

Multimorbidity: clinical assessment and management

Multimorbidity: assessment, prioritisation and management of care for people with commonly occurring multimorbidity

NICE guideline NG56

Appendices A – Q

August 2016

Final

Commissioned by the National Institute for Health and Care Excellence

Disclaimer

Healthcare professionals are expected to take NICE guidelines fully into account when exercising their clinical judgement. However, the guidance does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of each patient, in consultation with the patient and, where appropriate, their guardian or carer.

Copyright

National Guideline Centre, 2016

Funding

National Institute for Health and Care Excellence

Update information

December 2016: The full version and appendices were updated to correct the risk of bias given in the evidence reviews for Hippisley-Cox 2013. The change does not affect any recommendations.

Contents

Appendices.....	5
Appendix A: Scope.....	5
Appendix B: Declarations of interest	14
Appendix C: Clinical review protocols.....	27
Appendix D: Health economic review protocol	44
Appendix E: Clinical study selection.....	46
Appendix F: Health economic study selection.....	64
Appendix G: Literature search strategies	65
Appendix H: Clinical evidence tables.....	126
Appendix I: Health economic evidence tables.....	471
Appendix J: GRADE tables	480
Appendix K: Forest plots	536
Appendix L: Excluded clinical studies	587
Appendix M: Excluded health economic studies.....	660
Appendix N: Cost-effectiveness analysis: holistic assessment compared to usual care	664
Appendix O: Research recommendations	682
Appendix P: NICE technical team.....	693
Appendix Q: References	694

Appendices

Appendix A: Scope

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

SCOPE

1 Guideline title

Multimorbidity: the assessment, prioritisation and management of care for people with commonly occurring multimorbidity

1.1 Short title

Multimorbidity: assessment and management

2 The remit

NHS England has asked NICE: to develop a clinical guideline on the following topic: Multimorbidity: Assessment, prioritisation and management of care for people with commonly occurring multimorbidity.

3 Need for the guideline

3.1 Epidemiology

- a) Multimorbidity in its broadest sense has been defined as the combination of 1 chronic disease with at least 1 other disease (acute or chronic) or biopsychosocial (biological, psychological or social) factor (associated or not) or somatic (related to or affected by the body) risk factor. It is often defined more simply as the co-existence of 2 or more long term conditions. Generalist and multiagency care is particularly relevant to people with multimorbidity, while specialist care is usually organised around care for a single condition. Multimorbidity increases markedly with age, but it is also found in younger people, especially in socially deprived areas where the co-existence of physical and mental health problems is particularly common. Multimorbidity is associated with poor quality of life, disability, psychological

problems and increased mortality. Multimorbidity is also associated with increased frequency of health service use including emergency hospital admission, adverse drug events, polypharmacy, duplicate testing and poor care co-ordination. Polypharmacy is often significantly driven by the introduction of multiple drugs intended to prevent future morbidity and mortality, but the case for using such drugs weakens as life expectancy reduces. The absolute difference made by each additional drug may also reduce when people are taking multiple preventative medicines.

- b) Some conditions are commonly found together because one can be caused by the other (for example, diabetes can cause chronic kidney disease) or because they share an aetiology, (for example, smoking is an important cause of both lung cancer and coronary heart disease). Other conditions such as pain and depression are not known to share an aetiology, but are common comorbidities of many conditions. The implications of multimorbidity for healthcare are highly variable depending on which conditions an individual has. For some people, a single condition such as a potentially fatal cancer may be dominant, at least for a time. Groups of conditions which have closely related or concordant treatment, such as diabetes, hypertension and angina pose fewer problems of co-ordination than groups where treatment is discordant, such as people who experience both physical and mental health conditions.
- c) Management of care in some people with multimorbidity may be difficult because of limited access to healthcare or because most care is received from a specialist service which does not address all of their needs. These include people who are homeless and those who are usually cared for by services focusing on a particular morbidity (for example, people with learning difficulties or people with severe mental illness who may not have their physical health needs addressed, or people with chronic physical health problems

who may not have their mental health needs identified and effectively managed).

- d) NICE guidelines have already been developed for the management of many individual diseases and conditions. The aim of this guideline is to inform patient and clinical decision-making and models of care for people with multimorbidity who would benefit from a tailored approach. The guideline will not develop recommendations on management of individual conditions or on organisation of care for individual conditions.

3.2 Current practice

Clinical care is largely informed by evidence and guidelines for single systems or diseases. Current clinical practice is increasingly specialist, with healthcare professionals often basing treatment decisions on relatively narrow aspects of an individual's health problems. Issues associated with multimorbidity, such as polypharmacy and related adverse events, are considered in some settings, such as general practice and services caring for older people. However, there is a lack of information to guide decisions about multiple medicine use, including information on the effect of stopping some treatments and information comparing the benefits of different drug combinations when managing patients with multimorbidity.

4 The guideline

The guideline development process is described in detail on the NICE website (see section 6, 'Further information').

This scope defines what the guideline will (and will not) examine, and what the guideline developers will consider. The scope is based on the referral from NHS England. The areas that will be addressed by the guideline are described in the following sections.

4.1 Population

4.1.1 Groups that will be covered

- a) Adults (18 years and over) with multimorbidity.

4.1.2 Groups that will not be covered:

- a) Children and young people under 18 years.
- b) People who only have multiple mental health problems and no physical health problems.
- c) People with a single long-term condition.

4.2 Setting

- a) All settings in which NHS care is delivered.

4.3 Management

4.3.1 Key issues that will be covered

- a) Identifying people with multimorbidity who need a tailored approach to healthcare. The guideline will consider both individual indicators and multi-variable prediction tools for identifying people who most need a tailored approach, using the following as potential indicators for risk stratification, for example:
- taking large numbers of prescribed drugs
 - having unplanned hospital admissions
- b) Principles for assessing and prioritising health care interventions for individuals with multimorbidity, including the values and preferences of the individual
- c) Assessing methods for estimating life expectancy, evaluating frailty and assessing burden of treatment.
- d) Ranking absolute risks and benefits of interventions for prevention or improving prognosis of common morbidity (for example,

treatments to improve glucose and blood pressure control, statins, angiotensin-converting enzyme [ACE] inhibitors, drugs for osteoporosis).

- d) Effects of stopping common drug treatments.
- e) Strategies for managing healthcare for people with multimorbidity
 -
 - strategies to improve continuity of care e.g. case management, care plans, named healthcare professionals
 - format of consultations with healthcare professionals
 - models of multi-professional healthcare (for example co-ordinated care for common patterns of co-morbidity such as joint clinics across specialties)
 - self-management and expert patient programmes.
- f) Barriers to optimising healthcare for people with multimorbidity.

4.3.2 Clinical issues that will not be covered

- a) Symptomatic treatment.
- b) The management and organisation of healthcare for individual conditions
- c) End of life care

4.4 Main outcomes

- a) Services and interventions will be evaluated based on outcomes defined by the guideline development group. Examples could include:
 - health-related quality of life (for example, EQ-5D)
 - mortality
 - patient and carer experience of care

- continuity of care
- healthcare utilisation, for example:
 - unplanned hospital admissions
 - length of hospital stay
 - number of primary care appointments.

4.5 Review questions

Review questions guide a systematic review of the literature. They address only the key issues covered in the scope, and usually relate to interventions, diagnosis, prognosis, service delivery or patient experience. Please note that these review questions are draft versions and will be finalised with the Guideline Development Group.

4.5.1 Population identification

- a) What indicators or tools identify people who need a tailored approach to the care of their multimorbidity?

4.5.2 Assessment and prioritisation

- a) What principles are important for assessing and prioritising healthcare interventions for people with multimorbidity?
- b) What is the clinical and cost-effectiveness of tools used to elicit patient and carer preferences about treatments?
- c) What is the clinical and cost effectiveness of using prognostic indices or tools for estimating life expectancy or evaluating frailty to support decisions on prioritising or stopping treatment?
- d) What is the clinical and cost effectiveness of tools to estimate burden of treatment?
- e) How might data from condition-specific guidance best be used and presented to inform a ranking of treatments based on absolute risk and benefit and time to achieve benefits?
- f) What are the effects of stopping common drug treatments?

4.5.3 Management of care

- a) What is the clinical and cost effectiveness of strategies to improve continuity of healthcare, for example care plans, case management and named health professionals to improve outcomes for people with multimorbidity?
- b) What format(s) of consultations with healthcare professionals improve outcomes for people with multimorbidity?
- c) What models of multi-professional care improve outcomes for people with multimorbidity?
- d) What is the clinical and cost effectiveness of self-management and expert patient programmes in improving outcomes for people with multimorbidity?

4.5.4 Barriers to management in people with multimorbidity

- a) What are the barriers that prevent healthcare professionals from stopping preventative treatments?
- b) What are barriers to healthcare professionals optimising care for people with multimorbidity?

4.6 Economic aspects

Developers will take into account both clinical and cost effectiveness when making recommendations involving a choice between alternative interventions. A review of the economic evidence will be conducted and analyses will be carried out as appropriate. In particular, the management of care for people with multimorbidity is likely to be a high priority in terms of health economic analysis.

In cost effectiveness analyses the preferred unit of effectiveness is the quality-adjusted life year (QALY), and the costs considered will usually be only from an NHS and personal social services (PSS) perspective. Further detail on the methods can be found in 'The guidelines manual'.

4.7 Status

4.7.1 Scope

This is the final scope.

4.7.2 Timing

The development of guideline recommendations will begin in November 2014.

5 Related NICE guidance

5.1 Published guidance

- Psychosis with co-existing substance misuse. NICE clinical guideline 120 (2011).
- Depression in adults with a chronic physical health problem. NICE clinical guideline 91 (2009).
- Medicines Adherence: involving patients in decisions about prescribed medicines and supporting adherence. NICE clinical guideline 76 (2009).

5.2 Guidance under development

NICE is currently developing the following related guidance (details available from the NICE website):

- Medicines optimisation. NICE clinical guideline. Publication expected March 2015.
- Social care of older people with multiple long-term conditions. NICE social care guidance. Publication expected October 2015.
- Transition between inpatient hospital settings and community or care home settings for adults with social care needs. NICE social care guidance. Publication expected November 2015.
- Older people: independence and mental wellbeing. NICE public health guidance. Publication expected November 2015.
- Dual diagnosis: meeting people's wider health and social care needs when they have a severe mental illness and misuse substances. NICE public health guidance. Publication expected September 2016

- **Multimorbidities: system integration to meet population needs.** NICE public health guidance. Publication date to be confirmed.
- **Care of the dying adult.** NICE clinical guideline. Publication date to be confirmed.

6 Further information

Information on the guideline development process is provided in the following documents, available from the NICE website:

- **How NICE clinical guidelines are developed: an overview for stakeholders the public and the NHS: 5th edition**
- **The guidelines manual.**

Information on the progress of the guideline will also be available from the NICE website.

Appendix B: Declarations of interest

The Chair and GDG members were recruited to this guideline using NICE DOI policy published Oct 2008

Nina Barnett			
Date	Item declared	Classification	Action taken
Application	Part of a project to develop patient information videos. Financial investment in the Patient Support programme.	None	No action required
GDG1 (5/11/14)	Shareholder for a company that produces patient information videos. Teaches health coaching for a company that receives funding from health companies and the NHS. Produces training packages for care homes with Aged Care Channel (ACC). Publishes narrative articles related to multimorbidity and specialist polypharmacy.	Personal pecuniary interest	Declare and participate
GDG2 (17/12/14)	None	-	-
GDG3 (4/2/15)	None	-	-
GDG4 (17/3/15)	Supporting Aged Care Channel with filming to provide information on good practice for care staff in care homes.	Personal pecuniary interest	Declare and participate
GDG5 (5/5/15)	None	-	-
GDG6 (6/5/15)	None	-	-
GDG7 (23/6/15)	None	-	-
GDG8 (9/9/15)	None	-	-
GDG9 (23/10/15)	None	-	-
GDG10 (27/11/15)	None	-	-
GDG11 (22/1/16)	Talk on respiratory medications and adherence, funded for by drug company. Talk at upcoming congress on medications and dysphagia, aphasia and patient centred polypharmacy. Organisation receives funding from pharmaceutical companies. Talk on pharmacy management on medicines optimisation and adherence. Organisation receives funding from pharmaceutical companies.	Personal pecuniary interest	Declare and participate

Nina Barnett			
GDG12 (10/6/16)	None	-	-

Sam Barnett-Cormack			
Date	Item declared	Classification	Action taken
Application	Has been part of ad-hoc groups organised to campaign on issues around disability. No such work has focussed on multimorbidity, though it has come up in passing. Has made comments publicly on the importance of proper care in multimorbidity (probably without using that term).	Personal non-pecuniary interest	No action required.
GDG1 (5/11/14)	Has made statements on social media that care for people with multimorbidity needs to be better. Involved with a small national charity that is developing concerns for mental wellbeing.	Personal non-pecuniary	Declare and participate
GDG2 (17/12/14)	None	-	-
GDG3 (4/2/15)	None	-	-
GDG4 (17/3/15)	None	-	-
GDG5 (5/5/15)	None	-	-
GDG6 (6/5/15)	None	-	-
GDG7 (23/6/15)	None	-	-
GDG8 (9/9/15)	None	-	-
GDG9 (23/10/15)	None	-	-
GDG10 (27/11/15)	None	-	-
GDG11 (22/1/16)	None	-	-
GDG12 (10/6/16)	None	-	-

Julia Botsford			
Date	Item declared	Classification	Action taken
Application	None	None	No action required
GDG1 (5/11/14)	Currently on secondment to Dementia UK with a role to specifically promote admiral nursing. Specialist adviser to the CQC.	Personal pecuniary	Declare and participate
GDG2 (17/12/14)	None	-	-

Julia Botsford			
GDG3 (4/2/15)	None	-	-
GDG4 (17/3/15)	None	-	-
GDG5 (5/5/15)	Resigned on 26 March 2015	-	-
GDG6 (6/5/15)	Not applicable	-	-
GDG7 (23/6/15)	Not applicable	-	-
GDG8 (9/9/15)	Not applicable	-	-
GDG9 (23/10/15)	Not applicable	-	-
GDG10 (27/11/15)	Not applicable	-	-
GDG11 (22/1/16)	Not applicable	-	-
GDG12 (10/6/16)	Not applicable	-	-

Carolyn Chew-Graham			
Date	Item declared	Classification	Action taken
Application	I am a grant-holder on a number of research studies, some of which involve the evaluation of primary care interventions for people with multimorbidity.	Personal non-pecuniary	Declare and participate.
GDG1 (5/11/14)	A member of the Dialogue on Diabetes and Depression (DDD) and will be delivering training to a group of family physicians in Slovenia in November 2014 (unpaid work; travel and accommodation paid). Works with the Royal College of General Physicians (RCGP).	Personal non-pecuniary Personal pecuniary	Declare and participate.
GDG2 (17/12/14)	None	-	-
GDG3 (4/2/15)	None	-	-
GDG4 (17/3/15)	None	-	-
GDG5 (5/5/15)	None	-	-
GDG6 (6/5/15)	None	-	-
GDG7 (23/6/15)	None	-	-
GDG8 (9/9/15)	None	-	-
GDG9 (23/10/15)	None	-	-

Carolyn Chew-Graham			
GDG10 (27/11/15)	None	-	-
GDG11 (22/1/16)	None	-	-
GDG12 (10/6/16)	Co-investigator on NIHR funded study PHR Project: 14/186/11 - Community pHarmacists Mood Intervention Study (CHEMIST). Feasibility and Pilot Study	Personal non-pecuniary	Declare and participate.

Andrew Clegg			
Date	Item declared	Classification	Action taken
Application	None	None	No action required
GDG1 (5/11/14)	None	-	-
GDG2 (17/12/14)	None	-	-
GDG3 (4/2/15)	Leading work to develop and validate a frailty index based on routine primary care data. Funded by the NIHR (National Institute for Health Research) CLAHREC (The Collaboration for Leadership in Applied Health Research and Care) Programme.	Personal non-pecuniary	It was agreed that this declaration did not present a conflict for items on the day's agenda as the group would not be asked to consider evidence or draft recommendations on the topic. However, as AC is a recognized expert in this field, his contribution to introducing the topic to the group was very welcome. Later in development, however, during presentation of future reviews on this topic, AC

Andrew Clegg			
			may be asked to reclude himself from discussions when group-work on drafting recommendations begins.
GDG4 (17/3/15)	None	-	-
GDG5 (5/5/15)	None	-	-
GDG6 (6/5/15)	None	-	-
GDG7 (23/6/15)	None	-	-
GDG8 (9/9/15)	None	-	-
GDG9 (23/10/15)	None	-	-
GDG10 (27/11/15)	None	-	-
GDG11 (22/1/16)	None	-	-
GDG12 (10/6/16)	Leading work to develop and validate a frailty index based on routine primary care data. Funded by the NIHR (National Institute for Health Research) CLAHREC (The Collaboration for Leadership in Applied Health Research and Care) Programme.	Personal non-pecuniary	Declare and withdraw

Bruce Guthrie (GDG Chair)			
Date	Item declared	Classification	Action taken
Application	I have a research interest in multimorbidity, polypharmacy and guideline development for people with multimorbidity. Specifically, I have published papers that relate to guidelines and multimorbidity (cited below), and currently am Chief Investigator on a research grant from NIHR Health Services and Delivery Research Programme which is exploring how multimorbidity might be better accounted for in clinical guidelines (http://www.nets.nihr.ac.uk/projects/hsdr/11200327). This project includes NICE staff as co-applicants (Dr Phil Alderson and Dr Bhaish Naidoo). Finally, I was a co-applicant on a Scottish Government Chief Scientist Office funded study to develop and evaluate in a pilot trial a complex intervention to improve quality of life in younger people with multimorbidity living in very deprived	Personal non-pecuniary interest	No action required.

Bruce Guthrie (GDG Chair)			
	<p>area, and am a co-applicant on a current NIHR HS&DR funded study to develop and evaluate a general practice based complex intervention for people with multimorbidity (http://www.nets.nihr.ac.uk/projects/hsdr/1213015). I am therefore on record as stating that clinical guidelines do not currently address multimorbidity very effectively, and work is needed to remedy this, and am involved in several projects either seeking to improve guideline development in this regard or to provide evidence of effectiveness of interventions.</p>		
GDG1 (5/11/14)	<p>Has research interests in multimorbidity and is working with NICE in this field. He has received funding to develop an intervention for management of people with multimorbidity. He has publicly stated that he believes current guidelines are unhelpful for multimorbidity.</p>	<p>Personal pecuniary Personal non-pecuniary</p>	<p>Declare and participate</p>
GDG2 (17/12/14)	<p>None</p>	-	-
GDG3 (4/2/15)	<p>None</p>	-	-
GDG4 (17/3/15)	<p>None</p>	-	-
GDG5 (5/5/15)	<p>Research interest in multimorbidity, polypharmacy and guideline development for people with multimorbidity. Specifically, published papers that relate to guidelines and multimorbidity (cited below), and currently is Chief Investigator on a research grant from NIHR Health Services and Delivery Research Programme which is exploring how multimorbidity might be better accounted for in clinical guidelines (http://www.nets.nihr.ac.uk/projects/hsdr/11200327). This project includes NICE staff as co-applicants (Dr Phil Alderson and Dr Bhaish Naidoo).</p> <p>An element of this study was examining how best to compare treatments for different conditions in terms of absolute benefit.</p> <p>Finally, was a co-applicant on a Scottish Government Chief Scientist Office funded study to develop and evaluate in a pilot trial a complex intervention to improve quality of life in younger people with multimorbidity living in very deprived area, and is a co-applicant on a current NIHR HS&DR funded study to develop and evaluate a general practice based complex intervention for people with multimorbidity (http://www.nets.nihr.ac.uk/projects/hsdr/1213015). Therefore on record as stating that clinical guidelines do not currently address multimorbidity</p>	<p>Personal non-pecuniary</p>	<p>Declare and participate. Will not chair sessions examining this area of guideline.</p>

Bruce Guthrie (GDG Chair)			
	very effectively, and work is needed to remedy this, and is involved in several projects either seeking to improve guideline development in this regard or to provide evidence of effectiveness of interventions.		
GDG6 (6/5/15)	None	-	-
GDG7 (23/6/15)	None	-	-
GDG8 (9/9/15)	None	-	-
GDG9 (23/10/15)	Declared academic interest in the ways of presenting effectiveness of interventions.	Personal non-specific non-pecuniary interest	Agreed to act as an expert to the GDG when this area was discussed and the guideline lead would chair this section of the meeting.
GDG10 (27/11/15)	None	-	-
GDG11 (22/1/16)	None	-	-
GDG12 (10/6/16)	None	-	-

John Hindle			
Date	Item declared	Classification	Action taken
Application	<p>The declared interests are not directly relevant to the Guideline on Multimorbidity.</p> <p>Honoraria received for provision of general educational events in the field of Parkinson's disease from-</p> <p>Lundbeck- £750 plus economy travel- An all-day board with other specialists, neurologists and geriatricians from around the UK discussing the Pharmaceutical management of Parkinson's. Includes reading and preparation time. Learning from other specialists was my key objective. January 2014.</p> <p>Teva- £1500 plus accommodation and economy travel- Chaired and organised a major two day national educational meeting- "Positive steps in Parkinson's disease". 238 attendees from the UK. Geriatricians, neurologists and nurses. Birmingham March 2014. One year preparation time including 4 teleconferences, organising the agenda, chairing the</p>	Personal pecuniary interests	No action required.

John Hindle			
	<p>meeting. Excellent educational feedback.</p> <p>Teva- £500 plus economy travel and registration for the British Geriatrics Society national meeting Manchester- presented a debate on non-levodopa treatments in Parkinson's disease. Reading and preparation time, presentation of slides and delivery of the debate. April 2014</p> <p>I do not have any directorships or paid position and do not hold any consultancy post. I have not received any hospitality above what would be reasonably expected to attend meetings and conferences.</p>		
Application	<p>Reviewer for Parkinson's UK Research Advisory panel. Research funding:</p> <p>NISCHR Rfppb. Cognitive rehabilitation in Parkinson's disease dementia. £178,000. 2013-15. PI J V Hindle.</p> <p>ESRC. IDEAL- Living well with dementia. £4.3m Hindle J V Co-applicant. PI Clare L. 2013-18.</p> <p>NISCHR AHSC Clinical research Fellowship. Hindle J V. £143,000. 2011-14</p> <p>HTA. £2,037,487 over 3 years. MUSTARDD-PD. A multicentre study of the acetylcholinesterase inhibitor Donepezil in dementia of Parkinson's disease. PI Prof David Burn. 2012-15</p>	Non-personal Pecuniary	No action required.
GDG1 (5/11/14)	<p>Received honoraria for provision of general educational events in the field of Parkinson's disease from Teva pharmaceutical company.</p> <p>Assistant Clinical Director at Bangor University and is paid by his NHS employer and Bangor University for his work there (2 sessions per week).</p> <p>Was trustee of the British Geriatric Society until May 2014. He receives research funding from the government and the Michael J Fox Foundation.</p>	<p>Personal pecuniary</p> <p>Personal pecuniary</p> <p>Personal pecuniary</p>	Declare and participate
GDG2 (17/12/14)	None	-	-
GDG3 (4/2/15)	None	-	-
GDG4 (17/3/15)	None	-	-
GDG5 (5/5/15)	None	-	-
GDG6 (6/5/15)	Undertaken occasional fee paying medico-legal work which has included estimates of life expectancy.	Personal pecuniary non-specific	Declare and participate
GDG7 (23/6/15)	None	-	-
GDG8 (9/9/15)	None	-	-

John Hindle			
GDG9 (23/10/15)	None	-	-
GDG10 (27/11/15)	Received a grant to do a study on EEG neuro impact funded by the Betsi Cadwaladr Health Board.	Personal non-financial specific	Declare and participate.
GDG11 (22/1/16)	None	-	-
GDG12 (10/6/16)	None	-	-

Jonathan Inglesfield			
Date	Item declared	Classification	Action taken
Application	GP Partner at an NHS Medical Practice (The Cranleigh Medical Practice, Surrey), with a significant cohort of individuals with multiple morbidity in respect of which the practice receives capitated income. Medical Director at NHS Guildford and Waverley CCG, employee status, with responsibilities including Commissioning of services in respect of Multiple Morbidity.	Personal pecuniary interest	No action required.
GDG1 (5/11/14)	Currently a GP in a large group practice.	Personal pecuniary	Declare and participate
GDG2 (17/12/14)	None	-	-
GDG3 (4/2/15)	None	-	-
GDG4 (17/3/15)	None	-	-
GDG5 (5/5/15)	Leads programme on models of care in his practice.	Personal non-pecuniary	Declare and participate.
GDG6 (6/5/15)	None	-	-
GDG7 (23/6/15)	None	-	-
GDG8 (9/9/15)	None	-	-
GDG9 (23/10/15)	None	-	-
GDG10 (27/11/15)	None	-	-
GDG11 (22/1/16)	None	-	-
GDG12 (10/6/16)	None	-	-

David Kernick

David Kernick			
Date	Item declared	Classification	Action taken
Application	None	None	No action required.
GDG1 (5/11/14)	Holds positions on headache groups that receive pharmaceutical funding.	Personal pecuniary	Declare and participate
GDG2 (17/12/14)	None	-	-
GDG3 (4/2/15)	None	-	-
GDG4 (17/3/15)	None	-	-
GDG5 (5/5/15)	None	-	-
GDG6 (6/5/15)	None	-	-
GDG7 (23/6/15)	None	-	-
GDG8 (9/9/15)	None	-	-
GDG9 (23/10/15)	None	-	-
GDG10 (27/11/15)	None	-	-
GDG11 (22/1/16)	None	-	-
GDG12 (10/6/16)	None	-	-

Emily Lam			
Date	Item declared	Classification	Action taken
Application	None	None	No action required
GDG1 (5/11/14)	None	-	-
GDG2 (17/12/14)	Lay member on the technical appraisal team at NICE.	Personal non-pecuniary	Declare and participate
GDG3 (4/2/15)	None	-	-
GDG4 (17/3/15)	None	-	-
GDG5 (5/5/15)	None	-	-
GDG6 (6/5/15)	None	-	-
GDG7 (23/6/15)	None	-	-
GDG8 (9/9/15)	None	-	-

Emily Lam			
GDG9 (23/10/15)	None	-	-
GDG10 (27/11/15)	None	-	-
GDG11 (22/1/16)	None	-	-
GDG12 (10/6/16)	None	-	-

Rupert Payne			
Date	Item declared	Classification	Action taken
Application	Conducts and publishes research in the field of multimorbidity and polypharmacy	Personal Non-pecuniary	No action required.
GDG2 (17/12/14)	Received funding for research from the NIHR.	Non-personal pecuniary	Declare and participate
GDG3 (4/2/15)	None	-	-
GDG4 (17/3/15)	None	-	-
GDG5 (5/5/15)	None	-	-
GDG6 (6/5/15)	None	-	-
GDG7 (23/6/15)	None	-	-
GDG8 (9/9/15)	None	-	-
GDG9 (23/10/15)	None	-	-
GDG10 (27/11/15)	Submitted a research grant proposal to NIHR RFPB to do a qualitative examination of de-prescribing anti-hypertensions. Will not start prior to the guideline finishing.	Personal non-pecuniary specific	Declare and participate
GDG11 (22/1/16)	Has taken on a paid role as clinical editor for Prescriber Journal (from January 2016). Has also accepted a commitment (remunerated) to talk at a Clinical Pharmacy Congress in London in April 2016.	Personal pecuniary interest	Declare and participate
GDG12 (10/6/16)	None	-	-

Alaster Rutherford			
Date	Item declared	Classification	Action taken
Application	Director, Rutherford Health Consulting Ltd [provides/provided expert pharmacist services to Bath & NESomerset CCG, SW CSU and other NHS bodies]	Personal Pecuniary interest	No action required.

Alaster Rutherford			
	Director, Verto Health Consulting [payment received from Astellas Pharma] Received travel expenses for one UK meeting from Astra Zeneca Received fees from Shire for a NICE implementation project.		
Application	My wife is the owner and sole director of Banwell Village Pharmacy Limited which provides NHS Community Pharmacy Services in Banwell, North Somerset.	Personal family interest	No action required.
GDG1 (5/11/14)	Director of his own company to provide expert pharmacist services to Bath and North East Somerset Clinical Commissioning Groups (CCG), Bath University, NICE and other NHS bodies. Received payment from Astellas Pharma for a NICE implementation project.	Personal pecuniary Personal pecuniary Non-personal pecuniary	Declare and participate
	Wife owns and is the sole director of Banwell Village Pharmacy Limited which provides NHS Community Pharmacy Services in Banwell, North Somerset.	Personal family interest	Declare and participate
GDG2 (17/12/14)	None	-	-
GDG3 (4/2/15)	None	-	-
GDG4 (17/3/15)	Fee received from Insmmed Incorporated [US orphan respiratory drug maker – no UK products either in own right or franchised] for advice on UK health system and NHS Specialised Commissioning. Drug currently with EMA is for specific rare chest infections not associated with multimorbidity.	Personal pecuniary interest	Declare and participate
GDG5 (5/5/15)	None	-	-
GDG6 (6/5/15)	None	-	-
GDG7 (23/6/15)	None	-	-
GDG8 (9/9/15)	None	-	-
GDG9 (23/10/15)	None	-	-
GDG10 (27/11/15)	None	-	-
GDG11 (22/1/16)	None	-	-
GDG12 (10/6/16)	None	-	-

Cate Seton-Jones			
Date	Item declared	Classification	Action taken

Cate Seton-Jones			
Application	None	None	No action required.
GDG1 (5/11/14)	Works with a care organisation for over 65s.	Personal pecuniary	
GDG2 (17/12/14)	Works with the Phyllis Tuckwell Hospice, which receives numerous corporate and individual donations as it is a charity. Work with this organisation is as a palliative care consultant and senior manager, no direct involvement with fundraising.	Non-personal pecuniary	No additional action required
GDG3 (4/2/15)	None	-	-
GDG4 (17/3/15)	None	-	-
GDG5 (5/5/15)	None	-	-
GDG6 (6/5/15)	None	-	-
GDG7 (23/6/15)	None	-	-
GDG8 (9/9/15)	None	-	-
GDG9 (23/10/15)	None	-	-
GDG10 (27/11/15)	None	-	-
GDG11 (22/1/16)	None	-	-
GDG12 (10/6/16)	None	-	-

Appendix C: Clinical review protocols

C.1 Principles/Barriers of care

C.1.1 Principles of care

Table 1: Review protocol: what principles are important for assessing, prioritising and managing care for people with multimorbidity?

Component	Description
Review question	What principles are important for assessing, prioritising and managing care for people with multimorbidity?
Objective	To identify key principles that healthcare professionals should consider when assessing, prioritising and managing care for people with multimorbidity
Population and setting	Adults (aged 18 years and over) with multimorbidity; healthcare professionals treating adults with multimorbidity
Exclusions	None
Search strategy	Databases: Medline, Embase Date: All years Language: Restrict to English only
The review strategy	Study designs to be considered: Guidelines and other grey literature that provide guidance for healthcare professionals on the assessment, prioritisation and management of care for people with multimorbidity Appraisal of methodological quality The methodological quality of each study will be assessed using the AGREE II criteria. Data synthesis Themes identified will be analysed using thematic analysis. Extraction of available evidence will continue until themes are saturated. Results to be presented as a narrative, and diagrammatically where appropriate.

C.1.2 Barriers of care

Table 2: Review protocol: barriers to optimising care for people with multimorbidity

Review question	What are barriers to healthcare professionals optimising care for people with multimorbidity?
Objective	To identify what patients, carers and healthcare professionals believe are the barriers to optimising care for people with multimorbidity
Population and setting	Adults with multimorbidity, their family/carers, and healthcare professionals who provide care to people with multimorbidity
Exclusions	None
Search strategy	Databases: Embase, Medline, PsychINFO, CINAHL Date: All years Language: Restrict to English only
The review strategy	Study designs to be considered: Qualitative studies (for example, interviews, focus groups, observations); surveys if

Review question	What are barriers to healthcare professionals optimising care for people with multimorbidity?
	no qualitative studies retrieved Review strategy: Studies will be added until saturation is reached. Studies will be analysed using thematic analysis. Results to be presented as a narrative, and diagrammatically where appropriate. Study quality will be assessed using CERQUAL and GRADE.

C.2 Identification

C.2.1 Unplanned hospital admissions

Table 3: Review protocol: What risk tool best identifies people with multimorbidity who are at risk of unplanned hospital admission?

Review question	What risk tool best identifies people with multimorbidity who are at risk of unplanned hospital admission?
Objective	To evaluate which multivariable prediction tools can best identify those people with multimorbidity who have adverse outcomes, in order to identify those patients who may need an approach to care that takes account of their multimorbidity
Population	Adults (aged >17 years) with multimorbidity
Risk tools	Validated risk tools identified in the literature
Outcomes	Unplanned hospital admissions (max time point = 3 years) Statistical outputs may include: <ul style="list-style-type: none"> – Area under the ROC curve (c-index, c-statistic) – Sensitivity, specificity, predictive values – Predicted risk versus observed risk (calibration) – Other Statistical measures: for example, Somers' D statistic, R² statistic and Brier score – Reclassification
Exclusions	<ul style="list-style-type: none"> • Children and young people with multimorbidity (age <18 years) • Patients with multiple mental health conditions and no physical health condition • Adults with multimorbidity who are at the end of life (<1 year of death) • Adults who are experiencing acute life threatening illness • Tools not externally validation/tools only validated internally • Tools aimed at predicting unplanned hospital admission in a specific patient group only (for example, a tool validated in a group of patients with heart failure, where the tool includes items specific to heart failure)
Search strategy	Databases: Medline, Embase, the Cochrane Library Date: All years Language: Restrict to English only Study designs: Retrospective and prospective cohort studies
The review strategy	Appraisal of methodological quality: The methodological quality of each study will be assessed using PROBAST

C.2.2 Health-related quality of life

Table 4: PICO characteristics of review question

Review question	What risk tool best identifies people with multimorbidity who are at risk of reduced health-related quality of life?
Objective	To evaluate which multi-variable prediction tools can best identify those people with multimorbidity who have adverse outcomes, in order to identify those patients who may need an approach to care that takes account of their multimorbidity
Population	Adults (aged >17 years) with multimorbidity
Risk tools	Validated risk tools identified in the literature
Outcomes	Reductions in health related quality of life (max time point = 3 years) Statistical outputs may include: <ul style="list-style-type: none"> – Area under the ROC curve (c-index, c-statistic) – Sensitivity, specificity, predictive values – Predicted risk versus observed risk (calibration) – Other Statistical measures: for example, Somers' D statistic, R² statistic and Brier score – Reclassification
Exclusions	<ul style="list-style-type: none"> • Children and young people with multimorbidity (age <18 years) • Patients with multiple mental health conditions and no physical health condition • Adults with multimorbidity who are at the end of life (<1 year of death) • Adults who are experiencing acute life threatening illness • Tools not externally validation/tools only validated internally • Tools aimed at predicting unplanned hospital admission in a specific patient group only (for example, a tool validated in a group of patients with heart failure, where the tool includes items specific to heart failure)
Search strategy	Databases: Medline, Embase, the Cochrane Library Date: All years Language: Restrict to English only Study designs: Retrospective and prospective cohort studies
The review strategy	Appraisal of methodological quality: The methodological quality of each study will be assessed using PROBAST
Analysis	If many validated risk tools are identified, we will use the following rules (in order) to prioritise inclusion (1) only include tools that have been externally validated (i.e. not split-half validation) (2) only include studies from the UK and (3) only include tools that have been derived and validated in a community sample Where a tool has been updated, we will only evaluate the most recent version unless earlier versions are more applicable to a MM population

C.2.3 Admission to care facility

Table 5: Review protocol: What risk tool best identifies people with multimorbidity who are at risk of admission to a care facility?

Review question	What risk tool best identifies people with multimorbidity who are at risk of admission to a care facility?
Objective	To evaluate which multivariable prediction tools can best identify those people with

	multimorbidity who have adverse outcomes, in order to identify those patients who may need an approach to care that takes account of their multimorbidity
Population	Adults (aged >17 years) with multimorbidity
Risk tools	Validated risk tools identified in the literature
Outcomes	Admission to care facility (max time point = 3 years) Statistical outputs may include: <ul style="list-style-type: none"> – Area under the ROC curve (c-index, c-statistic) – Sensitivity, specificity, predictive values – Predicted risk versus observed risk (calibration) – Other Statistical measures: for example, Somers' D statistic, R² statistic and Brier score – Reclassification
Exclusions	<ul style="list-style-type: none"> • Children and young people with multimorbidity (age <18 years) • Patients with multiple mental health conditions and no physical health condition • Adults with multimorbidity who are at the end of life (<1 year of death) • Adults who are experiencing acute life threatening illness • Tools not externally validation/tools only validated internally • Tools aimed at predicting unplanned hospital admission in a specific patient group only (for example, a tool validated in a group of patients with heart failure, where the tool includes items specific to heart failure)
Search strategy	Databases: Medline, Embase, the Cochrane Library Date: All years Language: Restrict to English only Study designs: Retrospective and prospective cohort studies
The review strategy	Appraisal of methodological quality: The methodological quality of each study will be assessed using PROBAST

C.2.4 Life expectancy risk tools

Table 6: Review protocol: What risk tool best identifies people with multimorbidity who are at risk of reduced life expectancy?

Review question	What risk tool best identifies people with multimorbidity who are at risk of reduced life expectancy?
Objective	To determine which prognostic risk tool is the most accurate at predicting mortality to support decisions on prioritising treatment
Population	Adults (18 years and over) with multimorbidity Stratum: community-dwelling, inpatient
Index tests (risk assessment tools)	Validated risk tools identified in the literature
Patient outcome or target	Mortality (all cause at ≥ 1 year)

conditions	
Statistical measures (in terms of discrimination and calibration)	<ul style="list-style-type: none"> • Area under the ROC curve (c-index, c-statistic) • Sensitivity, specificity, predictive values • Predicted risk versus observed risk (calibration) • Other Statistical measures: for example, Somers' D statistic, R² statistic and Brier score • Reclassification
Exclusions	<ul style="list-style-type: none"> • Children and young people with multimorbidity (age <18 years) • People with multiple mental health conditions and no physical health condition • Adults with multimorbidity who are at the end of life (<1 year of death) • Adults who are experiencing acute life threatening illness • Internally validated tools (i.e. not split-half validation) • Tools aimed at predicting mortality in a specific patient group only (for example, a tool validated in a group of patients with heart failure, where the tool includes items specific to heart failure)
Search strategy	<p>Databases: Medline, Embase, the Cochrane Library Date: All years Language: Restrict to English only Study designs: Retrospective and prospective cohort studies</p>
The review strategy	Appraisal of methodological quality: The methodological quality of each study will be assessed using PROBAST

C.2.5 Polypharmacy: unplanned hospital admissions

Table 7: Review protocol: Is polypharmacy associated with a greater risk of unplanned hospital admissions amongst people with multimorbidity?

Component	Description
Review question	Is polypharmacy associated with a greater risk of unplanned hospital admissions amongst people with multimorbidity?
Objectives	To evaluate whether polypharmacy is associated with a greater risk of adverse outcomes amongst people with multimorbidity, in order to identify whether people who are taking multiple medications may benefit from an approach to care that takes account of their multimorbidity
Population	Adults (aged >17 years) with multimorbidity
Presence / absence of prognostic variable	Polypharmacy (stratify by how defined; i.e. the number of drugs individuals are taking; ≥ 5 , ≥ 8 , ≥ 10)
Outcomes	Unplanned hospital admissions at ≥ 1 year Statistical outputs may include: Sensitivity, specificity, AUC, R ² , beta coefficients, OR/RR, HR, MD will be extracted if no sensitivity/specificity data
Study design	Prognostic studies
Exclusions	Children aged 17 years and under People with single conditions and polypharmacy

Component	Description
	People who have multiple mental health conditions and no physical health condition
How the information will be searched	Databases: Medline, Embase, the Cochrane Library Date: Published since 2000 Language: Restrict to English only
The review strategy	Where we extract R ² , beta coefficients, OR/RR, HR, or MD, we will prioritise the extraction of unadjusted data. Any adjusted data extracted will be analysed separately.

C.2.6 Polypharmacy: health-related quality of life

Table 8: Review protocol: Is polypharmacy associated with a greater risk of reductions in health-related quality of life amongst people with multimorbidity?

Component	Description
Review question	Is polypharmacy associated with a greater risk of reductions in health-related quality of life amongst people with multimorbidity?
Objectives	To evaluate whether polypharmacy is associated with a greater risk of adverse outcomes amongst people with multimorbidity, in order to identify whether people who are taking multiple medications may benefit from an approach to care that takes account of their multimorbidity
Population	Adults (aged >17 years) with multimorbidity
Presence / absence of prognostic variable	Polypharmacy (stratify by how defined; i.e. the number of drugs individuals are taking; ≥5, ≥8, ≥10)
Outcomes	Health-related quality of life at ≥ 1 year Statistical outputs may include: Sensitivity, specificity, AUC, R ² , beta coefficients, OR/RR, HR, MD will be extracted if no sensitivity/specificity data
Study design	Prognostic studies
Exclusions	Children aged 17 years and under People with single conditions and polypharmacy People who have multiple mental health conditions and no physical health condition
How the information will be searched	Databases: Medline, Embase, the Cochrane Library Date: Published since 2000 Language: Restrict to English only
The review strategy	Where we extract R ² , beta coefficients, OR/RR, HR, or MD, we will prioritise the extraction of unadjusted data. Any adjusted data extracted will be analysed separately.

C.2.7 Polypharmacy: admission to care facilities

Table 9: Review protocol: Is polypharmacy associated with a greater risk of admission to care facility amongst people with multimorbidity?

Component	Description
Review question	Is polypharmacy associated with a greater risk of admission to care facility

Component	Description
	amongst people with multimorbidity?
Objectives	To evaluate whether polypharmacy is associated with a greater risk of adverse outcomes amongst people with multimorbidity, in order to identify whether people who are taking multiple medications may benefit from an approach to care that takes account of their multimorbidity
Population	Adults (aged >17 years) with multimorbidity
Presence / absence of prognostic variable	Polypharmacy (stratify by how defined; that is the number of drugs individuals are taking; ≥ 5 , ≥ 8 , ≥ 10)
Outcomes	Admission to care facility at ≥ 1 year Statistical outputs may include: Sensitivity, specificity, AUC, R^2 , beta coefficients, OR/RR, HR, MD will be extracted if no sensitivity/specificity data
Study design	Prognostic studies
Exclusions	Children aged 17 years and under People with single conditions and polypharmacy People who have multiple mental health conditions and no physical health condition
How the information will be searched	Databases: Medline, Embase, the Cochrane Library Date: Published since 2000 Language: Restrict to English only
The review strategy	Where we extract R^2 , beta coefficients, OR/RR, HR, or MD, we will prioritise the extraction of unadjusted data. Any adjusted data extracted will be analysed separately.

C.2.8 Polypharmacy: mortality

Table 10: Review protocol: Is polypharmacy associated with a greater risk of mortality amongst people with multimorbidity?

Component	Description
Review question	Is polypharmacy associated with a greater risk of mortality amongst people with multimorbidity?
Objectives	To evaluate whether polypharmacy is associated with a greater risk of adverse outcomes amongst people with multimorbidity, in order to identify whether people who are taking multiple medications may benefit from an approach to care that takes account of their multimorbidity
Population	Adults (aged >17 years) with multimorbidity
Presence / absence of prognostic variable	Polypharmacy (stratify by how defined; i.e. the number of drugs individuals are taking; ≥ 5 , ≥ 8 , ≥ 10)
Outcomes	Mortality at ≥ 1 year Statistical outputs may include:

Component	Description
	Sensitivity, specificity, AUC, R ² , beta coefficients, OR/RR, HR, MD will be extracted if no sensitivity/specificity data
Study design	Prognostic studies
Exclusions	Children aged 17 years and under People with single conditions and polypharmacy People who have multiple mental health conditions and no physical health condition
How the information will be searched	Databases: Medline, Embase, the Cochrane Library Date: Published since 2000 Language: Restrict to English only
The review strategy	Where we extract R ² , beta coefficients, OR/RR, HR, or MD, we will prioritise the extraction of unadjusted data. Any adjusted data extracted will be analysed separately.

C.3 Frailty

Table 11: Review protocol: What is the most accurate tool for assessing frailty?

Component	Description
Review question	What is the most accurate tool for assessing frailty?
Objectives	To determine which tool is the best for assessing frailty
Study design	Cross-sectional studies, cohort studies
Population	<ul style="list-style-type: none"> Adults (18 years and over) with multimorbidity
Setting	All settings
Index test	Tools and brief assessments identified in the literature for assessing frailty; including: <ul style="list-style-type: none"> Abbreviated Comprehensive Geriatric Assessment (aCGA) Vulnerable Elders-Survey-13 (VES-13) Groningen Frailty Indicator (GFI) Geriatric 8 (G8) Tilburg frailty indicator PRISMA 7 Timed up and go test (TUG) Edmonton frail scale Brief assessments (for example, gait speed, grip strength)
Reference standards	<ul style="list-style-type: none"> Cardiovascular Health Study (Fried) phenotype model Comprehensive geriatric assessment (CGA) Cumulative deficit model
Statistical measures	Sensitivity, specificity, AUC
Other exclusions	Children and young people with multiple morbidity (aged <18 years) Adults with more than 1 mental health condition and no physical condition Adults with cancer
Search strategy	Databases: Medline, Embase, the Cochrane Library Date: All years Language: Restrict to English only
Review strategy	Stratification – groups that cannot be combined:

	<ul style="list-style-type: none"> • <i>Data from different reference standards will not be pooled</i> <p>In the case of heterogeneity, subgroup by age <65 years versus ≥65 years</p> <p>Appraisal of methodological quality:</p> <ul style="list-style-type: none"> • The methodological quality of each study will be assessed using the QUADAS-2 checklist (per target condition). <p>Synthesis of data:</p> <ul style="list-style-type: none"> • Diagnostic meta-analysis will be conducted where appropriate using hierarchical methods.
--	--

C.4 Delivering an approach to care that takes account of multimorbidity

Table 12: Review protocol: how can treatment burden be assessed?

Component	Description
Review question	How can treatment burden be assessed?
Objective	To identify what methods can be used to assess treatment burden Definition of treatment burden: impact of health care on patients' functioning and well-being, apart from specific treatment side effects. It takes into account everything patients do to take care of their health: visits to the doctor, medical tests, treatment management, and lifestyle changes
Population	Adults (18 years and over) with multimorbidity
Intervention	Questionnaires identified in the literature that aim to assess people's experience on treatment burden
Statistical measures	Reliability Validity Reproducibility Responsiveness Interpretability Time to complete User friendliness
Study design	Questionnaire validation studies
Search strategy	Databases: Medline, Embase, the Cochrane Library, CINAHL, PsycINFO Date: All years Language: Restrict to English only
Analysis	Quality assessment will be conducted using Q-BAST ⁴²⁰

C.4.1 Ranking

Table 13: Review protocol: How might data from condition-specific guidance best be used and presented to inform a ranking of treatments based on absolute risk and benefit and time to achieve benefits?

Objective	To develop an example of how data from condition-specific guidance may be presented to inform a ranking of treatments as part of decisions to optimise care amongst people with multimorbidity .
Conditions and	

interventions	<ul style="list-style-type: none"> • Hyperlipidemia (statins) • Hypertension (ACE inhibitors, beta blockers, calcium channel blockers, thiazides, angiotensin receptor blockers) • Type II diabetes (Metformin hydrochloride, sulfonylureas, DPP4 inhibitors) • Chronic heart failure (ACE inhibitors, beta blockers) • Atrial fibrillation (anticoagulants) • Chronic kidney disease (ACE inhibitors, angiotensin receptor blockers, spironolactone) • Angina (aspirin) • Depression (antidepressants) • Schizophrenia (anti-psychotics) • Migraine (prophylaxis)
Outcomes	<p>The following metrics will be reported/calculated:</p> <ul style="list-style-type: none"> • Demographics of trial participants • Duration of treatment • Outcome (critical outcomes; including mortality and serious adverse events) • Length of follow-up • Event rate as reported/calculated • Relative risk (95% CI) • Absolute benefit (95% CI) • Annualised absolute benefit (95% CI) • Number needed to treat (95% CI) • Annualised number needed to treat (95% CI)
Study design	<p>Published NICE guidelines. Quality assessment of data will not be conducted.</p>

C.4.2 Stopping antihypertensive treatment

Table 14: Review protocol: What is the clinical- and cost-effectiveness of stopping antihypertensive treatment?

Review question	What is the clinical- and cost-effectiveness of stopping antihypertensive treatment?
Area of scope	Effects of stopping treatment
Objective:	To evaluate the risks and benefits of stopping antihypertensive therapy to inform a recommendation
Population	Adults taking drugs for primary prevention of hypertension Adults taking drugs for secondary prevention of hypertension (excluding pregnancy)
Intervention	Stopping: Anti-hypertensive agents (thiazides, beta blockers, alpha blockers, calcium-channel blockers, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers)
Comparison	Continuing anti hypertension agents
Outcomes	Critical:

Review question	What is the clinical- and cost-effectiveness of stopping antihypertensive treatment?
	<ul style="list-style-type: none"> • All-cause mortality • Cardiovascular mortality • Non-fatal myocardial infarction • Stroke • Quality of life • Hospitalisation • Admission to care facility <p>Important:</p> <ul style="list-style-type: none"> • Blood pressure • Falls
Exclusion	Pregnant women taking anti-hypertensives for secondary prevention Drugs used for other indications Duration of treatment less than 1 year
Search strategy	Databases: Medline, Embase, the Cochrane Library Date: all years Language: restrict to English only Study designs: RCTs and systematic reviews of RCTs; cohort studies if no RCTs are retrieved
The review strategy	Quality of life data: collect all data for the stated QoL measure, for meta-analysis and GRADE report only overall scores. Appraisal of methodological quality: the methodological quality of each study will be assessed using NICE checklists and GRADE.
Confounders	Multimorbidity, age (over or under 65)

C.4.3 Stopping drugs for osteoporosis

Table 15: Review protocol: Stopping drugs for osteoporosis

Review question	Stopping drugs for osteoporosis
Area of scope	Effects of stopping treatment

C.4.4 Stopping statins

Table 16: Review protocol: What is the clinical and cost effectiveness of stopping statin treatment?

Review question	What is the clinical and cost effectiveness of stopping statin treatment?
Area of scope	Effects of stopping treatment
Objectives	To evaluate the risks and benefits of stopping statin therapy to inform a recommendation
Review population	Adults taking statins for primary or secondary prevention of cardiovascular events for at least 1 year
Interventions and comparators:	Stopping statins
Comparisons	Continuing statins
Outcomes	<p>Critical:</p> <ul style="list-style-type: none"> • Quality of life (continuous) • Hospitalisation (dichotomous) • All-cause mortality (time to event) • Cardiovascular mortality (time to event) • Stroke (dichotomous) • Non-fatal myocardial infarction (dichotomous) • Admission to care home (dichotomous) <p>Important:</p> <ul style="list-style-type: none"> • Myalgia (dichotomous)
Study design	RCTs and systematic reviews of RCTs; cohort studies if no RCTs are retrieved
Unit of randomisation	Patient
Crossover study	Permitted
Minimum duration of study	Not defined
Other exclusions	<p>Patients not matched at baseline or analysis not adjusted</p> <p>Wrong comparison</p> <p>Adherence studies (where non-adherence is identified as the primary reason for stopping statins)</p>
Population stratification	<p>Primary prevention</p> <p>Secondary prevention</p>
Reasons for stratification	Risks of stopping may be different
Subgroup analyses if there is heterogeneity	<ul style="list-style-type: none"> • Multimorbidity (<50%; >50%); multimorbidity patients may be at greater risks of events • Age (Under 65 years; 65 years or over); Older adults at greater risk of events • Reason for stopping (Adverse effects; Clinical event; Frailty/life expectancy); as this may alter the risk of events
Search criteria	<p>Databases: Medline, Embase, the Cochrane Library</p> <p>Date limits for search: all years</p> <p>Language: restrict to English only</p>

C.5 Interventions

C.5.1 Interventions: Models of Care and Holistic assessment

Table 17: Review protocol: models of care and holistic assessment

Review question	What models of care improve outcomes in patients with multimorbidity? What is the clinical and cost effectiveness of holistic assessment in patients with multimorbidity?
Guideline condition and its definition	Multimorbidity. Definition: Co-existence of 2 or more long-term conditions
Review population	Adults (18 years and over) with multimorbidity
Interventions	<p>Interventions targeted at improving outcomes and continuity of care for patients with multimorbidity. Examples include:</p> <ul style="list-style-type: none"> • Collaborative care • Integrated care • Case management (note different levels of involvement, for example <ul style="list-style-type: none"> ○ Case manager sets up care plan only ○ Case manager as single point of contact throughout patient journey) • Provider continuity (for example, facilitating regular appointments with the same clinician) • Care plan • Patient held medical records • Multi-professional team working • Interventions to improve continuity of information (including interventions to improve exchange of information across healthcare settings; discharge planning) • Medication management (not including patient self-management) • A combination of the above <p>Note: Interventions for multimorbidity patients where the intervention is targeted at improving outcomes for a single condition only will be excluded</p>
Comparison	<p>Standard care</p> <p>A comparison of the above</p>
Outcomes	<p>Critical:</p> <ul style="list-style-type: none"> • Health-related quality of life • Mortality • Functional outcomes (for example mobility, activities of daily living) • Patient and carer satisfaction • Length of hospital stay • Unscheduled care • Admission to care facility <p>Important:</p> <ul style="list-style-type: none"> • Continuity of care • Patient/carers burden
Study design	RCTs and systematic reviews of RCTs; cohort studies if no RCTs are retrieved
Unit of randomisation	<p>Patient</p> <p>Cluster</p>

Review question	What models of care improve outcomes in patients with multimorbidity? What is the clinical and cost effectiveness of holistic assessment in patients with multimorbidity?
Other exclusions	Children aged 17 years and under People with more than 1 mental health condition but no physical condition
Subgroup analyses if there is heterogeneity	<ul style="list-style-type: none"> • Ethnicity (White (>80%); Black (>80%); Asian (>80%); ethnicity as defined by studies); interventions may have varying efficacy in people from different ethnicities due to variations in language and culture. • Age (<65 years; >65 years); interventions may have varying efficacy in older and younger patients. • Type of conditions (only physical conditions; physical and mental conditions); interventions may have varying efficacy in patients with only physical conditions versus those with physical and mental conditions. This may be due to difficulties in continuity of care across physical and mental health services. • Deprivation (low SES; medium SES; high SES); interventions may have varying efficacy in patients with different socio-economic status, due to varying levels of education and engagement with health services. • Number of conditions (2 chronic conditions; 3 chronic conditions; more than 3 chronic conditions). Interventions may have varying efficacy in those patients with differing number of chronic conditions, which may be due to self-management being more difficult in those patients with more conditions to manage.
Search criteria	The searches from a Cochrane review ¹¹³⁰ will be updated. Databases: Medline, Embase, the Cochrane Library, CINAHL, AMED Date limits for search: 2011 Language: restrict to English only

C.6 Self-Management

Table 18: Review protocol: Self-management

Review question	What is the clinical- and cost-effectiveness of self-management and expert patient programmes for people with multimorbidity?
Guideline condition and its definition	Multimorbidity. Definition: Co-existence of 2 or more long-term conditions.
Review population	Adults (aged 18 years and over) with multimorbidity Strata: Type of conditions (only physical conditions; physical and mental conditions); interventions may have varying efficacy in patients with only physical conditions versus those with physical and mental conditions. This may be due to difficulties in continuity of care across physical and mental health services.
	Line of therapy not an inclusion criterion
Interventions	Self-management programmes Expert patient programmes Combination of the above
Comparison	Standard care Inactive control intervention

Review question	What is the clinical- and cost-effectiveness of self-management and expert patient programmes for people with multimorbidity?
Outcomes	<p>Critical:</p> <ul style="list-style-type: none"> • Health-related quality of life (continuous) • Mortality (time to event/dichotomous) • Functional outcomes (mobility, activities of daily living) (continuous) • Patient and carer satisfaction (continuous) • Unplanned hospital admissions (dichotomous) • Length of hospital stay (continuous) <p>Important:</p> <ul style="list-style-type: none"> • Continuity metrics (continuous) • Patient/carer treatment burden (continuous) • Patient self-efficacy (continuous)
Study design	RCTs and systematic reviews of RCTs; cohort studies if no RCTs are retrieved
Unit of randomisation	Patient Cluster
Crossover study	Not permitted
Minimum duration of study	None
Other exclusions	<p>Children and young people under 18 years</p> <p>People who only have multiple mental health problems and no physical health problems</p> <p>People with a single long-term condition</p> <p>Interventions targeted at a single condition only</p>
Sensitivity/other analysis	Combine different studies across different types of intervention
Subgroup analyses if there is heterogeneity	<ul style="list-style-type: none"> • Ethnicity (White [>80%]; Black [>80%]; Asian [>80%]; ethnicity as defined by studies). Interventions may have varying efficacy in people from different ethnicities due to variations in language and culture. • Age (<65 years; >65 years). Interventions may have varying efficacy in older and younger patients. • Deprivation (low SES; medium SES; high SES). Interventions may have varying efficacy in patients with different socio-economic status due to varying levels of education and engagement with health services. • Number of conditions (2 chronic conditions; 3 chronic conditions; more than 3 chronic conditions). Interventions may have varying efficacy in those patients with differing number of chronic conditions, which may be due to self-management being more difficult in those patients with more conditions to manage.
Search criteria	<p>Databases: Medline, Embase, the Cochrane Library</p> <p>Date limits for search: All years</p> <p>Language: English language only (except studies translated for Cochrane reviews or as directed by the GDG)</p>

C.7 Format of encounters

Table 19: Review protocol: What format of encounters with healthcare professionals improves outcomes for people with multimorbidity?

Review question	What format of encounters with healthcare professionals improves outcomes for people with multimorbidity?
Guideline condition and its definition	Multimorbidity
Objectives	To determine which is the most clinically- and cost-effective format of healthcare encounters between health professionals and adults with multimorbidity
Review population	Adults with multimorbidity
	Adults (aged 18 years and over)
Interventions and comparators: generic/class; specific/drug (All interventions will be compared with each other, unless otherwise stated)	<p>Formats of healthcare encounters targeted at improving outcomes for people with multimorbidity, as specified in papers. For example, interventions comparing:</p> <ul style="list-style-type: none"> • Time allocated for consultations (including inpatient care) (for example longer time allocation) • Planned recall and structured review • Method of communication (for example face to face, telephone, email, virtual) • Methods of arranging appointments (for example advanced booking, booking with chosen healthcare professional) • Methods to involve patient in planning content of appointments (for example patient setting agenda) • Multi-professional appointments (including ward rounds/clinics) • Setting of encounter (for example community visits) • Combination of the above
Outcomes	<p>Critical:</p> <ul style="list-style-type: none"> • Quality of life (continuous) • Mortality (dichotomous) • Functional outcomes (continuous) • Patient/carer satisfaction (continuous) • Length of hospital stay (continuous) • Unscheduled care (dichotomous) <p>Important:</p> <ul style="list-style-type: none"> • Continuity of care (dichotomous) • Patient/carer treatment burden (dichotomous) • Admission to care facility (dichotomous)
Study design	RCTs; cohort studies if no RCTs retrieved
Unit of randomisation	Patient Healthcare setting
Crossover study	Not permitted
Minimum duration of study	Not defined
Population stratification	Inpatient Outpatient
Reasons for stratification	The format of healthcare encounters will be relevant to the setting.

Review question	What format of encounters with healthcare professionals improves outcomes for people with multimorbidity?
	Furthermore, some formats may be more effective in 1 setting than another.
Subgroup analyses if there is heterogeneity	<ul style="list-style-type: none"> • Age (adult [18-65 years]; older adult [65+ years]). Some interventions may be more effective in some age groups than others. • Number of conditions (2 conditions; 3-4 conditions; >4 conditions). The efficacy of interventions may vary depending on the number of comorbid conditions people have. • Type of comorbid conditions (physical multimorbidity; physical and mental health multimorbidity). Mental health and physical health services may be organised differently, and there may be poorer continuity of care between the 2 than may occur in solely physical health service. • Ethnicity (predominantly 1 population; mixed population). Language and culture barriers may influence the efficacy of healthcare encounters. • Deprivation (low deprivation/high SES; high deprivation/low SES; mixed population). Greater deprivation is associated with poorer health outcomes amongst adults with multimorbidity.
Search criteria	Databases: Medline, Embase, the Cochrane Library Date limits for search: all years Language: English only

Appendix D: Health economic review protocol

Table 20: Health economic review protocol

Review question	All questions – health economic evidence
Objectives	To identify economic evaluations relevant to any of the review questions.
Search criteria	<ul style="list-style-type: none"> • Populations, interventions and comparators must be as specified in the individual review protocol above. • Studies must be of a relevant economic study design (cost–utility analysis, cost-effectiveness analysis, cost–benefit analysis, cost–consequences analysis, comparative cost analysis). • Studies must not be an abstract only, a letter, editorial or commentary, or a review of economic evaluations. (Recent reviews will be ordered although not reviewed. The bibliographies will be checked for relevant studies, which will then be ordered.) • Unpublished reports will not be considered unless submitted as part of a call for evidence. • Studies must be in English.
Search strategy	<p>An economic study search will be undertaken using population-specific terms and an economic study filter – see Appendix G [in the Full guideline].</p> <p>In addition, an economic study search will be undertaken for the following reviews using the same terms as the clinical review and an economic study filter:</p> <ul style="list-style-type: none"> - Treatment burden - Stopping antihypertensive - Stopping bisphosphonates - Stopping statins - Cochrane interventions review
Review strategy	<p>Studies not meeting any of the search criteria above will be excluded. Studies published before 1999, abstract-only studies and studies from non-OECD countries or the USA will also be excluded.</p> <p>Each remaining study will be assessed for applicability and methodological limitations using the NICE economic evaluation checklist which can be found in Appendix G of the NICE guidelines manual (2012).⁸⁹³</p> <p>Inclusion and exclusion criteria</p> <ul style="list-style-type: none"> • If a study is rated as both ‘Directly applicable’ and with ‘Minor limitations’ then it will be included in the guideline. An economic evidence table will be completed and it will be included in the economic evidence profile. • If a study is rated as either ‘Not applicable’ or with ‘Very serious limitations’ then it will usually be excluded from the guideline. If it is excluded then an economic evidence table will not be completed and it will not be included in the economic evidence profile. • If a study is rated as ‘Partially applicable’, with ‘Potentially serious limitations’ or both then there is discretion over whether it should be included. <p>Where there is discretion</p> <p>The health economist will make a decision based on the relative applicability and quality of the available evidence for that question, in discussion with the GDG if required. The ultimate aim is to include studies that are helpful for decision-making in the context of the guideline and the current NHS setting. If several studies are considered of sufficiently high applicability and methodological quality that they could all be included, then the health economist, in discussion with the GDG if required, may decide to include only the most applicable studies and to selectively exclude the remaining studies. All studies excluded on the basis of</p>

applicability or methodological limitations will be listed with explanation as excluded economic studies in Appendix M.

The health economist will be guided by the following hierarchies.

Setting:

- UK NHS (most applicable).
- OECD countries with predominantly public health insurance systems (for example, France, Germany, Sweden).
- OECD countries with predominantly private health insurance systems (for example, Switzerland).
- Studies set in non-OECD countries or in the USA will have been excluded before being assessed for applicability and methodological limitations.

Economic study type:

- Cost–utility analysis (most applicable).
- Other type of full economic evaluation (cost–benefit analysis, cost-effectiveness analysis, cost–consequences analysis).
- Comparative cost analysis.
- Non-comparative cost analyses including cost-of-illness studies will have been excluded before being assessed for applicability and methodological limitations.

Year of analysis:

- The more recent the study, the more applicable it will be.
- Studies published in 1999 or later but that depend on unit costs and resource data entirely or predominantly from before 1999 will be rated as ‘Not applicable’.
- Studies published before 1999 will have been excluded before being assessed for applicability and methodological limitations.

Quality and relevance of effectiveness data used in the economic analysis:

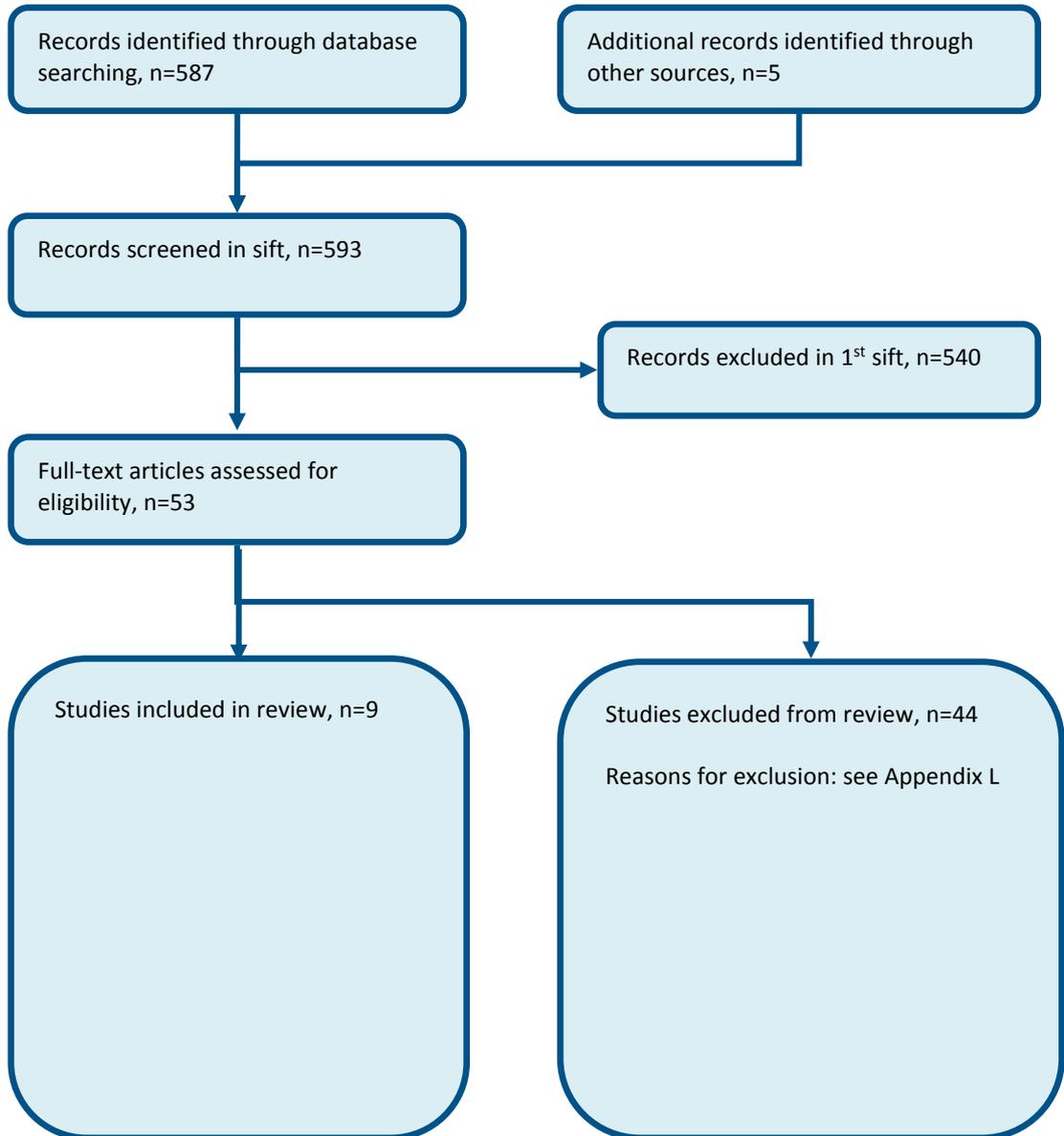
- The more closely the effectiveness data used in the economic analysis matches with the outcomes of the studies included in the clinical review the more useful the analysis will be for decision-making in the guideline.

Appendix E: Clinical study selection

E.1 Principles/Barriers of care

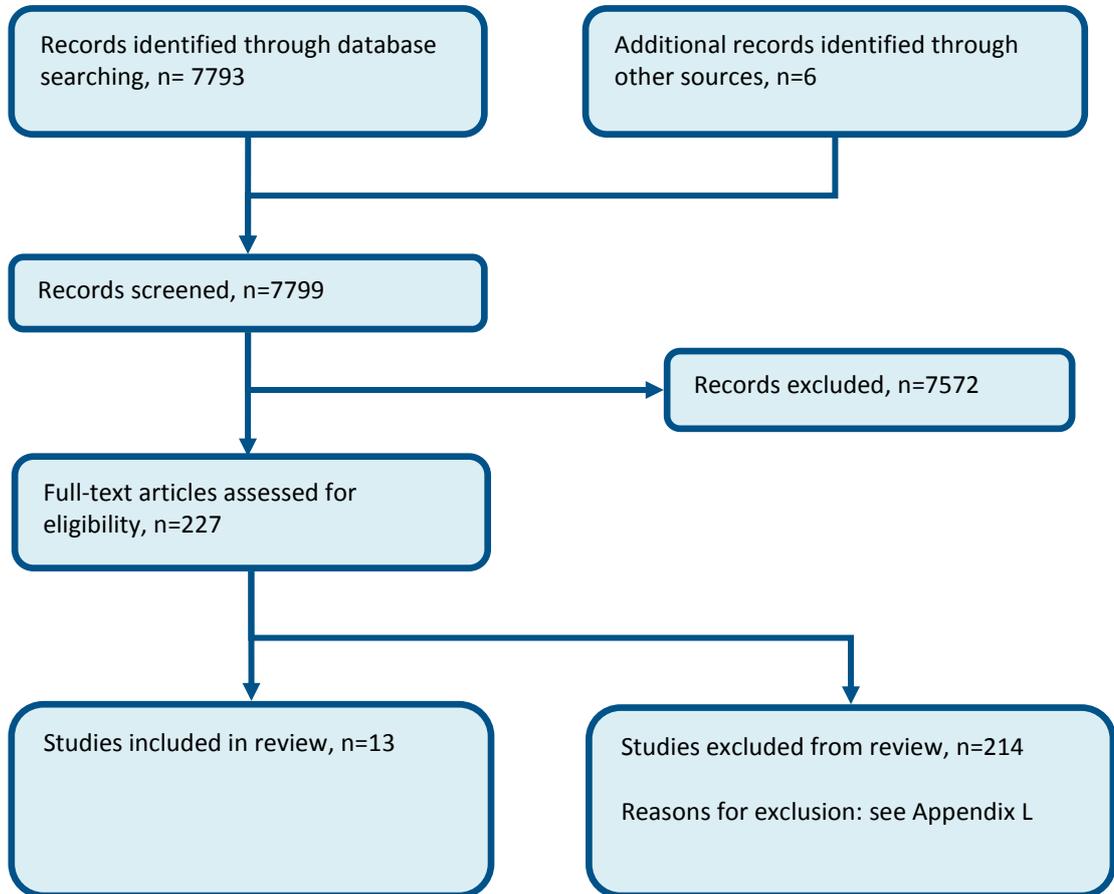
E.1.1 Principles of care

Figure 1: Flow chart of clinical article selection for the review of principles in multimorbidity



E.1.2 Barriers of care

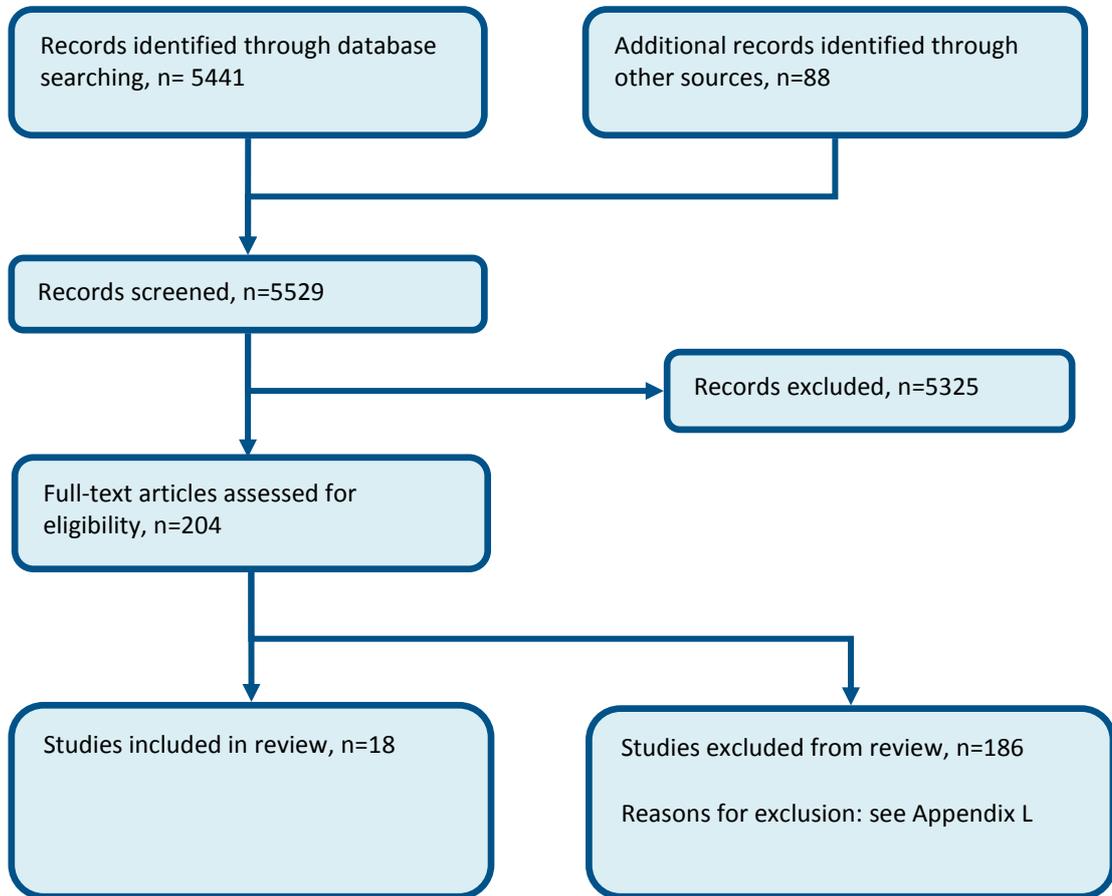
Figure 2: Flow chart of clinical article selection for the review of barriers to optimising care for people with multimorbidity



E.2 Identification

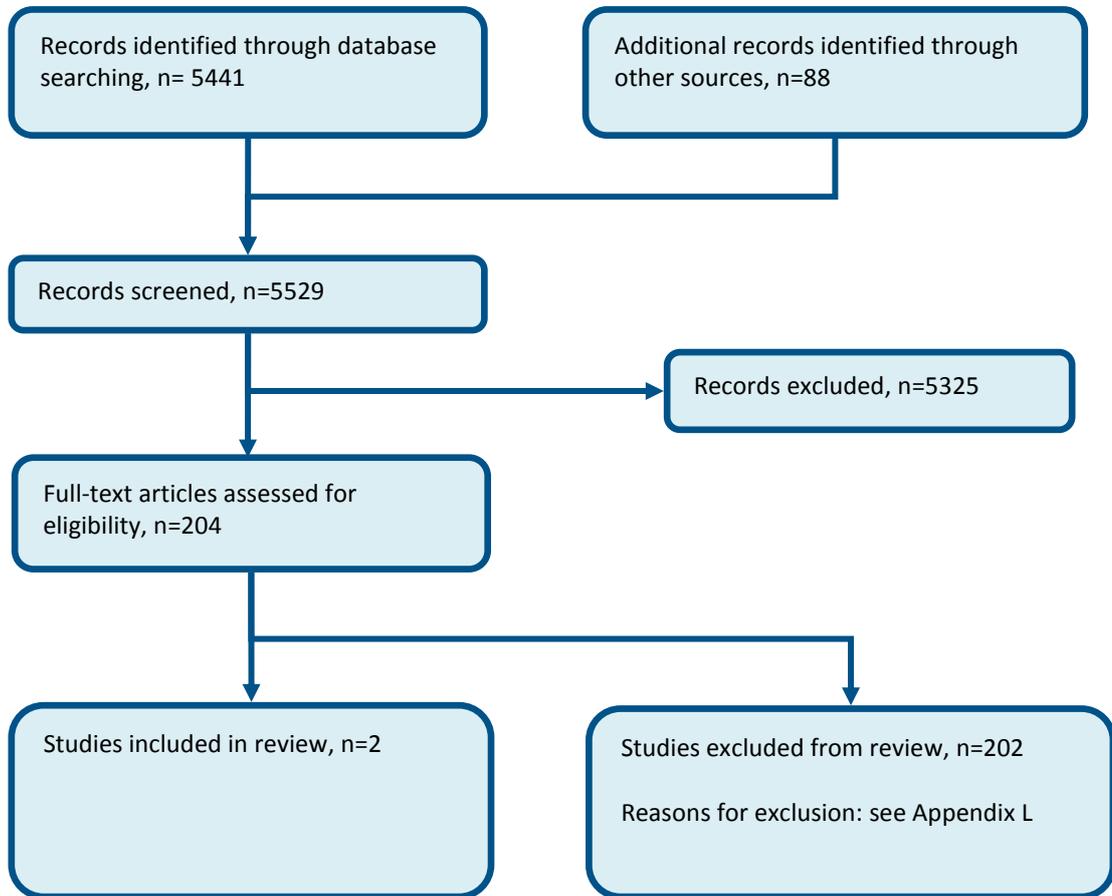
E.2.1 Unplanned hospital admissions

Figure 3: Flow chart of clinical article selection for the review of: What risk tool best identifies people with multimorbidity who are at risk of unplanned hospital admission?



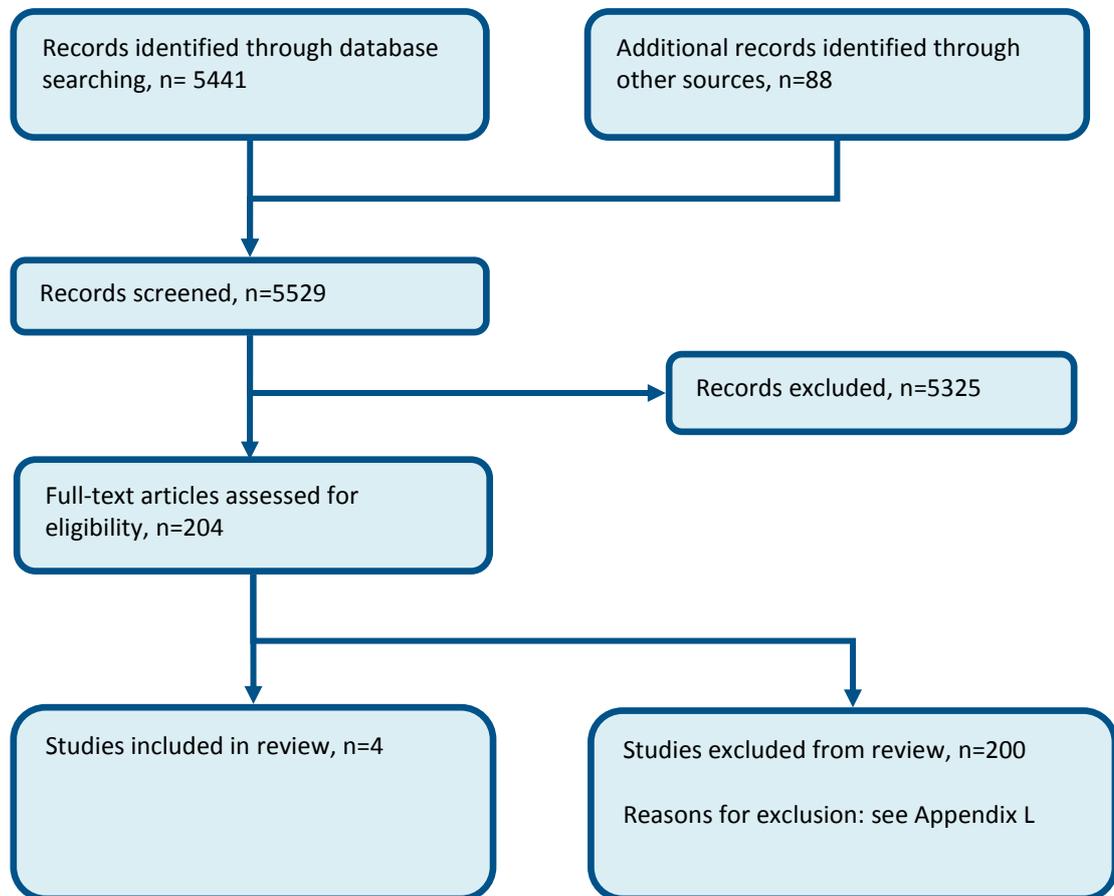
E.2.2 Health-related quality of life

Figure 4: Flow chart of clinical article selection for the review of: What risk tool best identifies people with multimorbidity who are at risk of reduced health-related quality of life?



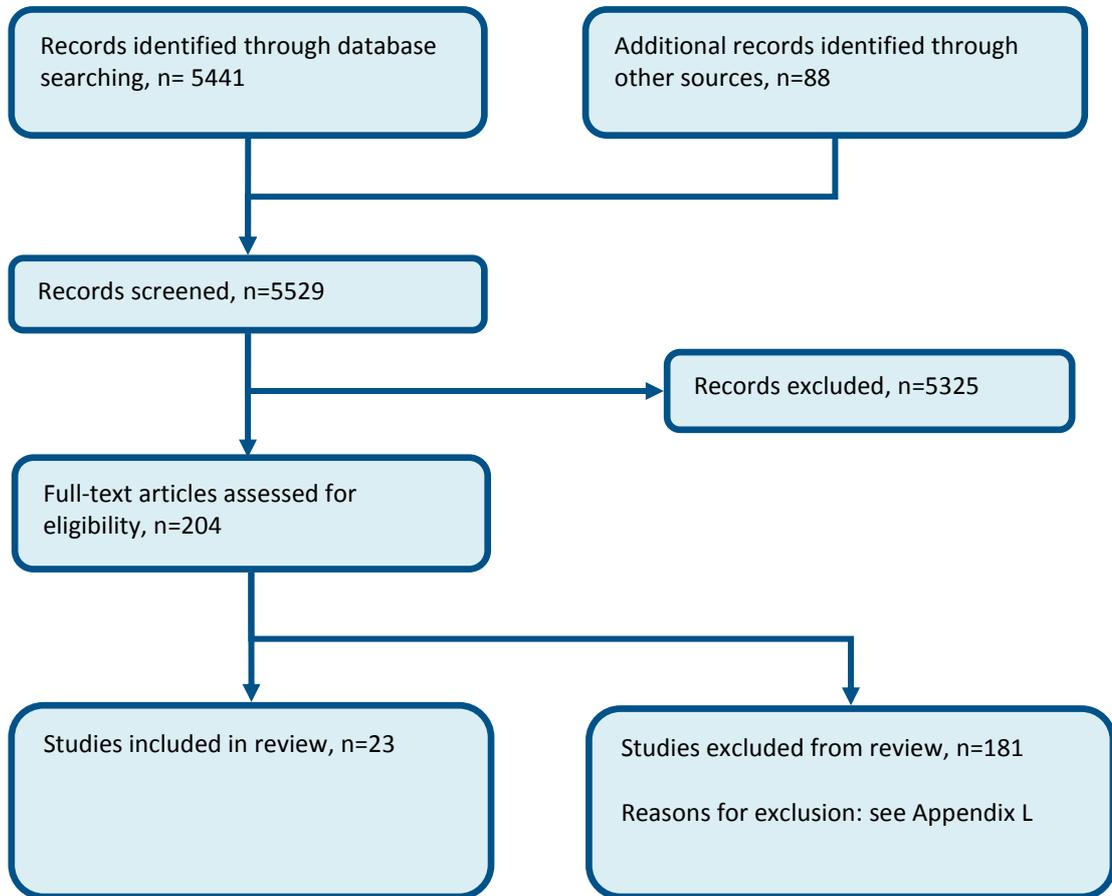
E.2.3 Admission to care facility

Figure 5: Flow chart of clinical article selection for the review of: What risk tool best identifies people with multimorbidity who are at risk of admission to a care facility?



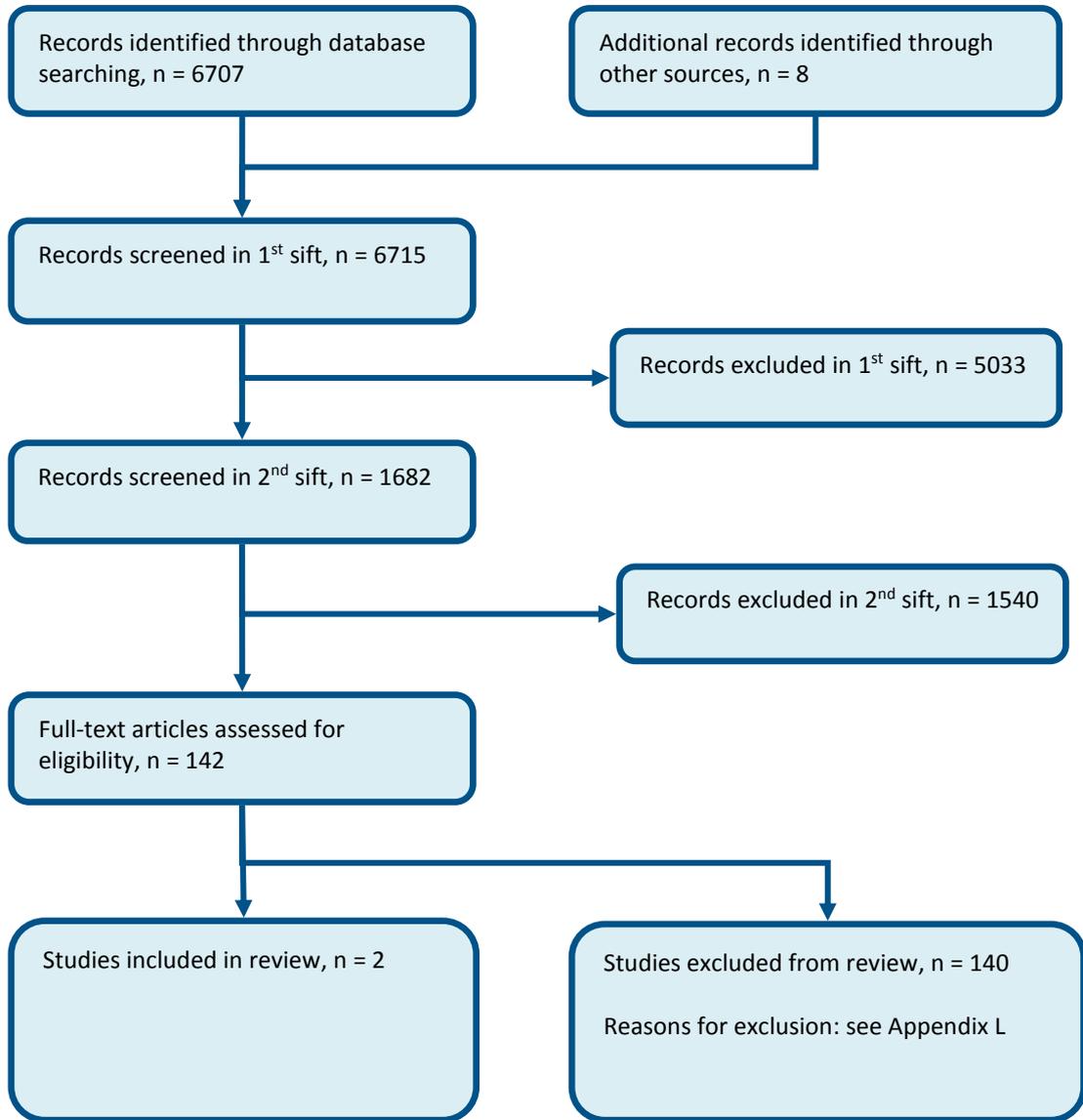
E.2.4 Life expectancy risk tools

Figure 6: Flow chart of clinical article selection for the review of: What risk tool best identifies people with multimorbidity who are at risk of reduced life expectancy?



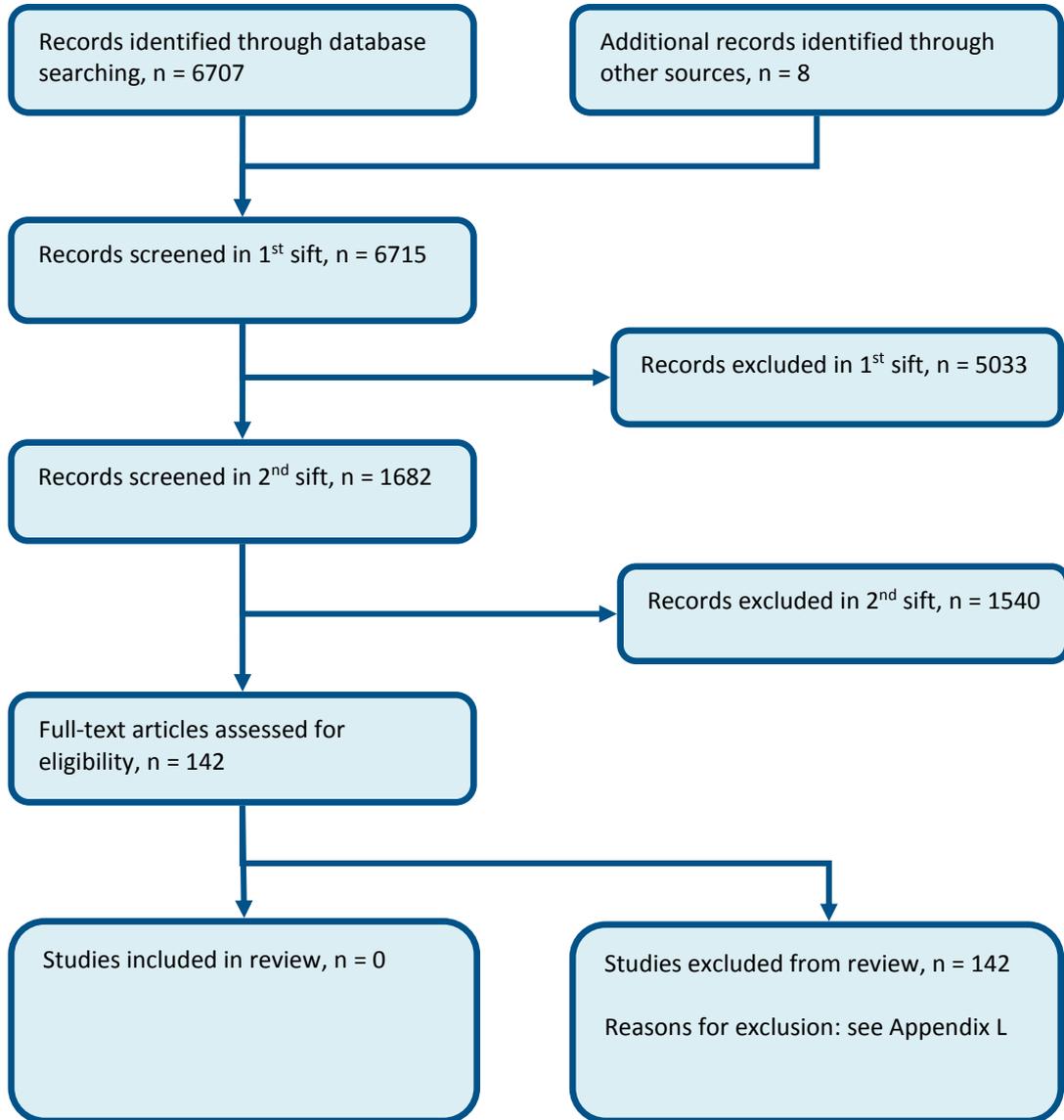
E.2.5 Polypharmacy: unplanned hospital admissions

Figure 7: Flow diagram of clinical article selection for: is polypharmacy associated with a greater risk of unplanned admissions amongst people with multimorbidity?



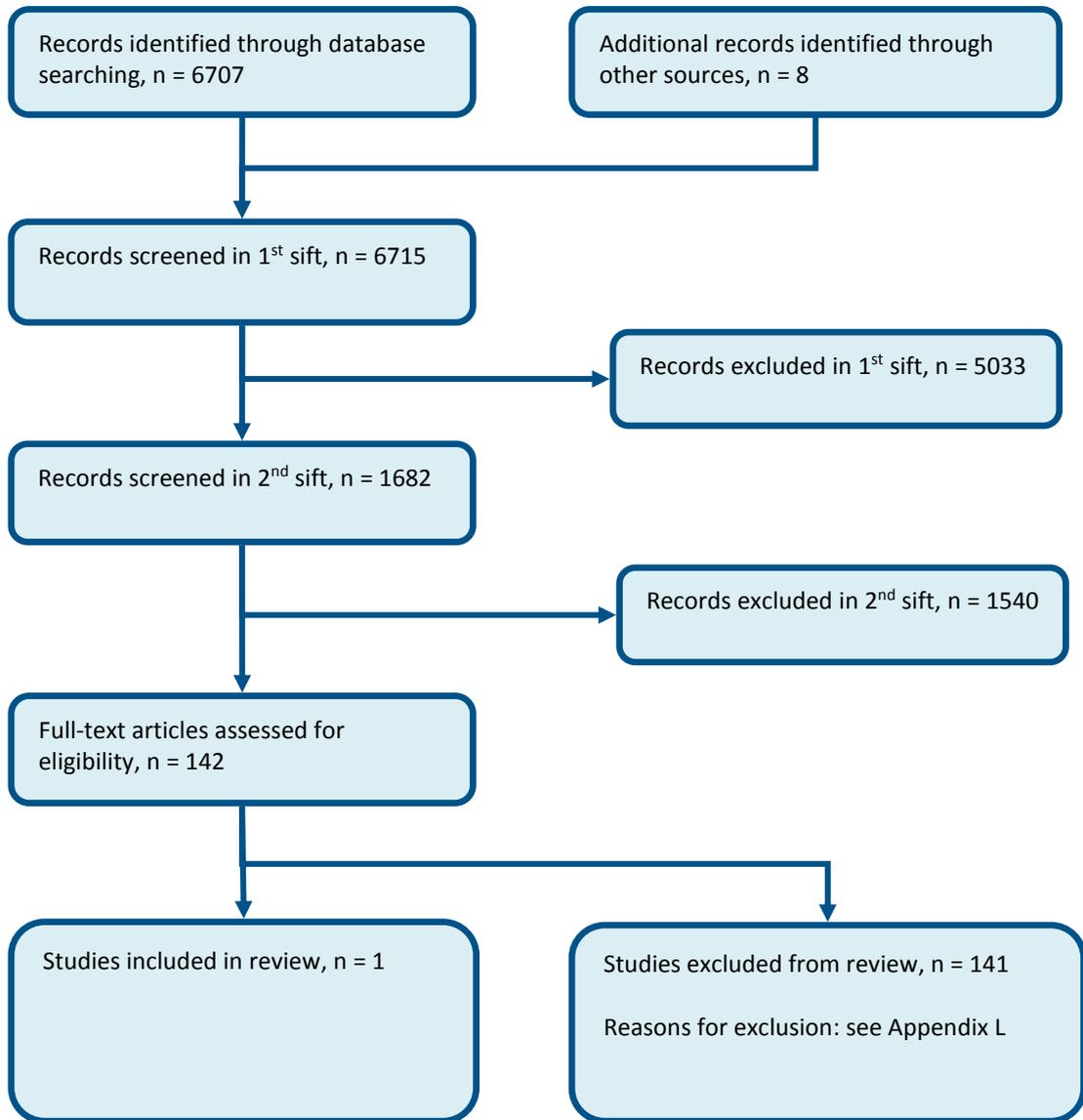
E.2.6 Polypharmacy: health-related quality of life

Figure 8: Flow diagram of clinical article selection: Is polypharmacy associated with a greater risk of reductions in health-related quality of life amongst people with multimorbidity?



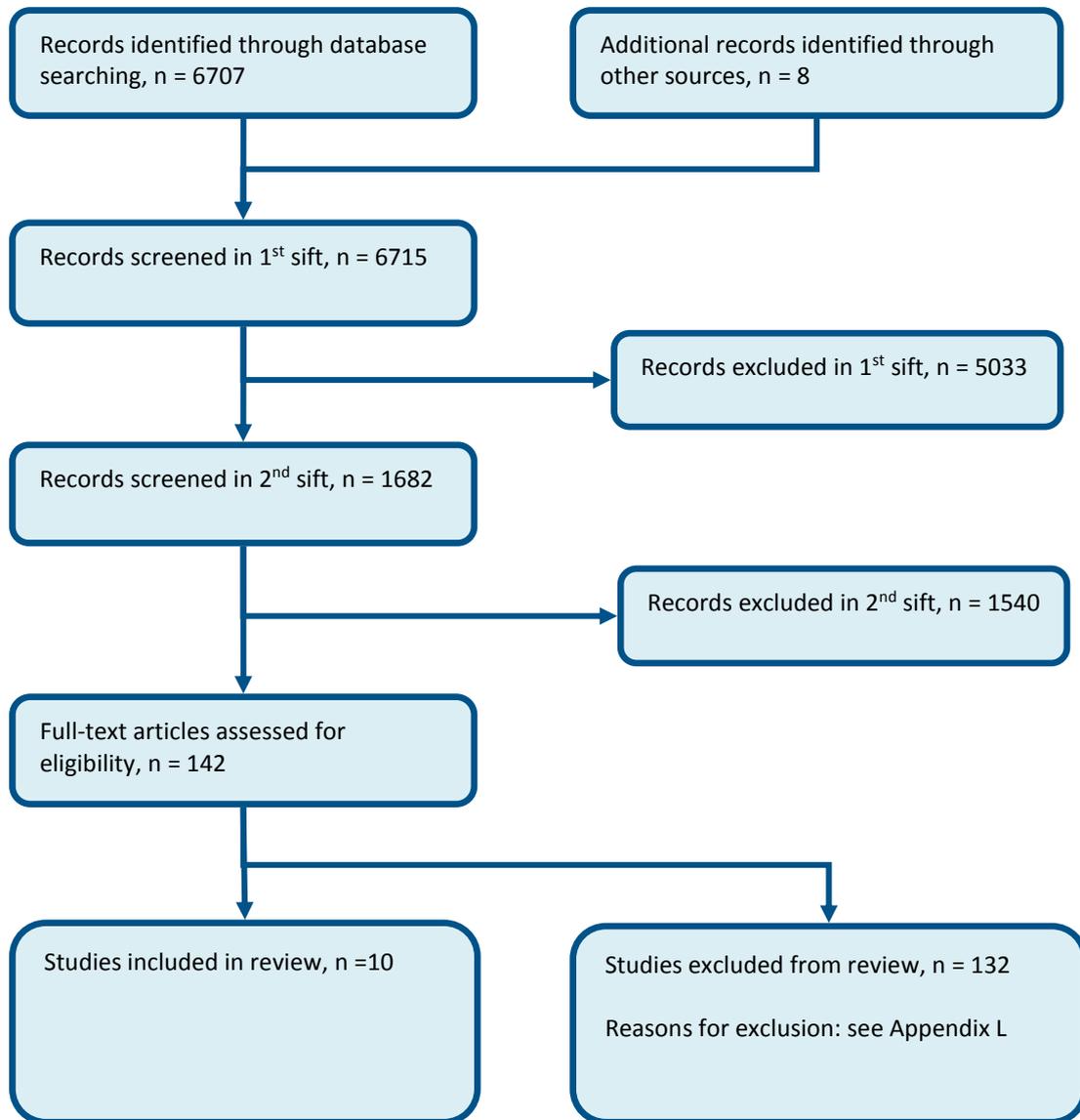
E.2.7 Polypharmacy: admission to care facilities

Figure 9: Flow diagram of clinical article selection for: Is polypharmacy associated with a greater risk of admission to care facility amongst people with multimorbidity?



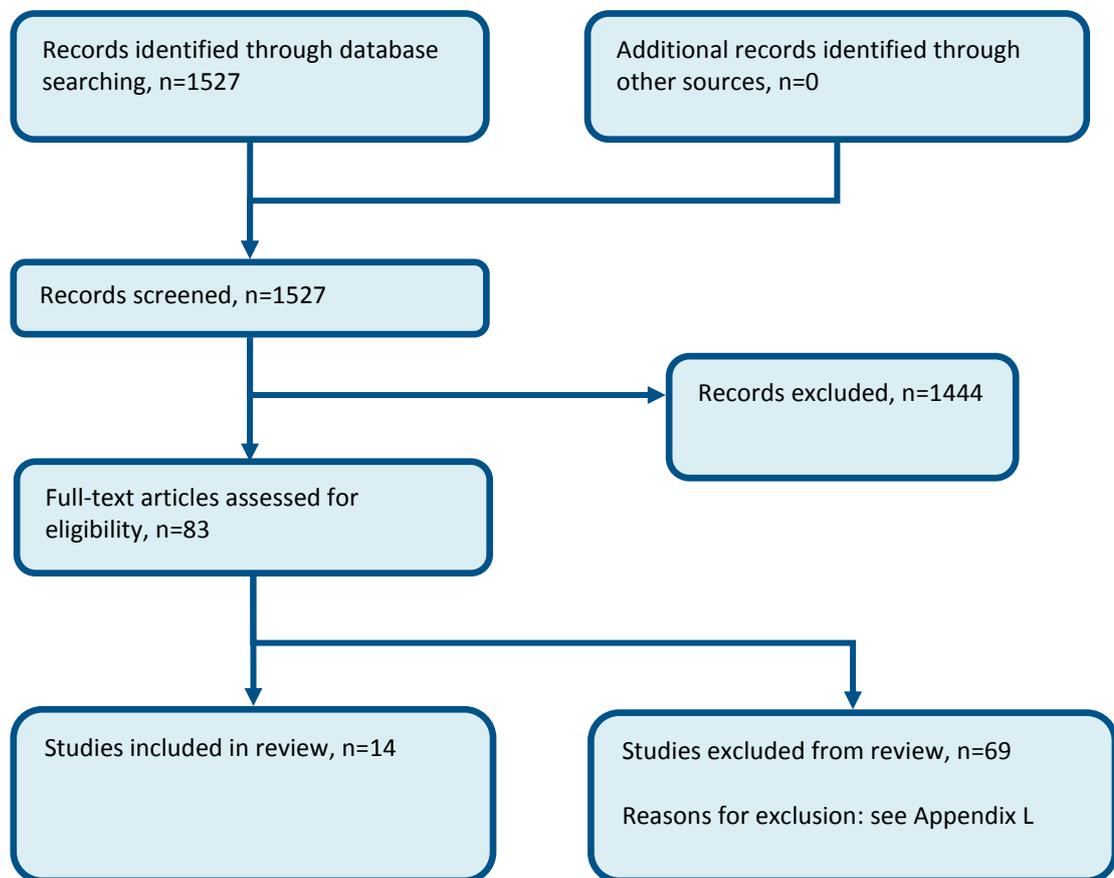
E.2.8 Polypharmacy: mortality

Figure 10: Flow diagram of clinical article selection for: Is polypharmacy associated with a greater risk of mortality amongst people with multimorbidity?



E.3 Frailty

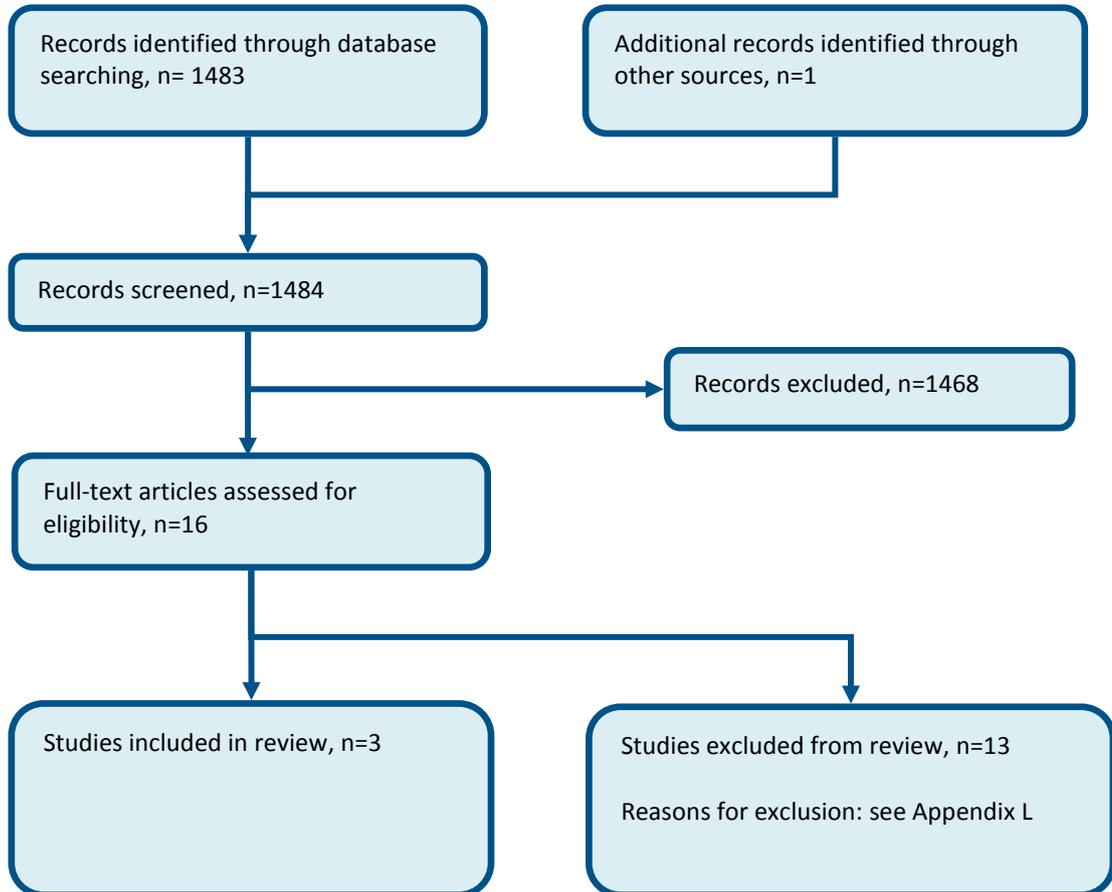
Figure 11: Flow chart of clinical article selection for the review of diagnostic test accuracy of tools for frailty



E.4 Delivering an approach to care that takes account of multimorbidity

E.4.1 Treatment burden

Figure 12: Flow chart of clinical article selection for the review of assessing treatment burden

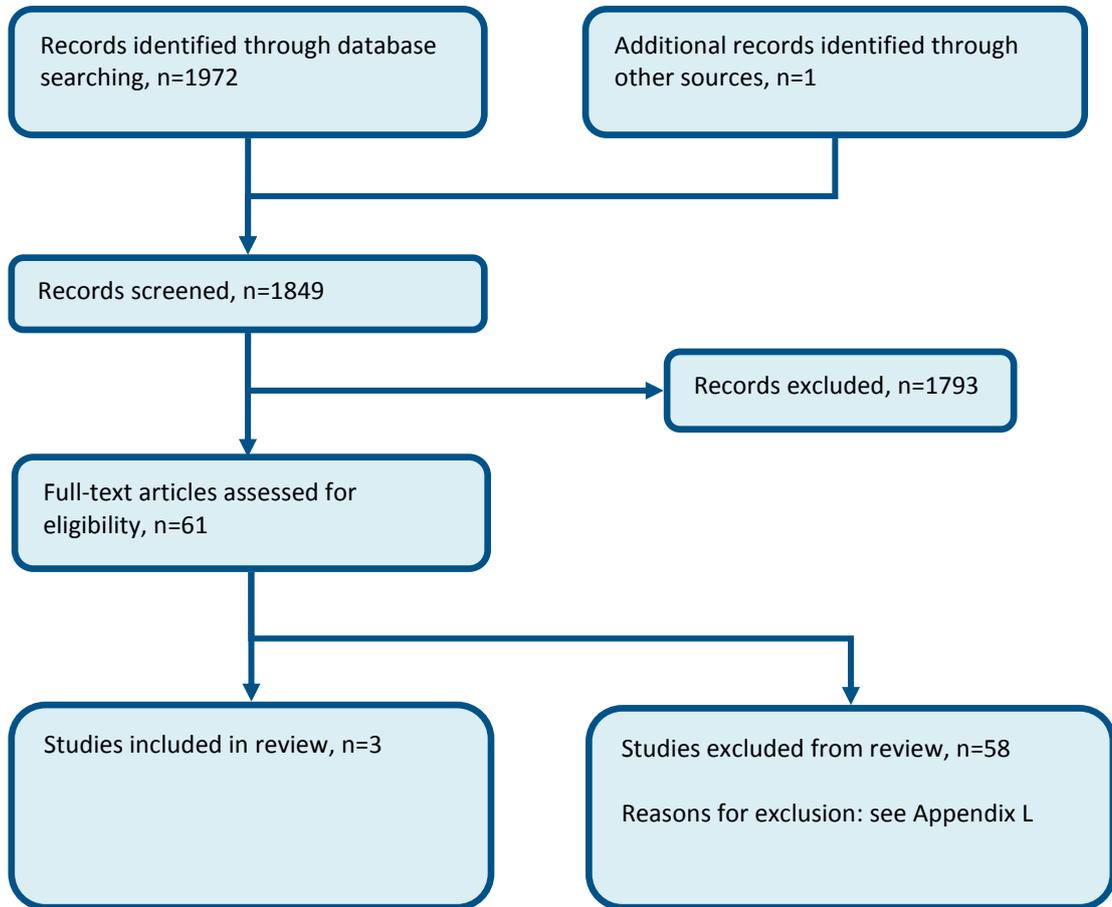


E.4.2 Ranking

None.

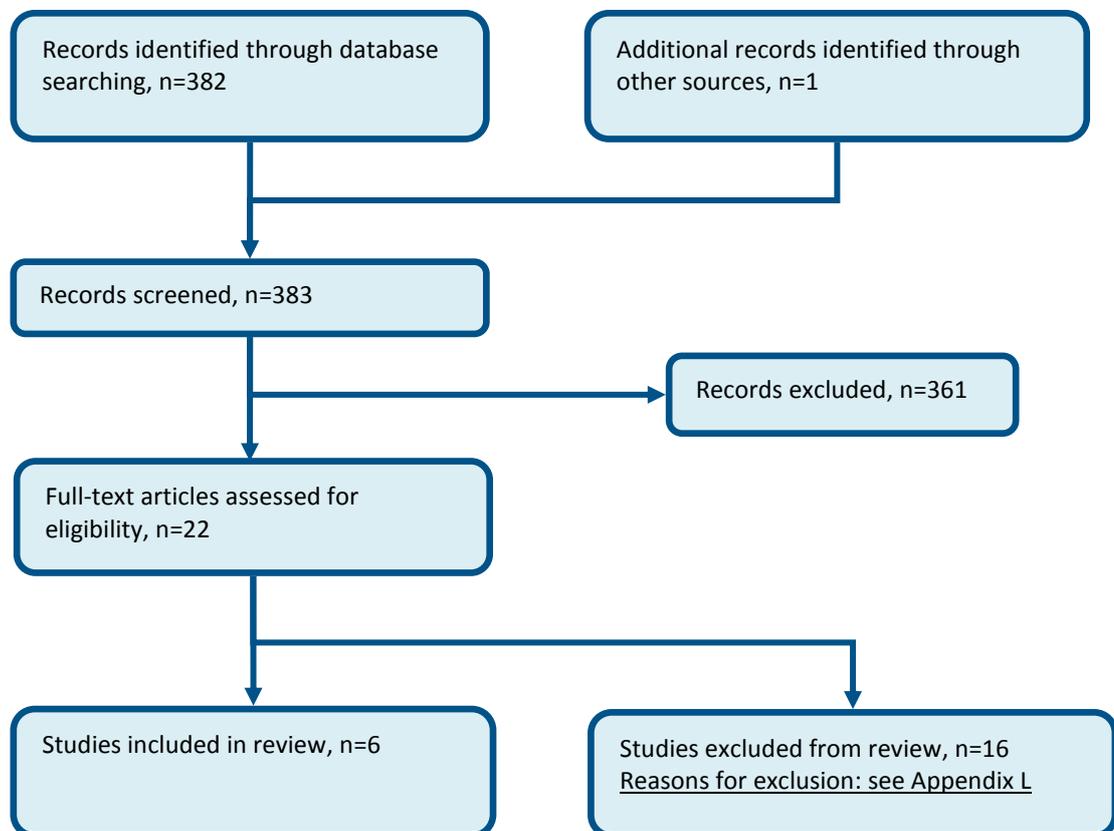
E.4.3 Stopping antihypertensive treatment

Figure 13: Flow chart of clinical article selection for the review of stopping antihypertensive treatment



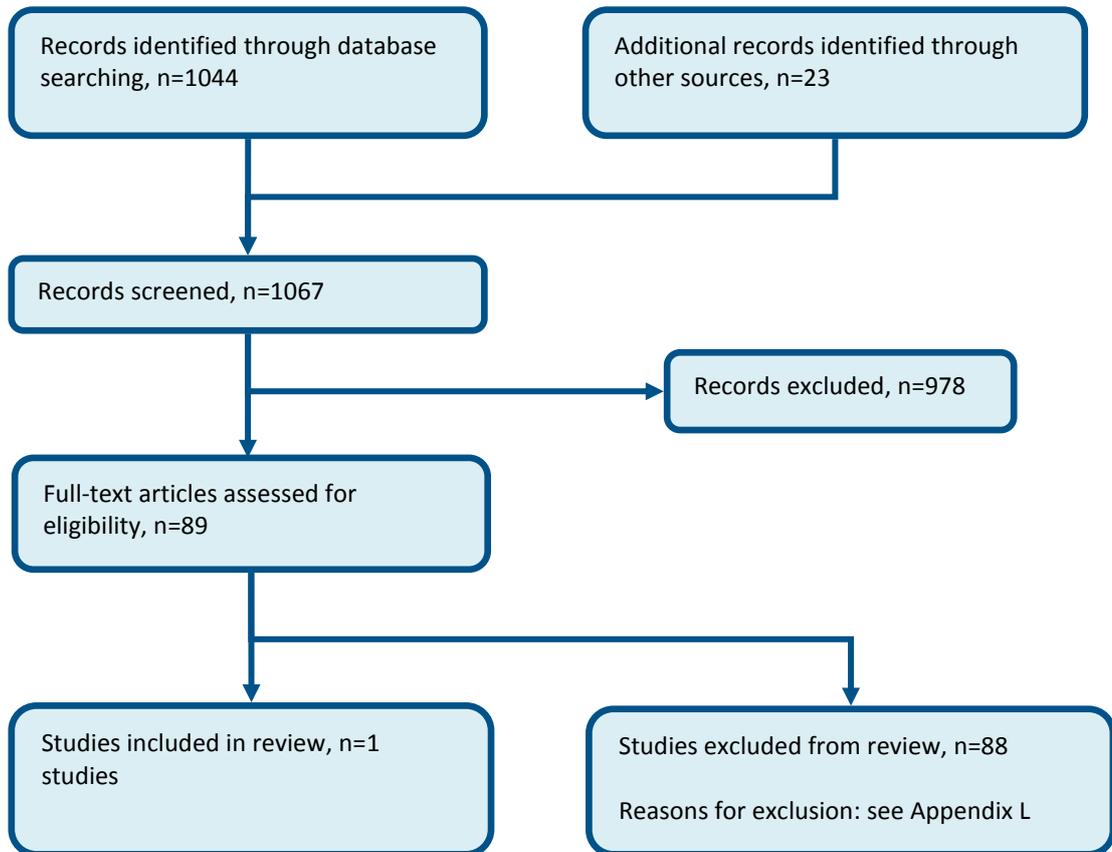
E.4.4 Stopping drugs for osteoporosis

Figure 14: Flow chart of clinical article selection for the review of stopping bisphosphonate treatment



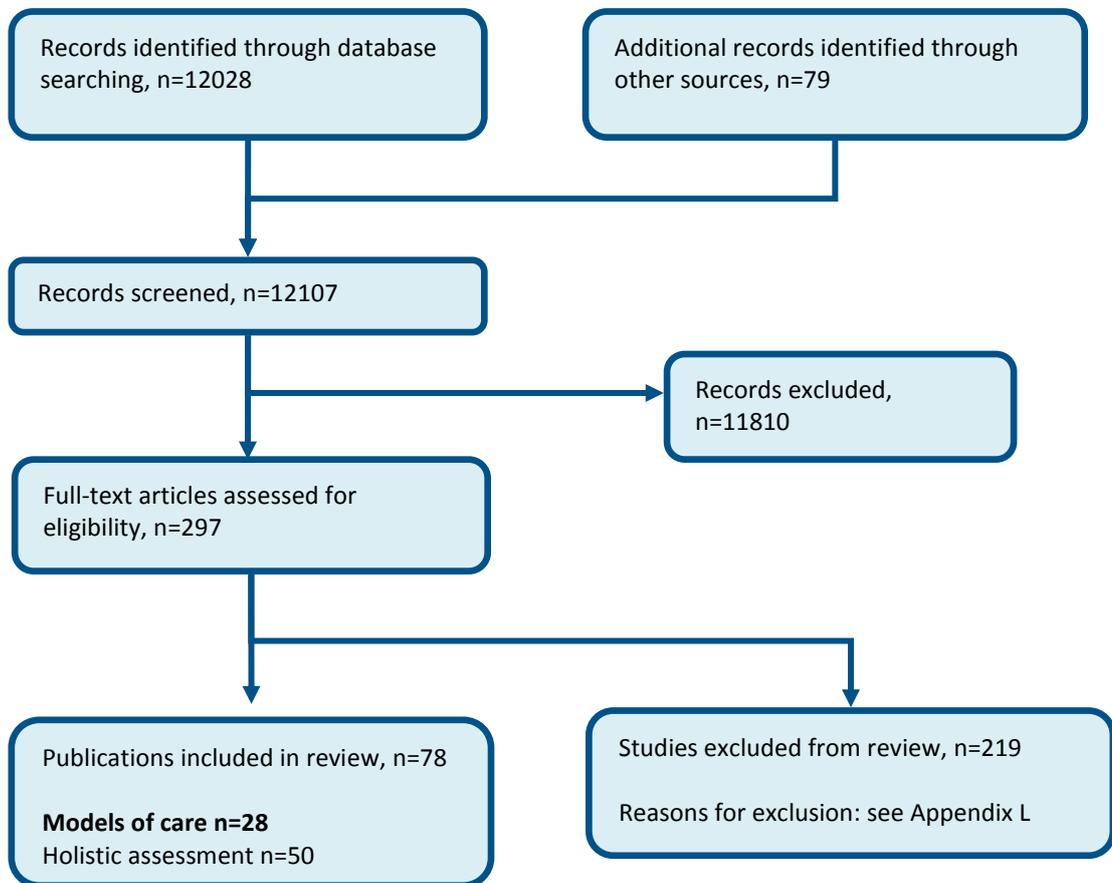
E.4.5 Stopping statins

Figure 15: Flow chart of clinical article selection for the review of stopping treatments (statins)



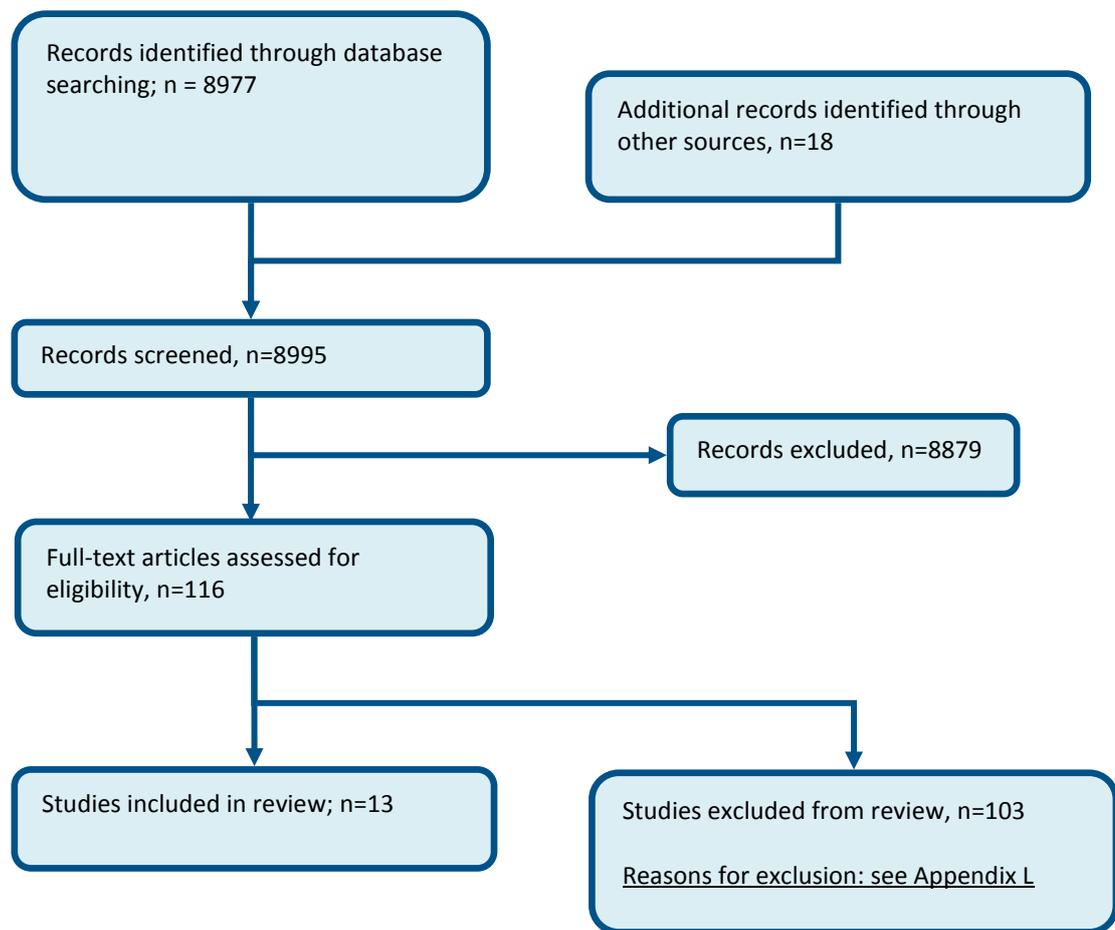
E.5 Interventions

Figure 16: Flow chart of clinical article selection for the review of models of care and holistic assessment



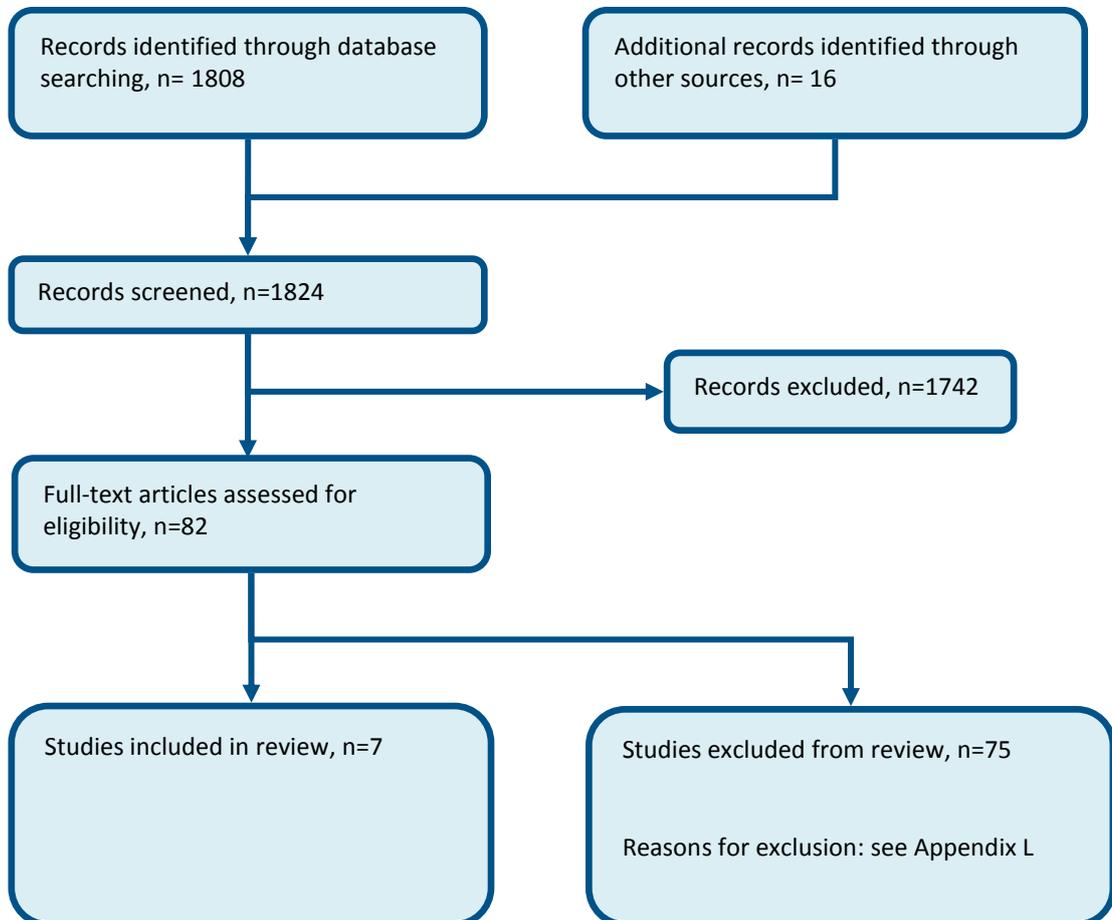
E.6 Self-Management

Figure 17: Flow chart of clinical article selection for the review of self-management



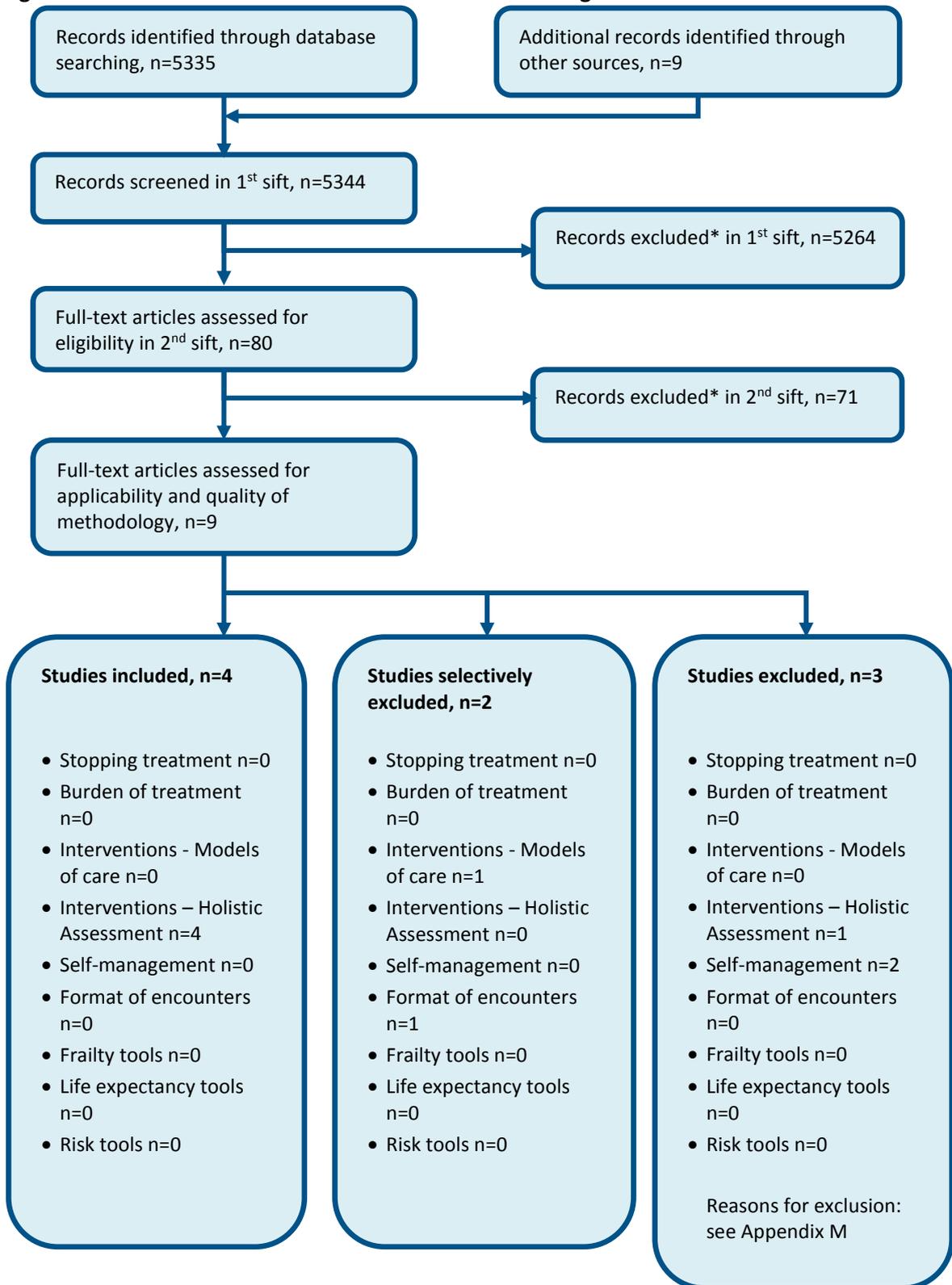
E.7 Format of encounters

Figure 18: Flow chart of clinical article selection for the review of: What format of encounters with healthcare professionals improves outcomes for people with multimorbidity?



Appendix F: Health economic study selection

Figure 19: Flow chart of economic article selection for the guideline



Appendix G: Literature search strategies

G.1 Contents

Introduction	Search methodology
Section G.2	Search population
Section G.3	Study filters and exclusions terms
G.3.1	Excluded study designs and publication types
G.3.2	Randomised controlled trials (RCT)
G.3.3	Systematic reviews (SR)
G.3.4	Health economic studies (HE)
G.3.5	Quality of life studies (QoL)
G.3.6	Health economic modelling (MOD)
G.3.7	Observational studies (OBS)
G.3.8	Qualitative reviews (QUAL)
Section G.4	Searches for specific questions
G.4.1	Identification: risk tools
G.4.2	Identification: polypharmacy
G.4.3	Principles
G.4.4	Barriers
G.4.5	Burden of treatment
G.4.6	Stopping treatment: antihypertensives
G.4.7	Stopping treatment: bisphosphonates
G.4.8	Stopping treatment: statins
G.4.9	Frailty assessment
G.4.10	Models of care
G.4.11	Holistic assessment
G.4.12	Expert patient programmes
G.4.13	Format of consultation
Section G.5	Health economics searches
G.5.1	General multimorbidity economics
G.5.2	Models of care
G.5.3	Holistic assessment
G.5.4	Burden of treatment
G.5.5	Stopping treatment: antihypertensives
G.5.6	Stopping treatment: bisphosphonates
G.5.7	Stopping treatment: statins
G.5.8	EQ5D
G.5.9	Quality of life (QOL) in care homes
G.5.10	Mortality in care homes

Search strategies used for the multimorbidity guideline are outlined below and were run in accordance with the methodology in the NICE guidelines manual.⁸⁹⁰ All searches were run up to **4 January 2016** unless otherwise stated. Any studies added to the databases after this date (even those published prior to this date) were not included unless specifically stated in the text. We do not routinely search for electronic, ahead of print or 'online early' publications. Where possible searches were limited to retrieve material published in English.

Table 21: Database date parameters

Database	Dates searched
Medline	1946 – 04 January 2016
Embase	1974 – 2015 Week 52
The Cochrane Library	Cochrane Reviews to Issue 1 of 12, January 2016 CENTRAL to Issue 12 of 12, December 2015 DARE and NHSEED to Issue 2 of 4, April 2015 HTA to Issue 4 of 4, October 2015
CINAHL	Inception – 04 January 2016
PsycINFO	Inception – 04 January 2016
AMED	Inception – 04 January 2016

Searches for the **clinical reviews** were run in Medline (OVID), Embase (OVID) and the Cochrane Library (Wiley). Additional searches were run in CINAHL, Cumulative Index to Nursing and Allied Health Literature (EBSCO), PsycINFO (ProQuest), AMED, Allied and Complementary Medicine (Ovid), see Table 2.

Table 22: Databases searched

Question	Question number	Databases
Barriers	G.4.4	Medline, Embase, CINAHL, PsycINFO
Burden of treatment	G.4.5	Medline, Embase, the Cochrane Library, CINAHL, PsycINFO
Expert patient programmes	G.4.12	Medline, Embase, the Cochrane Library
Format of consultation	G.4.13	Medline, Embase, the Cochrane Library
Frailty assessment	G.4.9	Medline, Embase, the Cochrane Library
Holistic assessment	G.4.11	Medline, Embase, the Cochrane Library
Identification: polypharmacy	G.4.2	Medline, Embase, the Cochrane Library
Identification: risk tools	G.4.1	Medline, Embase, the Cochrane Library
Models of care	G.4.10	Medline, Embase, the Cochrane Library, CINAHL, AMED
Principles	G.4.3	Medline, Embase
Stopping treatment: antihypertensives	G.4.6	Medline, Embase, the Cochrane Library
Stopping treatment: bisphosphonates	G.4.7	Medline, Embase, the Cochrane Library

Question	Question number	Databases
Stopping treatment: statins	G.4.8	Medline, Embase, the Cochrane Library

Searches for **intervention and diagnostic studies** were usually constructed using a PICO format where population (P) terms were combined with Intervention (I) and sometimes Comparison (C) terms. An intervention can be a drug, a procedure or a diagnostic test. Outcomes (O) are rarely used in search strategies for interventions. Search filters were also added to the search where appropriate.

Searches for the health economic reviews were run in Medline, Embase, the NHS Economic Evaluations Database (NHS EED), the Health Technology Assessment (HTA) database and the Health Economic Evaluation Database (HEED). NHS EED and HTA databases were hosted by the Centre for Research and Dissemination (CRD). The Health Economic Evaluation Database (HEED) ceased production in 2014 with access ceasing in January 2015. For the final dates of HEED searches, please see individual economic questions.

For Medline and Embase an economic filter (instead of a study type filter) was added to the same clinical search strategy.

G.2 Population search strategies

There is no standard population search strategy for this guideline. Population search terms were either not used or are included with the intervention terms in section G.4.

G.3 Study filter search terms

G.3.1 Excluded study designs and publication types

The following study designs and publication types were removed from retrieved results using the NOT operator.

Medline search terms

1.	letter/
2.	editorial/
3.	news/
4.	exp historical article/
5.	anecdotes as topic/
6.	comment/
7.	case report/
8.	(letter or comment*).ti.
9.	or/1-8
10.	randomized controlled trial/ or random*.ti,ab.
11.	9 not 10
12.	animals/ not humans/
13.	exp animals, laboratory/
14.	exp animal experimentation/
15.	exp models, animal/
16.	exp rodentia/
17.	(rat or rats or mouse or mice).ti.

18.	or/11-17
-----	----------

Embase search terms

1.	letter.pt. or letter/
2.	note.pt.
3.	editorial.pt.
4.	case report/ or case study/
5.	(letter or comment*).ti.
6.	or/1-5
7.	randomized controlled trial/ or random*.ti,ab.
8.	6 not 7
9.	animal/ not human/
10.	nonhuman/
11.	exp animal experiment/
12.	exp experimental animal/
13.	animal model/
14.	exp rodent/
15.	(rat or rats or mouse or mice).ti.
16.	or/8-15

CINAHL search terms

S1.	pt anecdote or pt audiovisual or pt bibliography or pt biography or pt book or pt book review or pt brief item or pt cartoon or pt commentary or pt computer program or pt editorial or pt games or pt glossary or pt historical material or pt interview or pt letter or pt listservs or pt masters thesis or pt obituary or pt pamphlet or pt pamphlet chapter or pt pictorial or pt poetry or pt proceedings or pt "questions and answers" or pt response or pt software or pt teaching materials or pt website
-----	--

G.3.2 Randomised controlled trials (RCT) search terms

Medline search terms

1.	randomized controlled trial.pt.
2.	controlled clinical trial.pt.
3.	randomi#ed.ab.
4.	placebo.ab.
5.	randomly.ab.
6.	clinical trials as topic.sh.
7.	trial.ti.
8.	or/1-7

Embase search terms

1.	random*.ti,ab.
2.	factorial*.ti,ab.
3.	(crossover* or cross over*).ti,ab.
4.	((doubl* or singl*) adj blind*).ti,ab.
5.	(assign* or allocat* or volunteer* or placebo*).ti,ab.
6.	crossover procedure/
7.	double blind procedure/

8.	single blind procedure/
9.	randomized controlled trial/
10.	or/1-9

G.3.3 Systematic review (SR) search terms

Medline search terms

1.	meta-analysis/
2.	meta-analysis as topic/
3.	(meta analy* or metanaly* or metaanaly*).ti,ab.
4.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
5.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
6.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
7.	(search* adj4 literature).ab.
8.	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
9.	cochrane.jw.
10.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
11.	or/1-10

Embase search terms

1.	systematic review/
2.	meta-analysis/
3.	(meta analy* or metanaly* or metaanaly*).ti,ab.
4.	((systematic or evidence) adj3 (review* or overview*)).ti,ab.
5.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
6.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
7.	(search* adj4 literature).ab.
8.	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
9.	cochrane.jw.
10.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
11.	or/1-10

G.3.4 Health economics (HE) search terms

Medline search terms

1.	economics/
2.	value of life/
3.	exp "costs and cost analysis"/
4.	exp economics, hospital/
5.	exp economics, medical/
6.	economics, nursing/
7.	economics, pharmaceutical/
8.	exp "fees and charges"/
9.	exp budgets/
10.	budget*.ti,ab.

11.	cost*.ti.
12.	(economic* or pharmaco?economic*).ti.
13.	(price* or pricing*).ti,ab.
14.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
15.	(financ* or fee or fees).ti,ab.
16.	(value adj2 (money or monetary)).ti,ab.
17.	or/1-16

Embase search terms

1.	health economics/
2.	exp economic evaluation/
3.	exp health care cost/
4.	exp fee/
5.	budget/
6.	funding/
7.	budget*.ti,ab.
8.	cost*.ti.
9.	(economic* or pharmaco?economic*).ti.
10.	(price* or pricing*).ti,ab.
11.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
12.	(financ* or fee or fees).ti,ab.
13.	(value adj2 (money or monetary)).ti,ab.
14.	or/1-13

G.3.5 Quality of life (QOL) search terms

Medline search terms

1.	quality-adjusted life years/
2.	sickness impact profile/
3.	(quality adj2 (wellbeing or well-being)).ti,ab.
4.	sickness impact profile.ti,ab.
5.	disability adjusted life.ti,ab.
6.	(qal* or qtime* or qwb* or daly*).ti,ab.
7.	(euroqol* or eq5d* or eq 5d*).ti,ab.
8.	(qol* or hql* or hqol* or h qol* or hrqol* or hr qol*).ti,ab.
9.	(health utility* or utility score* or disutilit*).ti,ab.
10.	(hui or hui1 or hui2 or hui3).ti,ab.
11.	health* year* equivalent*.ti,ab.
12.	(hye or hyes).ti,ab.
13.	rosser.ti,ab.
14.	(willingness to pay or time tradeoff or time trade off or tto or standard gamble*).ti,ab.
15.	(sf36 or sf 36 or short form 36 or shortform 36 or shortform36).ti,ab.
16.	(sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab.
17.	(sf12 or sf 12 or short form 12 or shortform 12 or shortform12).ti,ab.
18.	(sf8 or sf 8 or short form 8 or shortform 8 or shortform8).ti,ab.
19.	(sf6 or sf 6 or short form 6 or shortform 6 or shortform6).ti,ab.

20.	or/1-19
-----	---------

Embase search terms

1.	quality adjusted life year/
2.	"quality of life index"/
3.	short form 12/ or short form 20/ or short form 36/ or short form 8/
4.	sickness impact profile/
5.	(quality adj2 (wellbeing or well-being)).ti,ab.
6.	sickness impact profile.ti,ab.
7.	disability adjusted life.ti,ab.
8.	(qal* or qtime* or qwb* or daly*).ti,ab.
9.	(euroqol* or eq5d* or eq 5d*).ti,ab.
10.	(qol* or hq1* or hqol* or h qol* or hrqol* or hr qol*).ti,ab.
11.	(health utility* or utility score* or disutilit*).ti,ab.
12.	(hui or hui1 or hui2 or hui3).ti,ab.
13.	health* year* equivalent*.ti,ab.
14.	(hye or hyes).ti,ab.
15.	rosser.ti,ab.
16.	(willingness to pay or time tradeoff or time trade off or tto or standard gamble*).ti,ab.
17.	(sf36 or sf 36 or short form 36 or shortform 36 or shortform36).ti,ab.
18.	(sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab.
19.	(sf12 or sf 12 or short form 12 or shortform 12 or shortform12).ti,ab.
20.	(sf8 or sf 8 or short form 8 or shortform 8 or shortform8).ti,ab.
21.	(sf6 or sf 6 or short form 6 or shortform 6 or shortform6).ti,ab.
22.	or/1-21

G.3.6 Health economic modelling (MOD) search terms

Medline search terms

1.	exp models, economic/
2.	*models, theoretical/
3.	*models, organizational/
4.	markov chains/
5.	monte carlo method/
6.	exp decision theory/
7.	(markov* or monte carlo).ti,ab.
8.	econom* model*.ti,ab.
9.	(decision* adj2 (tree* or analy* or model*)).ti,ab.
10.	or/1-9

Embase search terms

1.	statistical model/
2.	exp economic aspect/
3.	1 and 2
4.	*theoretical model/
5.	*nonbiological model/
6.	stochastic model/

7.	decision theory/
8.	decision tree/
9.	monte carlo method/
10.	(markov* or monte carlo).ti,ab.
11.	econom* model*.ti,ab.
12.	(decision* adj2 (tree* or analy* or model*)).ti,ab.
13.	or/3-12

G.3.7 Observational studies (OBS) search terms

Medline search terms

1.	epidemiologic studies/
2.	exp case control studies/
3.	exp cohort studies/
4.	cross-sectional studies/
5.	case control.ti,ab.
6.	(cohort adj (study or studies or analys*)).ti,ab.
7.	((follow up or observational or uncontrolled or non randomi#ed or nonrandomi#ed or epidemiologic*) adj (study or studies)).ti,ab.
8.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort*)).ti,ab.
9.	or/1-8

Embase search terms

1.	clinical study/
2.	exp case control study/
3.	family study/
4.	longitudinal study/
5.	retrospective study/
6.	prospective study/
7.	cross-sectional study/
8.	cohort analysis/
9.	follow-up/
10.	cohort*.ti,ab.
11.	9 and 10
12.	case control.ti,ab.
13.	(cohort adj (study or studies or analys*)).ti,ab.
14.	((follow up or observational or uncontrolled or non randomi#ed or nonrandomi#ed or epidemiologic*) adj (study or studies)).ti,ab.
15.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort*)).ti,ab.
16.	or/1-8,11-15

G.3.8 Qualitative reviews (QUAL) search terms

Medline search terms

1.	qualitative research/ or narration/ or exp interviews as topic/ or exp questionnaires/ or health care surveys/
----	--

2.	(qualitative or interview* or focus group* or theme* or questionnaire* or survey*).ti,ab.
3.	(metasynthes* or meta-synthes* or metasummar* or meta-summar* or metastud* or meta-stud* or metathem* or meta-them* or ethno* or emic or etic or phenomenolog* or grounded theory or constant compar* or (thematic* adj3 analys*) or theoretical sampl* or purposive sampl* or hermeneutic* or heidegger* or husserl* or colaizzi* or van kaam* or van manen* or giorgi* or glaser* or strauss* or ricoeur* or spiegelberg* or merleau*).ti,ab.
4.	or/1-3

Embase search terms

1.	health survey/ or exp questionnaire/ or exp interview/ or qualitative research/ or narrative/
2.	(qualitative or interview* or focus group* or theme* or questionnaire* or survey*).ti,ab.
3.	(metasynthes* or meta-synthes* or metasummar* or meta-summar* or metastud* or meta-stud* or metathem* or meta-them* or ethno* or emic or etic or phenomenolog* or grounded theory or constant compar* or (thematic* adj3 analys*) or theoretical sampl* or purposive sampl* or hermeneutic* or heidegger* or husserl* or colaizzi* or van kaam* or van manen* or giorgi* or glaser* or strauss* or ricoeur* or spiegelberg* or merleau*).ti,ab.
4.	or/1-3

CINAHL search terms

S1.	(mh "qualitative studies+")
S2.	(mh "qualitative validity+")
S3.	(mh "interviews+") or (mh "focus groups") or (mh "surveys") or (mh "questionnaires+")
S4.	(qualitative or interview* or focus group* or theme* or questionnaire* or survey*)
S5.	(metasynthes* or meta-synthes* or metasummar* or meta-summar* or metastud* or meta-stud* or metathem* or meta-them* or ethno* or emic or etic or phenomenolog* or grounded theory or constant compar* or (thematic* adj3 analys*) or theoretical sampl* or purposive sampl* or hermeneutic* or heidegger* or husserl* or colaizzi* or van kaam* or van manen* or giorgi* or glaser* or strauss* or ricoeur* or spiegelberg* or merleau*)
S6.	S1 or s2 or S3 or S4 or S5

PsycINFO search terms

1.	(su.exact("qualitative research") or (su.exact("narratives") or su.exact("interviews")) or (su.exact("questionnaires") or su.exact.explode("surveys")) or (qualitative or interview* or focus-group* or theme*) or (questionnaire* or survey*) or (metasynthes* or meta-synthes*) or (metasummar* or meta-summar*) or (metastud* or meta-stud*) or (metathem* or meta-them*) or ethno* or (emic or etic) or (phenomenolog* or "grounded theory") or (constant-compar* or thematic* near/3 analys*) or (theoretical-sampl* or purposive-sampl*) or (hermeneutic* or heidegger*) or (husserl* or colaizzi*) or (van-kaam* or van-manen*) or (giorgi* or glaser*) or (strauss* or ricoeur*) or (spiegelberg* or merleau*))
----	---

G.4 Searches for specific questions

G.4.1 Identification: risk tools

Searches for the following four questions were run as one search:

- What risk tool best identifies people with multimorbidity who are at risk of reduced life expectancy?
- What risk tool best identifies people with multimorbidity who are at risk of admission to a care facility?
- What risk tool best identifies people with multimorbidity who are at risk of reduced health-related quality of life?

- What risk tool best identifies people with multimorbidity who are at risk of unplanned hospital admission?

Medline search terms

1.	comorbidity/
2.	(comorbid* or co-morbid*).ti,ab.
3.	(multimorbid* or multi-morbid*).ti,ab.
4.	(multidisease? or multi-disease? or (multiple adj (ill* or disease? or condition? or syndrom* or disorder?))).ti,ab.
5.	((coocur* or co-ocur* or coexist* or co-exist* or multipl* or concord* or discord*) adj3 (disease? or ill* or care or condition? or disorder* or health* or medication* or symptom* or syndrom*).ti,ab.
6.	or/1-5
7.	chronic disease scor*.ti,ab.
8.	mortality risk* ind*.ti,ab.
9.	((charlson* or elixhauser* or comorbid* or co-morbid*) adj2 (index or indices)).ti,ab.
10.	cumulative illness rating scale*.ti,ab.
11.	adjusted clinical group*.ti,ab.
12.	(risk* adj2 (tool* or index or indices or score* or scale* or predict*).ti,ab.
13.	((prognos* or predict*) adj2 (tool* or index or indices or score* or scale*).ti,ab.
14.	or/12-13
15.	valid*.ti,ab.
16.	14 and 15
17.	or/7-11,16
18.	6 and 17
19.	(rxrisk* or rx risk*).ti,ab.
20.	(medication* adj3 burden* ind*).ti,ab.
21.	burden of illness scor*.ti,ab.
22.	functional morbidity ind*.ti,ab.
23.	multidimension* prognos* ind*.ti,ab.
24.	silver code.ti,ab.
25.	health intelligence system*.ti,ab.
26.	combined predict* model*.ti,ab.
27.	hospital admission risk profile*.ti,ab.
28.	(predict* emergency admission* adj3 next year*).ti,ab.
29.	predictive risk stratification model*.ti,ab.
30.	(qadmission* or q-admission*).ti,ab.
31.	(sparra or "scottish patients at risk of readmission and admission" or "scottish patients at risk of re-admission and admission").ti,ab.
32.	sussex predictor of key event*.ti,ab.
33.	("patients at risk" adj2 (re-hospitali#ation or rehospitali#ation)).ti,ab.
34.	probability of repeated admission.ti,ab.
35.	or/19-34
36.	18 or 35
37.	Excluded study designs and publication types [G.3.1]

38.	36 not 37
39.	Limit 38 to English language
	Date parameters: see Table 21

Embase search terms

1.	*comorbidity/
2.	(comorbid* or co-morbid*).ti,ab.
3.	(multimorbid* or multi-morbid*).ti,ab.
4.	(multidisease? or multi-disease? or (multiple adj (ill* or disease? or condition? or syndrom* or disorder?))).ti,ab.
5.	((coocur* or co-ocur* or coexist* or co-exist* or multipl* or concord* or discord*) adj3 (disease? or ill* or care or condition? or disorder* or health* or medication* or symptom* or syndrom*)).ti,ab.
6.	or/1-5
7.	chronic disease scor*.ti,ab.
8.	mortality risk* ind*.ti,ab.
9.	((charlson* or elixhauser* or comorbid* or co-morbid*) adj2 (index or indices)).ti,ab.
10.	charlson comorbidity index/ or elixhauser comorbidity index/
11.	cumulative illness rating scale*.ti,ab.
12.	adjusted clinical group*.ti,ab.
13.	(risk* adj2 (tool* or index or indices or score* or scale* or predict*)).ti,ab.
14.	((prognos* or predict*) adj2 (tool* or index or indices or score* or scale*)).ti,ab.
15.	13 or 14
16.	valid*.ti,ab.
17.	15 and 16
18.	or/7-12,17
19.	6 and 18
20.	(rxrisk* or rx risk*).ti,ab.
21.	(medication* adj3 burden* ind*).ti,ab.
22.	burden of illness scor*.ti,ab.
23.	functional morbidity ind*.ti,ab.
24.	multidimension* prognos* ind*.ti,ab.
25.	silver code.ti,ab.
26.	health intelligence system*.ti,ab.
27.	combined predict* model*.ti,ab.
28.	hospital admission risk profile*.ti,ab.
29.	(predict* emergency admission* adj3 next year*).ti,ab.
30.	predictive risk stratification model*.ti,ab.
31.	(qadmission* or q-admission*).ti,ab.
32.	(sparra or "scottish patients at risk of readmission and admission" or "scottish patients at risk of re-admission and admission").ti,ab.
33.	sussex predictor of key event*.ti,ab.
34.	("patients at risk" adj2 (re-hospitali#ation or rehospitali#ation)).ti,ab.
35.	probability of repeated admission.ti,ab.
36.	or/19-35

37.	Excluded study designs and publication types [G.3.1]
38.	36 not 37
39.	Limit 38 to English language
	Date parameters: see Table 21

Cochrane search terms

#1.	[mh ^comorbidity]
#2.	(comorbid* or co-morbid*):ti,ab
#3.	(multimorbid* or multi-morbid*):ti,ab
#4.	(multidisease* or multi-disease* or (multiple next (ill* or disease* or condition* or syndrom* or disorder*)):ti,ab
#5.	((coocur* or co-ocur* or coexist* or co-exist* or multipl* or concord* or discord*) near/3 (disease* or ill* or care or condition* or disorder* or health* or medication* or symptom* or syndrom*)):ti,ab
#6.	{or #1-#5}
#7.	chronic next disease next scor*:ti,ab
#8.	mortality next risk* next ind*:ti,ab
#9.	((charlson* or elixhauser* or comorbid* or co-morbid*) near/2 (index or indices)):ti,ab
#10.	cumulative next illness next rating next scale*:ti,ab
#11.	adjusted next clinical next group*:ti,ab
#12.	(risk* near/2 (tool* or index or indices or score* or scale* or predict*)):ti,ab
#13.	((prognos* or predict*) near/2 (tool* or index or indices or score* or scale*)):ti,ab
#14.	{or #12-#13}
#15.	valid*:ti,ab
#16.	#14 and #15
#17.	#6 and #16
#18.	{or #7-#11}
#19.	(rxrisk* or rx next risk*):ti,ab
#20.	(medication* near/3 burden* next ind*):ti,ab
#21.	burden next of next illness next scor*:ti,ab
#22.	functional next morbidity next ind*:ti,ab
#23.	multidimension* next prognos* next ind*:ti,ab
#24.	silver next code:ti,ab
#25.	health next intelligence next system*:ti,ab
#26.	combined next predict* next model*:ti,ab
#27.	hospital next admission next risk next profile*:ti,ab
#28.	(predict* next emergency next admission* near/4 year*):ti,ab
#29.	predictive next risk next stratification next model*:ti,ab
#30.	(qadmission* or q next admission*):ti,ab
#31.	(sparra or "scottish patients at risk of readmission and admission" or "scottish patients at risk of re-admission and admission"):ti,ab
#32.	sussex next predictor next of next key next event*:ti,ab
#33.	("patients at risk" near/2 (re-hospitalization or rehospitalization or re-hospitalisation or rehospitalisation)):ti,ab
#34.	probability of repeated admission:ti,ab

#35.	{or #17-#34}
	Date parameters: see Table 21

G.4.2 Identification: polypharmacy

Searches for the following four questions were run as one search:

- Is polypharmacy associated with a greater risk of admission to care facility amongst people with multimorbidity?
- Is polypharmacy associated with a greater risk of reductions in health-related quality of life amongst people with multimorbidity?
- Is polypharmacy associated with a greater risk of mortality amongst people with multimorbidity?
- Is polypharmacy associated with a greater risk of unplanned hospital admissions amongst people with multimorbidity?

Medline search terms

1.	polypharmacy/
2.	(hyperpolypharmacy or polypharmacy).ti,ab.
3.	((medicat* or drug* or prescri*) adj2 (number* or multiple or excessive)).ti,ab.
4.	or/1-3
5.	(risk* or predict* or correlat* or associat* or prognos*).ti.
6.	(validat* or rule*).ti,ab.
7.	(predict* and (outcome* or risk* or model*)).ti,ab.
8.	((history or variable* or criteria or scor* or characteristic* or finding* or factor*) and (predict* or model* or decision* or identif* or prognos*)).ti,ab.
9.	decision*.ti,ab. and Logistic models/
10.	logistic regression.ti,ab.
11.	(decision* and (model* or clinical*)).ti,ab.
12.	(prognostic and (history or variable* or criteria or scor* or characteristic* or finding* or factor* or model*)).ti,ab.
13.	(stratification or discrimination or discriminate or c statistic or "area under the curve" or auc or calibration or indices or algorithm or multivariable).ti,ab.
14.	roc curve/
15.	exp risk/
16.	or/5-15
17.	4 and 16
18.	Excluded study designs and publication types [G.3.1]
19.	17 not 18
20.	Limit 19 to English language
	Date parameters: 2000-04 January 2016

Embase search terms

1.	*polypharmacy/
2.	(hyperpolypharmacy or polypharmacy).ti,ab.
3.	((medicat* or drug* or prescri*) adj2 (number* or multiple or excessive)).ti,ab.
4.	or/1-3
5.	(risk* or predict* or correlat* or associat* or prognos*).ti.
6.	(validat* or rule*).ti,ab.

7.	(predict* and (outcome* or risk* or model*)).ti,ab.
8.	((history or variable* or criteria or scor* or characteristic* or finding* or factor*) and (predict* or model* or decision* or identif* or prognos*)).ti,ab.
9.	decision*.ti,ab. and Statistical model/
10.	(decision* and (model* or clinical*)).ti,ab.
11.	(prognostic and (history or variable* or criteria or scor* or characteristic* or finding* or factor* or model*)).ti,ab.
12.	(stratification or discrimination or discriminate or c statistic or "area under the curve" or auc or calibration or indices or algorithm or multivariable).ti,ab.
13.	receiver operating characteristic/
14.	exp *risk/
15.	or/5-14
16.	4 and 15
17.	Excluded study designs and publication types [G.3.1]
18.	16 not 17
19.	Limit 18 to English language
	Date parameters: 2000-04 Janaury 2016

Cochrane search terms

#1.	[mh ^polypharmacy]
#2.	(hyperpolypharmacy or polypharmacy):ti,ab
#3.	((medicat* or drug* or prescri*) near/2 (number* or multiple or excessive)):ti,ab
#4.	#1 or #2 or #3
	Date parameters: 2000-04 Janaury 2016

G.4.3 Principles

- What principles are important for assessing, prioritising and managing care for people with multimorbidity?

Medline search terms

1.	*comorbidity/
2.	(multimorbid* or multi-morbid* or polymorbidity or polypathy or pluralpathology).ti,ab.
3.	(multidisease? or multi-disease? or (multiple adj (ill* or disease? or condition? or syndrom* or disorder?))).ti,ab.
4.	(multifactorial disease* or dual diagnosis).ti,ab.
5.	((coocur* or co-ocur* or cooccur* or co-occur* or coexist* or co-exist* or multipl*) adj3 (disease? or ill* or care or condition? or disorder* or health* or medication* or symptom* or syndrom*)).ti,ab.
6.	or/1-5
7.	guidelines as topic/ or practice guidelines as topic/
8.	exp guideline/
9.	health planning guidelines/
10.	(guideline or practice guideline).pt.
11.	guideline*.ti.
12.	or/7-11
13.	(implement* or validation or impact or compliance or adherence).ti.
14.	12 not 13
15.	6 and 14

16.	Excluded study designs and publication types [G.3.1]
17.	15 not 16
18.	Limit 17 to English language
	Date parameters: see Table 21

Embase search terms

1.	*comorbidity/
2.	(multimorbid* or multi-morbid* or polymorbidity or polypathy or pluralpathology).ti,ab.
3.	(multidisease? or multi-disease? or (multiple adj (ill* or disease? or condition? or syndrom* or disorder?))).ti,ab.
4.	(multifactorial disease* or dual diagnosis).ti,ab.
5.	((coocur* or co-ocur* or cooccur* or co-occur* or coexist* or co-exist* or multipl*) adj3 (disease? or ill* or care or condition? or disorder* or health* or medication* or symptom* or syndrom*)).ti,ab.
6.	or/1-5
7.	*practice guideline/
8.	guideline*.ti.
9.	7 or 8
10.	(implement* or validation or impact or compliance or adherence).ti.
11.	9 not 10
12.	6 and 11
13.	Excluded study designs and publication types [G.3.1]
14.	12 not 13
15.	Limit 14 to English language
	Date parameters: see Table 21

G.4.4 Barriers

- What are barriers to healthcare professionals optimising care for people with multimorbidity?

Medline search terms

1.	comorbidity/
2.	(comorbid* or co-morbid*).ti,ab.
3.	(multimorbid* or multi-morbid*).ti,ab.
4.	(multidisease? or multi-disease? or (multiple adj (ill* or disease? or condition? or syndrom* or disorder?))).ti,ab.
5.	((coocur* or co-ocur* or coexist* or co-exist* or multipl* or concord* or discord*) adj3 (disease? or ill* or care or condition? or disorder* or health* or medication* or symptom* or syndrom*)).ti,ab.
6.	or/1-5
7.	Excluded study designs and publication types [G.3.1]
8.	6 not 7
9.	Limit 8 to English language
10.	attitude of health personnel/
11.	health priorities/
12.	exp consumer participation/
13.	patient care planning/
14.	patient preference/

15.	exp professional-patient relations/
16.	"continuity of patient care"/ or patient handoff/
17.	((health professional or health personnel or physician* or consultant* or nurse* or doctor* or health care assistant* or healthcare assistant*) adj4 (knowledge or preference* or satisfaction or satisfied or satisfy or experience* or facilitator or facilitation or facilitate or barrier* or relation* or attitude*)).ti,ab.
18.	((consumer* or client* or resident* or patient* or people or person or spouse* or wife or wives or husband* or carer* or caregiver* or care giver* or significant other* or family or families or individual*) adj4 (preference* or satisfaction or satisfied or satisfy or experience* or facilitator or facilitation or facilitate or barrier* or relation* or attitude* or wish* or choice*)).ti,ab.
19.	(priorit* adj2 set*).ti,ab.
20.	((treat* or care or health*) adj4 (preference* or experience* or facilitator or facilitation or facilitate or barrier*)).ti,ab.
21.	((medic* or treat* or care) adj3 (optimi* or concord* or priorit* or continu*)).ti,ab.
22.	((medic* or treat* or intervention* or appointment*) adj3 (stop* or reduc* or discontinu* or withdraw* or withhold* or access*)).ti,ab.
23.	or/10-22
24.	9 and 23
25.	Study filters QUAL (G.3.8)
26.	24 and 25
	Date parameters: see Table 21

Embase search terms

1.	*comorbidity/
2.	(comorbid* or co-morbid*).ti,ab.
3.	(multimorbid* or multi-morbid*).ti,ab.
4.	(multidisease? or multi-disease? or (multiple adj (ill* or disease? or condition? or syndrom* or disorder?))).ti,ab.
5.	((coocur* or co-ocur* or coexist* or co-exist* or multipl* or concord* or discord*) adj3 (disease? or ill* or care or condition? or disorder* or health* or medication* or symptom* or syndrom*)).ti,ab.
6.	or/1-5
7.	Excluded study designs and publication types [G.3.1]
8.	6 not 7
9.	Limit 8 to English language
10.	exp *health personnel attitude/
11.	*health care planning/
12.	*patient care planning/
13.	exp *patient attitude/
14.	*doctor patient relation/ or *nurse patient relationship/
15.	exp *clinical handover/
16.	((health professional or health personnel or physician* or consultant* or nurse* or doctor* or health care assistant* or healthcare assistant*) adj4 (knowledge or preference* or satisfaction or satisfied or satisfy or experience* or facilitator or facilitation or facilitate or barrier* or relation* or attitude*)).ti,ab.
17.	(priorit* adj2 set*).ti,ab.
18.	((treat* or care or health*) adj4 (preference* or experience* or facilitator or facilitation or facilitate or barrier*)).ti,ab.

19.	((medic* or treat* or care) adj3 (optimi* or concord* or priorit* or continu*)).ti,ab.
20.	((medic* or treat* or intervention* or appointment*) adj3 (stop* or reduc* or discontinu* or withdraw* or withhold* or access*)).ti,ab.
21.	or/10-20
22.	9 and 21
23.	Study filters QUAL (G.3.8)
24.	22 and 23
	Date parameters: see Table 21

CINAHL search terms

S1.	(mh "comorbidity")
S2.	comorbid* or co-morbid*
S3.	multimorbid* or multi-morbid*
S4.	(multidisease* or multi-disease* or (multiple n1 (ill* or disease* or condition* or syndrom* or disorder*)))
S5.	((coocur* or co-ocur* or coexist* or co-exist* or multipl* or concord* or discord*) n3 (disease* or ill* or care or condition* or disorder* or health* or medication* or symptom* or syndrom*))
S6.	S1 or S2 or S3 or S4 or S5
S7.	Excluded study designs and publication types [G.3.1]
S8.	S6 not S7
S9.	Limit S8 to English language
S10.	(mh "attitude of health personnel+") or (mh "consumer participation") or (mh "patient care plans+") or (mh "professional-patient relations+") or (mh "continuity of patient care+") or (mh "hand off (patient safety)")
S11.	((health professional or health personnel or physician* or consultant* or nurse* or doctor* or health care assistant* or healthcare assistant*) n4 (knowledge or preference* or satisfaction or satisfied or satisfy or experience* or facilitator or facilitation or facilitate or barrier* or relation* or attitude*))
S12.	((consumer* or client* or resident* or patient* or people or person or spouse* or wife or wives or husband* or carer* or caregiver* or care giver* or significant other* or family or families or individual*) n4 (preference* or satisfaction or satisfied or satisfy or experience* or facilitator or facilitation or facilitate or barrier* or relation* or attitude* or wish* or choice*))
S13.	priorit* n2 set*
S14.	((treat* or care or health*) n4 (preference* or experience* or facilitator or facilitation or facilitate or barrier*))
S15.	((medic* or treat* or care) n3 (optimi* or concord* or priorit* or continu*))
S16.	((medic* or treat* or intervention* or appointment*) n3 (stop* or reduc* or discontinu* or withdraw* or withhold* or access*))
S17.	S10 or S11 or S12 or S13 or S14 or S15 or S16
S18.	S9 and S17
S19.	Study filters QUAL (G.3.8)
S20.	S18 and S19
	Date parameters: see Table 21

PsycINFO search terms

1.	(su.exact("comorbidity") or ti,ab(comorbid* or co-morbid* or multimorbid* or multi-morbid*) or ti,ab(multidisease* or multi-disease* or (multiple pre/1 (ill* or disease* or condition* or syndrom* or disorder*))) or ti,ab((coocur* or co-ocur* or coexist* or co-exist* or multipl* or concord* or discord*) near/3 (disease* or ill* or care or condition* or disorder* or health* or
----	---

	medication* or symptom* or syndrom*))
2.	(su.exact.explode("health personnel attitudes") or su.exact("client participation") or su.exact.explode("treatment planning") or su.exact.explode("consumer attitudes") or su.exact("continuum of care") or su.exact("communication barriers") or su.exact("treatment barriers") or ti,ab(("health professional" or "health personnel" or physician* or consultant* or nurse* or doctor* or health-care-assistant* or healthcare-assistant*) near/4 (knowledge or preference* or satisfaction or satisfied or satisfy or experience* or facilitator or facilitation or facilitate or barrier* or relation* or attitude*)) or ti,ab((consumer* or client* or resident* or patient* or people or person or spouse* or wife or wives or husband* or carer* or caregiver* or care-giver* or significant-other* or family or families or individual*) near/4 (preference* or satisfaction or satisfied or satisfy or experience* or facilitator or facilitation or facilitate or barrier* or relation* or attitude* or wish* or choice*)) or ti,ab(priorit* near/2 set*) or ti,ab((treat* or care or health*) near/4 (preference* or experience* or facilitator or facilitation or facilitate or barrier*)) or ti,ab((medic* or treat* or care) near/3 (optimi* or concord* or priorit* or continu*)) or ((medic* or treat* or intervention* or appointment*) near/3 (stop* or reduc* or discontinu* or withdraw* or withhold* or access*)))
3.	Study filters QUAL (G.3.8)
4.	1 and 2 and 3
5.	Limit 4 to English language
	Date parameters: see Table 21

G.4.5 Burden of treatment

- How can treatment burden be assessed?

Medline search terms

1.	((treat* or therap*) adj2 burden*).ti,ab.
2.	Excluded study designs and publication types [G.3.1]
3.	1 not 2
4.	Limit 3 to English language
	Date parameters: see Table 21

Embase search terms

1.	((treat* or therap*) adj2 burden*).ti,ab.
2.	Excluded study designs and publication types [G.3.1]
3.	1 not 2
4.	Limit 3 to English language
	Date parameters: see Table 21

Cochrane search terms

#1.	((treat* or therap*) near/2 burden*).ti,ab
	Date parameters: see Table 21

CINAHL search terms

S1.	treat* n2 burden* or therap* n2 burden*
S2.	Excluded study designs and publication types [G.3.1]
S3.	1 not 2
S4.	Limit 3 to English language
	Date parameters: see Table 21

PyscINFO search terms

1.	ti,ab((treat* or therap*) near/2 burden*)
----	---

2.	Limit 1 to English language
	Date parameters: see Table 21

G.4.6 Stopping treatment: antihypertensives

- What are the effects of stopping common drug treatments (antihypertensives)?

Medline search terms

1.	exp hypertension/
2.	hypertens*.ti,ab.
3.	((elevat* or high or increas*) adj3 blood adj pressur*).ti,ab.
4.	or/1-3
5.	exp *thiazides/
6.	(thiazide* or bendrofluazide or bendroflumethazide or aprinox or neo-naclex or chlorthalidone or chlortalidone or hygroton or cyclopenthiazide or navidrex or indapamide or natrilix or metolazone or xipamide or diurexan or hydrochlorthiazide or hydrochlorothiazide or neo-naclex-k).ti,ab.
7.	exp *calcium channel blockers/
8.	(calcium adj3 (block* or inhibit* or antagonist*)).ti,ab.
9.	(diltiazem or optil or tildiem or adizem or angitil or calcicard or dilcardia or dilzem or slozem or viazem or zemtard or verapamil or zolvera or cordilox or securon or univer or verapress or vertab).ti,ab.
10.	(amlodipine or amlostin or istin or exforge or felodipine or plendil or lacidipine or motens or lercanidipine or zanidip or nicardipine or cardene or nifedipine or adalat or nimodipine or nimotop or coracten or adipine or fortipine or tensipine or valni or nifedipress).ti,ab.
11.	exp *adrenergic beta-antagonists/
12.	(propranolol or angilol or inderal-1a or half-inalderal or inderal or bedranol or syprol or prograne or slo-pro or acebutolol or sectral or atenolol or tenormin or bisoprolol or cardiacor or emcor or carvedilol or eucardic or celiprolol or celectol or co-tenidone or tenoret or tenoretic or labetalol or trandate or metoprolol or betaloc or lopresor or nadolol or corgard or nebivolol or nebilet or hypoloc or oxprenolol or trasicor or slow-trasicor or pindolol or visken or viskaldix or timolol or betim).ti,ab.
13.	((beta or b) adj3 (block* or antagonist*)).ti,ab.
14.	exp *angiotensin ii type 1 receptor blockers/ or *angiotensin ii type 2 receptor blockers/
15.	((angiotensin adj3 (receptor* adj2 (antagonist* or blocker*))) or arb or arbs).ti,ab.
16.	(candesartan or amias or eprosartan or teveten or irbesartan or aprovel or coaprovel or losartan or cozaar or cozaar-comp or olmesartan or olmetec or sevikar or telmisartan or micardis or valsartan or diovan or co-diovan or azilsartan or edarbi).ti,ab.
17.	exp *angiotensin-converting enzyme inhibitors/
18.	((ace or acei or ((angiotensin adj converting adj2 enzyme*) or ace or kininase)) adj2 (inhibit* or antagonist*)).ti,ab.
19.	(captopril or ecopace or kaplon or capoten or co-zidocapt or capto-co or capozide or cilazapril or vascace or enalapril or ednyt or innovace or innozide or fosinopril or imidapril or tanatril or lisinopril or zestril or carace or zestoretic or moexipril or perdex or perindopril or coversyl or quinapril or quinil or accupro or accuretic or ramipril or tritace or triapin or trandolapril or gopten or tarka).ti,ab.
20.	*antihypertensive agents/
21.	(antihypertens* adj2 (drug* or agent* or treat* or therap* or intervention*)).ti,ab.
22.	or/5-21
23.	4 and 22
24.	(deprescri* or de-prescri*).ti,ab.

25.	(stop adj3 (criteria or criterion or rule or standard or benchmark or bench mark or decision* or take or taking)).ti,ab.
26.	(discontin* or withdraw* or cessat* or down-titrat* or step-down or "step down").ti.
27.	((discontin* or withdraw* or cessat* or down-titrat* or step-down or "step down" or stop* or cease* or taper*) adj2 (dose* or drug* or treatment* or therap* or medicat* or intervention*)).ti,ab.
28.	polypharmacy/
29.	polypharmacy.ti,ab.
30.	*medication adherence/
31.	*patient compliance/
32.	*treatment refusal/
33.	(adheren* or nonadheren* or non-adheren* or non adheren* or complian* or noncomplian* or non-complian* or non complian*).ti.
34.	((adheren* or nonadheren* or non-adheren* or non adheren* or complian* or noncomplian* or non-complian* or non complian* or persist*) adj2 (patient* or participant* or dose* or drug* or treatment* or therap* or medicat* or intervention*)).ti,ab.
35.	or/24-34
36.	23 and 35
37.	Excluded study designs and publication types [G.3.1]
38.	36 not 37
39.	Limit 38 to English language
40.	Study filters RCT (G.3.2) or SR (G.3.3) or OBS (G.3.7)
41.	39 and 40
	Date parameters: see Table 21

Embase search terms

1.	exp *hypertension/
2.	hypertens*.ti,ab.
3.	((elevat* or high or increas*) adj3 blood adj pressur*).ti,ab.
4.	or/1-3
5.	exp *thiazide diuretic agent/
6.	(thiazide* or bendrofluazide or bendroflumethazide or aprinox or neo-naclex or chlorthalidone or chlortalidone or hygroton or cyclopenthiazide or navidrex or indapamide or natrilix or metolazone or xipamide or diurexan or hydrochlorthiazide or hydrochlorothiazide or neo-naclex-k).ti,ab.
7.	exp *calcium channel blocking agent/
8.	(calcium adj3 (block* or inhibit* or antagonist*)).ti,ab.
9.	(diltiazem or optil or tildiem or adizem or angitil or calcicard or dilcardia or dilzem or slozem or viazem or zemtard or verapamil or zolvera or cordilox or securon or univer or verapress or vertab).ti,ab.
10.	(amlodipine or amlostin or istin or exforge or felodipine or plendil or lacidipine or motens or lercanidipine or zanidip or nifedipine or cardene or nifedipine or adalat or nimodipine or nimotop or coracten or adipine or fortipine or tensipine or valni or nifedipress).ti,ab.
11.	exp *beta adrenergic receptor blocking agent/
12.	(propranolol or angilol or inderal-la or half-inalderal or inderal or bedranol or syprol or prograne or slo-pro or acebutolol or sectral or atenolol or tenormin or bisoprolol or cardicor or emcor or carvedilol or eucardic or celiprolol or celectol or co-tenidone or tenoret or tenoretic or labetalol or trandate or metoprolol or betaloc or lopresor or nadolol or corgard or nebivolol or nebilet or hypoloc or oxprenolol or trasicor or slow-trasicor or pindolol or visken or viskaldix or

	timolol or betim).ti,ab.
13.	((beta or b) adj3 (block* or antagonist*).ti,ab.
14.	exp *angiotensin receptor antagonist/
15.	((angiotensin adj3 (receptor* adj2 (antagonist* or blocker*))) or arb or arbs).ti,ab.
16.	(candesartan or amias or eprosartan or teveten or irbesartan or aprovel or coaprovel or losartan or cozaar or cozaar-comp or olmesartan or olmetec or sevikar or telmisartan or micardis or valsartan or diovan or co-diovan or azilsartan or edarbi).ti,ab.
17.	exp *dipeptidyl carboxypeptidase inhibitor/
18.	((ace or acei or ((angiotensin adj converting adj2 enzyme*) or ace or kininase)) adj2 (inhibit* or antagonist*).ti,ab.
19.	(captopril or ecopace or kaplon or capoten or co-zidocapt or capto-co or capozide or cilazapril or vascace or enalapril or ednyt or innovace or innozide or fosinopril or imidapril or tanatril or lisinopril or zestril or carace or zestoretic or moexipril or perdex or perindopril or coversyl or quinapril or quinil or accupro or accuretic or ramipril or tritace or triapin or trandolapril or gopten or tarka).ti,ab.
20.	*antihypertensive agent/
21.	(antihypertens* adj2 (drug* or agent* or treat* or therap* or intervention*).ti,ab.
22.	or/5-21
23.	4 and 22
24.	(deprescri* or de-prescri*).ti,ab.
25.	(stop adj3 (criteria or criterion or rule or standard or benchmark or bench mark or decision* or take or taking)).ti,ab.
26.	(discontin* or withdraw* or cessat* or down-titrat* or step-down or "step down").ti.
27.	((discontin* or withdraw* or cessat* or down-titrat* or step-down or "step down" or stop* or cease* or taper*) adj2 (dose* or drug* or treatment* or therap* or medicat* or intervention*).ti,ab.
28.	*polypharmacy/
29.	polypharmacy.ti,ab.
30.	*patient compliance/ or *medication compliance/
31.	*treatment refusal/
32.	(adheren* or nonadheren* or non-adheren* or non adheren* or complian* or noncomplian* or non-complian* or non complian*).ti.
33.	((adheren* or nonadheren* or non-adheren* or non adheren* or complian* or noncomplian* or non-complian* or non complian* or persist*) adj2 (patient* or participant* or dose* or drug* or treatment* or therap* or medicat* or intervention*).ti,ab.
34.	or/24-33
35.	23 and 34
36.	Excluded study designs and publication types [G.3.1]
37.	35 not 36
38.	Limit 37 to English language
39.	Study filters RCT (G.3.2) or SR (G.3.3) or OBS (G.3.7)
40.	38 and 39
	Date parameters: see Table 21

Cochrane search terms

#1.	[mh hypertension]
#2.	hypertens*.ti,ab
#3.	((elevat* or high or increas*) near/3 blood next pressur*).ti,ab
#4.	#1 or #2 or #3

#5.	[mh thiazides]
#6.	(thiazide* or bendrofluazide or bendroflumethazide or aprinox or neo-naclex or chlorthalidone or chlortalidone or hygroton or cyclopenthiazide or navidrex or indapamide or natrilix or metolazone or xipamide or diurexan or hydrochlorthiazide or hydrochlorothiazide or neo-naclex-k):ti,ab
#7.	[mh "calcium channel blockers"]
#8.	(calcium near/3 (block* or inhibit* or antagonist*)):ti,ab
#9.	(diltiazem or optil or tildiem or adizem or angitil or calcicard or dilcardia or dilzem or slozem or viazem or zemtard or verapamil or zolvera or cordilox or securon or univer or verapress or vertab):ti,ab
#10.	(amlodipine or amlostin or istin or exforge or felodipine or plendil or lacidipine or motens or lercanidipine or zanidip or nicardipine or cardene or nifedipine or adalat or nimodipine or nimotop or coracten or adipine or fortipine or tensipine or valni or nifedipress):ti,ab
#11.	[mh "adrenergic beta-antagonists"]
#12.	(propranolol or angilol or inderal-la or half-inalderal or inderal or bedranol or syprol or prograne or slo-pro or acebutolol or sectral or atenolol or tenormin or bisoprolol or cardicor or emcor or carvedilol or eucardic or celiprolol or celectol or co-tenidone or tenoret or tenoretic or labetalol or trandate or metoprolol or betaloc or lopresor or nadolol or corgard or nebivolol or nebilet or hypoloc or oxprenolol or trasicor or slow-trasicor or pindolol or visken or viskaldix or timolol or betim):ti,ab
#13.	((beta or b) near/3 (block* or antagonist*)):ti,ab
#14.	[mh "angiotensin ii type 1 receptor blockers"]
#15.	[mh "angiotensin ii type 2 receptor blockers"]
#16.	((angiotensin near/3 (receptor* near/2 (antagonist* or blocker*))) or arb or arbs):ti,ab
#17.	(candesartan or amias or eprosartan or teveten or irbesartan or aprovel or coaprovel or losartan or cozaar or cozaar-comp or olmesartan or olmetec or sevikar or telmisartan or micardis or valsartan or diovan or co-diovan or azilsartan or edarbi):ti,ab
#18.	[mh "angiotensin-converting enzyme inhibitors"]
#19.	((ace or acei or ((angiotensin next converting near/2 enzyme*) or ace or kininase)) near/2 (inhibit* or antagonist*)):ti,ab
#20.	(captopril or ecopace or kaplon or capoten or co-zidocapt or capto-co or capozide or cilazapril or vascace or enalapril or ednyt or innovace or innozide or fosinopril or imidapril or tanatril or lisinopril or zestril or carace or zestoretic or moexipril or perdix or perindopril or coversyl or quinapril or quinil or accupro or accuretic or ramipril or tritace or triapin or trandolapril or gopten or tarka):ti,ab
#21.	[mh "antihypertensive agents"]
#22.	(antihypertens* near/2 (drug* or agent* or treat* or therap* or intervention*)):ti,ab
#23.	{or #5-#22}
#24.	(deprescri* or de-prescri*):ti,ab
#25.	(stop near/3 (criteria or criterion or rule or standard or benchmark or bench mark or decision* or take or taking)):ti,ab
#26.	(discontin* or withdraw* or cessat* or down-titrat* or step-down or "step down") .ti
#27.	((discontin* or withdraw* or cessat* or down-titrat* or step-down or "step down" or stop* or cease* or taper*) near/2 (dose* or drug* or treatment* or therap* or medicat* or intervention*)):ti,ab
#28.	[mh ^polypharmacy]
#29.	polypharmacy:ti,ab
#30.	[mh ^"medication adherence"]
#31.	[mh ^"treatment refusal"]
#32.	(adheren* or nonadheren* or non-adheren* or non next adheren* or complian* or

	noncompliant* or non-compliant* or non next compliant*):ti
#33.	((adheren* or nonadheren* or non-adheren* or non next adheren* or complian* or noncompliant* or non-compliant* or non next complian* or persist*) near/2 (patient* or participant* or dose* or drug* or treatment* or therap* or medicat* or intervention*)):ti,ab
#34.	{or #24-#33}
#35.	[mh "adrenergic alpha-antagonists"]
#36.	(doxazosin or cardura or indoramin or baratol or prazosin or hypovase or terazosin or hytrin):ti,ab
#37.	#23 or #35 or #36
#38.	#4 and #37
#39.	#38 and #34
	Date parameters: see Table 21

G.4.7 Stopping treatment: bisphosphonates

- What are the effects of stopping common drug treatments (drugs for osteoporosis)?

Medline search terms

1.	diphosphonates/
2.	alendronate/
3.	etidronic acid/
4.	clodronic acid/
5.	bone density conservation agents/
6.	raloxifene/
7.	teriparatide/
8.	(bisphosphonate* or diphosphonate*).ti,ab.
9.	(alendronate or alendronic or fosamax or fosavance or etidronate or didronel or etidronic or risedronate or risedronic or actonel or ibandronate or ibandronic or bondronat or bonviva).ti,ab.
10.	(clodronate or clodronic or bonefos or clasteon or loron or zoledronate or zoledronic or aclasta or zometa or pamidronate or aredia or denosumab or prolia or xgeva).ti,ab.
11.	(raloxifene or evista or strontium ranelate or protelos or teriparatide or forsteo or forteo).ti,ab.
12.	or/1-11
13.	(deprescri* or de-prescri*).ti,ab.
14.	(stop* adj3 (criteria or criterion or rule* or standard* or benchmark* or bench mark* or decision* or take or taking)).ti,ab.
15.	(discontin* or withdraw* or cessat* or down-titrat* or step-down or "step down").ti.
16.	((discontin* or withdraw* or cessat* or down-titrat* or step-down or "step down" or stop* or cease* or taper*) adj2 (dose* or drug* or treatment* or therap* or medicat* or intervention* or group* or arm*)).ti,ab.
17.	polypharmacy/
18.	polypharmacy.ti,ab.
19.	or/13-18
20.	12 and 19
21.	Excluded study designs and publication types [G.3.1]
22.	20 not 21
23.	Limit 22 to English language
24.	Study filters RCT (G.3.2) or SR (G.3.3) or OBS (G.3.7)

25.	23 and 24
	Date parameters: see Table 21

Embase search terms

1.	*bisphosphonic acid derivative/ or *alendronic acid/ or *alendronic acid plus alfacalcidol/ or *alendronic acid plus colecalciferol/ or *etidronic acid/ or *ibandronic acid/ or *risedronic acid/
2.	*clodronic acid/ or *pamidronic acid/ or *zoledronic acid/
3.	*raloxifene/
4.	*strontium ranelate/
5.	*"parathyroid hormone[1-34]"/
6.	*bone density conservation agent/
7.	*denosumab/
8.	(bisphosphonate* or diphosphonate*).ti,ab.
9.	(alendronate or alendronic or fosamax or fosavance or etidronate or didronel or etidronic or risedronate or risedronic or actonel or ibandronate or ibandronic or bondronat or bonviva).ti,ab.
10.	(clodronate or clodronic or bonefos or clasteon or loron or zoledronate or zoledronic or aclasta or zometa or pamidronate or aredia or denosumab or prolia or xgeva).ti,ab.
11.	(raloxifene or evista or strontium ranelate or protelos or teriparatide or forsteo or forteo).ti,ab.
12.	or/1-11
13.	(deprescri* or de-prescri*).ti,ab.
14.	(stop* adj3 (criteria or criterion or rule* or standard* or benchmark* or bench mark* or decision* or take or taking)).ti,ab.
15.	(discontin* or withdraw* or cessat* or down-titrat* or step-down or "step down").ti.
16.	((discontin* or withdraw* or cessat* or down-titrat* or step-down or "step down" or stop* or cease* or taper*) adj2 (dose* or drug* or treatment* or therap* or medicat* or intervention* or group* or arm*)).ti,ab.
17.	*polypharmacy/
18.	polypharmacy.ti,ab.
19.	or/13-18
20.	12 and 19
21.	Excluded study designs and publication types [G.3.1]
22.	20 not 21
23.	Limit 22 to English language
24.	Study filters RCT (G.3.2) or SR (G.3.3) or OBS (G.3.7)
25.	23 and 24
	Date parameters: see Table 21

Cochrane search terms

#1.	[mh ^diphosphonates]
#2.	[mh ^alendronate]
#3.	[mh ^"etidronic acid"]
#4.	[mh ^"clodronic acid"]
#5.	[mh ^"bone density conservation agents"]
#6.	[mh ^raloxifene]
#7.	[mh ^teriparatide]

#8.	(bisphosphonate* or diphosphonate*):ti,ab
#9.	(alendronate or alendronic or fosamax or fosavance or etidronate or didronel or etidronic or risedronate or risedronic or actonel or ibandronate or ibandronic or bondronat or bonviva):ti,ab
#10.	(clodronate or clodronic or bonefos or clasteon or liron or zoledronate or zoledronic or aclasta or zometa or pamidronate or aredia or denosumab or prolia or xgeva):ti,ab
#11.	(raloxifene or evista or strontium ranelate or protelos or teriparatide or forsteo or forteo):ti,ab
#12.	{or #1-#11}
#13.	(deprescri* or de-prescri*):ti,ab
#14.	(stop* near/3 (criteria or criterion or rule* or standard* or benchmark* or bench next mark* or decision* or take or taking)):ti,ab
#15.	(discontin* or withdraw* or cessat* or down-titrat* or step-down or "step down"):ti
#16.	((discontin* or withdraw* or cessat* or down-titrat* or step-down or "step down" or stop* or cease* or taper*) near/2 (dose* or drug* or treatment* or therap* or medicat* or intervention* or group* or arm*)):ti,ab
#17.	[mh ^polypharmacy]
#18.	polypharmacy:ti,ab
#19.	{or #13-#18}
#20.	#12 and #19
	Date parameters: see Table 21

G.4.8 Stopping treatment: statins

- What are the effects of stopping common drug treatments (statins)?

Medline search terms

1.	*hydroxymethylglutaryl-coa reductase inhibitors/
2.	statin*.ti,ab.
3.	((hydroxymethylglutaryl-coa or hmg-coa) adj3 (reductase or inhibitors)).ti,ab.
4.	exp *simvastatin/
5.	(simvastatin* or zocor).ti,ab.
6.	(atorvastatin* or lipitor).ti,ab.
7.	(rosuvastatin* or crestor).ti,ab.
8.	exp *pravastatin/
9.	(pravastatin* or lipostat).ti,ab.
10.	(fluvastatin* or lescol).ti,ab.
11.	or/1-10
12.	(deprescri* or de-prescri*):ti,ab.
13.	(stop adj3 (criteria or criterion or rule or standard or benchmark or bench mark or decision* or take or taking)).ti,ab.
14.	(discontin* or withdraw* or cessat* or down-titrat* or step-down or "step down").ti.
15.	((discontin* or withdraw* or cessat* or down-titrat* or step-down or "step down" or stop* or cease* or taper*) adj2 (dose* or drug* or treatment* or therap* or medicat* or intervention*)):ti,ab.
16.	polypharmacy/
17.	polypharmacy.ti,ab.
18.	or/12-17
19.	*medication adherence/
20.	*patient compliance/

21.	*treatment refusal/
22.	(adheren* or nonadheren* or non-adheren* or non adheren* or complian* or noncomplian* or non-complian* or non complian*).ti.
23.	((adheren* or nonadheren* or non-adheren* or non adheren* or complian* or noncomplian* or non-complian* or non complian* or persist*) adj2 (patient* or participant* or dose* or drug* or treatment* or therap* or medicat* or intervention*)).ti,ab.
24.	or/19-23
25.	18 or 24
26.	11 and 25
27.	Excluded study designs and publication types [G.3.1]
28.	26 not 27
29.	Limit 28 to English language
30.	Study filters RCT (G.3.2) or SR (G.3.3) or OBS (G.3.7)
31.	29 and 30
	Date parameters: see Table 21

Embase search terms

1.	*hydroxymethylglutaryl-coa reductase inhibitor/
2.	((hydroxymethylglutaryl-coa or hmg-coa) adj3 (reductase or inhibitors)).ti,ab.
3.	statin*.ti,ab.
4.	exp *simvastatin/
5.	(simvastatin* or zocor).ti,ab.
6.	(atorvastatin* or lipitor).ti,ab.
7.	(rosuvastatin* or crestor).ti,ab.
8.	exp *pravastatin/
9.	(pravastatin* or lipostat).ti,ab.
10.	(fluvastatin* or lescol).ti,ab.
11.	exp *atorvastatin/ or exp *rosuvastatin/
12.	or/1-11
13.	(deprescri* or de-prescri*).ti,ab.
14.	(stop adj3 (criteria or criterion or rule or standard or benchmark or bench mark or decision* or take or taking)).ti,ab.
15.	(discontin* or withdraw* or cessat* or down-titrat* or step-down or "step down").ti.
16.	((discontin* or withdraw* or cessat* or down-titrat* or step-down or "step down" or stop* or cease* or taper*) adj2 (dose* or drug* or treatment* or therap* or medicat* or intervention*)).ti,ab.
17.	*polypharmacy/
18.	polypharmacy.ti,ab.
19.	or/13-18
20.	*patient compliance/ or *medication compliance/
21.	*treatment refusal/
22.	(adheren* or nonadheren* or non-adheren* or non adheren* or complian* or noncomplian* or non-complian* or non complian*).ti.
23.	((adheren* or nonadheren* or non-adheren* or non adheren* or complian* or noncomplian* or non-complian* or non complian* or persist*) adj2 (patient* or participant* or dose* or drug* or treatment* or therap* or medicat* or intervention*)).ti,ab.
24.	or/20-23

25.	19 or 24
26.	12 and 25
27.	Excluded study designs and publication types [G.3.1]
28.	26 not 27
29.	Limit 28 to English language
30.	Study filters RCT (G.3.2) or SR (G.3.3) or OBS (G.3.7)
31.	29 and 30
	Date parameters: see Table 21

Cochrane search terms

#1.	[mh ^"hydroxymethylglutaryl-coa reductase inhibitors"]
#2.	((hydroxymethylglutaryl-coa or hmg-coa) near/3 (reductase or inhibitors)):ti,ab
#3.	statin*:ti,ab
#4.	[mh ^simvastatin]
#5.	(simvastatin* or zocor):ti,ab
#6.	(atorvastatin* or lipitor):ti,ab
#7.	(rosuvastatin* or crestor):ti,ab
#8.	[mh ^pravastatin]
#9.	(pravastatin* or lipostat):ti,ab
#10.	(fluvastatin* or lescol):ti,ab
#11.	{or #1-#10}
#12.	(deprescri* or de-prescri*):ti,ab
#13.	(stop near/3 (criteria or criterion or rule or standard or benchmark or bench mark or decision* or take or taking)):ti,ab
#14.	(discontin* or withdraw* or cessat* or down-titrat* or step-down or "step down"):ti
#15.	((discontin* or withdraw* or cessat* or down-titrat* or step-down or "step down" or stop* or cease* or taper*) near/2 (dose* or drug* or treatment* or therap* or medicat* or intervention*)):ti,ab
#16.	[mh ^polypharmacy]
#17.	polypharmacy:ti,ab
#18.	{or #12-#17}
#19.	[mh ^"medication adherence"]
#20.	[mh ^"patient compliance"]
#21.	[mh ^"treatment refusal"]
#22.	(adheren* or nonadheren* or non-adheren* or non next adheren* or complian* or noncomplian* or non-complian* or non next complian*):ti
#23.	((adheren* or nonadheren* or non-adheren* or non next adheren* or complian* or noncomplian* or non-complian* or non next complian* or persist*) near/2 (patient* or participant* or dose* or drug* or treatment* or therap* or medicat* or intervention*)):ti,ab
#24.	{or #19-#23}
#25.	#18 or #24
#26.	#11 and #25
	Date parameters: see Table 21

G.4.9 Frailty assessment

- What is the most accurate tool for assessing frailty?

Medline search terms

1.	(abbreviat* adj1 (comprehensive geriatric assessment or cga)).ti,ab.
2.	(ves13 or ves 13 or vulnerable elders survey*).ti,ab.
3.	groningen frailty ind*.ti,ab.
4.	(geriatric 8 or geriatric8 or (g8 adj4 (risk* or tool* or ind* or scor* or assess* or scale* or question*))).ti,ab.
5.	tilburg frailt* ind*.ti,ab.
6.	(prisma 7 or prisma7).ti,ab.
7.	edmonton frail* scale*.ti,ab.
8.	(frail* adj3 (assess* or tool* or scor* or index or indices or indicat* or scale* or question* or survey*).ti,ab.
9.	((gait or walk*) adj speed*) or (grip adj2 strength*).ti,ab.
10.	("timed up and go test" or tugt).ti,ab.
11.	(or/9-10) and frail*.ti,ab.
12.	or/1-8,11
13.	Excluded study designs and publication types [G.3.1]
14.	12 not 13
15.	Limit 14 to English language
	Date parameters: see Table 21

Embase search terms

1.	(abbreviat* adj1 (comprehensive geriatric assessment or cga)).ti,ab.
2.	(ves13 or ves 13 or vulnerable elders survey*).ti,ab.
3.	groningen frailty ind*.ti,ab.
4.	(geriatric 8 or geriatric8 or (g8 adj4 (risk* or tool* or ind* or scor* or assess* or scale* or question*))).ti,ab.
5.	tilburg frail* ind*.ti,ab.
6.	(prisma 7 or prisma7).ti,ab.
7.	edmonton frail* scale*.ti,ab.
8.	(frail* adj3 (assess* or tool* or scor* or index or indices or indicat* or scale* or question* or survey*).ti,ab.
9.	((gait or walk*) adj speed*) or (grip adj2 strength*).ti,ab.
10.	("timed up and go test" or tugt).ti,ab.
11.	(or/9-10) and frail*.ti,ab.
12.	or/1-8,11
13.	Excluded study designs and publication types [G.3.1]
14.	12 not 13
15.	Limit 14 to English language
	Date parameters: see Table 21

Cochrane search terms

#1.	(abbreviat* near/1 ("comprehensive geriatric assessment" or cga)).ti,ab
#2.	(ves13 or ves 13 or vulnerable next elders next survey*).ti,ab
#3.	groningen next frailty next ind*.ti,ab
#4.	("geriatric 8" or geriatric8 or (g8 near/4 (risk* or tool* or ind* or scor* or assess* or scale* or question*))).ti,ab
#5.	tilburg next frail* next ind*.ti,ab

#6.	("prisma 7" or prisma7):ti,ab
#7.	edmonton next frail* next scale*:ti,ab
#8.	(frail* near/3 (assess* or tool* or scor* or index or indices or indicat* or scale* or question* or survey*)):ti,ab
#9.	((gait or walk*) next speed*) or (grip near/2 strength*):ti,ab
#10.	("timed up and go test" or tugt):ti,ab
#11.	#9 or #10
#12.	frail*:ti,ab
#13.	#11 and #12
#14.	{or #1-#8, #13}
	Date parameters: see Table 21

G.4.10 Models of care

- What models of care improve outcomes in patients with multimorbidity?

The searches from a relevant Cochrane review¹¹³⁰ were updated as follows:

Medline search terms

1.	comorbidity/
2.	(comorbid* or co-morbid*).ti,ab.
3.	(multimorbid* or multi-morbid*).ti,ab.
4.	(multidisease? or multi-disease? or (multiple adj (ill* or disease? or condition? or syndrom* or disorder?))).ti,ab.
5.	or/1-4
6.	chronic disease/
7.	(chronic* adj3 (disease? or ill* or care or condition? or disorder* or health* or medication* or syndrom* or symptom*)).ti,ab.
8.	or/6-7
9.	5 or 8
10.	exp diabetes mellitus/ or diabet*.ti,ab.
11.	exp hypertension/ or (hypertens* or "high blood pressure?").ti,ab.
12.	exp heart diseases/ or (((heart or cardiac or cardiovascular or coronary) adj (disease? or disorder? or failure)) or arrythmia?).ti,ab.
13.	exp cerebrovascular disorders/ or ((cerebrovascular or vascular or carotoid* or arter*) adj (disorder? or disease?)).ti,ab.
14.	exp asthma/ or asthma*.ti,ab.
15.	exp pulmonary disease chronic obstructive/ or (copd or (pulmonary adj2 (disease? or disorder?))).ti,ab.
16.	exp hyperlipidemia/ or (hyperlipidem* or hypercholesterolemia* or hypertriglyceridemia*).ti,ab.
17.	exp thyroid diseases/ or ((thyroid adj (disease? or disorder)) or hyperthyroid* or hypothyroid*).ti,ab.
18.	exp arthritis rheumatoid/ or rheumatoid arthritis.ti,ab.
19.	exp mental disorders/ or (((mental or anxiety or mood or psychological or sleep) adj (disease? or disorder?)) or ((substance or drug or marijuana or cocaine or amphetamine) adj2 abuse) or depression or schizophren* or psychos* or "substance abuse" or addiction?).ti,ab.
20.	exp epilepsy/ or (epileps* or seizure?).ti,ab.
21.	exp hiv infections/ or (hiv or acquired immune* deficiency syndrome? or (aids adj (associated or related or arteritis))).ti,ab.

22.	exp neoplasms/ or (neoplasm? or cancer?).ti,ab.
23.	exp kidney diseases/ or (kidney adj (disease? or disorder?)).ti,ab.
24.	exp liver diseases/ or (liver adj (disease? or disorder?)).ti,ab.
25.	exp osteoporosis/ or osteoporosis.ti,ab.
26.	or/10-25
27.	((coocur* or co-ocur* or coexist* or co-exist* or multipl*) adj3 (disease? or ill* or care or condition? or disorder* or health* or medication* or symptom* or syndrom*)).ti,ab.
28.	chronic*.ti,ab,hw.
29.	27 or 28
30.	26 and 29
31.	exp *education, continuing/
32.	(education* adj2 (program* or intervention? or meeting? or session? or strateg* or workshop? or visit?)).tw.
33.	(behavio?r* adj2 intervention?).tw.
34.	*pamphlets/
35.	(leaflet? or booklet? or poster or posters).tw.
36.	((written or printed or oral) adj information).tw.
37.	(information* adj2 campaign).tw.
38.	(education* adj1 (method? or material?)).tw.
39.	*advance directives/
40.	outreach.tw.
41.	((opinion or education* or influential) adj1 leader?).tw.
42.	facilitator?.tw.
43.	academic detailing.tw.
44.	consensus conference?.tw.
45.	*guideline adherence/
46.	practice guideline?.tw.
47.	(guideline? adj2 (introduc* or issu* or impact or effect? or disseminat* or distribut*)).tw.
48.	((effect? or impact or evaluat* or introduc* or compar*) adj2 training program*).tw.
49.	*reminder systems/
50.	reminder?.tw.
51.	(recall adj2 system*).tw.
52.	(prompter? or prompting).tw.
53.	algorithm?.tw.
54.	*feedback/ or feedback.tw.
55.	chart review*.tw.
56.	((effect? or impact or records or chart?) adj2 audit).tw.
57.	compliance.tw.
58.	marketing.tw.
59.	or/31-58
60.	exp *reimbursement mechanisms/
61.	fee for service.tw.
62.	*capitation fee/
63.	*"deductibles and coinsurance"/
64.	cost shar*.tw.

65.	(copayment? or co payment?).tw.
66.	(prepay* or prepaid or prospective payment?).tw.
67.	*hospital charges/
68.	formular?.tw.
69.	fundhold?.tw.
70.	*medicaid/
71.	*medicare/
72.	blue cross.tw.
73.	or/60-72
74.	*nurse clinicians/
75.	*nurse midwives/
76.	*nurse practitioners/
77.	(nurse adj (rehabilitator? or clinician? or practitioner? or midwi*)).tw.
78.	*pharmacists/
79.	clinical pharmacist?.tw.
80.	paramedic?.tw.
81.	*patient care team/
82.	exp *patient care planning/
83.	(team? adj2 (care or treatment or assessment or consultation)).tw.
84.	(integrat* adj2 (care or service?)).tw.
85.	(care adj2 (coordinat* or program* or continuity)).tw.
86.	(case adj1 management).tw.
87.	exp *ambulatory care facilities/
88.	*ambulatory care/
89.	or/74-88
90.	*home care services/
91.	*hospices/
92.	*nursing homes/
93.	*office visits/
94.	*house calls/
95.	*day care/
96.	*aftercare/
97.	*community health nursing/
98.	(chang* adj1 location?).tw.
99.	domiciliary.tw.
100.	(home adj1 treat*).tw.
101.	day surgery.tw.
102.	*medical records/
103.	*medical records systems, computerized/
104.	(information adj2 (management or system?)).tw.
105.	*peer review/
106.	*utilization review/
107.	exp *health services misuse/
108.	or/90-107
109.	*physician's practice patterns/

110.	quality assurance.tw.
111.	*process assessment/ [health care]
112.	*program evaluation/
113.	*length of stay/
114.	(early adj1 discharg*).tw.
115.	discharge planning.tw.
116.	offset.tw.
117.	triage.tw.
118.	exp *"referral and consultation"/ and "consultation"/
119.	*drug therapy, computer assisted/
120.	near patient testing.tw.
121.	*medical history taking/
122.	*telephone/
123.	(physician patient adj (interaction? or relationship?)).tw.
124.	*health maintenance organizations/
125.	managed care.tw.
126.	(hospital? adj1 merg*).tw.
127.	or/109-126
128.	((standard or usual or routine or regular or traditional or conventional or pattern) adj2 care).tw.
129.	(program* adj2 (reduc* or increas* or decreas* or chang* or improv* or modify* or monitor* or care)).tw.
130.	(program* adj1 (health or care or intervention?)).tw.
131.	((effect? or impact or evaluat* or introduc* or compar*) adj2 treatment program*).tw.
132.	((effect? or impact or evaluat* or introduc* or compar*) adj2 care program*).tw.
133.	((effect? or impact or evaluat* or introduc* or compar*) adj2 screening program*).tw.
134.	((effect? or impact or evaluat* or introduc* or compar*) adj2 prevent* program*).tw.
135.	(computer* adj2 (dosage or dosing or diagnosis or therapy or decision?)).tw.
136.	((introduc* or impact or effect? or implement* or computer*) adj2 protocol?).tw.
137.	((effect or impact or introduc*) adj2 (legislation or regulations or policy)).tw.
138.	or/128-137
139.	or/59,73,89,108,127,138
140.	9 or 30
141.	139 and 140
142.	Excluded study designs and publication types [G.3.1]
143.	141 not 142
144.	Limit 143 to English language
145.	Study filters RCT (G.3.2)
146.	(control* adj2 (trial? or study or studies)).ti,ab.
147.	double-blind method/ or random allocation/ or single-blind method/
148.	((double or single or triple or treble) adj2 blind*).ti,ab.
149.	(quasi-experiment* or quasiexperiment*).ti,ab.
150.	interrupt* time series.ti,ab.
151.	or/146-150
152.	145 or 151

153.	144 and 152
154.	Date parameters: 2011-04 January 2016

Embase search terms

1.	comorbidity/
2.	(comorbid* or co-morbid*).ti,ab.
3.	(multimorbid* or multi-morbid*).ti,ab.
4.	(multidisease? or multi-disease? or (multiple adj (ill* or disease? or condition? or syndrom* or disorder?))).ti,ab.
5.	or/1-4
6.	chronic disease/
7.	(chronic* adj3 (disease? or ill* or care or condition? or disorder* or health* or medication* or syndrom* or symptom*).ti,ab.
8.	or/6-7
9.	5 or 8
10.	exp diabetes mellitus/ or diabet*.ti,ab.
11.	exp hypertension/ or (hypertens* or "high blood pressure?").ti,ab.
12.	exp heart disease/ or exp myocardial disease/ or (((heart or cardiac or cardiovascular or coronary) adj (disease? or disorder? or failure)) or arrythmia?).ti,ab.
13.	cerebrovascular disease/ or carotid artery disease/ or ((cerebrovascular or vascular or carotoid* or arter*) adj (disorder? or disease?)).ti,ab.
14.	exp asthma/ or asthma*.ti,ab.
15.	chronic obstructive lung disease/ or (copd or ((pulmonary or lung?) adj2 (disease? or disorder?))).ti,ab.
16.	exp hyperlipidemia/ or exp hypercholesterolemia/ or (hyperlipidem* or hypercholesterolemia* or hypertriglyceridemia*).ti,ab.
17.	exp thyroid diseases/ or ((thyroid adj (disease? or disorder)) or hyperthyroid* or hypothyroid*).ti,ab.
18.	exp rheumatoid arthritis/ or rheumatoid arthritis.ti,ab.
19.	exp mental disease/ or (((mental or anxiety or mood or psychological or sleep) adj (disease? or disorder?)) or ((substance or drug or marijuana or cocaine or amphetamine) adj2 abuse) or depression or schizophren* or psychos* or "substance abuse" or addiction?).ti,ab.
20.	exp epilepsy/ or (epileps* or seizure?).ti,ab.
21.	human immunodeficiency virus/ or (hiv or acquired immune* deficiency syndrome? or (aids adj (associated or related or arteritis)) or human immunodeficiency).ti,ab.
22.	exp neoplasm/ or (neoplasm? or cancer?).ti,ab.
23.	exp kidney disease/ or ((kidney? or renal) adj (disease? or disorder? or failure)).ti,ab.
24.	exp liver disease/ or (liver adj (disease? or disorder?)).ti,ab.
25.	exp osteoporosis/ or osteoporosis.ti,ab.
26.	or/10-25
27.	((coocur* or co-ocur* or coexist* or co-exist* or multipl*) adj3 (disease? or ill* or care or condition? or disorder* or health* or medication* or symptom* or syndrom*).ti,ab.
28.	chronic*.ti,ab,hw.
29.	27 or 28
30.	26 and 29
31.	exp primary health care/ or exp primary medical care/
32.	(primary adj2 (care? or medical* or health* or clinic* or practitioner? or doctor?)).ti,ab.
33.	general practitioner/

34.	((family or general or generalist? or communit*) adj2 (physician? or doctor? or practitioner? or practice)) or GP).ti,ab.
35.	general practice/
36.	exp community care/
37.	(communit* adj2 (health or healthcare or service? or clinic* or setting? or centre? or center?)).ti,ab.
38.	or/31-37
39.	(education* adj2 (program* or intervention? or meeting? or session? or strateg* or workshop? or visit?)).tw.
40.	(behavior*r* adj2 intervention?).tw.
41.	(leaflet? or booklet? or poster or posters).tw.
42.	((written or printed or oral) adj information).tw.
43.	(information* adj2 campaign).tw.
44.	(education* adj1 (method? or material?)).tw.
45.	outreach.tw.
46.	((opinion or education* or influential) adj1 leader?).tw.
47.	facilitator?.tw.
48.	academic detailing.tw.
49.	consensus conference?.tw.
50.	practice guideline?.tw.
51.	(guideline? adj2 (introduc* or issu* or impact or effect? or disseminat* or distribut*)).tw.
52.	((introduc* or impact or effect? or implement* or computer* or compli*) adj2 protocol?).tw.
53.	((introduc* or impact or effect? or implement* or computer* or compli*) adj2 algorithm?).tw.
54.	clinical pathway?.tw.
55.	critical pathway?.tw.
56.	((effect? or impact or evaluat* or introduc* or compar*) adj2 training program*).tw.
57.	reminder?.tw.
58.	(recall adj2 system*).tw.
59.	(prompter? or prompting).tw.
60.	advance directive?.tw.
61.	*feedback/ or feedback.tw.
62.	chart review*.tw.
63.	((effect? or impact or records or chart?) adj2 audit).tw.
64.	compliance.tw.
65.	marketing.tw.
66.	((cost or clinical or medical) adj information).tw.
67.	*medical education/
68.	*medical audit/
69.	continuing education/
70.	postgraduate education/
71.	or/39-70
72.	fee for service.tw.
73.	cost shar*.tw.
74.	(copayment? or co payment?).tw.
75.	(prepay* or prepaid or prospective payment?).tw.
76.	formular?.tw.

77.	fundhold?.tw.
78.	blue cross.tw.
79.	voucher?.tw.
80.	(free adj2 care).tw.
81.	exp *health insurance/
82.	*health care costs/
83.	*health care financing/
84.	*medical fee/
85.	*prospective payment/
86.	or/72-85
87.	(nurse adj (rehabilitator? or clinician? or practitioner? or midwi*)).tw.
88.	((nurse or midwi* or practitioner) adj managed).tw.
89.	clinical pharmacist?.tw.
90.	paramedic?.tw.
91.	exp *paramedical personnel/
92.	*general practitioner/
93.	*physician/
94.	(team? adj2 (care or treatment or assessment or consultation)).tw.
95.	(integrat* adj2 (care or service?)).tw.
96.	(care adj2 (coordinat* or program* or continuity)).tw.
97.	(case adj1 management).tw.
98.	*patient care/
99.	(chang* adj1 location?).tw.
100.	domiciliary.tw.
101.	(home adj1 (treat* or visit?)).tw.
102.	day surgery.tw.
103.	exp *primary health care/
104.	*ambulatory surgery/
105.	*nursing home/
106.	*day hospital/
107.	*outpatient care/
108.	*terminal care/
109.	*group practice/
110.	*general practice/
111.	*rural health care/
112.	*community mental health center/
113.	information system/
114.	*medical record/
115.	(information adj2 (management or system?)).tw.
116.	*peer review/
117.	*professional standards review organization/
118.	exp *clinical practice/
119.	quality assurance.tw.
120.	exp *health care delivery/
121.	*health care quality/

122.	*professional practice/
123.	(early adj1 discharg*).tw.
124.	discharge planning.tw.
125.	offset.tw.
126.	triage.tw.
127.	near patient testing.tw.
128.	*patient referral/
129.	(physician patient adj (interaction? or relationship?)).tw.
130.	managed care.tw.
131.	*health care organization/
132.	*health maintenance organization/
133.	*health care system/
134.	*health care access/
135.	(hospital? adj1 merg*).tw.
136.	(computer* adj2 (dosage or dosing or diagnosis therapy or decision?)).tw.
137.	(computer* adj2 (diagnosis or therapy)).tw.
138.	gatekeep*.tw.
139.	or/87-138
140.	((standard or usual or routine or regular or traditional or conventional or pattern) adj2 care).tw.
141.	(program* adj2 (reduc* or increas* or decreas* or chang* or improv* or modify* or monitor* or care)).tw.
142.	(program* adj1 (health or care or intervention?)).tw.
143.	((effect or impact or introduc*) adj2 (legislation or regulations or policy)).tw.
144.	((effect? or impact or evaluat* or introduc* or compar*) adj2 treatment program*).tw.
145.	((effect? or impact or evaluat* or introduc* or compar*) adj2 care program*).tw.
146.	((effect? or impact or evaluat* or introduc* or compar*) adj2 screening program*).tw.
147.	((effect? or impact or evaluat* or introduc* or compar*) adj2 prevent* program*).tw.
148.	or/140-147
149.	71 or 86 or 139 or 148
150.	9 or 30
151.	150 and 38 and 149
152.	Excluded study designs and publication types [G.3.1]
153.	151 not 152
154.	Limit 153 to English language
155.	Study filters RCT (G.3.2)
156.	(control* adj2 (trial? or study or studies)).ti,ab.
157.	((double or single or triple or treble) adj2 blind*).ti,ab.
158.	(quasi-experiment* or quasiexperiment*).ti,ab.
159.	interrupt* time series.ti,ab.
160.	intervent*.ti,ab,pt. or evaluat*.ti,hw. or impact*.ti.
161.	or/156-160
162.	155 or 161
163.	154 and 162
	Date parameters: 2011-04 January 2016

Cochrane search terms

#1.	[mh ^comorbidity]
#2.	(comorbid* or co-morbid* or multimorbid* or multi-morbid* or multidisease or multidiseases or multi-disease or multi-diseases):ti
#3.	[mh ^"chronic disease"]
#4.	(#1 or #2 or (#2 and #3))
#5.	[mh "diabetes mellitus"]
#6.	diabet*:ti,ab
#7.	[mh hypertension]
#8.	(hypertens* or "high blood pressure"):ti,ab
#9.	[mh "heart diseases"]
#10.	[mh "cerebrovascular disorders"]
#11.	(cerebrovascular disorder* or cerebrovascular disease* or vascular disorder* or vascular disease* or carotid* disorder* or carotid disease* or arter* disorder* or arter* disease*):ti
#12.	[mh asthma]
#13.	asthma*:ti
#14.	[mh "pulmonary disease, chronic obstructive"]
#15.	(copd or pulmonary disease* or pulmonary disorder*):ti
#16.	[mh hyperlipidemias]
#17.	(hyperlipidem* or hypercholesterolemia* or hypertriglyceridemia*):ti
#18.	[mh "thyroid diseases"]
#19.	(thyroid disease* or thyroid disorder*):ti
#20.	[mh "mental disorders"]
#21.	((mental or anxiety or mood or psychological or sleep) near/2 (disease* or disorder*)):ti
#22.	((substance or drug or marijuana or cocaine or amphetamine) near/2 abuse):ti
#23.	(depression or schizophren* or psychos* or "substance abuse" or addiction or addictions):ti
#24.	[mh epilepsy]
#25.	(epileps* or seizure or seizures):ti
#26.	[mh "hiv infections"]
#27.	(hiv or acquired immune* deficiency syndrome*):ti
#28.	[mh neoplasms]
#29.	(neoplasm or cancer):ti
#30.	[mh "kidney diseases"]
#31.	(kidney disease* or kidney disorder*):ti
#32.	[mh "liver diseases"]
#33.	(liver disease* or liver disorder*):ti
#34.	[mh osteoporosis]
#35.	osteoporosis:ti
#36.	(#5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35)
#37.	((coocur* or co-ocur* or coexist* or co-exist* or multipl*) near/2 (disease or diseases or ill* or care or condition or conditions or disorder* or health* or medication* or symptom* or syndrom*)):ti,ab
#38.	(#36 and #37)
#39.	(#4 or #38)

Date parameters: 2011-04 January 2016

AMED search terms

1.	comorbidity/
2.	(comorbid* or co-morbid*).ti,ab.
3.	(multimorbid* or multi-morbid*).ti,ab.
4.	(multidisease? or multi-disease? or (multiple adj (ill* or disease? or condition? or syndrom* or disorder?))).ti,ab.
5.	or/1-4
6.	chronic disease/
7.	(chronic* adj3 (disease? or ill* or care or condition? or disorder* or health* or medication* or syndrom* or symptom*).ti,ab.
8.	or/6-7
9.	5 or 8
10.	exp diabetes mellitus/ or diabet*.ti,ab.
11.	exp hypertension/ or (hypertens* or "high blood pressure?").ti,ab.
12.	exp heart diseases/ or (((heart or cardiac or cardiovascular or coronary) adj (disease? or disorder? or failure)) or arrythmia?).ti,ab.
13.	exp cerebrovascular disorders/ or ((cerebrovascular or vascular or carotoid* or arter*) adj (disorder? or disease?)).ti,ab.
14.	exp asthma/ or asthma*.ti,ab.
15.	exp pulmonary disease chronic obstructive/ or (copd or (pulmonary adj2 (disease? or disorder?))).ti,ab.
16.	exp hyperlipidemia/ or (hyperlipidem* or hypercholesterolemia* or hypertriglyceridemia*).ti,ab.
17.	exp thyroid diseases/ or ((thyroid adj (disease? or disorder)) or hyperthyroid* or hypothyroid*).ti,ab.
18.	exp arthritis rheumatoid/ or rheumatoid arthritis.ti,ab.
19.	exp mental disorders/ or (((mental or anxiety or mood or psychological or sleep) adj (disease? or disorder?)) or ((substance or drug or marijuana or cocaine or amphetamine) adj2 abuse) or depression or schizophren* or psychos* or "substance abuse" or addiction?).ti,ab.
20.	exp epilepsy/ or (epileps* or seizure?).ti,ab.
21.	exp hiv infections/ or (hiv or acquired immune* deficiency syndrome? or (aids adj (associated or related or arteritis))).ti,ab.
22.	exp neoplasms/ or (neoplasm? or cancer?).ti,ab.
23.	exp kidney diseases/ or (kidney adj (disease? or disorder?)).ti,ab.
24.	exp liver diseases/ or (liver adj (disease? or disorder?)).ti,ab.
25.	exp osteoporosis/ or osteoporosis.ti,ab.
26.	or/10-25
27.	((coocur* or co-ocur* or coexist* or co-exist* or multipl*) adj3 (disease? or ill* or care or condition? or disorder* or health* or medication* or symptom* or syndrom*).ti,ab.
28.	chronic*.ti,ab,hw.
29.	27 or 28
30.	26 and 29
31.	exp education/
32.	(education* adj2 (program* or intervention? or meeting? or session? or strateg* or workshop? or visit?)).tw.
33.	(behavio?r* adj2 intervention?).tw.

34.	(leaflet? or booklet? or poster or posters).tw.
35.	((written or printed or oral) adj information).tw.
36.	(information* adj2 campaign).tw.
37.	(education* adj1 (method? or material?)).tw.
38.	advance directives/
39.	outreach.tw.
40.	((opinion or education* or influential) adj1 leader?).tw.
41.	facilitator?.tw.
42.	academic detailing.tw.
43.	consensus conference?.tw.
44.	practice guideline?.tw.
45.	(guideline? adj2 (introduc* or issu* or impact or effect? or disseminat* or distribut*)).tw.
46.	((effect? or impact or evaluat* or introduc* or compar*) adj2 training program*).tw.
47.	reminder?.tw.
48.	(recall adj2 system*).tw.
49.	(prompter? or prompting).tw.
50.	algorithm?.tw.
51.	*feedback/ or feedback.tw.
52.	chart review*.tw.
53.	((effect? or impact or records or chart?) adj2 audit).tw.
54.	compliance.tw.
55.	marketing.tw.
56.	or/31-55
57.	fee for service.tw.
58.	cost shar*.tw.
59.	(copayment? or co payment?).tw.
60.	(prepay* or prepaid or prospective payment?).tw.
61.	formular?.tw.
62.	fundhold?.tw.
63.	insurance health/
64.	medicare/
65.	blue cross.tw.
66.	or/57-65
67.	(nurse adj (rehabilitator? or clinician? or practitioner? or midwi*)).tw.
68.	clinical pharmacist?.tw.
69.	paramedic?.tw.
70.	exp patient care management/
71.	(team? adj2 (care or treatment or assessment or consultation)).tw.
72.	(integrat* adj2 (care or service?)).tw.
73.	(care adj2 (coordinat* or program* or continuity)).tw.
74.	(case adj1 management).tw.
75.	exp ambulatory care facilities/
76.	ambulatory care/
77.	or/67-76
78.	home care services/

79.	hospices/
80.	nursing homes/
81.	day care/
82.	community health nursing/
83.	(chang* adj1 location?).tw.
84.	domiciliary.tw.
85.	(home adj1 treat*).tw.
86.	day surgery.tw.
87.	medical records/
88.	(information adj2 (management or system?)).tw.
89.	peer review/
90.	or/78-89
91.	professional practice/
92.	quality assurance.tw.
93.	program evaluation/
94.	length of stay/
95.	(early adj1 discharg*).tw.
96.	discharge planning.tw.
97.	offset.tw.
98.	triage.tw.
99.	"referral and consultation"/
100.	near patient testing.tw.
101.	medical history taking/
102.	telephone/
103.	(physician patient adj (interaction? or relationship?)).tw.
104.	health maintenance organizations/
105.	managed care.tw.
106.	(hospital? adj1 merg*).tw.
107.	or/91-106
108.	((standard or usual or routine or regular or traditional or conventional or pattern) adj2 care).tw.
109.	(program* adj2 (reduc* or increas* or decreas* or chang* or improv* or modify* or monitor* or care)).tw.
110.	(program* adj1 (health or care or intervention?)).tw.
111.	((effect? or impact or evaluat* or introduc* or compar*) adj2 treatment program*).tw.
112.	((effect? or impact or evaluat* or introduc* or compar*) adj2 care program*).tw.
113.	((effect? or impact or evaluat* or introduc* or compar*) adj2 screening program*).tw.
114.	((effect? or impact or evaluat* or introduc* or compar*) adj2 prevent* program*).tw.
115.	(computer* adj2 (dosage or dosing or diagnosis or therapy or decision?)).tw.
116.	((introduc* or impact or effect? or implement* or computer*) adj2 protocol?).tw.
117.	((effect or impact or introduc*) adj2 (legislation or regulations or policy)).tw.
118.	or/108-117
119.	or/56,66,77,90,107,118
120.	9 or 30
121.	animals/ not humans/

122.	120 not 121
123.	randomized controlled trial.pt.
124.	controlled clinical trial.pt.
125.	random*.ti,ab.
126.	(control* adj2 (trial? or study or studies)).ti,ab.
127.	double-blind method/ or random allocation/ or single-blind method/
128.	((double or single or triple or treble) adj2 blind*).ti,ab.
129.	(quasi-experiment* or quasiexperiment*).ti,ab.
130.	interrupt* time series.ti,ab.
131.	or/123-130
132.	122 and 131
133.	Limit 133 to English language
	Date parameters: 2011-04 January 2016

CINAHL search terms

S1.	(mh "comorbidity")
S2.	ti (multimorbid* or multi-morbid* or comorbid* or co-morbid* or multidisease? or multi-disease?) or ab (multimorbid* or multi-morbid* or comorbid* or co-morbid* or multidisease? or multi-disease?) or ti (multiple n2 ill* or multiple n2 disease? or multiple n2 condition? or multiple n2 syndrom* or multiple n2 disorder?) or ab (multiple n2 ill* or multiple n2 disease? or multiple n2 condition? or multiple n2 syndrom* or multiple n2 disorder?) or ti (coocur* n3 disease? or coocur* n3 ill* or coocur* n3 care or coocur* n3 condition? or coocur* n3 disorder* or coocur* n3 health* or coocur* n3 medication* or coocur* n3 symptom* or coocur* n3 syndrom* or coexist* n3 disease? or coexist* n3 ill* or coexist* n3 condition? or coexist* n3 disorder* or coexist* n3 symptom* or coexist* n3 syndrom* or multipl* n3 disease? or multipl* n3 ill* or multipl* n3 condition? or multipl* n3 disorder* or multipl* n3 medication* or multipl* n3 symptom* or multipl* n3syndrom* or co-exist* n3 disease? or co-exist* n3 ill* or co-exist* n3 condition? or co-exist* n3 disorder* or co-exist* n3 health* co-exist* n3 symptom* or co-exist* n3 syndrom* or co-ocur* n3 disease? or co-ocur* n3 ill* or co-ocur* n3 condition? or co-ocur* n3 disorder* or co-ocur* n3 health* or co-ocur* n3 symptom* or co-ocur* n3 syndrom*) or ab (coocur* n3 disease? or coocur* n3 ill* or coocur* n3 care or coocur* n3 condition? or coocur* n3 disorder* or coocur* n3 health* or coocur* n3 medication* or coocur* n3 symptom* or coocur* n3 syndrom* or coexist* n3 disease? or coexist* n3 ill* or coexist* n3 condition? or coexist* n3 disorder* or coexist* n3 symptom* or coexist* n3 syndrom* or multipl* n3 disease? or multipl* n3 ill* or multipl* n3 condition? or multipl* n3 disorder* or multipl* n3 medication* or multipl* n3 symptom* or multipl* n3syndrom* or co-exist* n3 disease? or co-exist* n3 ill* or co-exist* n3 condition? or co-exist* n3 disorder* or co-exist* n3 health* co-exist* n3 symptom* or co-exist* n3 syndrom* or co-ocur* n3 disease? or co-ocur* n3 ill* or co-ocur* n3 condition? or co-ocur* n3 disorder* or co-ocur* n3 health* or co-ocur* n3 symptom* or co-ocur* n3 syndrom*)
S3.	S1 or S2
S4.	(mh "chronic disease")
S5.	ti (chronic* w3 disease? or chronic* w3 ill* or chronic* w3 care or chronic* w3 condition? or chronic* w3 disorder* or chronic* w3 health* or chronic* w3 medication* or chronic* w3 syndrom* or chronic* w3 symptom*) or ab (chronic* w3 disease? or chronic* w3 ill* or chronic* w3 care or chronic* w3 condition? or chronic* w3 disorder* or chronic* w3 health* or chronic* w3 medication* or chronic* w3 syndrom* or chronic* w3 symptom*)
S6.	S4 or S5
S7.	(mh "diabetes mellitus+") or (mm "hypertension+") or (mm "cerebrovascular disorders+")
S8.	(mm "cardiovascular diseases+")
S9.	(mm "lung diseases, obstructive+") or (mm "pulmonary disease, chronic obstructive+") or (mm "asthma+")

S10.	(mm "thyroid diseases+") or (mm "arthritis+") or (mm "epilepsy+")
S11.	(mh "mental disorders, chronic") or (mm "mental disorders+") or (mm "human immunodeficiency virus+")
S12.	(mm "liver diseases+") or (mm "neoplasms+") or (mm "osteoporosis+")
S13.	(mm "kidney diseases+")
S14.	(mw (disease or diseases)) or mw syndrome? or mw chronic
S15.	ti diabet* or asthma* or chronic or disease
S16.	S7 or S8 or S9 or S10 or S11 or S12 or S13 or S14 or S15
S17.	ti (coocurr* or coexist* or co-ocurr* or coexist* or co-exist*) or ab (coocurr* or coexist* or co-ocurr* or coexist* or co-exist*)
S18.	S6 and S17
S19.	S16 and S17
S20.	(ti (multimorbid* or multi-morbid*)) or (ab (multimorbid* or multi-morbid*))
S21.	(mh "quasi-experimental studies")
S22.	ti (intervention* or multiintervention* or multi-intervention* or postintervention* or post-intervention* or preintervention* or pre-intervention*) or ab (intervention* or multiintervention* or multi-intervention* or postintervention* or post-intervention* or preintervention* or pre-intervention*)
S23.	ti (pre-test* or pretest* or posttest* or post-test*) or ab (pre-test* or pretest* or posttest* or "post test*") or ti (preimplement*" or pre-implement*) or ab (pre-implement* or preimplement*)
S24.	mh experimental studies or community trials or community trials or pretest-posttest design + or quasi-experimental studies + pilot studies or policy studies + multicenter studies
S25.	ti ((comparative n2 study) or (comparative n2 studies) or evaluation study or evaluation studies) or ab ((comparative n2 study) or (comparative n2 studies) or evaluation study or evaluation studies)
S26.	mh "multiple time series" or mh "time series"
S27.	ti pre w7 post or ab pre w7 post
S28.	ti ((quasi-experiment* or quasiexperiment* or quasi-random* or quasirandom* or quasi control* or quasicontrol* or quasi* w3 method* or quasi* w3 study or quasi* w3 studies or quasi* w3 trial or quasi* w3 design* or experimental w3 method* or experimental w3 study or experimental w3 studies or experimental w3 trial or experimental w3 design*)) or ab ((quasi-experiment* or quasiexperiment* or quasi-random* or quasirandom* or quasi control* or quasicontrol* or quasi* w3 method* or quasi* w3 study or quasi* w3 studies or quasi* w3 trial or quasi* w3 design* or experimental w3 method* or experimental w3 study or experimental w3 studies or experimental w3 trial or experimental w3 design*))
S29.	ti ((time point*) or (period* n4 interrupted) or (period* n4 multiple) or (period* n4 time) or (period* n4 various) or (period* n4 varying) or (period* n4 week*) or (period* n4 month*) or (period* n4 year*)) or ab ((time point*) or (period* n4 interrupted) or (period* n4 multiple) or (period* n4 time) or (period* n4 various) or (period* n4 varying) or (period* n4 week*) or (period* n4 month*) or (period* n4 year*))
S30.	(ab (before* n10 during or before n10 after)) or (au (before* n10 during or before n10 after))
S31.	ti time series or ab time series or ab "before-and-after"
S32.	(mh "pilot studies") or ti pilot
S33.	ti (collaborativ* or collaboration* or tailored or personalised or personalized) or ab (collaborativ* or collaboration* or tailored or personalised or personalized)
S34.	(intervention n6 clinician*) or (intervention n6 community) or (intervention n6 complex) or (intervention n6 design*) or (intervention n6 doctor*) or (intervention n6 educational) or (intervention n6 family doctor*) or (intervention n6 family physician*) or (intervention n6 family practitioner*) or (intervention n6 financial) or (intervention n6 gp) or (intervention n6

	general practice*) or (intervention n6 hospital*) or (intervention n6 impact*) or (intervention n6 improv*) or (intervention n6 individualize*) or (intervention n6 individualise*) or (intervention n6 individualizing) or (intervention n6 individualising) or (intervention n6 interdisciplin*) or (intervention n6 multicomponent) or (intervention n6 multi-component) or (intervention n6 multidisciplin*) or (intervention n6 multi-disciplin*) or (intervention n6 multifacet*) or (intervention n6 multi-facet*) or (intervention n6 multimodal*) or (intervention n6 multi-modal*) or (intervention n6 personalize*) or (intervention n6 personalise*) or (intervention n6 personalizing) or (intervention n6 personalising) or (intervention n6 pharmaci*) or (intervention n6 pharmacist*) or (intervention n6 pharmacy) or (intervention n6 physician*) or (intervention n6 practitioner*) or (intervention n6 prescrib*) or (intervention n6 prescription*) or (intervention n6 primary care) or (intervention n6 professional*) or (intervention* n6 provider*) or (intervention* n6 regulatory) or (intervention n6 regulatory) or (intervention n6 tailor*) or (intervention n6 target*) or (intervention n6 team*) or (intervention n6 usual care)
S35.	ti (demonstration project or demonstration projects or preimplement* or pre-implement* or post-implement* or postimplement*) or ab (demonstration project or demonstration projects or preimplement* or pre-implement* or post-implement* or postimplement*)
S36.	ti (pre-workshop or preworkshop or post-workshop or postworkshop or (before n3 workshop) or (after n3 workshop)) or ab (pre-workshop or preworkshop or post-workshop or postworkshop or (before n3 workshop) or (after n3 workshop))
S37.	ti (trial or (study n3 aim) or "our study") or ab ((study n3 aim) or "our study")
S38.	ti random* or controlled
S39.	(ti (multicentre or multicenter or multi-centre or multi-center)) or ab random*
S40.	ti ((control w3 area) or (control w3 cohort*) or (control w3 compar*) or (control w3 condition) or (control w3 group*) or (control w3 intervention*) or (control w3 participant*) or (control w3 study)) or ab ((control w3 area) or (control w3 cohort*) or (control w3 compar*) or (control w3 condition) or (control w3 group*) or (control w3 intervention*) or (control w3 participant*) or (control w3 study))
S41.	ti ((time points n3 over) or (time points n3 multiple) or (time points n3 three) or (time points n3 four) or (time points n3 five) or (time points n3 six) or (time points n3 seven) or (time points n3 eight) or (time points n3 nine) or (time points n3 ten) or (time points n3 eleven) or (time points n3 twelve) or (time points n3 month*) or (time points n3 hour*) or (time points n3 day*) or (time points n3 "more than")) or ab ((time points n3 over) or (time points n3 multiple) or (time points n3 three) or (time points n3 four) or (time points n3 five) or (time points n3 six) or (time points n3 seven) or (time points n3 eight) or (time points n3 nine) or (time points n3 ten) or (time points n3 eleven) or (time points n3 twelve) or (time points n3 month*) or (time points n3 hour*) or (time points n3 day*) or (time points n3 "more than"))
S42.	S21 or S22 or S23 or S24 or S25 or S26 or S27 or S28 or S29 or S30 or S31 or S32 or S33 or S34 or S35 or S36 or S37 or S38 or S39 or S40 or S41
S43.	ti ((multicent* n2 design*) or (multicent* n2 study) or (multicent* n2 studies) or (multicent* n2 trial*)) or ab ((multicent* n2 design*) or (multicent* n2 study) or (multicent* n2 studies) or (multicent* n2 trial*))
S44.	(mm "clinical trials+")
S45.	(ti ("clinical study" or "clinical studies")) or (ab ("clinical study" or "clinical studies"))
S46.	ti random* or ab random*
S47.	ti ("control* n1 clinical" or "control* n1 group*" or "control* n1 trial*" or "control* n1 study" or "control* n1 studies" or "control* n1 design*" or "control* n1 method*") or ab ("control* n1 clinical" or "control* n1 group*" or "control* n1 trial*" or "control* n1 study" or "control* n1 studies" or "control* n1 design*" or "control* n1 method*")
S48.	ti controlled
S49.	S43 or S44 or S45 or S46 or S47 or S48
S50.	(mh "family practice") or (family practice) or (general practice) or (family practitioner*) or (general practitioner*) or (family doctor*)

S51.	(mh "physicians, family") or ti (family physician? or family doctor?) or ab (family doctor? or family physician?)
S52.	(mh "primary health care") or (mh "community health services+") or (mw care or patient or community)
S53.	S50 or S51 or S52
S54.	S3 and S49
S55.	S18 or S19
S56.	S49 and S55
S57.	S42 and S55
S58.	S3 and S42 and S53
S59.	S20 or S54 or S56 or S57 or S58
S60.	Limit S59 to English language
	Date parameters: 2011-04 January 2016

G.4.11 Holistic assessment

- What is the clinical and cost effectiveness of holistic assessment in patients with multimorbidity?

The searches from a relevant Cochrane review³⁹⁸ were updated as follows:

Medline search terms

1.	geriatric assessment/
2.	health services for the aged/
3.	needs assessment/
4.	risk assessment/
5.	exp diagnostic services/
6.	"health services needs and demand"/
7.	exp health services/
8.	exp "delivery of health care"/
9.	exp "outcome and process assessment (health care)"/
10.	or/3-9
11.	geriatrics/ or exp *aged/
12.	10 and 11
13.	or/1-2,12
14.	((geriatric or aged or elderly or old age) adj5 (assess* or evaluation or consultation)).tw.
15.	(gemu or gemus).tw.
16.	11 and (multidisciplinary adj5 assess*).tw.
17.	or/13-16
18.	Excluded study designs and publication types [G.3.1]
19.	17 not 18
20.	Limit 19 to English language
21.	Study filters RCT (G.3.2)
22.	20 and 21
	Date parameters: 2010-04 January 2016

Embase search terms

1.	geriatric assessment/
2.	exp geriatric care/

3.	geriatrics/ or exp *aged/
4.	needs assessment/
5.	*risk assessment/
6.	preventive health service/
7.	*health services/
8.	*health status/
9.	treatment outcome/ or *outcome assessment/
10.	health care delivery/ or integrated health care system/
11.	*patient care/
12.	or/4-11
13.	3 and 12
14.	((geriatric or aged or elderly or old age) adj5 (assess* or evaluation or consultation)).tw.
15.	(gemu or gemus).tw.
16.	3 and (multidisciplinary adj5 assess*).tw.
17.	or/1-2,13-16
18.	Excluded study designs and publication types [G.3.1]
19.	17 not 18
20.	Limit 19 to English language
21.	Study filters RCT (G.3.2)
22.	20 and 21
23.	Date parameters: 2010-04 January 2016

Cochrane search terms

#1.	[mh ^"geriatric assessment"]
#2.	[mh ^"health services for the aged"]
#3.	[mh ^"needs assessment"]
#4.	[mh ^"risk assessment"]
#5.	[mh "diagnostic services"]
#6.	[mh ^"health services needs and demand"]
#7.	[mh "health services"]
#8.	[mh "delivery of health care"]
#9.	[mh "outcome and process assessment (health care)"]
#10.	{or #3-#9}
#11.	[mh ^geriatrics]
#12.	[mh aged]
#13.	#11 or #12
#14.	#10 and #13
#15.	((geriatric or aged or elderly or old age) near/5 (assess* or evaluation or consultation)):ti,ab
#16.	(gemu or gemus):ti,ab
#17.	(multidisciplinary near/5 assess*):ti,ab
#18.	#13 and #17
#19.	#1 or #2 or #14 or #15 or #16 or #18
	Date parameters: 2010-04 January 2016

G.4.12 Expert patient programmes

- What is the clinical- and cost-effectiveness of self-management and expert patient programmes for people with multimorbidity?

Medline search terms

1.	comorbidity/
2.	(comorbid* or co-morbid*).ti,ab.
3.	(multimorbid* or multi-morbid*).ti,ab.
4.	(multidisease? or multi-disease? or (multiple adj (ill* or disease? or condition? or syndrom* or disorder?))).ti,ab.
5.	((coocur* or co-ocur* or coexist* or co-exist* or multipl* or concord* or discord*) adj3 (disease? or ill* or care or condition? or disorder* or health* or medication* or symptom* or syndrom*)).ti,ab.
6.	or/1-5
7.	patient education as topic/
8.	health education/
9.	(patient* adj2 (educat* or expert*).ti,ab.
10.	(self adj3 (manage* or care or motivat*).ti,ab.
11.	exp self care/
12.	10 or 11
13.	(program* or educat* or teach* or train* or support* or instruct* or coach*).ti,ab.
14.	12 and 13
15.	or/7-9,14
16.	6 and 15
17.	Excluded study designs and publication types [G.3.1]
18.	16 not 17
19.	Limit 18 to English language
20.	Study filters RCT (G.3.2) or SR (G.3.3) or OBS (G.3.7)
21.	19 and 20
	Date parameters: see Table 21

Embase search terms

1.	*comorbidity/
2.	(comorbid* or co-morbid*).ti,ab.
3.	(multimorbid* or multi-morbid*).ti,ab.
4.	(multidisease? or multi-disease? or (multiple adj (ill* or disease? or condition? or syndrom* or disorder?))).ti,ab.
5.	((coocur* or co-ocur* or coexist* or co-exist* or multipl* or concord* or discord*) adj3 (disease? or ill* or care or condition? or disorder* or health* or medication* or symptom* or syndrom*)).ti,ab.
6.	or/1-5
7.	*health education/ or *patient education/
8.	(patient* adj2 (educat* or expert*).ti,ab.
9.	(self adj3 (manage* or care or motivat*).ti,ab.
10.	*self care/
11.	or/9-10
12.	(program* or educat* or teach* or train* or support* or instruct* or coach*).ti,ab.
13.	11 and 12

14.	or/7-8,13
15.	6 and 14
16.	Excluded study designs and publication types [G.3.1]
17.	15 not 16
18.	Limit 17 to English language
19.	Study filters RCT (G.3.2) or SR (G.3.3) or OBS (G.3.7)
20.	18 and 19
	Date parameters: see Table 21

Cochrane search terms

#1.	[mh ^comorbidity]
#2.	(comorbid* or co-morbid*):ti,ab
#3.	(multimorbid* or multi-morbid*):ti,ab
#4.	(multidisease* or multi-disease* or (multiple next (ill* or disease* or condition* or syndrom* or disorder*)):ti,ab
#5.	((coocur* or co-ocur* or coexist* or co-exist* or multipl* or concord* or discord*) near/3 (disease* or ill* or care or condition* or disorder* or health* or medication* or symptom* or syndrom*)):ti,ab
#6.	{or #1-#5}
#7.	[mh ^"patient education as topic"]
#8.	[mh ^"health education"]
#9.	(patient* near/2 (educat* or expert*)):ti,ab
#10.	(self near/3 (manage* or care or motivat*)):ti,ab
#11.	[mh "self care"]
#12.	#10 or #11
#13.	(program* or educat* or teach* or train* or support* or instruct* or coach*):ti,ab
#14.	#12 and #13
#15.	#7 or #8 or #9 or #14
#16.	#6 and #15
	Date parameters: see Table 21

G.4.13 Format of consultation

- What format of encounters with healthcare professionals improves outcomes for people with multimorbidity?

Medline search terms

1.	comorbidity/
2.	(comorbid* or co-morbid*).ti,ab.
3.	(multimorbid* or multi-morbid*).ti,ab.
4.	(multidisease? or multi-disease? or (multiple adj (ill* or disease? or condition? or syndrom* or disorder?)):ti,ab.
5.	((coocur* or co-ocur* or coexist* or co-exist* or multipl* or concord* or discord*) adj3 (disease? or ill* or care or condition? or disorder* or health* or medication* or symptom* or syndrom*)):ti,ab.
6.	or/1-5
7.	*patient care team/
8.	"appointments and schedules"/
9.	(telemed* or telecare*).ti,ab.

10.	"delivery of health care, integrated"/ or exp telemedicine/ or exp patient-centered care/
11.	((consultation* or appointment* or ((patient* or health* or communit*) adj2 (encounter* or visit* or meeting*)) or (review* adj2 (plan* or structur*)) or ward round*) adj4 (time* or length* or long* or extend* or extension* or remote* or virtual* or email* or telephon* or book* or choos* or chose or choice* or prefer* or plan* or discharge* or multidisciplinary or multiprofession* or ((multi or multiple) adj profession*) or (patient* adj (activat* or centre* or center*))))).ti,ab.
12.	or/7-11
13.	6 and 12
14.	Excluded study designs and publication types [G.3.1]
15.	13 not 14
16.	Limit 15 to English language
	Date parameters: see Table 21

Embase search terms

1.	*comorbidity/
2.	(comorbid* or co-morbid*).ti,ab.
3.	(multimorbid* or multi-morbid*).ti,ab.
4.	(multidisease? or multi-disease? or (multiple adj (ill* or disease? or condition? or syndrom* or disorder?))).ti,ab.
5.	((coocur* or co-ocur* or coexist* or co-exist* or multipl* or concord* or discord*) adj3 (disease? or ill* or care or condition? or disorder* or health* or medication* or symptom* or syndrom*)).ti,ab.
6.	or/1-5
7.	*patient decision making/
8.	exp *consultation/
9.	*integrated health care system/
10.	exp *telehealth/
11.	*telecommunication/
12.	(telemed* or telecare*).ti,ab.
13.	((consultation* or appointment* or ((patient* or health* or communit*) adj2 (encounter* or visit* or meeting*)) or (review* adj2 (plan* or structur*)) or ward round*) adj4 (time* or length* or long* or extend* or extension* or remote* or virtual* or email* or telephon* or book* or choos* or chose or choice* or prefer* or plan* or discharge* or multidisciplinary or multiprofession* or ((multi or multiple) adj profession*) or (patient* adj (activat* or centre* or center*))))).ti,ab.
14.	or/7-13
15.	6 and 14
16.	Excluded study designs and publication types [G.3.1]
17.	15 not 16
18.	Limit 17 to English language
	Date parameters: see Table 21

Cochrane search terms

#1.	[mh ^comorbidity]
#2.	(comorbid* or co-morbid*):ti,ab
#3.	(multimorbid* or multi-morbid*):ti,ab
#4.	(multidisease* or multi-disease* or (multiple next (ill* or disease* or condition* or syndrom* or disorder*))).ti,ab

#5.	((coocur* or co-ocur* or coexist* or co-exist* or multipl* or concord* or discord*) near/3 (disease* or ill* or care or condition* or disorder* or health* or medication* or symptom* or syndrom*)):ti,ab
#6.	{or #1-#5}
#7.	[mh ^"patient care team"]
#8.	[mh ^"appointments and schedules"]
#9.	(telemed* or telecare*):ti,ab
#10.	[mh ^"delivery of health care, integrated"]
#11.	[mh telemedicine]
#12.	[mh "patient-centered care"]
#13.	((consultation* or appointment* or ((patient* or health* or communit*) near/2 (encounter* or visit* or meeting*)) or (review* near/2 (plan* or structur*)) or ward next round*) near/4 (time* or length* or long* or extend* or extension* or remote* or virtual* or email* or telephon* or book* or choos* or chose or choice* or prefer* or plan* or discharge* or multidisciplinary or multiprofession* or ((multi or multiple) next profession*) or (patient* next (activat* or centre* or center*))))):ti,ab
#14.	{or #7-#13}
#15.	#6 and #14
	Date parameters: see Table 21

G.5 Health economics search

A general economics search was run, as well as specific searches for additional economic studies on other questions. These searches used the same search terms as the corresponding clinical searches, with the addition of an economic filter rather than a study design filter.

G.5.1 General multimorbidity economics

Economic searches were conducted in Medline, Embase, HEED, and NHS EED and HTA databases via the CRD interface.

Medline search terms

1.	*comorbidity/
2.	(multimorbid* or multi-morbid* or polymorbidity or polypathy or pluralpathology).ti,ab.
3.	(multidisease? or multi-disease? or (multiple adj (ill* or disease? or condition? or syndrom* or disorder?))):ti,ab.
4.	(multifactorial disease* or dual diagnosis).ti,ab.
5.	((coocur* or co-ocur* or cooccur* or co-occur* or coexist* or co-exist* or multipl*) adj3 (disease? or ill* or care or condition? or disorder* or health* or medication* or symptom* or syndrom*)):ti,ab.
6.	or/1-5
7.	*multiple sclerosis/
8.	*multiple myeloma/
9.	or/7-8
10.	6 not 9
11.	Excluded study designs and publication types [G.3.1]
12.	10 not 11
13.	Limit 12 to English language
14.	Study filter HE (G.3.4)

15.	13 and 14
	Date parameters: 2013 – 04 January 2016

Embase search terms

1.	*comorbidity/
2.	(multimorbid* or multi-morbid* or polymorbidity or polypathy or pluralpathology).ti,ab.
3.	(multidisease? or multi-disease? or (multiple adj (ill* or disease? or condition? or syndrom* or disorder?))),ti,ab.
4.	(multifactorial disease* or dual diagnosis).ti,ab.
5.	((coocur* or co-ocur* or cooccur* or co-occur* or coexist* or co-exist* or multipl*) adj3 (disease? or ill* or care or condition? or disorder* or health* or medication* or symptom* or syndrom*)).ti,ab.
6.	or/1-5
7.	*multiple sclerosis/
8.	*multiple myeloma/
9.	or/7-8
10.	6 not 9
11.	Excluded study designs and publication types [G.3.1]
12.	10 not 11
13.	Limit 21 to English language
14.	Study filter HE (G.3.4)
15.	13 and 14
16.	Date parameters: 2013 – 04 January 2016

CRD search terms

#1.	MeSH descriptor comorbidity in NHSEED,HTA
#2.	(multimorbid* or multi-morbid* or polymorbidity or polypathy or pluralpathology) in NHSEED, HTA
#3.	((multidisease* or multi-disease* or (multiple adj (ill* or disease* or condition* or syndrom* or disorder*)))) in NHSEED, HTA
#4.	(multifactorial disease* or dual diagnosis) in NHSEED, HTA
#5.	((coocur* or co-ocur* or cooccur* or co-occur* or coexist* or co-exist* or multipl*) adj3 (disease* or ill* or care or condition* or disorder* or health* or medication* or symptom* or syndrom*)) in NHSEED, HTA
#6.	#1 or #2 or #3 or #4 or #5
	Date parameters: Inception – 04 January 2016

HEED search terms

1.	ax=multimorbid* or multi-morbid* or polymorbidity or polypathy or pluralpathology
2.	ax=multidisease* or multi-disease*
3.	ax='multiple illnesses' within 3
4.	ax='multiple illness'
5.	ax='multiple disease' within 3
6.	ax='multiple conditions' within 2
7.	ax='multiple disorders' within 3
8.	ax='multiple syndromes' within 3
9.	ax='multifactorial disease'
10.	ax='dual diagnosis'

11.	ax=coocur* or co-ocur* or cooccur* or co-occur* or coexist* or co-exist*
12.	ax=disease* or ill* or care or condition* or disorder* or health* or medication* or symptom* or syndrom*
13.	cs=11 and 12
14.	cs=1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 13
	Date parameters: Inception – 08 August 2014

G.5.2 Models of care

This search used the same terms as the Cochrane review,¹¹³⁰ with the addition of economic filters. Searches were conducted in Medline, Embase, HEED, and NHS EED and HTA databases via the CRD interface.

Medline search terms

1.	Interventions search terms [G.4.10, line 141]
2.	Excluded study designs and publication types [G.3.1]
3.	1 not 2
4.	Limit 3 to English language
5.	Study filter HE (G.3.4)
6.	4 and 5
	Date parameters: 2013 – 04 January 2016

Embase search terms

1.	Interventions search terms [G.4.10, line 151]
2.	Excluded study designs and publication types [G.3.1]
3.	1 not 2
4.	Limit 3 to English language
5.	Study filter HE (G.3.4)
6.	4 and 5
	Date parameters: 2013 – 04 January 2016

CRD search terms

#1.	MeSH descriptor comorbidity explode all trees in NHSEED,HTA
#2.	(comorbid* or co-morbid* or multimorbid* or multi-morbid* or multidisease or multidiseases or multi-disease or multi-diseases) in NHSEED, HTA
#3.	((((coocur* or co-ocur* or coexist* or co-exist* or multipl*) adj2 (disease or diseases or ill* or care or condition or conditions or disorder* or health* or medication* or symptom* or syndrom*))) in NHSEED, HTA
#4.	#1 or #2 or #3
	Date parameters: 1999 – 04 January 2016

HEED search terms

1.	ax=comorbid* or co-morbid* or multimorbid* or multi-morbid* or multidisease or multidiseases or multi-disease or multi-diseases
2.	ax=coocur* or co-ocur* or cooccur* or co-occur* or coexist* or co-exist*
3.	cs=1 or 2
	Date parameters: 1999 – 06 October 2014

G.5.3 Holistic assessment

This search used the same terms as the Cochrane review,³⁹⁸ with the addition of economic filters. Searches were conducted in Medline, Embase, HEED, and NHS EED and HTA databases via the CRD interface.

Medline search terms

1.	CGA search terms [G.4.11, line 17]
2.	Excluded study designs and publication types [G.3.1]
3.	1 not 2
4.	Limit 3 to English language
5.	Study filter HE (G.3.4)
6.	4 and 5
	Date parameters: 2013 – 04 January 2016

Embase search terms

1.	CGA search terms [G.4.11, line 17]
2.	Excluded study designs and publication types [G.3.1]
3.	1 not 2
4.	Limit 3 to English language
5.	Study filter HE (G.3.4)
6.	4 and 5
	Date parameters: 2013 – 04 January 2016

CRD search terms

#1.	MeSH descriptor geriatric assessment in NHSEED,HTA
#2.	MeSH descriptor health services for the aged in NHSEED,HTA
#3.	MeSH descriptor needs assessment in NHSEED,HTA
#4.	MeSH descriptor risk assessment in NHSEED,HTA
#5.	MeSH descriptor health services needs and demand in NHSEED,HTA
#6.	MeSH descriptor health services in NHSEED,HTA
#7.	MeSH descriptor delivery of health care in NHSEED,HTA
#8.	MeSH descriptor diagnostic services in NHSEED,HTA
#9.	#3 or #4 or #5 or #6 or #7 or #8
#10.	MeSH descriptor geriatrics in NHSEED,HTA
#11.	MeSH descriptor aged explode all trees in NHSEED,HTA
#12.	#10 or #11
#13.	#9 and #12
#14.	((geriatric or aged or elderly or old age) adj5 (assess* or evaluation or consultation))) in NHSEED, HTA
#15.	((gemu or gemus)) in NHSEED, HTA
#16.	((multidisciplinary adj5 assess*)) in NHSEED, HTA
#17.	#12 and #16
#18.	#1 or #2 or #13 or #14 or #15 or #17
#19.	Date parameters: Inception – 04 January 2016

G.5.4 Burden of treatment

Economic searches were conducted in Medline, Embase, and NHS EED and HTA databases via the CRD interface.

Medline search terms

1.	((treat* or therap*) adj2 burden*).ti,ab.
2.	Excluded study designs and publication types [G.3.1]
3.	1 not 2
4.	Limit 3 to English language
5.	Study filter HE (G.3.4)
6.	4 and 5
	Date parameters: see Table 21

Embase search terms

1.	((treat* or therap*) adj2 burden*).ti,ab.
2.	Excluded study designs and publication types [G.3.1]
3.	1 not 2
4.	Limit 3 to English language
5.	Study filter HE (G.3.4)
6.	4 and 5
	Date parameters: see Table 21

CRD search terms

#1.	((treat* or therap*) adj2 burden*) in NHSEED, HTA
	Date parameters: Inception – 04 January 2016

G.5.5 Stopping treatment: antihypertensives

Economic searches were conducted in Medline, Embase, HEED, and NHS EED and HTA databases via the CRD interface.

Medline search terms

1.	Stopping antihypertensives search terms [G.4.6, line 36]
2.	Excluded study designs and publication types [G.3.1]
3.	1 not 2
4.	Limit 3 to English language
5.	Study filter HE (G.3.4)
6.	4 and 5
	Date parameters: see Table 21

Embase search terms

1.	Stopping antihypertensives search terms [G.4.6, line 35]
2.	Excluded study designs and publication types [G.3.1]
3.	1 not 2
4.	Limit 3 to English language
5.	Study filter HE (G.3.4)
6.	4 and 5
	Date parameters: see Table 21

CRD search terms

#1.	MeSH descriptor thiazides explode all trees in NHSEED,HTA
#2.	((thiazide* or bendrofluazide or bendroflumethazide or aprinox or neo-naclex or chlorthalidone or hygroton or cyclopenthiiazide or navidrex or indapamide or natrilix or metolazone or xipamide or diurexan)) in NHSEED, HTA
#3.	MeSH descriptor calcium channel blockers explode all trees in NHSEED,HTA
#4.	((calcium adj3 (block* or inhibit* or antagonist*))) in NHSEED, HTA
#5.	((diltiazem or optil or tildiem or adizem or angitil or calcicard or dilcardia or dilzem or slozem or viazem or zemtard or verapamil or zolvera or cordilox or securon or univer or verapress or verstab)) in NHSEED, HTA
#6.	((amlodipine or amlostin or istin or exforge or felodipine or plendil or lacidipine or motens or lercanidipine or zanidip or nicardipine or cardene or nifedipine or adalat or nimodipine or nimotop)) in NHSEED, HTA
#7.	MeSH descriptor adrenergic beta-antagonists explode all trees in NHSEED,HTA
#8.	((propranolol or angilol or angilol or inderal-1a or half-inalderal or inderal or bedranol or prograne or slo-pro or acebutolol or sectral or atenolol or tenormin or bisoprolol or cardicor or emcor or carvedilol or eucardic or celiprolol or celectol or co-tenidone or tenoret or tenoretic or esmolol or brevibloc or labetalol or trandate or metoprolol or betaloc or lopresor or nadolol or corgard or nebivolol or nebilet or hypoloc or oxprenolol or trasicor or slow-trasicor or pindolol or visken or sotalol or beta-cardone or sotacor or timolol or betim)) in NHSEED, HTA
#9.	((beta or b) adj3 (block* or antagonist*)) in NHSEED, HTA
#10.	MeSH descriptor angiotensin receptor antagonists explode all trees in NHSEED,HTA
#11.	((angiotensin adj3 (receptor* adj2 (antagonist* or blocker*))) or arb or arbs)) in NHSEED, HTA
#12.	((candesartan or amias or eprosartan or teveten or irbesartan or aprovel or coaprovel or losartan or cozaar or cozaar-comp or olmesartan or olmetec or sevikar or telmisartan or micardis or valsartan or diovan or co-diovan or azilsartan or edarbi)) in NHSEED, HTA
#13.	MeSH descriptor angiotensin-converting enzyme inhibitors explode all trees in NHSEED,HTA
#14.	((ace or acei or ((angiotensin adj converting adj2 enzyme*) or ace or kininase)) adj2 (inhibit* or antagonist*)) in NHSEED, HTA
#15.	((captopril or ecopace or kaplon or capoten or co-zidocapt or capto-co or capozide or cilazapril or vascace or enalapril or ednyt or innovace or innozide or fosinopril or imidapril or tanatril or lisinopril or zestril or carace or zestoretic or moexipril or perdex or perindopril or coversyl or quinapril or quinil or accupro or accuretic or ramipril or tritace or triapin or trandolapril or gopten or tarka)) in NHSEED, HTA
#16.	MeSH descriptor antihypertensive agents explode all trees in NHSEED,HTA
#17.	((antihypertens* adj2 (drug* or agent* or treat* or therap* or intervention*)) in NHSEED, HTA
#18.	MeSH descriptor adrenergic alpha-antagonists explode all trees in NHSEED,HTA
#19.	((doxazosin or cardura or indoramin or doraleso or prazosin or hypovase or terazosin or hytrin or phenoxybenzamine or phentolamine)) in NHSEED, HTA
#20.	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19
#21.	((deprescri* or de-prescri*)) in NHSEED, HTA
#22.	((stop adj3 (criteria or criterion or rule or standard or benchmark or bench mark or decision* or take or taking))) in NHSEED, HTA
#23.	((discontin* or withdraw* or cessat* or down-titrat* or step-down or "step down")):ti in NHSEED, HTA
#24.	((discontin* or withdraw* or cessat* or down-titrat* or step-down or "step down" or stop* or cease* or taper*) adj2 (dose* or drug* or treatment* or therap* or medicat* or intervention*)) in NHSEED, HTA
#25.	MeSH descriptor polypharmacy in NHSEED,HTA

#26.	(polypharmacy) in NHSEED, HTA
#27.	MeSH descriptor medication adherence in NHSEED,HTA
#28.	MeSH descriptor treatment refusal in NHSEED,HTA
#29.	((adheren* or nonadheren* or non-adheren* or non adheren* or complian* or noncomplian* or non-complian* or non complian*)):ti in NHSEED, HTA
#30.	((adheren* or nonadheren* or non-adheren* or non adheren* or complian* or noncomplian* or non-complian* or non complian* or persist*) adj2 (patient* or participant* or dose* or drug* or treatment* or therap* or medicat* or intervention*)) in NHSEED, HTA
#31.	#21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30
#32.	#20 and #31
	Date parameters: Inception – 04 January 2016

HEED search terms

1.	ax=thiazide* or bendrofluazide or aprinox or neo-naclex or chlorthalidone or hygroton or cyclopenthiiazide or navidrex or indapamide or natrilix or metolazone or xipamide or diurexan
2.	ax=calcium channel or diltiazem or optil or tildiem or adizem or angitil or calcicard or dilcardia or dilzem or slozem or viazem or zemtard or verapamil or zolvera or cordilox or securon or univer or verapress or vertab or amlodipine or amlostin or istin or exforge or felodipine or plendil or lacidipine or motens or lercanidipine or zanidip or nicardipine or cardene or nifedipine or adalat or nimodipine or nimotop
3.	ax= beta blocker or beta blockers
4.	ax=propranolol or angilol or angilol or inderal or bedranol or prograne or acebutolol or sectral or atenolol or tenormin or bisoprolol or cardicor or emcor or carvedilol or eucardic or celiprolol or celectol or co-tenidone or tenoret or tenoretic or esmolol or brevibloc or labetalol or trandate or metoprolol or betaloc or loproresor or nadolol or corgard or nebivolol or nebilet or hypoloc or oxprenolol or trasicor or slow-trasicor or pindolol or visken or sotalol or beta-cardone or sotacor or timolol or betim
5.	ax=angiotensin receptor or arb or arbs or candesartan or amias or eprosartan or teveten or irbesartan or aprovel or coaprovel or losartan or cozaar or olmesartan or olmetec or sevikar or telmisartan or micardis or valsartan or diovan or azilsartan or edarbi
6.	ax=ace or acei or captopril or ecopace or kaplon or capoten or co-zidocapt or capto-co or capozide or cilazapril or vascace or enalapril or ednyt or innovace or innozide or fosinopril or imidapril or tanatril or lisinopril or zestril or carace or zestoretic or moexipril or perdix or perindopril or coversyl or quinapril or quinil or accupro or accuretic or ramipril or tritace or triapin or trandolapril or gopten or tarka
7.	ax=antihypertens*
8.	ax= alpha blocker or alpha blockers or doxazosin or cardura or indoramin or doralese or prazosin or hypovase or terazosin or hytrin or phenoxybenzamine or phentolamine
9.	cs=1 or 2 or 3 or 4 or 5 or 6 or 7 or 8
10.	ax=polypharmacy
11.	ax=deprescri* or de-prescri*
12.	ax=discontin* or withdraw* or cessat* or down-titrat* or step-down or step down or stop* or cease* or taper*
13.	ax=adheren* or nonadheren* or non-adheren* or complian* or noncomplian* or non-complian*
14.	cs=10 or 11 or 12 or 13
15.	cs=9 and 14
	Date parameters: Inception – 03 December 2014

G.5.6 Stopping treatment: bisphosphonates

Economic searches were conducted in Medline, Embase, and NHS EED and HTA databases via the CRD interface.

Medline search terms

1.	Stopping bisphosphonates search terms [G.4.7, line 20]
2.	Excluded study designs and publication types [G.3.1]
3.	1 not 2
4.	Limit 3 to English language
5.	Study filter HE (G.3.4)
6.	4 and 5
	Date parameters: 1999 – 04 January 2016

Embase search terms

1.	Stopping bisphosphonates search terms [G.4.7, line 20]
2.	Excluded study designs and publication types [G.3.1]
3.	1 not 2
4.	Limit 3 to English language
5.	Study filter HE (G.3.4)
6.	4 and 5
	Date parameters: 1999 – 04 January 2016

CRD search terms

#1.	MeSH descriptor diphosphonates in NHSEED,HTA
#2.	MeSH descriptor alendronate in NHSEED,HTA
#3.	MeSH descriptor etidronic acid in NHSEED,HTA
#4.	MeSH descriptor bone density conservation agents in NHSEED,HTA
#5.	MeSH descriptor raloxifene in NHSEED,HTA
#6.	MeSH descriptor teriparatide in NHSEED,HTA
#7.	((bisphosphonate* or diphosphonate*)) in NHSEED, HTA
#8.	((alendronate or alendronic or fosamax or fosavance or etidronate or didronel or etidronic or risedronate or risedronic or actonel or ibandronate or ibandronic or bondronat or bonviva)) in NHSEED, HTA
#9.	((raloxifene or evista or strontium ranelate or protelos or teriparatide or forsteo or forteo)) in NHSEED, HTA
#10.	MeSH descriptor clodronic acid in NHSEED,HTA
#11.	((clodronate or clodronic or bonefos or clasteon or loron or zoledronate or zoledronic or aclasta or zometa or pamidronate or aredia or denosumab or prolia or xgeva)) in NHSEED, HTA
#12.	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11
#13.	((deprescri* or de-prescri*)) in NHSEED, HTA
#14.	((stop* adj3 (criteria or criterion or rule* or standard* or benchmark* or bench mark* or decision* or take or taking))) in NHSEED, HTA
#15.	(discontinu* or withdraw* or cessat* or down-titrat* or step-down or "step down" or stop* or cease* or taper*) in NHSEED, HTA
#16.	MeSH descriptor polypharmacy in NHSEED,HTA
#17.	(polypharmacy) in NHSEED, HTA
#18.	#13 or #14 or #15 or #16 or #17
#19.	#12 and #18

Date parameters: 1999 – 04 January 2016

G.5.7 Stopping treatment: statins

Economic searches were conducted in Medline, Embase, HEED, and NHS EED and HTA databases via the CRD interface.

Medline search terms

1.	Stopping statins search terms [G.4.8, line 26]
2.	Excluded study designs and publication types [G.3.1]
3.	1 not 2
4.	Limit 3 to English language
5.	Study filter HE (G.3.4)
6.	4 and 5
	Date parameters: see Table 21

Embase search terms

1.	Stopping statins search terms [G.4.8, line 26]
2.	Excluded study designs and publication types [G.3.1]
3.	1 not 2
4.	Limit 3 to English language
5.	Study filter HE (G.3.4)
6.	4 and 5
	Date parameters: see Table 21

CRD search terms

#1.	MeSH descriptor hydroxymethylglutaryl-coa reductase inhibitors in NHSEED,HTA
#2.	(statin*) in NHSEED, HTA
#3.	(((((hydroxymethylglutaryl-coa or hmg-coa) adj3 (reductase or inhibitors)))) in NHSEED, HTA
#4.	MeSH descriptor simvastatin in NHSEED,HTA
#5.	(simvastatin* or zocor) in NHSEED, HTA
#6.	(atorvastatin* or lipitor) in NHSEED, HTA
#7.	(rosuvastatin* or crestor) in NHSEED, HTA
#8.	MeSH descriptor pravastatin in NHSEED,HTA
#9.	(pravastatin* or lipostat) in NHSEED, HTA
#10.	(fluvastatin* or lescol) in NHSEED, HTA
#11.	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10
#12.	(deprescri* or de-prescri*) in NHSEED, HTA
#13.	(stop adj3 (criteria or criterion or rule or standard or benchmark or bench mark or decision* or take or taking)) in NHSEED, HTA
#14.	(discontin* or withdraw* or cessat* or down-titrat* or step-down or "step down"):ti in NHSEED, HTA
#15.	((((discontin* or withdraw* or cessat* or down-titrat* or step-down or "step down" or stop* or cease* or taper*) adj2 (dose* or drug* or treatment* or therap* or medicat* or intervention*))) in NHSEED, HTA
#16.	MeSH descriptor polypharmacy in NHSEED,HTA
#17.	(polypharmacy) in NHSEED, HTA
#18.	MeSH descriptor medication adherence in NHSEED,HTA

#19.	MeSH descriptor patient compliance in NHSEED,HTA
#20.	MeSH descriptor treatment refusal in NHSEED,HTA
#21.	((adheren* or nonadheren* or non-adheren* or non adheren* or complian* or noncomplian* or non-complian* or non complian*)):ti in NHSEED, HTA
#22.	((((adheren* or nonadheren* or non-adheren* or non adheren* or complian* or noncomplian* or non-complian* or non complian* or persist*) adj2 (patient* or participant* or dose* or drug* or treatment* or therap* or medicat* or intervention*))) in NHSEED, HTA
#23.	#12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22
#24.	#11 and #23
	Date parameters: Inception – 04 Janaury 2016

HEED search terms

1.	ax=statin* or hydroxymethylglutaryl-coa or hmg-coa
2.	ax=simvastatin* or zocor or atorvastatin* or lipitor or rosuvastatin* or crestor or pravastatin* or lipostat or fluvastatin* or lescol
3.	cs=1 or 2
4.	ax=polypharmacy
5.	ax=deprescri* or de-prescri*
6.	ax=discontin* or withdraw* or cessat* or down-titrat* or step-down or step down or stop* or cease* or taper*
7.	ax=adheren* or nonadheren* or non-adheren* or complian* or noncomplian* or non-complian*
8.	cs=4 or 5 or 6 or 7
9.	cs=3 and 8
	Date parameters: Inception – 14 November 2014

G.5.8 EQ5D

QoL searches were conducted in Medline and Embase only. A truncated version of the full QoL filter was used, to look for the EQ5D utility score alone.

Medline search terms

1.	comorbidity/
2.	(comorbid* or co-morbid*).ti,ab.
3.	(multimorbid* or multi-morbid*).ti,ab.
4.	(multidisease? or multi-disease? or (multiple adj (ill* or disease? or condition? or syndrom* or disorder?))).ti,ab.
5.	((coocur* or co-ocur* or coexist* or co-exist* or multipl* or concord* or discord*) adj3 (disease? or ill* or care or condition? or disorder* or health* or medication* or symptom* or syndrom*).ti,ab.
6.	or/1-5
7.	(euroqol* or eq5d* or eq 5*).ti,ab.
8.	6 and 7
9.	Excluded study designs and publication types [G.3.1]
10.	8 not 9
11.	Limit 10 to English language
	Date parameters: see Table 21

Embase search terms

1.	*comorbidity/
2.	(comorbid* or co-morbid*).ti,ab.
3.	(multimorbid* or multi-morbid*).ti,ab.
4.	(multidisease? or multi-disease? or (multiple adj (ill* or disease? or condition? or syndrom* or disorder?))).ti,ab.
5.	((coocur* or co-ocur* or coexist* or co-exist* or multipl* or concord* or discord*) adj3 (disease? or ill* or care or condition? or disorder* or health* or medication* or symptom* or syndrom*)).ti,ab.
6.	or/1-5
7.	(euroqol* or eq5d* or eq 5*).ti,ab.
8.	6 and 7
9.	Excluded study designs and publication types [G.3.1]
10.	8 not 9
11.	Limit 10 to English language
	Date parameters: see Table 21

G.5.9 Quality of life (QOL) in care homes

QoL searches were conducted in Medline and Embase only.

Medline search terms

1.	exp aged/
2.	(elder* or old* or aged or geriatric* or senior* or pensioner*).ti,ab.
3.	or/1-2
4.	residential facilities/ or homes for the aged/ or exp nursing homes/
5.	((care or residential or nursing or respite) adj (home* or facilit*)).ti,ab.
6.	4 or 5
7.	3 and 6
8.	Excluded study designs and publication types [G.3.1]
9.	7 not 8
10.	Limit 9 to English language
11.	Study filter QOL (G.3.5)
12.	10 and 11
	Date parameters: see Table 21

Embase search terms

1.	exp aged/
2.	(elder* or old* or aged or geriatric* or senior* or pensioner*).ti,ab.
3.	or/1-2
4.	assisted living facility/ or nursing home/ or residential home/
5.	home for the aged/
6.	((care or residential or nursing or respite) adj (home* or facilit*)).ti,ab.
7.	or/4-6
8.	3 and 7
9.	Excluded study designs and publication types [G.3.1]
10.	8 not 9
11.	Limit 10 to English language

12.	Study filter QOL (G.3.5)
13.	11 and 12
	Date parameters: see Table 21

G.5.10 Mortality in care homes

Searches were conducted in Medline and Embase only.

Medline search terms

1.	residential facilities/ or homes for the aged/ or exp nursing homes/
2.	((care or residential or nursing or respite) adj (home* or facilit*)).ti,ab.
3.	1 or 2
4.	*life expectancy/
5.	(mortality or survival or life expectanc*).ti,ab.
6.	or/4-6
7.	3 and 7
8.	Excluded study designs and publication types [G.3.1]
9.	7 not 8
10.	Limit 9 to English language
11.	Study filter MOD (G.3.6)
12.	exp regression analysis/
13.	regression analys*.ti,ab.
14.	((hazard or risk) adj ratio*).ti,ab.
15.	relative risk.ti,ab.
16.	or/12-15
17.	11 or 16
18.	10 and 17
	Date parameters: see Table 21

Embase search terms

1.	assisted living facility/ or nursing home/ or residential home/
2.	home for the aged/
3.	((care or residential or nursing or respite) adj (home* or facilit*)).ti,ab.
4.	or/1-3
5.	mortality/ or *standardized mortality ratio/
6.	exp *survival/
7.	(mortality or survival or life expectanc*).ti,ab.
8.	or/5-7
9.	4 and 8
10.	Excluded study designs and publication types [G.3.1]
11.	9 not 10
12.	Limit 11 to English language
13.	Study filter MOD (G.3.6)
14.	exp regression analysis/
15.	hazard ratio/
16.	((hazard or risk) adj ratio*).ti,ab.
17.	regression analys*.ti,ab.

18.	relative risk.ti,ab.
19.	or/14-18
20.	13 or 19
21.	12 and 20
	Date parameters: see Table 21

Appendix H: Clinical evidence tables

H.1 Principles/Barriers of care

H.1.1 Principles of care

Table 23: Medicines Adherence

Guideline (ref id)	Medicines Adherence	
Aim	This guideline gives recommendations to clinicians and others on how to involve adults and carers in decisions about prescribed medicine	
Population	Adults, including those with co morbidities, learning disabilities or language and cultural differences	
Setting	Across the NHS	
Themes with recommendations	Theme in guideline	Recommendation(s)
	1. Patient involvement in decisions about medicines	Healthcare professionals should adapt their consultation style to the needs of individual patients so that all patients have the opportunity to be involved in decisions about their medicines at the level they wish
		Encourage patients to ask about their condition and treatment.
		Be aware that the consultation skills needed for increasing patient involvement can be improved.
		Offer all patients the opportunity to be involved in making decisions about prescribed medicines. Establish what level of involvement in decision making the patient would like.
		Discuss with the patient why they might benefit from the treatment. Clearly explain the disease or condition and how the medicine will influence this.
		Explain the medical aims of the treatment to patients and openly discuss the pros and cons of proposed medicines. The discussion should be at the level preferred by the patient.
		Clarify what the patient hopes the treatment will achieve.
		Avoid making assumptions about patient preferences about treatment. Talk to the patient to find out their preferences, and note any non-verbal cues that may indicate you need to explore the patient's perspective further.
		Healthcare professionals have a duty to help patients to make decisions about their treatment based on an understanding of the likely benefits and risks rather than on misconceptions.
Accept that patients may have different views from healthcare professionals about the balance of risks, benefits and		

Guideline (ref id)	Medicines Adherence	
		side effects of medicines.
		Be aware that increasing patient involvement may mean that the patient decides not to take or to stop taking a medicine. If in the healthcare professional's view this could have an adverse effect, then the information provided to the patient on risks and benefits and the patient's decision should be recorded.
		Encourage and support patients, families and carers to keep an up to date list of all medicines the patient is taking. The list should include the names and dosages of prescription and non-prescription medicines and herbal and nutritional supplements. If the patient has any allergic or adverse reactions to medicines, these should be noted.
		Be aware that patients may wish to minimise how much medicine they take
		Be aware that patients may wish to discuss what will happen if they do not take the medicine suggested by their healthcare professional, non-pharmacological alternatives to medicines, how to reduce and stop medicines they may have been taking for a long time, particularly those known to be associated with withdrawal symptoms, how to fit taking the medicine into their daily routine, how to make a choice between medicines if they believe they are taking too many medicines.
	2. Supporting adherence	Recognise that non adherence is common and that most patients are non-adherent sometimes. Routinely assess adherence in a non-judgemental way whenever you prescribe, dispense and review medicines.
		Consider assessing non adherence by asking the patient if they have missed any doses of medicine recently. Make it easier for them to report non adherence by asking the question in a way that does not apportion blame, explaining why you are asking the question, mentioning a specific time period such as 'in the past week', asking about medicine-taking behaviours such as reducing the dose, stopping and starting medicines.
		Consider using records of prescription re ordering, pharmacy patient medication records and return of unused medicines to identify potential non adherence and patients needing additional support.
		If a patient is not taking their medicines, discuss with them whether this is because of beliefs and concerns or problems about the medicines (intentional non adherence) or because of practical problems (unintentional non adherence).
		Be aware that although adherence can be improved, no specific intervention can be recommended for all patients. Tailor any intervention to increase adherence to the specific difficulties with adherence the patient is experiencing.
	3. Reviewing medicines	Review patient knowledge, understanding and concerns about medicines, and a patient's view of their need for medicine at intervals agreed with the patient, because these may change over time. Offer repeat information and review to patients, especially when treating long term conditions with multiple medicines.
	Review at regular intervals the decision to prescribe medicines, according to patient choice and need.	
	Be aware that patients sometimes evaluate prescribed medicines using their own criteria such as their understanding	

Guideline (ref id)	Medicines Adherence						
		of their condition or the symptoms most troubling to them. They may, for example, stop and start the medicine or alter the dose and check how this affects their symptoms. Ask the patient whether they have done this.					
	4. Communication between healthcare professionals	Healthcare professionals involved in prescribing, dispensing or reviewing medicines should ensure that there are robust processes for communicating with other healthcare professionals involved in the patient's care.					
		Healthcare professionals involved in reviewing medicines should inform the prescriber of the review and its outcome. This is particularly important if the review involves discussion of difficulties with adherence and further review is necessary.					
Limitations	Generally well formulated guidelines, GDG member list did not explicitly state inclusion of a pharmacist, although there were a number of members who worked in the academic pharmacy fields that could be consistent with also practicing as a pharmacist.						
AGREE II score	Scope and purpose: 89%	Stakeholder involvement: 94%	Rigour of development: 92%	Clarity of presentation: 92%	Applicability: 79%	Editorial independence: 67%	Overall assessment: 6
Applicability of evidence	Moderate, wide-ranging guidelines not specific to those with multimorbidity although many of the recommendations were more relevant to those with multimorbidity than those with single conditions						

Table 24: Polypharmacy Guidance (NHS Scotland)

Guideline (ref id)	Polypharmacy Guidance (NHS Scotland)	
Aim	This guidance aims to provide information about patient groups that NHS boards should consider as a priority for polypharmacy review, an outline of medication review process in these patients and provide NHS boards with tools to be adapted for local guideline use	
Population	Patients on multiple medications or is "frail" in a medical sense	
Setting	Across the NHS	
Themes with recommendations	Theme in guideline	Recommendation(s)
	1. Reviewing medicines	Patients with a 40-60% risk of emergency admission within the next 12 months (as per iSPARRA), on multiple medicines from 10 or more particular BNF sections and high risk medicines, reviews should be started on patients >75 years.
		Question whether each prescription is preventing rapid symptomatic deterioration or fulfilling an essential replacement function as these should be continued or only discontinued with specialist input.
		For medicines without clear essential indications or contraindications, check their effectiveness in the specific patient group against a reference summary (version included in guideline – based on NNTs in specific situations).
	High risk combinations should be avoided unless completely necessary, these combinations include: NSAID +	

Guideline (ref id)	Polypharmacy Guidance (NHS Scotland)						
	ACEi/diuretic, NSAID + tricyclic antidepressant/glitazone, warfarin + antiplatelet drug/macrolide/NSAID/quinolone.						
	PPIs and H2 antagonists should be considered for reduction particularly if antibiotics are required due to the increased risk of <i>C.difficile</i> .						
	When using diuretics for ankle oedema consider alternative ways to manage the oedema particularly if there is medication causes (for example, calcium channel blockers).						
	Consider stopping or reducing dose of digoxin if being used in presence of CKD.						
	Review of combinations of antidepressants such as tricyclic antidepressants for analgesia used in combination with other antidepressants for depression.						
	In general SSRIs are better tolerated in people with dementia who also have depression.						
	Consider cumulative GI effects when co-prescribing SSRIs & NSAIDs/aspirin.						
	Use metformin with caution in renal impairment and avoid if eGFG <30 ml/min.						
Limitations	No systematic search for evidence, some references included to support specific recommendations but no evidence that a systematic search was conducted.						
AGREE II score	Scope and purpose: 61%	Stakeholder involvement: 72%	Rigour of development: 23%	Clarity of presentation: 50%	Applicability: 67%	Editorial independence: 17%	Overall assessment: 3
Applicability of evidence	Moderate, polypharmacy applies to a subset of patients with MM but a relatively large subset, some recommendations were specific to individual combinations of medications and therefore less appropriate for this review, but others were more guiding principles						

Table 25: Guiding principles for the care of older adults with multimorbidity

Guideline (ref id)	Guiding principles for the care of older adults with MM	
Aim	To present the guiding principles for the clinical management of older adults with MM	
Population	Older adults with multiple chronic conditions	
Setting	USA, community	
Themes with recommendations	Theme in guideline	Recommendation(s)
	Patient preferences	Recognise when the older adult with multimorbidity (OLDER ADULT WITH MULTIMORBIDITY) is facing a “preference sensitive” decision.
		Ensure that older adult with multimorbidity are adequately informed about the expected benefits and harms of different treatment options.

Guideline (ref id)	Guiding principles for the care of older adults with MM							
			Elicit preferences only after the older adult with multimorbidity is sufficiently informed.					
	Interpreting the evidence			Question whether a study is applicable to the population in question.				
				Consider the quality of a study (for example, RCT vs NRS) and tend to prefer reviews of multiple studies.				
				Consider whether the outcomes reported are clinically important and important to patients.				
				Consider the balance between any benefits and the harms incurred including the burden required to commit to treatment.				
				Always consider the baseline risk not just a relative risk change, that is, ARR is more useful than RRR.				
			NNT and NNH data should be interpreted in conjunction with time factors, clinicians should look for a time horizon to benefit or harm (that is, the length of time needed to accrue an observable clinically meaningful benefit or harm).					
	Prognosis			Clinicians should offer to discuss prognosis but not all older adult with multimorbidity may wish to do so.				
				It is helpful to prioritise decisions based on life expectancy so they are categorised as short term (within the next year), midterm (within the next 5 years) or long term (beyond 5 years).				
	Clinical feasibility			An MDT should assess the ability of older adult with multimorbidity to manage or adhere to a treatment plan on an ongoing basis.				
				In older adult with multimorbidity, evidence-based medicine alone does not provide an adequate guide to the best clinical management and condition specific guidelines are often not feasible, feasibility should inform decisions in these situations.				
				Where there are conflicts between what clinicians wants and what older adult with multimorbidity want there should be consideration, education and re-evaluation on both sides.				
	Optimising therapies			The first step is to identify treatments that may be inappropriate in older adult with multimorbidity; consensus statements and expert derived criteria exist to identify these potentially inappropriate medications (PIMs) and should be consulted.				
				Medication appropriateness should be evaluated at hospital admission, ICU admission and hospital discharge.				
				Medication should ideally be stopped 1 at a time.				
				Little evidence exists to guide stopping of medications and if there is uncertainty it is sensible to use a tapering regimen when stopping drugs.				
Limitations	Panel discussion supported by a review of the evidence that is in the author’s own words “not systematic” however their approach seems relatively consistent with a systematic review. Funded by the American Geriatric Society and there is no discussion of the potential for bias here.							
AGREE II score	Scope and	Stakeholder	Rigour of	Clarity of	Applicability: 63%	Editorial	Overall	

Guideline (ref id)	Guiding principles for the care of older adults with MM						
	purpose: 50%	involvement: 72%	development: 42%	presentation: 92%		independence: 58%	assessment: 4
Applicability of evidence	High, specifically about patients with MM, although a subset, “older adults”, there is no strict age defined in the review and the principles are not overly skewed towards the extremes of old age.						

Table 26: AHA/ACC/HHS strategies to enhance application of clinical practice guidelines in patients with cardiovascular disease and comorbid conditions

Guideline (ref id)	AHA/ACC/HHS Strategies to enhance application of clinical practice guidelines in patients with cardiovascular disease and comorbid conditions						
Aim	To identify core principles for CPGs (clinical practice guidelines) in the effective management of people with multiple chronic conditions and related actions that might be taken by developers of CPGs						
Population	US patients with cardiovascular disease and co-morbid conditions						
Setting	USA, community						
Themes with recommendations	Theme in guideline	Recommendation(s)					
	Need for research	There is a need for external validation of clinical and drug approval trials to ensure that people with multiple comorbid conditions are not excluded unnecessarily.					
		The use of electronic health records and clinical registries can allow for longitudinal evaluation of the management strategies and clinical outcomes of patients with multimorbidity.					
		Comorbidity data for selected CPG conditions to outline the most common combinations should be developed to inform further CPG research.					
	Guideline development	Organisations that develop CPGs must now consider comorbidities in the development process.					
		Involving patients in the CPG development process is critically important to fully appreciate patient perspectives, this becomes even more important when dealing with MM.					
		In light of the paucity of evidence around MM, CPGs need to be nuanced to account for clinical judgement and acknowledge the role of individualised, patient-centred decision making in implementation.					
CPGs should explicitly discuss the applicability and quality of recommendations for the most frequent combinations of comorbidities that accompany the named condition.							
Limitations	No search for evidence was conducted, panel discussion by physicians only without any other disciplinary input.						
AGREE II score	Scope and purpose:56%	Stakeholder involvement: 33%	Rigour of development: 7%	Clarity of presentation: 42%	Applicability: 8%	Editorial independence: 67%	Overall assessment: 2

Guideline (ref id)	AHA/ACC/HHS Strategies to enhance application of clinical practice guidelines in patients with cardiovascular disease and comorbid conditions
Applicability of evidence	Moderate, specifically about patients with comorbid conditions but only those patients with cardiovascular disease.

Table 27: The Ariadne principles: how to handle multimorbidity in primary care consultations

Guideline (ref id)	The Ariadne principles: how to handle multimorbidity in primary care consultations	
Aim	To develop a set of principles for handling multimorbidity in primary care consultations	
Population	Patients with multimorbidity	
Setting	Global, primary care consultations	
Themes with recommendation s	Theme in guideline	Recommendation(s)
	Interaction assessments	In contrast to single disease patients, interactions rather than single diseases need assessment. These include drug-drug, drug-disease and disease-disease interactions.
		Complex medication regimens should trigger awareness of increased risk of reduced adherence.
		It is important to keep a list of all individual diagnoses and to assess impact on quality of life and functioning.
		Medication should be reviewed regularly.
		A list of other physicians and therapists should be kept and updated regularly.
		Active monitoring for signs and symptoms of psychological disorders, cognitive dysfunction and deleterious social circumstances that may influence care seeking, is vital.
		Patients' social participation, functional autonomy, coping strategies and health seeking behaviour should be elicited and considered.
	Prioritisation & patient preferences	Healthcare decisions need to be made on a background of the patient's values and preferences, these should be thoroughly elucidated and treatment goals agreed upon as a consequence. Patients may prioritise desired outcomes <u>or</u> the avoidance of negative outcomes.
		Family physicians should be aware of their own potentially differing preferences.
		Patient's prognosis should always be taken into consideration.
		Treatment goals should be defined in terms of time, this clarification will support monitoring and re-discussing priorities at appropriate time points.
	Individualised	We (clinicians) should generally be more conservative when introducing additional treatments, while at the same time

Guideline (ref id)	The Ariadne principles: how to handle multimorbidity in primary care consultations						
	management	remaining aware of the risk of under-treatment.					
		We (clinicians) should anticipate unintended consequences of new treatment both prior to starting the treatment and during follow up.					
		It is important to be aware of the existence of simple solutions to aid patients with complex medications.					
		Appointments should be prioritised by applying a minimally disruptive approach to meeting agreed treatment goals.					
		It is important the patient has a family physician in charge of his or her overall health process.					
Limitations	No evidence search conducted but involves a well detailed semiformal consensus approach with many opportunities for feedback from primary care physicians.						
AGREE II score	Scope and purpose: 67%	Stakeholder involvement: 56%	Rigour of development: 48%	Clarity of presentation: 75%	Applicability: 38%	Editorial independence: 67%	Overall assessment: 5
Applicability of evidence	High, multimorbidity of all ages covered here, specifically in primary care consultations.						

Table 28: Patient experience in adult NHS services: improving the experience of care for people using adult NHS services

Guideline (ref id)	Patient experience in adult NHS services: improving the experience of care for people using adult NHS services	
Aim	To provide the NHS with clear guidance on the components of a good patient experience	
Population	Patients using adult NHS services	
Setting	UK, NHS across all settings	
Themes with recommendations ^s	Theme in guideline	Recommendation(s)
	Knowing the patient as an individual	Ask the patient about and take into account any factors, such as their domestic, social and work situation and their previous experience of healthcare, that may impact on their health condition and/or affect their ability or willingness to engage with healthcare services and affect their ability to manage their own care and make decisions about self-management and lifestyle choices.
		Listen to and address any health beliefs, concerns and preferences that the patient has, and be aware that these affect how and whether they engage with treatment. Respect their views and offer support if needed to help them.
Individualised services	Adopt an individualised approach to healthcare services that is tailored to the patient's needs and circumstances, taking into account their ability to access services, personal preferences and coexisting conditions. Review the patient's needs and circumstances regularly.	

Guideline (ref id)	Patient experience in adult NHS services: improving the experience of care for people using adult NHS services						
	Hold discussions in a way that encourages the patient to express their personal needs and preferences for care, treatment, management and self-management. Allow adequate time so that discussions do not feel rushed.						
	Continuity of care and relationships		For patients who use a number of different services ensure effective co-ordination and prioritisation of care to minimise the impact on the patient.				
			Ensure clear and timely exchange of patient information between healthcare professionals and between healthcare and social care professionals.				
	Promote patient autonomy		Explore patient’s preferences about the level and type of information they want. Based on this, give the patient (and their family members and carers if appropriate) clear, consistent, evidence-based, tailored information throughout all stages of their care.				
	Discussing risks and benefits with a patient		Personalise risks and benefits as far as possible.				
			Use absolute risk rather than relative risk.				
			Use natural frequency rather than a percentage (for example, 10 in 100 not 10%).				
			Be consistent in the use of data (for example, 1 in 100 vs 10 in 100, not 1 in 100 vs 1 in 10).				
			Present a risk over a defined period of time.				
			Include both positive and negative framing.				
			Be aware that different people interpret terms such as rare, unusual and common in different ways, and use numerical data if available.				
			Think about using a mixture of numerical and pictorial formats.				
	Offer support to the patient when they are considering options. Use the principles of shared decision making, that the patient is aware of the options available, understands the risks, benefits and consequence of these, that the patient understands the information and encourage the patient to clarify what is important to them and check their choice is consistent with this.						
Limitations	Rigorous methodology,						
AGREE II score	Scope and purpose: 100%	Stakeholder involvement: 100%	Rigour of development: 94%	Clarity of presentation: 83%	Applicability: 67%	Editorial independence: 83%	Overall assessment: 6
Applicability of evidence	Moderate very wide-ranging guideline with some recommendations of particular relevance to multimorbidity						

Table 29: IOM and DHHS meeting on making clinical practice guidelines appropriate for patients with multiple chronic conditions

Guideline (ref id)	IOM and DHHS Meeting on Making Clinical Practice Guidelines Appropriate for Patients with Multiple Chronic Conditions						
Aim	To identify guiding principles for clinical guidelines in the effective management of multiple chronic conditions and identifying actions that should be taken by developers and users of guidelines for people with multiple chronic conditions						
Population	Patients with multiple chronic conditions						
Setting	USA, all settings						
Themes with recommendations	Theme in guideline	Recommendation(s)					
	Improving stakeholder process	Guideline development should harmonize co-morbidity related content across guidelines created by different groups.					
		Guideline development panels should include appropriate expert representation for conditions other than the index condition.					
	Strengthen substance and content	Guidelines should take into account factors associated with adherence as a function of the number and types of comorbid conditions in individual patients.					
		Guidelines should prompt clinicians to consider comorbidities in addition to the index condition.					
		Discussion of comorbidities should be integrated into guidelines rather than addressed in supplemental sections.					
		In addition to addressing what is known about relevant comorbidities, condition-specific guidelines should concisely summarise what key information is unknown.					
		Guidelines should call attention to and integrate, preventative measures across certain index conditions which may have implications for other conditions and modifiable risk factors.					
	Increase focus on patient-centeredness	Guidelines should address care co-ordination across providers and settings.					
		Guidelines should be patient-centred rather than focused solely on the management of specific conditions.					
Because of the complexity of management plans for persons with multiple chronic conditions, the application of guidelines should take into account the need for and importance of shared decision making.							
Limitations	Representation on their panel lacking patient groups, clinicians and other HEALTHCARE PROFESSIONALSs – composed of Department of Health employees, guideline organisations and “academics”. No search for evidence.						
AGREE II score	Scope and purpose: 78%	Stakeholder involvement: 56%	Rigour of development: 7%	Clarity of presentation: 75%	Applicability: 12.5%	Editorial independence: 17%	Overall assessment: 3
Applicability of	High, applicable to care of all patients with multimorbidity, about specific subset of care in the generation of guidelines and their use in these						

Guideline (ref id)	IOM and DHHS Meeting on Making Clinical Practice Guidelines Appropriate for Patients with Multiple Chronic Conditions
evidence	patients.

Table 30: Medicines Optimisation

Guideline (ref id)	Medicines Optimisation	
Aim	To review the evidence available to support health and social care practitioners, and health and social care organisations, in considering the systems and processes required to ensure safe and effective medicines optimisation.	
Population	All adults in the NHS	
Setting	NHS, UK	
Themes with recommendations	Theme in guideline	Recommendation(s)
	Identifying incidents	Consider using a screening tool (for example, STOPP/START) to identify potential medicines related patient safety incidents in some patient groups, including those with polypharmacy or chronic conditions.
	Medicines-related communication systems for transitions	Organisations should ensure that robust and transparent processes are in place so that when a person is transferred to another setting complete and accurate information about medicines is shared, received, document and acted on.
		Organisations should ensure that information about medicines is shared with the person and their GP; they should identify when local systems are in place for this and take account of HSCIC’s guide to confidentiality.
		Organisations should consider additional support for some patient groups (including those with polypharmacy or chronic conditions) when they have been discharged from hospital, for example, pharmacist counselling, telephone follow up, GP and or nurse home visits.
	Medication review	Determine locally the most appropriate health professional to carry out a medication review, based on their knowledge and skills, including technical knowledge of medicine managing processes, therapeutic knowledge and effective communication skills.
During a medication review, take into account the person’s understanding about their medicines, their concerns about their medicines, all over the counter and complementary medicines, how safe & effective their medicines are and any monitoring tests that are needed.		
	Self-management plans	When discussing medicines with people who have chronic or long-term conditions, consider using an individualised self-management plan to support people who want to be involved in managing their medicines.
	Patient decision aids	Offer all people the opportunity to be involved in making decisions about their medicines. Find out what level of involvement in decision-making the person would like and avoid making assumptions about this.
		Find out about a patient’s values and preferences by discussing what is important to them about managing their conditions and their medicines. Recognise that the patient’s values and preferences may be different from those of the

Guideline (ref id)	Medicines Optimisation						
	health professional and avoid making assumptions about them.						
	Apply the principles of evidence based medicine when discussing the available treatment options with a person in a consultation about medicines. Use the best available evidence carefully when making decisions together with clinical expertise and the patients' values and preferences.						
	In a consultation about medicines, offer the person the opportunity to use a patient decision aid (when 1 is available) to help them make a preference-sensitive decision that involves trade-offs between benefits and risks. Ensure the patient aid is appropriate in the context of the consultation as a whole.						
	Do not use a patient decision aid (PDA) to replace discussions with a person in a consultation about medicine.						
	Recognise that it may be appropriate to have more than 1 consultation to ensure that a person can make an informed decision about their medicines. Give people the opportunity to review their decision as appropriate.						
	Ensure that PDAs have followed a robust and transparent development process, in line with IPDAS criteria.						
	Before using a PDA, read and understand its content paying particular attention to its limitations and the need to adjust discussions according to the patient's baseline risk.						
	Have the necessary skills and knowledge when using a PDA including clinical knowledge, communication skills, numeracy skills, ability to explain the trade-off between benefits and risks.						
	Consider training and education to support healthcare professionals and patients in developing the skills to use PDAs.						
Limitations	Well documented NICE methodology, full process available online						
AGREE II score	Scope and purpose: 78%	Stakeholder involvement: 100%	Rigour of development: 96%	Clarity of presentation: 75%	Applicability: 63%	Editorial independence: 83%	Overall assessment: 6
Applicability of evidence	Low, wide-ranging guideline with some subsets more relevant to patients with multimorbidity than the general population						

Table 31: Depression in adults with chronic physical health problems

Guideline (ref id)	Depression in adults with a chronic physical health problem	
Aim	The guideline makes recommendations for the treatment and management of depression in adults with a chronic physical health problem.	
Population	Patients with depression and a chronic physical health problem	
Setting	UK, NHS, all care levels	
Themes with	Theme in guideline	Recommendation(s)

Guideline (ref id)	Depression in adults with a chronic physical health problem						
recommendations	Principles of assessment		When assessing a patient with a chronic physical health problem who may have depression, conduct a comprehensive assessment that does not rely simply on a symptom count. Take into account both the degree of functional impairment.				
			When providing interventions for patients with a learning disability or acquired cognitive impairment who have a chronic physical health problem and a diagnosis of depression provide the same interventions as for other people with depression where possible but if necessary adjust the method of delivery or duration of the intervention to take account of the disability or impairment.				
	Effective delivery of care for depression		If a patient's chronic health problem restricts their ability to engage with a preferred psychosocial or psychological treatment for depression consider alternatives in discussion with the patient, such as antidepressants or delivery of psychosocial or psychological interventions by telephone if mobility or other difficulties prevent face to face contact.				
			When an antidepressant is to be prescribed for a patient with depression and a chronic physical health problem, take into account the presence of additional physical health disorders, the side effects of the antidepressants which may impact on the physical health disorders, that there is no evidence supporting the use of specific antidepressants for patients with particular physical health problems and interactions with other medicines.				
	Collaborative care		Consider collaborative care for patients with moderate to severe depression and a chronic physical health problem with associated functional impairment whose depression has not responded to initial high-intensity psychological interventions, pharmacological treatment or a combination of psychological and pharmacological interventions.				
			Collaborative care should normally include supervised case management with support from a senior mental health professional, close collaboration between primary and secondary physical health services and specialist mental health services, a range of interventions consistent with latest guidelines and long term co-ordination of care and follow-up.				
Limitations	Well documented NICE methodology, full process available online						
AGREE II score	Scope and purpose: 94%	Stakeholder involvement: 100%	Rigour of development: 90%	Clarity of presentation: 78%	Applicability: 75%	Editorial independence: 42%	Overall assessment: 5
Applicability of evidence	Moderate, specifically about patients who have multimorbidity but much defined subset of depression + chronic physical health problem.						

H.1.2 Barriers of care

Table 32: Allen 2015

Study (ref id)	Allen 2015 ³⁴
Aim	To better understand how patients with multimorbidity who receive care in institutions designed for treatment of acute illness experience and engage in health-related decisions
Population	n= 17 (patients and health professionals) Patients (n=6): ESRD and comorbid condition Health professionals (n=11): medical specialists, nurses, social worker (n=1), dietician (n=1)
Setting	Canada
Study design	44 interviews (25 with patients, 19 with health professionals); 2 focus groups (with physician, nurse, social worker, dietician); ethnographic study
Methods and analysis	Identified 6 co-morbid end stage renal disease patients who represented a wide range of ages, illness histories, and experience with haemodialysis. Data analysis occurred concurrent with and again after data collection. Post data-collection analysis was first conducted thematically within cases and then again across cases. A third level of analysis drew specifically on the interviews with health professionals and the field logs to provide a clear picture of the haemodialysis unit and the broader health care system of the hospital.
Themes with findings	<p>Patient decision making – embedded in uncertainty</p> <ul style="list-style-type: none"> Participants felt that the decision making for people with multimorbidity was a balance between a present known quality of life and an uncertain 1 in the future. Decision-making for this population is often about running the risk that decisions involving sacrifices to current quality-of-life will not pay off in one’s future quality-of-life. <p>Patient decision making – relational</p> <ul style="list-style-type: none"> Participants cited support from family, friends and health professionals in decision making <p>Systematic assumptions about and impact on decision making</p> <ul style="list-style-type: none"> Participants reported that specialists often only focused on 1 aspect of care Patients thought they had little support in making decisions about the complex interplay of their comorbidities Participants thought there was a lack of communication and coordination of care between health professionals Patients had a poor understanding about the complex interactions between their conditions
Limitations and applicability of evidence	<p>Very serious limitations</p> <ul style="list-style-type: none"> Researchers have not considered their own role, potential bias or influence during the design, data collection and analysis Research/design not rigorous - unclear how participants were selected

Study (ref id)	Allen 2015³⁴
	<ul style="list-style-type: none"> • Data collection not rigorous – unclear methods of data collection; unclear who collected data; unclear in what form data were collected; no discussion of data saturation • Data not rich

Table 33: Bardach 2012

Study (ref id)	Bardach 2012⁹³
Aim	To explore primary care physicians perspectives on prevention counseling among patients with multimorbidity
Population	<p>n=12 (primary care physicians)</p> <p>Primary care physicians Age range 31-57 years Family practice physicians n=6, internal medicine n=5, specialist in OB/GYN n=1</p> <p>Male/female ratio: 1:1</p>
Setting	Primary care, USA
Study design	Semi-structured interviews
Methods and analysis	<p>A purposive sample was used to obtain a diverse array of physicians—men and women from rural and urban practices, community and academic settings, and family and internal medicine specialties. Initial inclusion criteria: being a practicing internal medicine or family practice physician with a willingness to participate in the study. They subsequently included 1 physician in obstetrics-gynecology (OB/GYN), after initial interviews highlighted that for some women, their OB/GYN served as their primary care provider. Exclusion criteria: physicians who focused on pediatric populations. Potential participants were identified through a primary care physician email directory. Thirty potential participants were contacted via email and asked about their willingness to participate in an interview study about prevention practices among complex patients. Physicians who indicated a willingness to participate were re-contacted via email to schedule an interview session. Sixteen physicians never replied, 14 replied and were willing to participate, and 12 were scheduled and interviewed. The remaining 2 physicians who had indicated a willingness to participate were not interviewed because of scheduling difficulties and having already achieved saturation.</p> <p>Using the Theory of Triadic Influence, semi-structured questions were developed that encompassed a range of intrapersonal, interpersonal, and cultural/environmental factors related to physician prevention recommendations among patients with MM. Semi-structured interviews were conducted using the same questions in the same order. The first 3 interviews focused on colorectal cancer screening, after this the scope of the interview was expanded to include diet and physical activity. Interviews lasted approximately 1 hour and took place at a mutually agreeable location, usually the physician’s office.</p> <p>Interviews were audiotaped and then transcribed. Data were coded on completion of data collection. Coding was used to develop inductive</p>

Study (ref id)	Bardach 2012 ⁹³
	categories and emerging themes were identified. Resulting categories were compiled in a codebook. Discrepancies were discussed, codes clarified and the codebook modified as needed.
Themes with findings	<p>Relationship between disease management and prevention counselling</p> <ul style="list-style-type: none"> • Time constraints were the most frequently discussed systems factor influencing prevention recommendations • “Preventive care is also discussed once their chronic issues are on the right track.” [primary care physician] • “Number 1, triage them as far as create a hierarchy of what needs to be addressed first and foremost, what are the life-threatening immediately versus longer term preventative measures, and trying to find a healthy balance between the two.” [primary care physician] • “[prevention accounts for] 80% of my time, because it’s so important to people with chronic medical problems who already have established disease, preventing that from progressing.” • Physicians’ engagement in diet and physical activity counselling often did not match the high value they placed on this aspect of preventive care, due to time constraints and competing demands within the visit: “a lot of people can control a lot of their problems if they were just motivated to do these types of things. It’s unfortunate that I only spend a minute or two talking about these things with them.” [primary care physician]; “Not enough [time spent discussing prevention]. I mean, they’ve done the calculations right. If you did preventive care for every person, you’d be in the office 10 hours a day.” [primary care physician] • “Primary prevention, for another co-morbidity that we’re trying to think about in the mix of everything, that’s where it gets dropped because we just don’t have the time.” [primary care physician] <p>Complexity as constraint</p> <ul style="list-style-type: none"> • Some physicians hesitated to broach prevention issues given their desire not to overwhelm patients • “I think we make a lot of decisions based on what’s going to be simpler for the patient rather than what’s actually going to be better. Or we don’t and then we get a bad outcome when the patient can’t manage that... You can’t overwhelm them. Because their blood pressure is out of control and you have to give them another pill. If you start talking to them about a colonoscopy, it’s just too much” [primary care physician] • “I find it very hard to just be like, ‘you know, you’re overweight and I think we should work on it.’ Like I said, if there is a medical condition to tie it into, I’ll usually do that. And that is actually what prompts me to do it most of the time. It’s like, ‘yeah, I know your knees hurt, we’re going to work on this stuff, but I think you also, while we’re doing this, work on trying to lose a little bit of weight too.’ Like tie it in that way as part of the treatment plan.” [primary care physician] <p>Complexity as opportunity</p> <ul style="list-style-type: none"> • “If they have multiple issues, they can be more motivated [to take preventative action] because they know that it’ll affect every single health issue. And yet, when they have all these multiple issues they often have the pain issues that go along. You know, the arthritis and the disability secondary to their obesity or diabetes or something. So, it’s a catch 22” [primary care physician] • “Most patients with stable chronic conditions are very receptive to discussions of prevention because they do not want 1 more preventable condition to worry about and would like to improve their current condition. Those with uncontrolled conditions usually are not receptive to preventive discussions until the current condition is controlled.” [primary care physician]

Study (ref id)	Bardach 2012 ⁹³
	<p>Prevention counselling strategies</p> <ul style="list-style-type: none"> • Physicians also discussed the importance of tailoring prevention recommendations to a patient’s existing conditions: “Tailored to each patient’s individual needs is important, being able to have them see where their own weaknesses are, where they can improve. And oftentimes, have them offer those things, ‘what do you think is your biggest weakness with your diet?’” [primary care physician] • The establishment of a good relationship with patients was perceived to enhance patient trust and increase patient receptivity to prevention behaviors: “if they [the patients] trust you and that you’ve given them good advice and that you’ve listened to them, they are much more likely to take your advice.” [primary care physician]; “[trust is] a huge part of preventative health measures. And so that’s probably the biggest thing you’ve got to focus on, is just trying to connect with the patient. Then you can open up anything.” [primary care physician]; “Things that they won’t agree to now they’ll agree to after a year, after they trust you, that you are not going to force them to do something, but that you’ve treated them well and tried to listen to them over the year.” [primary care physician] • “I do personally have some discomfort in not wanting them to feel sort of overwhelmed in that first visit because it’s a lot of stuff to cover. So, when I bring it up, I would say, now it depends on the patient, but to an overweight or an obese patient, I would talk to them about the importance of losing weight either to make their current comorbidities better or to prevent comorbidities in the future.” [primary care physician] • “I won’t talk about it every time, because that is often too oppressive. Especially if there’s not any progress made and they say they’ve changed their diet. Generally if they say they’ve changed their diet in a positive way, there’s nothing like encouragement.” [primary care physician] <p>Perceived futility and benefit of prevention counselling</p> <ul style="list-style-type: none"> • Many physicians believed their patients lacked the resources needed to follow prevention recommendations: “What are the resources? What are my tools to fix this problem? They are extremely minimal. Facing a society where there is advertising everywhere, where many people live in places where they can’t access, where they can’t exercise safely. They don’t have the financial means to access exercise programs or really fresh fruits and vegetables. So I think that’s the reason that most of us don’t, not only time, but also this idea of futility.” [primary care physician] <p>System factors</p> <ul style="list-style-type: none"> • Absence of a centralised electronic medical record is a challenge to preventive care of patients • “You just don’t have enough time. You’re dealing with 5 or 6 things that are pressing to them and they want immediate responses for and so you don’t have as much time to tack on, ‘Do you need a colonoscopy? Or, do you need a PSA screen?’ Or some of the preventative health measures, and you say, well, ‘I’ll just postpone that to the next visit’, but what happens at the next visit is the exact same thing.” [primary care physician] • “If they come regularly, you are hoping that 1 of those times that don’t have much going on... If they are finally stable and they don’t have all those things that I’m needing to address or explain, then I’ll take that time to go over, kind of healthy stuff.” [primary care physician]
Limitations and applicability of	<p>Serious limitations</p> <ul style="list-style-type: none"> • Researchers have not considered their own role, potential bias or influence during the design, data collection and analysis

Study (ref id)	Bardach 2012⁹³
evidence	<ul style="list-style-type: none"> Data collection not rigorous – interview methods changed after first 3 interviews; unclear who conducted interviews

Table 34: Coventry 2014

Study (ref id)	Coventry 2014³⁰⁰
Aim	To evaluate patient and practitioner views about barriers to self-management in people with multimorbidity
Population	<p>n=40 (20 patients, 20 practitioners)</p> <p>Patients: Adults with multimorbidity (with 2 or more of 5 exemplar conditions: coronary heart disease, diabetes, osteoarthritis, chronic obstructive pulmonary disease).</p> <p>Practitioners: 16 GPs, 4 practice nurses</p>
Setting	Greater Manchester, England
Study design	1:1 semi-structured interviews
Methods and analysis	<p>Qualitative study nested within a larger qualitative study designed to explore predictors of self-management behaviour in patients with multimorbidity</p> <p>Patient recruitment: 516 (34%) responded to the invitation to complete the survey, of which 222 (43%) consented to be approached for interview. From this group 20 people were purposively sampled on socioeconomic deprivation (defined by the Index of Multiple Deprivation score), number and type of chronic conditions, age and gender.</p> <p>Practitioner recruitment: convenience sampling. 12 practitioners were initially recruited from 4 practices participating in the quantitative study, and a further 5 were recruited from 3 other practices where researchers had prior links. Attempts were made to interview subjects with varying characteristics of interest for example, deprivation status of practice area, role (that is, salaried GP, GP principal, practice nurse), number of years' experience</p> <p>Interviews were carried out by 1 of 2 authors. A topic guide covering main themes was used, which covered the following topics:</p> <p>Patient -</p> <ul style="list-style-type: none"> How does the patient define self-care/supported self-care, how do these differ, what is their understanding of these terms, how do they

Study (ref id)	Coventry 2014 ³⁰⁰
	<p>apply them</p> <ul style="list-style-type: none"> • Level of self-care, reliance on carers/professionals, confidence in maintaining self-care, social/emotional support, professional-patient relationship/patient-centeredness • Knowledge of local self-care support groups in your area or other resources such as on-line support groups? Yes - which ones, how referred (self/GP/other), feelings about it, how long attended. No - knowledge about resources, any referral by practice(GP/nurse), Why not tried= barriers (social, health, logistics), feeling 'ready', expectations • Disablement, financial constraints/costs, low level health literacy, logistical problems, persistent depressive symptoms, balance between illness and QoL • Any other issues not discussed, positive summary of the info they have given <p>Practitioner -</p> <ul style="list-style-type: none"> • Multimorbidity- outcome for patient health, diagnosis, role of depression/low mood, prioritising conditions, understanding of antagonism between conditions • How do they define self-care/supported self-care, how do these differ, what is their understanding of these terms, how do they apply them in practice • Promotion of self-care, active promotion, use of care plans, responses from patients, confidence and ability in this process • Promotion of supported self-care, awareness of CDSMP, for example EPP, active promotion, worth of such programmes, patients responses to suggestions (positive/negative, resistance) • Perceived/reported barriers to supported self-care programmes (Disablement, financial constraints, low level health literacy, logistical problems, persistent depressive symptoms, balance between illness and QoL), suitability of specific programmes for multimorbid conditions • For patients who do attend self-care services - motivations, benefit to patient/practice, impact on management of conditions/health/QoL, initial barriers- How were barriers overcome • Any other issues not discussed, summary of the info they have given <p>Patient interviews were conducted at their homes and practitioners were conducted at locations according to their preference. The average length of interview was 38 minutes (range 10-72). All interviews were digitally recorded with consent and transcribed verbatim.</p> <p>Interviews were analysed to explore a priori and emergent themes using an approach informed by Framework. Five key steps were followed: 1) familiarisation – the transcripts were read thoroughly by all researchers to identify key themes; 2) a preliminary thematic framework was constructed using the interview schedules to structure the early themes. 3) indexing – themes and emerging sub themes were labelled and indexed; 4) charting – each framework was converted into a series of thematic charts; 5) mapping and interpretation – the key characteristics across all the data were mapped and interpreted. Disconfirming evidence and deviant cases were sought throughout the analysis. Analysis was</p>

Study (ref id)	Coventry 2014 ³⁰⁰
	<p>carried out by 4 researchers from different backgrounds (general practice, health services research and health psychology) to increase trustworthiness of analysis. Each transcript was analysed individually and then in groups, with the healthcare professional transcripts analysed separately from the patient transcripts but with comparisons made across data sets. In doing so this qualitative study drew on the concept of investigator triangulation by sharing data collection and data analysis between researchers drawn from different disciplinary backgrounds, again increasing trustworthiness of the analysis.</p>
Themes with findings	<p>Capacity – included capacity external to the patient (access to social and economic infrastructure and time to support patient’s management of their conditions), their capacity in terms of know-how and confidence to accomplish complex self-care practices; and physical and emotional capacity to focus on self-management</p> <ul style="list-style-type: none"> • Practitioners focused on the fact that many patient with multiple health problems often expended a great deal of energy and time coping with day-to-day routines associated with living with illness, leaving them with little spare capacity to devote to more complex self-management tasks: “I speculate that with several conditions people are too busy just trying to survive. [Their day is spent] getting up in the morning out of bed (if they can), having a plateful, almost a meal full, of tablets every day, and just about coping on the edge of everyday life.” (GP principal, deprived area) • Practitioners also cited physiological barriers, generated from competing physical conditions: For example, practitioners knew of patients with combinations of illnesses or levels of physical incapacity that precluded self-management tasks that involved lifestyle changes such as exercise: “Somebody with diabetes... you encourage them to exercise, [but] maybe if they’ve got a respiratory condition, it stops them from doing that. So sometimes your advice conflicts, you know, when you’ve got multiple problems.”(Practice Nurse) • Some patients had greater interpretive capacity (that is, know-how or tacit knowledge) to spot opportunities to maximise the benefits of self-management for all their health problems: “in truth, a lot of the things are similar for both... exercise is good for my heart and it’s good for my diabetes, and paced exercise is good for the late effects of polio, improving your diet; it’s good for all conditions, really.” (patient) • Structural factors, such as access to transport or financial resources, were considered by patients as providing important and tangible ingredients in generating capacity to self-manage. Additionally, many patients spoke about how their capacity to cope with their multiple health problems was sustained through the perceived social and emotional support provided by their family (who often acted as informal carers), friends, and sometimes community and religious groups. • Practitioners also placed a high value on patients’ being able to mobilise a network of support to help them in managing their health problems. Social isolation was seen to reduce patients’ capacity to engage in self-management activities outside the home, often because they had no family nearby or poor access to social networks that might support them to learn about self-management: “I think if there’s social isolation that can be quite a big problem. So social isolation where they can’t get out, where they can’t use ordinary channels of communication... They’ve no relatives, no friends, and they’re just stuck at home.” (GP principal) • Practitioners suggested that poor access to material resources further eroded patients’ capacity to engage in self-management tasks. This was especially true for patients who lived in more socio-economically deprived areas. Patients who lived in more deprived areas were not only less likely to have fewer financial resources but also had limited access to public or private transport, leading to poorer up take of

Study (ref id)	Coventry 2014 ³⁰⁰
	<p>self-management options such as support groups: “Obviously, with low socioeconomic background.....you may not have the facilities...to do certain things; self-care depends, in some part on..., things like access to telephones, access to internet, being able to go to some of these classes by public transport, and...some patients may not have that.” (5 years qualified: GP trainee, deprived area)</p> <ul style="list-style-type: none"> Some patients from deprived backgrounds articulated how lack of financial resources dented their emotional capacity to invest in learning about and doing self-management. For these patients, especially those who relied on benefit payments, daily anxieties about money meant that their time and energy was spent on making ends meet, not seeking out opportunities to enhance self-management practices: “They’re only giving me £14 a week to live on. Out of that £14 I’ve got to pay £17 a week for water and heating. That’s another thing that does your head in because how are you supposed to live...? It’s playing on your mind all the time.” (patient, deprived area) By comparison patients with greater financial resources acknowledged that their relative affluence enhanced their emotional as well as structural capacity to devote to caring for themselves <p>Responsibility - centred on patients’ and practitioners’ attitudes about the division of labour associated with patients’ management of their care and medical management in multimorbidity, and how these attitudes were partly contingent on capacity</p> <ul style="list-style-type: none"> Practitioners believed that patients should take charge of all tasks associated with healthy lifestyles and medicines management: <i>“if the patient was at home, maybe, eating unhealthy food, not taking their medications and there’s little [I can do]...I can’t go in and, you know, do that for them, so, I think, people need to take more responsibility for their own conditions.”</i> (GP principal). However, practitioners were not inclined to believe that patients with multimorbidity should be less or more responsible for their health than patients with single long term conditions. Practitioners noted that all patients, regardless of the number of illnesses, have a responsibility to maintain their health, but the degree to which this was true might vary dependent on patients’ capacity, especially their interpretive capacity to process and understand complex advice about self-management tasks Practitioners noted that patients in deprived areas displayed lower capacity/levels of responsibility towards self-management and were thus more reliant on their support, entrusting their care instead to formal health care providers: <i>“I would probably say the patients here with chronic conditions probably expect doctors to fix it rather than taking care of themselves. They’re very dependent on GPs and doctors, I don’t know why. Maybe again, because it’s a deprived area.”</i> (salaried GP, deprived area) From more deprived areas commonly relied on a narrative that suggested that responsibility for health lay firmly with medical professionals. However, in doing so, some patients also alluded to the notion that responsibility for self-management might also equate to, or at least include, compliance with health professionals’ advice. <p>Motivation - drew on understandings that successful self-management was partly contingent on patients’ belief and expectation that self-management would improve their health, and how low mood can negatively influence patients’ capacity and sense of responsibility for self-management</p> <ul style="list-style-type: none"> Practitioners identified depression as being a common occurrence in patients with multiple health problems and recognised this as a

Study (ref id)	Coventry 2014 ³⁰⁰
	<p>barrier to adopting health-related lifestyle changes: <i>“if you have someone who has got COPD and is depressed then obviously I think tackling depression will be my first priority because that will help me to motivate the patient, maybe to adapt their diet, or stop [them] smoking rather than just ignore it or not tackle it.”</i> (salaried GP, deprived area)</p> <ul style="list-style-type: none"> • Patients concurred with practitioners that depression was an obstacle to self-management. Even where patients had expressed a commitment to adopt healthier lifestyles they recognised that depression could confound their desire to enact such self-management plans: <i>“as you get older like I want to be fitter in myself and then... these little conditions, they stop you doing things, and then your motivation, if you’re feeling down and you’re depressed, then your motivation’s not there.”</i> (patient, deprived area) • Practitioners also highlighted that some patients, even in the absence of depression, were unlikely to feel motivated to attend support groups for people with multiple health problems: <i>“this extra thing [a self-management support programme] is like an added hassle that they don’t perceive as being of any benefit. I see it that it probably would be beneficial and there’s no proof until they’ve been, and they don’t go because they don’t see it as a priority... It’s not as likely to work as a big red tablet.”</i> (GP principal, deprived area) • practitioner noted socioeconomic deprivation as a factor that negatively impacted motivation among some patients: <i>“there’s other ones who don’t have much aspirations, who don’t work and they’re in chronic poor health and they feel there’s nothing they can do, they feel powerless, probably...[and] the thing is, they’ve got other things to worry about, maybe, paying their bills, poor housing... I think health must come way down the list for these people.”</i> (GP principal) • Practitioners working in deprived areas also noted that patients were heavily influenced by their environment in which poor health and indeed poor life expectancy was an accepted feature of life. In this sense patients from more deprived areas were socialised into expecting ill health and consequently felt less motivated to improve their health by adopting health protective behaviours: <i>“sometimes people almost see it as normal, because they are surrounded by other people that are ill and neighbours that are ill and so I don’t think that necessarily they would look at themselves as being that unusual for the area.”</i> (GP principal, deprived area)
Limitations and applicability of evidence	<p>No serious limitations</p> <ul style="list-style-type: none"> • Researchers do not discuss reaching data saturation

Table 35: Cowie 2009

Study (ref id)	Cowie 2009 ³⁰⁴
Aim	To examine patients' experiences of continuity of care in the context of different long-term conditions and models of care, and to explore

Study (ref id)	Cowie 2009 ³⁰⁴
	implications for the future organisation care of long-term conditions
Population	<p>n=33 (patients)</p> <p>Adults (median age 67; range 42-83), 90.9% with multimorbidity Male/female ratio: 17:16</p> <p>Chronic conditions: arthritis (24.2%), coronary heart disease (18.2%), stroke (27.3), hypercholesterolaemia (21.2%), hypertension (54.5%), diabetes mellitus (36.4%), chronic obstructive pulmonary disease (30.3%); asthma 24.2%)</p>
Setting	Primary care, England
Study design	Semi-structured interviews
Methods and analysis	<p>Patients were recruited from 7 general practices of varying sizes in south London (2 to 11 GPs). Patients were recruited if they were being managed for 1 of 7 conditions: arthritis, coronary heart disease, stroke, hypercholesterolaemia, hypertension, diabetes mellitus or chronic obstructive pulmonary disease (COPD). Lists of patients with 1 or more of the target conditions were compiled. Each list provided a frame from which a purposive sample according to age and sex was selected in order to obtain a diverse range of patients to be invited for interview. Patient invitation letters (containing an information sheet) were sent from participating practices in order to ensure confidentiality.</p> <p>Semi-structured interviews were conducted in patients' homes by 1 researcher using a topic guide partly informed by concepts of continuity of care derived from the Freeman model. Topics included the history of the patient's condition(s), previous and current care, expectations and preferences relating to each type of care experienced, and experiences concerning informational, communicational, relational and management issues. Interviews were audio-taped and transcribed verbatim.</p> <p>Analysis was conducted through the initial identification of themes within and across different illness categories. Significant patient experiences were identified and coded using NVivo7 software. These were sorted into larger categories of experience, which could then be analysed in relation to various proposed dimensions of continuity.</p>
Themes with findings	<p>Longitudinal and relationship continuity</p> <ul style="list-style-type: none"> • Relationship continuity is valued by patients because it facilitates the establishment of a shared personal and clinical history between 2 individuals, rather than each visit constituting an unconnected encounter between relative strangers: "If like there's certain things that I need to discuss with that particular doctor, like my doctor, Dr B, I said 'No, I will have to try again' because nobody else can deal with it apart from him, you see. But if it's nothing [I'm] really too fussed about I'd say alright then I will have Dr whoever is available" [patient] • "it's a very busy practice ... it's very difficult to get an appointment with him because he's the more popular one ... so I have to settle for one of the other ones." [patient] • "when I got through eventually this morning, I wasn't able to see my own doctor but I didn't want to see anybody else ... I asked if it would be possible to make an appointment for Monday, [but] no he's going on 2 weeks leave after today." [patient] • "I'd like to see him [same doctor] because ... he sees thousands of people, but from your point of view, you've only seen the 1 consultant and that makes a difference to your mind, I think, rather than anything else." [patient] • Concerns such as whether or not the GP treats the patient as a whole person, shows an ability to listen, is sympathetic or takes time to

Study (ref id)	Cowie 2009 ³⁰⁴
	<p>explain things in a kind manner, were common regardless of the degree of longitudinal continuity experienced</p> <ul style="list-style-type: none"> • “I've only phoned a few times, but they do seem to have a problem with you being sick on the day, you have to sort of make an appointment to be sick ... sort of come back 2 or 3 days later and tell them you're sick.” [patient] • “When you ring up and say the appointment is not the right time; it's too early, too late and they change it for you but you're scared then they are going to move it on a long way ... you might have to wait 6 weeks so you say ‘Oh no, you'd better not change it’.” [patient] • Participants reported that it was difficult to address all of their health needs in a single appointment: “I remember one time I went there and I had 3 different problems and they said no sorry, we can only deal with at least two, you need to go and make another appointment and come back ... I was really annoyed ... I understand that there's other people waiting but they could at least hear me out because I'm not pretending, I've gone there with a serious problem.” [patient]
	<p>Management continuity between organisations</p> <ul style="list-style-type: none"> • Participants expressed concern about coordination of care across organisational boundaries • Patients often experienced delays due to miscommunication between sites • “They never sent for me or anything. And the doctor [GP] was concerned that I wasn't having, I had no medication. He said they should have put you on medication all the time. I said no, I was never on medication.” [patient, after heart surgery] • “I'm due for an operation, and the doctor said [that] to me 2 months ago ... I said ‘Well, what happens then, will I get an appointment off you?’ He said, ‘Oh no, the next person you'll hear from is the surgeon’. Now I haven't heard a word.” [patient]
	<p>Management continuity between professionals</p> <ul style="list-style-type: none"> • “... they are still getting no results ... [the consultant] wanted to prescribe me these 2 types of tablets for the heart problem ... But because of the renal problems that I had he couldn't prescribe me one of the tablets until he got the results of the blood tests. So he phoned up my GP surgery for the blood tests, they didn't have it ... Anyway, I had to wait then, they done blood tests on me at [the hospital] that day but he had to wait then a week to get the results of the blood tests back and then contact my GP for him to prescribe me the other type of tablets he wanted me on ... and I was up then the end of January for the renal clinic again and they hadn't got it again.” [patient] • “... when I had the accident and they got my records through ... they didn't have it [allergic to penicillin] down” [patient]
	<p>Management continuity: sharing information with patients</p> <ul style="list-style-type: none"> • Patients commonly referred to the necessity of receiving appropriate information, especially in terms of the routine communications that are intended to inform them of future appointments and what is required of them. • “When they write to you from the hospital, they'll write to you and say ‘You've got an appointment at so and so’, but if you've got a couple of things wrong with you at the same time, they don't actually specify. I know at one point I went up to [the hospital] and I had 2 things wrong with me, I had haemorrhoids and I had arthritis, and I thought I was going to an arthritic clinic ... but it wasn't, so I was quite surprised by the examination!” [patient] • “At [the hospital] recently I went up for a scan on my tummy, and ... he said ‘It's funny, we can see in one end but not the other’, and I said ‘Well, I've got a stent in there’. He said ‘No you haven't’. I said ‘I have’ ... And he said ‘Well, it's not on our records’ ... Anyhow, I was looking through yesterday and I have got a stent in there because I've got the records here.” [patient]

Study (ref id)	Cowie 2009³⁰⁴
Limitations and applicability of evidence	<p>No serious limitations</p> <ul style="list-style-type: none"> • Researchers have not considered their own role, potential bias or influence during the design, data collection and analysis • Researchers do not discuss reaching data saturation

Table 36: Fried 2008

Study (ref id)	Fried 2008⁴⁵⁴
Aim	To examine the ways in which older persons with multiple conditions think about potentially competing outcomes, in order to gain insight into how processes to elicit values regarding these outcomes can be grounded in the patient's perspective
Population	<p>n=66 (patients)</p> <p>Older adults (aged 65 years or older) with multimorbidity (median 5 chronic conditions; range 3-8)</p> <p>Community-dwelling</p> <p>Male/female ratio: 33:67</p>
Setting	Community-dwelling, USA
Study design	13 Focus groups
Methods and analysis	<p>Participants were recruited from sites selected to promote purposeful sampling by providing access to a population of older persons of diverse ethnic/racial, socioeconomic, and functional status (9 at senior centers, 3 at physicians' practices, and 1 at a congregate housing site).</p> <p>Eligibility was determined during a telephone screen. Inclusion criteria: aged ≥65 years; taking ≥5 medications; undergoing treatment for multiple conditions. Exclusion criteria: non-English speaking; severe hearing loss; cognitive impairment (inability to remember ≥ 2 items on a 3-item test of short-term recall)</p> <p>Focus groups consisted of 3-8 participants and were conducted at the site of recruitment. Focus groups were conducted by a single trained moderator using a discussion guide, which evolved over the course of the study to incorporate insights from the initial focus groups. The guide included the following: asking participants about their perceptions of whether their illnesses or treatment interacted with each other in any way; asking participants what they believed were the goals of their treatment, both from their own and their physicians' perspectives, whether they had any adverse effects from their treatments, and whether they had ever made a decision to change or stop a treatment. participants in later groups were asked in the final portion of the interview to consider how they would make a decision if faced with the following 2 scenarios: 1) they were having severe pain and the only effective medication treatment was associated with an increased risk of a heart attack, 2) the only available medication to decrease future risk of heart attack caused them fatigue and dizziness. At the end of the interview, participants were asked once</p>

Study (ref id)	Fried 2008⁴⁵⁴
	<p>again to think about the goals of their medical treatment.</p> <p>Focus groups were audiotaped and transcribed by an experienced medical transcriptionist. Using the constant comparative method, analysis of the transcripts took place simultaneously with data collection, so that issues arising in earlier focus groups could be explored in greater depth in later groups. Initially, small blocks of text were coded into discrete concepts using a coding scheme developed in an iterative process, in which 2 of the investigators each coded several interviews and met to review the scheme. These concepts were then compared within and across focus groups to organise them into larger themes. Sample size was determined by theoretical saturation; that is, focus groups were conducted until no new concepts emerged</p>
Themes with findings	<p>Recognition of competing outcomes</p> <ul style="list-style-type: none"> Participants discussed the adverse effects of medications as a competing outcome that influenced their treatment decision-making. Some participants were concerned that these effects were adverse outcomes of equal, if not greater importance, than the beneficial outcomes the medications could provide: “I have high cholesterol. I took something but... I had such pain in my calf, so I was taken off whatever that was. I think [my cholesterol] is 241, and I'm willing to live with that” [patient] <p>Shifting from disease-specific to global, cross-disease outcomes</p> <ul style="list-style-type: none"> “I have been trying to convince my doctor that I don't need the cholesterol medication any longer, because it has zapped me of my strength, and it is debilitating.” [patient] “If you don't feel good, you can't take care of yourself and you have to depend on somebody else, what's the good of living another 10 years?” [patient] “I never would like to take anything that would slow me down too much mentally.” [patient] “You will have a stroke or a heart attack from your blood pressure but you won't be dizzy when you die. I think it doesn't even bear asking. You have to be dizzy.” [patient] The consideration of symptoms, function, survival and quality of life outcomes facilitated participants' consideration of decision-making across different diagnoses: [how would you decide between treating your arthritis and heart disease, if therapy for one had the potential to make the other worse?] “I think I would go back to the thing that I fear most, being incapacitated and living, so I would choose whatever would prevent that.” [patient]
Limitations and applicability of evidence	<p>No serious limitations</p> <ul style="list-style-type: none"> Researchers have not considered their own role, potential bias or influence during the design, data collection and analysis Researchers do not discuss reaching data saturation

Table 37: Gill 2014

Study (ref id)	Gill 2014⁴⁸³
Aim	To explore the care challenges experienced by older patients with multimorbidity, their informal caregivers and family physicians

Study (ref id)	Gill 2014⁴⁸³
Population	<p>n=27 (patients, informal caregivers, physicians)</p> <p>Patients: older adults (aged 65 years or older; average 82.3±7.7 years) with multimorbidity; 56% male; diagnosed with median 5 conditions (SD=2.43)</p> <p>Carers: average 70.5±11.3 years; 79% female; 82% spousal caregivers</p>
Setting	Canada
Study design	Semi-structured interviews
Methods and analysis	<p>Two methods of patient recruitment were employed. Patients were first identified by the participating physicians during their team rounds from their patient rosters and using the study's inclusion criteria. If a patient had an upcoming clinic appointment, research associates were notified to attend the clinic to identify patients who might be interested in participating. After a patient's clinic visit, the primary care physician introduced the research study if the patient met the inclusion criteria, and was in good health to manage an interview. Inclusion criteria: 65 years of age or older, diagnosed with 2 or more chronic conditions, had an informal caregiver who participated in the patient's healthcare, spoke English as a first language and was able to provide informed consent. All members of the patient–caregiver–physician team had to agree to participate in order to be included in the study. If the primary care physician identified an eligible patient who was not being seen in clinic within the next month, administrative assistants phoned the patient at home, explained the research study and asked whether he or she would like to be contacted by a research associate to confirm his or her participation. The administrative assistants managed patient appointment scheduling and were considered a part of the clinical team.</p> <p>Two research associates conducted the study interviews, either at a research office at the academic health centre or the patient's home, depending upon the patient's preference and ease of transportation. Interviews were conducted in English and took approximately 1.5 hours to complete. The physician and caregiver interviews took approximately 30 minutes to complete as their interview guides were shorter than the patient version. Only the interviewer and interviewee were present during the interviews. All interviews were conducted separately to ensure confidentiality of responses. The research associate read from a script prior to asking the interview questions, which consisted of an introduction of herself, a description of the study objectives and details about the informed consent process. The research associates took notes during and after the interviews, which served as secondary information if questions arose during thematic coding of the transcripts. Given the short time period for the study, transcripts were not returned to participants for comment. Interviews were digitally recorded, transcribed verbatim by an external source and checked for accuracy by the 2 research associates.</p> <p>Qualitative description was used to generate general summaries and emerging themes from participant interviews. Themes were derived inductively from the data and not identified in advance. Furthermore, transparency of methods and conformability of themes were achieved by frequent meetings and discussion of the themes until consensus was reached among 3 of the authors. To ensure methodological rigour during data collection and analysis, the lead author consistently familiarized herself with the interview data by reading transcripts in their entirety for an initial</p>

Study (ref id)	Gill 2014 ⁴⁸³
	<p>understanding of key concepts and themes. An initial coding scheme was developed by the lead author and verified by the research associates after each researcher reviewed the first interview transcript in its entirety. Following that, data analysis was conducted simultaneously with data collection until saturation of themes occurred (that is, when themes became repetitive within each of the patient, caregiver and physician groups). After 14 patient–caregiver–physician triads were interviewed, data were reviewed to develop an initial coding scheme. A final coding scheme was then developed for all patient, caregiver and physician transcripts after 28 triads were interviewed, as no new themes emerged.</p>
Themes with findings	<p>Long wait times</p> <ul style="list-style-type: none"> • Patients experienced long waits for appointments (for example, for diagnostic testing), which complicated their ability to manage their illnesses: “I had to wait a long time for the MRI. Almost three-quarters of a year. Which I thought was excessive” [patient] • Caregivers were often balancing their caregiving duties with full-time employment. Thus, long wait times even after an appointment was scheduled were frustrating for caregivers • “Usually it's just the waiting and waiting and waiting for the next appointment or results. ... So, like, nothing is happening. Whether they're attempting to communicate or not.” [carer] • Caregivers noted that long waits also had a physical impact on patients: “She's 93, you know. So to go down and then sit in a waiting room for the doctor – but it's a morning out of your life or an afternoon out of your week, [and] that is very tiring for her.” [carer] <p>Poor communication</p> <ul style="list-style-type: none"> • Patients reported experiencing poor communication with health providers: “Well, I have frustrations if they don't follow up on tests. Because I think that if you go and have tests, ... someone should let you know if things are okay” [patient] • Patients also reported poor communication between health providers: “And I've always thought of a cardiologist as being a person who doesn't worry just about your heart pressures but also about the swelling in my feet. ... I just found out last fall that he thinks it's the problem of my family physician. ... Anyway, these silos are almost like people are hard-wired into them.” [patient] • Family physicians received little feedback from other healthcare providers involved in their patient's care and had to filter communication from multiple sources • Family physicians experienced delayed feedback from specialists: “Yes, thinking about her eyes, I actually don't think I get anything from her ophthalmologist. ... So I don't really know what's going on with her eyes and what's going on with her driving. And I have to rely on her [patient].” [physician] <p>Care management and adherence</p> <ul style="list-style-type: none"> • Patients experienced difficulties making decisions about their care, and were unsure how to prioritise and address competing health issues • Patients often feel alone when making decisions about their care: “So I put the plan together: ... I've got to do the carotid artery first. I've got to do whatever I can about my lungs. ... It was (specialist's name) that I said this to, and he said that he had a plan. But I never thought he had a plan” [patient] • Patients expressed uncertainty regarding their conditions, and were challenged to understand what was going on: “It's because I don't know what the answer is. I don't know what the problem is. And let's say that traditionally if there's a problem, I've always been geared to

Study (ref id)	Gill 2014 ⁴⁸³
	<p>try and find out what's wrong and take corrective action. That's how I've lasted 88 years." [patient]</p> <ul style="list-style-type: none"> • Informal caregivers reported that noncompliance often due to the patient's disease complexity and the difficulty of managing multimorbidity: "No, not the system because it's mostly around his lack of – I think it's from depression, his lack of willingness to do these things that might have helped him along the road. His attitude is very negative, and that's frustrating to deal with" [informal carer] • Carers at times felt helpless upon recognising that the situation was beyond their control: "Yes, there are some frustrations, but it's more to do with us knowing we can't achieve her goals 100%. Like she needs better pain control, but we can't find a drug that won't give her side effects that will achieve the pain control she needs. Right? So she is choosing to have less pain control so that she can avoid the side effects that she doesn't like... it's more the limitations of the medications that we currently have. That's my biggest frustration." [informal carer] • Caregivers were frustrated about (and felt pressured) making the appropriate decisions • Physicians frustrated about how to provide support to the patient and the caregiver when the situation extended beyond their clinical control • Physicians felt inability to prevent crises or acute exacerbations of the chronic disease • Physicians recognised that the patient's disease complexity was a barrier to complying with treatment recommendations • Physicians noted that often they were not able to diagnose conditions rapidly when these were confounded by other diseases

Study (ref id)	Gill 2014 ⁴⁸³
	<p>Lack of care coordination</p> <ul style="list-style-type: none"> • Patients reported poor coordination among providers when multiple medications had to be prescribed and various tests and procedures had to be coordinated: “I tried to get the system to put the 2 scans together because they were the bladder and the aneurism. I was trying to eliminate 2 scans and have one do the job of both. First of all, (specialist MD's name) wouldn't do it. He wouldn't return my call, even. And then when I got on the table, when I went to the room that morning to get the CT scan, they said that they couldn't do it because it hadn't been asked for” [patient] • Informal caregivers emphasised the need for a "point person" or single provider to manage the patient's care and to support communication and decision-making across the various specialties: “You want the expert in a given area to be addressing a certain thing. You want the person that is best trained in that area. And there's no question about that. But somehow you want them also to look at the other aspects. ... And that's hard to achieve because we do need the specialities.” [carer] • Caregivers recognised that family or specialist physicians did not always have up-to-date information, or were unaware of the patient's complete health history • Family physicians reported that when they have many specialist physicians to collaborate with, they are challenged by the number of tests that are ordered and are not always clear on the rationale behind the investigations • “I think with her, like I said, too many cooks in the kitchen is sort of my frustration with her. Sometimes I think we're all sort of – I feel this with the specialists. Like, the physiatrist orders another test and another thing and another. And for what purpose? You know, I find we do too many investigations without standing back and asking her, "What do you want?" ... But then it's hard when they go see the specialist who starts going on, and then I get kyboshed. And then off we go into some – I think we're doing some biological agent now, which is going to cause problems.” [physician]
Limitations and applicability of evidence	<p>Serious limitations</p> <ul style="list-style-type: none"> • Researchers have not considered their own role, potential bias or influence during the design, data collection and analysis • Researchers do not discuss reaching data saturation • Researchers do not provide an in-depth description of the analysis process

Table 38: Jowsey 2009

Study (ref id)	Jowsey 2009 ⁶⁶³
Aim	To identify the common challenges co-morbidity poses to patients and carers in their experiences of self-management; to detail the views and perceptions of health professionals about these challenges; and to discuss policy options to improve health care for people with co-morbid chronic illness
Population	<p>n=129 (52 patients; 12 carers, 63 health care professionals)</p> <p>Patients: adults (aged 45-85) with Type 2 diabetes, chronic obstructive pulmonary disease or chronic heart failure (index condition); 86.5% with multimorbidity. Common comorbidities included: arthritis, osteoporosis, asthma, and back pain. Male n=28 Carers: male n=1</p> <p>Patients and carers: over 65 years, n=42; BME n=23; experienced economic hardship n=42</p> <p>Health care professionals: RGN n=23, GPs n=15, specialists n=6, in addition to physiotherapists, care coordinators, managers, occupational therapists, podiatrists, psychologists and social workers. Female n=44</p>
Setting	Australia
Study design	Semi-structured interviews (patients and carers); focus groups (health professionals)
Methods and analysis	<p>Patients and carers were recruited through referrals from general practices, local hospitals, community health services, specialist clinics, health care consumer organisations, as well as Aboriginal health services located in the Australian Capital Territory (ACT) and western suburbs of Sydney in Australia. Inclusion criteria: patients aged between 45 and 85 with 1 or more of the 3 conditions of interest (DM, COPD and CHF), who at the time of interview were living in either the ACT or western Sydney. Exclusion criteria diagnosed cognitive impairment; family carers. Health care professionals who had specific experience in the management of the index conditions were recruited through Divisions of General Practice and Area Health Services to include hospital specialists, general practitioners, nurses and allied health professionals.</p> <p>Data collection and analysis were carried out by a group of 7 research workers with multidisciplinary backgrounds in health and social sciences, all of whom trained as a group in workshops and followed a data collection manual to ensure consistency in data collection and analysis. Data collection occurred between March 2007 and January 2008. Semi-structured in-depth interviews were conducted with patients and with carers; each interview running between 45 and 90 minutes. All health care professionals participated in 1-hour focus groups, with the exception of 2 healthcare professionals who were interviewed separately. The research team judged sufficient data had been gathered when interviews and focus groups were no longer providing new insights or ideas deemed central to the experience of patients and carers, indicating data saturation</p> <p>All interviews and focus groups were electronically recorded and transcribed verbatim. The data were analysed using qualitative content analysis,</p>

Study (ref id)	Jowsey 2009 ⁶⁶³
	<p>assisted by a computerised qualitative data analysis program, QSR NVivo7. A coding scheme was created during the data collection phase and used to facilitate consistent data analysis by 7 researchers across the 2 research sites. The coding scheme was refined by the collective researchers periodically throughout the data analysis and researchers regularly engaged in checking each other's interpretation accuracy of the data against the coding scheme.</p>
Themes with findings	<p>Capacity to act on risk factors</p> <ul style="list-style-type: none"> • For some patients co-morbid conditions such as arthritis delayed completion of rehabilitation programs or caused them to withdraw from the program: "There were people older than me [in the cardiac rehabilitation program] and I couldn't keep up with them because of my ankle" [patient] • Patients with comorbid depression found it difficult to maintain a healthy diet and exercise routine <p>Capacity to recognise signs and symptoms of distress</p> <ul style="list-style-type: none"> • "It is very hard for me to say whether it is my heart that I am short of breath with or asthma." [patient] • Patients indicated they learnt how to recognise signs and symptoms of exacerbation by applying information gained through various sources (written sources, conversations with health professionals, friends and family) to their personal experience in a process of trial and error. • Health care professionals reiterated the difficulty for patients in recognising signs and symptoms of co-morbid conditions, noting that this is a particular problem for patients with limited health knowledge. Healthcare professionals further explained that even when patients did correctly identify new symptoms they did not always know how to respond and so ended up in hospital or suffered unnecessarily at home. • Patients said they wanted more information that addresses the links between co-morbid conditions to facilitate management of their conditions <p>Capacity to manage medications</p> <ul style="list-style-type: none"> • Many patients demonstrated limited knowledge and understanding of their medications and were unable to differentiate between them: "Well I'm not too sure what they're for but I know they're either for diabetes or for me heart, or cholesterol, or high blood pressure" [patient]; "I have to do the medicines these days. ...I kept noticing she didn't know what to call the tablets and stuff and now she's got over 20 tablets [daily]" [carer about their patient] • Patients have insufficient knowledge about drug interactions and side-effects • Patients discussed the complex process of finding suitable medications to manage their conditions, noting that often this required good communication with health care professionals, which in turn was dependent on patient awareness of signs and symptoms associated with their numerous conditions • Patients, carers and healthcare professionals suggested that the capacity to manage medication could be improved through increased education, patient engagement and good communication between patients and their healthcare professionals. • Health professionals said that lack of awareness by healthcare professionals and patients concerning risks involved in using multiple

Study (ref id)	Jowsey 2009 ⁶⁶³
	<p>medication brand names could lead to patients unknowingly taking doses higher than prescribed, resulting in ill health, and that this could go unnoticed.</p> <ul style="list-style-type: none"> • Some patients did not follow medication recommendations because they did not like taking pills: "I'm on so many heart tablets and things like that, I didn't want to take any [more] medication, so I went for diet, and diet control." [patient] • Physicians said that patient honesty or recall/forgetfulness about which medications they were actually taking influences medication compliance • Several health care professionals indicated that medication management and non-compliance were particular problems with patients with mental illness • Financial constraints and the cost of filling scripts often caused patients with co-morbid conditions to skip medications they thought were less important than others: "They tend to pick and choose which... scripts they get filled, because they've got so many things going on at once... And the whole issue of medication management arises and it escalates their co-morbidity" [health professional]
Limitations and applicability of evidence	<p>Serious limitations</p> <ul style="list-style-type: none"> • Researchers have not considered their own role, potential bias or influence during the design, data collection and analysis • Data not rich

Table 39: Koch 2015

Study (ref id)	Koch 2015 ⁷⁰⁵
Aim	To conduct a systematic review of the literature on patient's perceptions of barriers and facilitators to managing multiple chronic conditions
Population	Adults (aged 18 years or older) with multimorbidity, n=426
Setting	England, Scotland, USA
Study design	Systematic review
Methods and analysis	<p>Cumulative Index of Nursing and Allied Health Literature (CINAHL), PubMed, and Scopus were searched from October 2012 through December 2012. No articles were excluded based on date of publication. Inclusion criteria were limited to peer-reviewed publications in English, adult's age 18 and above, studies that evaluated the burden of care from the patient's perspective and with a focus on patients with 2 or more chronic health conditions. Studies were excluded if they were focused on patient's age less than 18, single diseases, evaluation of specific interventions (for example, care management, guided care), providers or informal caregiver's perspective, and non-research based publications such as letters to the editor. 13 papers (12 studies) were identified.</p> <p>Data were analysed using content analysis to produce a descriptive summary of the content. Data analysis began with 1 investigator coding the data for individual themes within each article. Results were independently reviewed by a second investigator. Investigators then discussed the coding framework until consensus was reached. The 2 investigators then independently evaluated each article for barriers and facilitators, and</p>

Study (ref id)	Koch 2015 ⁷⁰⁵
	subthemes under each.
Themes with findings	<p>Financial resources (7 papers)</p> <ul style="list-style-type: none"> Patients reported financial resources to be a barrier to care for example, high cost of medications <p>Logistical challenges (7 papers)</p> <ul style="list-style-type: none"> Need to see multiple providers in multiple locations (n=1) challenges to scheduling and coordinating medications (n=1) inadequate transportation (n=2) Lack of time (n=2) <p>Physical limitations (7 papers):</p> <ul style="list-style-type: none"> For example, inability to exercise (n=1); pain (n=1); fatigue (n=1) <p>Lifestyle changes (5 papers):</p> <ul style="list-style-type: none"> symptoms affected participants' ability to work and work-related stress (n=1) inability to function routinely in their daily lives as individuals, as well as with family and friends (n=3) <p>Emotional impact (8 papers):</p> <ul style="list-style-type: none"> For example, depression (n=1); fear (n=2); "sense of giving up" (n=1) low self-efficacy and lack of control described as barriers to self-management <p>Informal support</p> <ul style="list-style-type: none"> Support of family and social relationships (For example, financial, emotional, informational, behavioural) served as motivators for many patients (7 papers) However some patients described lack family and social support as barriers to care management (n=5) for example, unwillingness to discuss their deteriorated health with others in an attempt to maintain identity and avoid negative labelling (n=1); reluctance to discuss health with family members (n=1) as family members less helpful or interfering, such as when the family member was financially unstable or discouraging to the patient's attempts to initiate or maintain healthy lifestyle choices. <p>Complexity of management of multiple conditions (10 papers)</p> <ul style="list-style-type: none"> For example, dealing with the escalating challenges of understanding a growing number of different clinical conditions while attempting to monitor combinations of different symptoms (n=5) For example, difficulties reporting symptom and functional status changes to multiple providers from different specialties (n=6) Patients mentioned lack of knowledge about their own health conditions <p>Complexity of medication management (5 papers):</p>

Study (ref id)	Koch 2015 ⁷⁰⁵
	<ul style="list-style-type: none"> • Lack of knowledge about medications and fear of combining medications as a barrier to adherence • complexity of medication regimens and burden of taking multiple medications at different times as a barrier to adherence • personal experience with negative side effects of medications as a barrier to adherence
	<p>Communicating with health care providers (9 papers):</p> <ul style="list-style-type: none"> • Patients reported that healthcare providers sometime had non-supportive attitudes toward the patient’s care management beliefs and abilities (n=1) • Patients reported receiving contradictory health care management information from multiple providers (n=1) • Patients reported not being able to obtain information and management strategies across conditions (n=1) • Patients discussed having disagreement between themselves and provider on the plan of care (n=1) • Patients reported physicians overlooking or ignoring concerns (n=1) • Patients discussed suspicion about physicians’ motivation for prescribing medication because of the relationship their doctor has with pharmaceutical companies (n=1) • Patients with cognitive impairment and hearing loss reported difficulty communicating with health care professionals when adjustments were not made for these comorbidities • Some patients also reported inadequate communication between multiple providers (n=2) for example, disagreement or lack of coordination between providers regarding diagnosis, medications, and diagnostic testing
	<p>Health system support (3 papers):</p> <ul style="list-style-type: none"> • access to an empathetic provider (n=2) • access to nurse practitioners • health care “team” approach • ability to use walk-in clinics when their personal providers were unavailable (n=1) • use of technology as a facilitator to communication between health care providers and participants (n=1)
	<p>Individualised care education and knowledge (4 papers):</p> <ul style="list-style-type: none"> • want focused health education tailored to them as individuals (n=4)
	<p>Personal mental and emotional strength (5 papers):</p> <ul style="list-style-type: none"> • commitment to self-discipline to achieve optimal health (n=2) • self-reliance (n=1) • active participation in one’s own health care decisions as giving a sense of empowerment (n=3) • faith in the ability to manage one’s own health was noted as an important aspect of care (n=2)

Study (ref id)	Koch 2015⁷⁰⁵
Limitations and applicability of evidence	<p>Very serious limitations</p> <ul style="list-style-type: none"> • Data not rich – sufficient data is not presented to support the finding, nor does the presented data illustrate the findings well. • Findings and conclusions not convincing – the findings are vague, unclear, and unsupported by data

Table 40: Schoenberg 2011

Study (ref id)	Schoenberg 2011¹⁰⁹¹
Aim	To improve understanding of how vulnerable rural residents experience and manage several simultaneously occurring chronic health conditions
Population	<p>n=20</p> <p>Adults (aged 41 years or older; mean age 55) with multimorbidity Average number of conditions: 4</p> <p>Heart disease or hypertension (90%) Arthritis (80%) Type 2 diabetes (75%) Cancer (10%) Stroke (10%)</p> <p>White 95% annual income less than \$10000 65% Unemployed 100% Rural</p> <p>Inclusion criteria: age 41 or over, diagnosis of 2 or more chronic illnesses; indicating having “just enough money to get by” or “not enough money to make ends meet”:</p>
Setting	USA
Study design	Interviews
Methods and analysis	Consecutive sampling. The interviewer visited the clinic, sat in the waiting room until a receptionist quickly reviewed the patient’s chart to determine eligibility and then asked permission of the patient to make an introduction to our interviewer. The interviewer then verified eligibility

Study (ref id)	Schoenberg 2011 ¹⁰⁹¹
	<p>via self-report, explained the study, and asked about a patient’s willingness to participate in an interview session. If the patient agreed, the interviewer would ask about a convenient time and location for the interview.</p> <p>Interviews were conducted in a private room. The interviewer then asked participants the open-ended and semi-structured questions on life and health history and MM, including self-management strategies. With the approval of the participants, all interviews were tape recorded. Interviews lasted 45–90 minutes, depending on the participant’s loquaciousness and fatigue level. On completion, participants were thanked and provided with a \$25 gift card.</p> <p>After each interview, the tape recorded sessions were subjected to professional transcription. Three members of the research team reviewed each transcript as soon as it was transcribed, independently engaged in line-by-line coding, and regularly met to ensure similar coding orientations and to discuss themes and patterns. We initiated line-by-line coding rather than culling themes according to the pre-established template of the interview questionnaire. We compiled a codebook, defining and adding new codes, as needed, to refine it and to determine consistency within the line-by-line coding. Differences among the codes were reviewed and discussed until a consensus was reached. Once the coding scheme and 13 drafts of the codebook were completed, 3 coders pursued additional line-by-line and axial coding and clustered codes into conceptual categories and themes</p>
Themes with findings	<p>Multifaceted challenges of multimorbidity</p> <ul style="list-style-type: none"> • Reported concerns about conditions affecting other conditions: “I know what complications you can get from it (diabetes). And it contributes to the heart disease and the arthritis and the high blood pressure...” [patient] • Some participants expressed concern that the treatment for 1 condition might be detrimental to another condition, especially in meeting dietary and medication requirements • Conflicting regimens, difficulty with recall, and the need for correct timing of numerous medications • “Well you have to keep up with what time you have to take this medicine and that medicine...and sometimes they react against each other...so you have to take them at different times.” [patient] • Depression impacting on ability to self-manage: “Sometimes I forget (my medicines) and I think, ‘well did I take that today?’ I have to sit and think if I took that or not and then you’re afraid to take it.” [patient] <p>Role of community</p> <ul style="list-style-type: none"> • Reported scarcity of personal resources for example, to purchase medication and inadequate transportation to healthcare appointments in relation to support from family and friends: “if you’re kin to me, you’re probably going to wind up helping me get somewhere, buy those pills, you know”
Limitations and applicability of evidence	<p>No serious limitations</p> <ul style="list-style-type: none"> • Researchers have not considered their own role, potential bias or influence during the design, data collection and analysis • Researchers do not discuss reaching data saturation

Table 41: Sinnott 2013

Study (ref id)	Sinnott 2013 ¹¹²⁴
Aim	To synthesise the existing published literature on the perceptions of general practitioners (GPs) or their equivalent on the clinical management of multimorbidity
Population	GPs, n=275
Setting	Belgium, England, Germany, Ireland, Scotland, The Netherlands, USA
Study design	Systematic review and meta-ethnographic synthesis
Methods and analysis	<p>EMBASE, MEDLINE, CINAHL, PsycInfo, Academic Search Complete, SocIndex, Social Science Full Text and digital theses/online libraries (database inception to September 2012) were searched to identify literature using qualitative methods (focus groups or interviews). Articles were excluded when, although they concerned patients with multiple chronic diseases, their exploration was focused on the management of an index disease</p> <p>The 7-step meta-ethnographic approach described by Noblit and Hare, which involves cross-interpretation between studies while preserving the context of the primary data. Included: <i>determining how the studies were related</i> to each other by comparing individual study findings; translation of the studies <i>into each other</i> by examining the contribution of each study to a key concept; synthesis of translations.</p> <p>10 papers were included (5 interviews, 5 focus groups)</p>
Themes with findings	<p>Disorganisation and fragmentation of healthcare</p> <ul style="list-style-type: none"> health systems lacked specific systems for treating patients with multimorbidity, lack of organisation hampered care by causing logistical difficulties and excess consultation demands on the patient and their GP Insufficient consultation time led to amended or suboptimal approaches (n=3), weighting consultation lengths to the complexity of multimorbidity would facilitate more effective management (n=2) <p>Inadequacy of guidelines and evidence-based medicine</p> <ul style="list-style-type: none"> Clinical guidelines are ‘generally written for sole conditions’ and do not account for ‘the unique circumstances of each patient’ (n=2) GPs used modified approaches to guidelines, involving, for example, the estimation of risk associated with particular diseases/treatments (n=2). However, some felt that this modification was in conflict with ‘best practice’ and felt guilty at not implementing guidelines fully (n=2) <p>Challenges in delivering patient-centred care</p> <ul style="list-style-type: none"> adopting a patient-centred approach was seen as a way of resolving the conflicts and uncertainty that can occur, particularly with co-implementation of multiple sets of guidelines (n=2) the longitudinal nature of the patient–GP relationship was seen as a ‘major facilitator’ and ‘elementary component’ of patient-centred care in multimorbidity (n=7)

Study (ref id)	Sinnott 2013 ¹¹²⁴
	<ul style="list-style-type: none"> • impact of treatment burden was an important consideration given the greater costs and risk of adverse drug events associated with the use of multiple medications (n=3)
	Barriers to shared decision-making <ul style="list-style-type: none"> • importance of eliciting patient's preferences was widely acknowledged, but GPs had difficulties doing this in practice (n=2) • for certain patients making choices could be a 'source of distress' and contributed to them becoming 'over the top anxious about their conditions' (n=1) • the risks and outcomes associated with treatment options in a way facilitated that patient involvement was particularly challenging, as was discussing the balance between quantity and quality of life (n=5) • Enhanced-communication skills were seen as necessary in multimorbidity to facilitate clear and concise discussion with patients on the interplay between their chronic diseases and to help with de-prescribing medications, which if carried out badly could be interpreted as withdrawing care (n=3)
Limitations and applicability of evidence	No serious limitations <ul style="list-style-type: none"> • Data not rich – data presented does illustrate findings well

Table 42: Townsend 2003

Study (ref id)	Townsend 2003 ¹²⁰⁹ ; Townsend 2008 ¹²¹¹
Aim	To examine attitudes towards drug use among middle aged respondents with high levels of chronic morbidity.
Population	n=23 Adults (aged 50 years or over) with multimorbidity (4 or more chronic conditions) Male/female ratio: 10:13
Setting	Scotland
Study design	43 semi-structured interviews
Methods and analysis	Sample comprised respondents purposively selected from the west of Scotland twenty-07 study. This is an ongoing longitudinal study of the social patterning of health among men and women resident in a large, socially varied (but mainly urban) area centred on Glasgow. Respondents have completed lengthy, home based interviews conducted by nurses at roughly 5-yearly intervals since 1987-8. Inclusion criteria: people (born in the early 1950s) who reported high morbidity (4 or more chronic conditions) in the interviews in 2000-2, half of whom were "low consulters" (≤ 3 consultations in previous year) and half were "high consulters" (≥ 7 consultations). We sent letters to 41 respondents who fulfilled our morbidity

Study (ref id)	Townsend 2003 ¹²⁰⁹ ; Townsend 2008 ¹²¹¹
	<p>and consultation criteria asking if they would be willing to take part in this additional qualitative study.</p> <p>Participants took part in 2 interviews, both which lasted about an hour. Interviews were tape recorded. The majority of interviews took place in participants' homes. Interviews covered the following: conditions and symptoms, the impact of conditions on daily life (including any action taken), the use of formal services and management of symptoms.</p> <p>The recorded interviews were transcribed in full, and the analysis was based on the transcripts. A constant comparative method was used, facilitated by the use of the software package nVivo. Transcripts were analysed in stages: 1 researcher checked the transcripts for accuracy against tape-recordings and made preliminary identification of themes; all authors read the transcripts separately to identify major themes; revised themes and the coding scheme after discussion and repeated reading of transcripts; generated codes to label passages and applied these to transcripts; and explored themes within and between respondents. Some themes related to drug use (such as people's aversion to drug use) were immediately obvious and were coded from an early stage of the analysis. Others (such as the higher order theme of "ambivalence") only emerged with further analysis. Once such a theme had emerged explicitly from some interviews, the data were re-analysed to establish whether others referred to the theme explicitly or implicitly and to look for deviant cases to develop and refine the findings.</p>
Themes with findings	<p>Control of symptoms and self-management strategies</p> <ul style="list-style-type: none"> • Differences in accounts of how effective self-management strategies were and the level of control people were able to achieve: "It's routine (pain) ... I've got that under control, yeah" [patient]; "I just don't let it (anxiety) get the better of me anymore" [patient]; "I'm fighting with myself ..." [patient]; "...as I think I'm getting on top of things something else smashes ... my life is turned upside down" [patient] <p>GP consultation as a last resort</p> <ul style="list-style-type: none"> • Participants described using GPs as "a last resort", that is, only when symptoms were severe, unpredictable, ongoing and resistant, or for unstable conditions: "I only go if I really need to go" [patient]; "...I try not to go unless it's something that's really annoying me" [patient]; "I would only go if I was in real bad pain or very, very sick ..." [patient] <p>Medical monitoring</p> <ul style="list-style-type: none"> • Regular attendance of GP consultations to monitor conditions were viewed as crucial for self-management strategy - they described being listened to, given time (which helped foster their sense of selves), thoroughly examined (which gave a sense of hope that something was being done) and provided with access to other support through referrals to professionals and services (which was perceived as both practical help and symbolic of improvement) • "He [GP] likes to see me, it used to be every fortnight ... it's a routine thing. He just likes to see me every 4 weeks ... to ask me how I am, to check how I am because of the ongoing things not only the MS ..." [patient] • [what makes the GP good?] "Because this doctor takes time to explain the procedures you are going through, he takes time to tell you

Study (ref id)	Townsend 2003 ¹²⁰⁹ ; Townsend 2008 ¹²¹¹
	<p>what is wrong with you, he takes time to examine you and he gets to the bottom of what's wrong with you. He doesn't leave you in limbo. There's none of this, give you a prescription and say: "Right try that, come back in 2 weeks" ... Somebody to be straight with me ... just get right down to the nitty gritty tell me what's wrong with me and give me something to help me along the way ... I'm not there a lot so when I do go he knows there's something really wrong. It's the only time I do go and this doctor knows that and he sits down, "Right what's the problem"? And he'll discuss it ... and that's what I like about him" [patient]</p> <ul style="list-style-type: none"> • "... it's all about the things that's wrong with me And her checking it up, and, my blood pressure... It's not just sitting talking about the weather or thingamy or anything like that, it's all about me. But she takes time to sit and listen to you, and if there's anything that she's concerned about it's referred to the hospital. Really brilliant doctor" [patient] <p>Place of GP consultation</p> <ul style="list-style-type: none"> • Participants discussed how their GP offered them neither symptom relief (medicines or treatment), knowledge (information which eased their symptoms) or hope of improvement (referrals or different treatments) nor moral support (empathic understanding) • "My GP doesn't really do very much. He's sort of just guided by what I want to do and how I feel, and what the hospital (pain clinic) sometimes says. Otherwise, he's just really a sort of innocent bystander, really just a man who fills out prescriptions and things like that, so I don't really speak to him very much" [patient] • "I have a lot of aches and pains on my legs, also my neck ... sometimes it's really, really bad ... but no I've never ever said to the doctor when I went "I've got a sore neck". I think maybe once I did and he said: "Ehm just wear and tear". You know, without examining or anything: "Just wear and tear" but of course I didn't make a big thing about it. Sometimes it's quite bad" [patient] <p>Reluctance to take drugs</p> <ul style="list-style-type: none"> • All respondents expressed their dislike of drugs to some extent, and drug use was often portrayed as the "last resort". Participants spoke of wanting to minimise use of drugs and maximise use of other management strategies for example, going to bed early, avoiding certain activities • "I've got 13 tablets I take in the morning; I take 4 at lunch time and 5 going to bed. It's a lot of tablets to be taking in a day.... Who wants to be on medication for the rest of your life? I certainly don't, but I know I've got to because of the strokes and the high blood pressure. I have to, I know I have to, take medication; I couldn't survive without it." [patient] • "... I would love to be able to turn round and come off all these things, but to be able to function half normally I've got to take them, and if that's the way it's got to be, that's the way it's got to be." [patient]
Limitations and applicability of evidence	<p>No serious limitations</p> <ul style="list-style-type: none"> • Researchers have not considered their own role, potential bias or influence during the design, data collection and analysis • Researchers do not discuss reaching data saturation

Table 43: Williams 2004A

Study (ref id)	Williams 2004A ¹³⁰⁵
Aim	To investigate perceptions of quality of care by patients experiencing comorbidities who required an acute hospital stay
Population	n=12 (patients) Adults (aged 18 years or over; range 34-77 years) with multimorbidity Average of 5.75 conditions Discharged from acute care Male/female ratio: 1:1
Setting	Discharged from acute care, Australia
Study design	Semi-structured interviews, 1:1
Methods and analysis	All prospective participants who met the inclusion criteria were contacted. Inclusion criteria: aged 18 years or over; more than 1 chronic illness; admitted to 1 hospital in Australia from their homes in 2000 and had received more than 4 days of acute care in the hospital; understand and speak English. All participants accepting the invitation to participate chose to be interviewed in their homes, where informed consent was obtained. Semi-structured interviews were conducted, which featured open-ended questions about the hospital stay. Questions were informed by the literature review and adapted from validated patient satisfaction measure. Data were analysed concurrently, as interviews continued until no new major themes were emerging (saturation). Analysis of the verbatim transcripts, field notes and patient medical histories was conducted according to the principles of qualitative description. The field notes and medical history were compared with the transcript data for congruence. A template analysis style was adopted, informed by Colaizzi's (1978) phenomenological method of theme development and using QSR NVivo, a code-and-retrieve computer software package. Independent data analysis was conducted by a second researcher, who confirmed the analysis. Additionally, a summary of the major findings was sent to each participant in an effort to verify interpretations, and was not contested by any participant.
Themes with findings	Poor continuity in the care of comorbidities <ul style="list-style-type: none"> Patients were annoyed that healthcare professionals did not take their comorbidities into attention: "I don't think they even considered it [leaky heart valves]. They were only concerned with the operation." [patient]; "You really need a doctor that can...put the whole thing together, the whole picture together. But because a GP sends you to a specialist for one thing and another specialist for another..." [patient]. Discharge planning was also only directed at the primary diagnosis and did not include care of comorbidities The length and complexity of the patient's history made it difficult and time-consuming to navigate: "My file is so...huge that there's no

Study (ref id)	Williams 2004A ¹³⁰⁵
	<p>way that they could ever keep up with all the things that you've got." [patient]</p> <ul style="list-style-type: none"> • Patients also stated that some information was kept in different places other than the hospital, such as at the doctor's surgery • They also had difficulty in recollecting what illnesses they thought they had, or their perceived importance and how they might impact on their hospital stay. This was augmented by the nature of some comorbidities, such as Meniere's disease. • Patients thought that health care professionals assumed that, as they were frequent consumers of health care services, they had knowledge of what to do with regards to their care and how to do it: "At best, they tell you what to do, but not how to get around those don'ts" [patient] • Patients reported that it was unclear, to them and health professionals, which health care provider was ultimately in control: "One of the nurses rang him and was told off by his secretary [who said] that I wasn't his patient at the moment, I was a surgeon's patient." [patient]; "As I told you before, I'm not too sure which doctor I'm supposed to ring." [patient] • Patients had multiple different health professional appointments, each disease was treated by a different specialist who was generally located in a different clinic, creating transport and parking difficulties for each appointment • The influence of the management of 1 disease on another was noted. For example, a patient perceived his reflux to be better from being nursed in a semi-upright position following a hip replacement. • Specialist appointments required a referral from a general practitioner and were difficult to obtain at short notice: "To get an appointment with him he's so busy that it's just about impossible, so it's better to go through your own doctor." [patients] • Letters from specialist to GPs often incomplete or delayed and, in the case of hospitalisation neglected to include other significant in hospital occurrences: "Doctors don't know we go elsewhere. They [bulk billing doctors] don't know who co-ordinates illnesses and how often you see the GP." [patient] • Patients reported receiving conflicting information from health professionals: "It's just so confusing...you get 1 doctor [who] says one thing, one doctor [who] says totally the opposite." [patient]
Limitations and applicability of evidence	<p>No serious limitations</p> <ul style="list-style-type: none"> • Researchers have not considered their own role, potential bias or influence during the design, data collection and analysis

H.2 Identification

H.2.1 Unplanned hospital admissions

Table 44: Abbatecola 2011⁴

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
Prospective cohort	Total n=3043	Older adults (aged 70 or older; mean age 81±6 years), previously hospitalised	Hospitalised Older Patient (HOPE) index Includes: functional status (BADL, IADL, dichotomised according to the interval 0-1); cognitive status (Mini-Mental State Examination); depression (Geriatric Depression Scale, GDS-15); comorbidity (CIRS); social isolation (Lubben Social Network Scale); self-perceived QoL SF-12). HOPE index was calculated as the sum of the 25 items, total score ranged from 0 (no evidence of clinical deficits) to 25 (clinically	Validation cohort, HOPE score ≥4		2 year	Italy	Italian National Research Centre on Aging	Risk of bias - low
	Development n=1533			Male to female ratio 47:53	Sensitivity				
		Specificity			16.7				
		AUC			0.60 (0.56-0.63)				
	Validation n=1510	Development cohort: consecutively admitted patient from January 2005 to December 2006. Validation cohort: consecutively admitted patient from January 2007 to December 2008. Uses data from Hospital Network of the Italian National Research Centre on Aging (INRCA). Inclusion criteria: aged over 70 years; admitted		Validation cohort, HOPE score ≥8					
				Sensitivity	65.6				
				Specificity	55.0				
AUC			0.60 (0.56-0.63)						

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
		to acute geriatric ward for unplanned admission; had complete Comprehensive Geriatric Assessment (CGA) data during hospital stay and was performed at discharge; data regarding survival after 24 months from their hospital stay; signed written informed consent (or by a relatives of critically ill or severely cognitively impaired patients) Unplanned readmission to an acute geriatric ward 76.8%	frail/vulnerable).						

Table 45: Boeckxstans 2015¹⁵¹

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
Prospective cohort	n=560	Older adults (aged 80-101 years; mean age 84.7±3.7), community-dwelling	Cumulative Illness Rating Scale (CIRS) Rates 14 body systems	Cumulative Illness Rating Scale (CIRS) >3		3 year	Belgium	Fondation Louvain	Risk of bias – high due to sample size and
				Sensitivity	61.4				
				Specificity	59.3				

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
		<p>Male to female ratio 37:63</p> <p>37.6% reported 5 or more diseases, range 1-16 diseases. Including: hypertension 66%; osteoarthritis 57.1%</p> <p>Part of BELFRAIL (BF_{c80+}) study.</p> <p>Exclusion criteria: known severe dementia; in palliative care; medical urgency</p> <p>Hospitalisation 50.9%</p>	<p>on a four-point severity scale (the CIRS is based on the number of body systems that present a severity score of at least 3, so the score can range from 0-14; optimal cut-off point (the cut-off value with the highest sensitivity and specificity for the outcome of interest): >3)</p> <p>Unweighted disease Count: included a number of diseases; including: hypertension, lipid disorder, angina pectoris, cardiomyopathy, myocardial infarction, etc.</p>	<p>AUC</p> <p>Unweighted Disease Count >3</p> <p>Sensitivity</p> <p>Specificity</p> <p>AUC</p>	<p>0.61 (0.57-0.66)</p> <p>66.7</p> <p>53.5</p> <p>0.63 (0.58-0.67)</p>				participant flow

Table 46: Clegg 2016^{275,276}

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
Retrospe	Total	Older adults (aged 65 to	Electronic frailty index	Moderate and above, internal cohort,		1 year, 3	UK	Governm	Risk of bias

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
Active cohort	n=931541	95; mean age 75±7 years)	(eFI)	3 years – sensitivity 0.26, specificity 0.88		years		ent	- low
	Development n=207814	Male to female ratio 45:55	Includes: activity limitation, anaemia, arthritis, atrial fibrillation, cerebrovascular disease, chronic kidney disease, diabetes, dizziness, dyspnoea, falls, foot problems, fragility fracture, hearing impairment, heart failure, heart valve disease, housebound, hypertension, hypotension/syncope, ischaemic heart disease, memory and cognitive problems, mobility problems, osteoporosis, Parkinsonism, peptic ulcer, peripheral vascular disease, polypharmacy, requirement for care, respiratory disease, skin ulcer, sleep disturbance, social vulnerability, thyroid	Moderate and above, external cohort, 3 years – sensitivity 0.36, specificity 0.82					
	Internal validation n=207720	Development and internal validation cohort: ResearchOne database of GP practices, randomly split		Severe, internal cohort, 3 years – sensitivity 0.06, specificity 0.98					
	External validation n=516007	External validation cohort: THIN database of GP practices		Severe, external cohort, 3 years – sensitivity 0.10, specificity 0.97					
				Moderate and above, internal cohort, 1 year – sensitivity 0.31, specificity 0.86					
				Moderate and above, external cohort, 1 year – sensitivity 0.42, specificity 0.81					
				Severe, internal cohort, 1 year – sensitivity 0.08, specificity 0.97					
				Severe, external cohort, 1 year – sensitivity 0.13, specificity 0.97					
				Internal cohort, 3 year – C statistics 0.64, pseudo R ² 0.05					

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
			disease, urinary incontinence, urinary system disease, visual impairment, weight loss and anorexia. Non-weighted tool, converted to 0 to 1 scale and categories of fit, mild frailty, moderate frailty and severe frailty defined by quartiles using the 99 th centile as the upper limit.	External cohort, 3 year – C statistics 0.69, pseudo R ² 0.02 Internal cohort, 1 year – C statistics 0.66, pseudo R ² 0.03 External cohort, 1 year – C statistics 0.71, pseudo R ² 0.02					

Table 47: Coleman 1998¹²

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
Prospective cohort	n=2174	HMO Enrolees 65 years and older (mean age not reported) 61% female Participants selected	Pra (administered and self-report)	Pra administrative AUC (SE) Pra self-report AUC (SE)	0.694% (0.014) 0.696% (0.014)	4 years	USA	Robert Wood Johnson Foundation	Risk of bias – high due to sample size/participant flow and analysis

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
		<p>from Group Health Cooperative of Puget Sound, a large Health Maintenance Organisation located in Washington State. Health plan enrollees were selected for a health promotion trial for older adults</p> <p>Inclusion criteria: aged 65 and older.</p> <p>Number ≥2 admissions: not reported</p>							

Table 48: Daniels 2012³²²

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
Prospective cohort	n=430	<p>Older adults (aged 70 or older), community-dwelling</p> <p>Age 70-74: 36.3%</p> <p>Age 75-79: 36.3%</p> <p>Age ≥80: 27.4%</p>	<p>Groningen Frailty Indicator</p> <p>15 items, focused on loss of functioning in 4 domains: physical (9 items), cognitive (1 item), social (3 items), psychological (2 items)</p>	Sensitivity	52 (40-64)	1 year	The Netherlands	Stichting Innovatie Alliantie and Zuyd University of Applied	Risk of bias – high due to sample size/participant flow
				Specificity	55 (50-60)				
				AUC	54 (46-61)				
				PPV	20 (15-26)				
				NPV	84 (79-89)				

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
		Male/female ratio 4:6 Education none/primary: 35.7% Income ≤900: 18.7% Disability, Groningen Activity and Restriction Scale (GARS): mean 24.9±9.3	Dutch Tilburg Frailty Indicator 2 subscales: socio-demographic, life event and chronic disease data (10 items); level of frailty – physical (8 items), social (3 items), psychological factors (4 items)	Sensitivity Specificity AUC PPV NPV	53 (41-64) 65 (60-70) 60 (52-67) 24 (18-32) 87 (82-90)			Sciences	
		Groningen Frailty Indicator (≥4): 46.3% Dutch Tilburg Frailty Indicator (≥5): 40.2% Sherbook Postal Questionnaire (≥2): 59.1%	Sherbook Postal Questionnaire 6 items: physical (4 items); social (1 item); cognitive (1 item)	Sensitivity Specificity AUC PPV NPV	76 (65-85) 44 (39-49) 60 (53-67) 22 (17-28) 90 (84-94)				
		Inclusion criteria: aged 70 years or older; people living in Limburg and Utrecht in the Netherlands, identified from panels of 4 GPs between November 2008 and April 2009 n=75 (17%)							

Table 49: Donate-Martinez 2013³⁶³

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
Retrospective cohort	n=500	Sample of elderly people (65+) from the Valencian region of Spain.	Probability of Repeated Admission (Pra)	Pra:		1 year	Spain	Ministry of Science and Innovation, through the Spanish National R+D+I Plan	Risk of bias – high due to analysis
	Pra: n=432			ROC statistic	0.67				
	CARS: n=500	Mean age: 74.76 years (SD 6.54). Male/female ratio: 58% female	Weighted score, 8 items: age, sex, self-perceived health, number of hospital admissions in previous year, number of physician visits in previous year, presence of diabetes mellitus, presence of coronary heart disease, and availability of a caregiver	Sensitivity	54%				
				Specificity	81%				
				CARS:					
				ROC statistic	0.69				
				Sensitivity	64%				
			Specificity	64%					
	Patients were recruited from three Health Departments.		Community Assessment Risk Screen (CARS)						
	Uses routinely collected data from general practice linked to hospital episode data. Patients were screened and recruited from 30 family doctors from six health centres.								
	Exclusion criteria: absence of patient data in databases, aged under 65 and exitus.		Includes: 3 factors to predict future hospitalisations; pre-existing chronic diseases (heart disease, diabetes, myocardial infarction,						
	Hospitalised once or more								

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
		in following year 15%	stroke, chronic obstructive pulmonary disease – COPD – or cancer), the number of prescriptions medications and hospitalisations or ED use in the preceding 6-12 months. A total score is obtained by adding the points of each question, with a possible range of 0-9. Patients with a total score of 4 or higher are classified in the high risk group, and those with a smaller score than 4 are classified in the low risk group.						

Table 50: Donnan 2008^{365,366}

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
Retropective	90,879 used for the	All subjects 40 years or older in the Tayside region of Scotland, registered with	Predicting Emergency admissions Over the Next Year (PEONY)	Accuracy of risk tool for predicting emergency hospital admission in the follow up year		1 year for validati	UK	Unrestricted local NHS trust grant	Risk of bias – high due to

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
cohort	validation portion of the study.	<p>a Tayside general practice.</p> <p>To be eligible each patient had to have data on the history of hospital use and drug prescribing over a 3 year period as well as a minimum of 12 months of follow-up information.</p> <p>No characteristics given for those in the validation data-set, but given that these were randomly chosen from the overall data set, the characteristics given for the derivation data set are probably a good approximation: mean age 61.5(12.5); 25.1% with previous hospital admission; 0.6 (1.4) previous admissions; 40% in 'most deprived' Carstairs deprivation category.</p> <p>Number emergency admissions: not reported for validation cohort; n=6793 in derivation cohort</p>	<p>Includes: gender; baseline age; age at previous emergency admission; Carstairs deprivation category; total bed days; previous emergency admissions relating to gastrointestinal drugs, antiplatelets and diuretics and use of respiratory drugs, hypnotics and anxiolytics, antipsychotic drugs, antidepressant drugs, analgesics, antiparkinson drugs, antibacterial drugs, diabetes medications, antiosteoporotic drugs and anaemia drugs</p>	Discrimination (c) – Area under ROC curve plotting the sensitivity and 1 – specificity for different thresholds of the tool.	0.79	on portion (implied)			<p>outcome, analysis</p> <p>Split half validation study.</p> <p>Validation portion of the study poorly described.</p> <p>No reports of blinding of assessors to algorithm score.</p>
				Raw diagnostic data at different thresholds for calculation of discrimination score above Cut off >50	Sensitivity 0.042; Specificity 0.998 PPV 67.1%				
				Cut off >46	Sensitivity 0.079; Specificity 0.996 PPV 59%				
				Cut off >37	Sensitivity 0.271; Specificity 0.998 PPV 40.6%				

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
				Cut off >32	Sensitivity 0.420; Specificity 0.926 PPV 31.5%				
				Cut off >23	Sensitivity 0.689; Specificity 0.774 PPV 19.8%				
				Cut off >20	Sensitivity 0.761; Specificity 0.695 PPV 16.8%				

Table 51: Hippisley-Cox 2013⁵⁸³

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
Prospective open cohort	Q Research validation cohort, n = 1340622	Primary care patients, aged 18-100 years old. Male to female ratio 51:49 Uses routinely collected data from general practice	QAdmissions Includes: demographic variables; lifestyle variables; chronic diseases; medication	QRes cohort, HES-GP linked data, women		2 years	UK	The North East London Commissioning support group; The	Risk of bias – low
				ROC statistic	0.773 (0.771 to 0.774)				
				Pseudo R ² (%)	40.6 (40.2 to				

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
	CPRD validation cohort, n = 2475360	linked to hospital episode data Development cohort: open cohort design, patients registered with eligible practices drawn from January 2010 and December 2011. Validation cohort: open cohort design, patients registered with eligible practices drawn from January 2010 and December 2011. Used V.35 of the QResearch database, a large validated primary care electronic database containing health records of 13 million patients registered from 600 general practices. Practices and patients are nationally representative. Additional validation cohort from 343 practices contributing to the Clinical Practice	use; clinical values; laboratory test results; emergency admissions in the year before study entry.		40.9)			National School for Primary Care Research	
				QRes cohort, HES-GP linked data, men					
				ROC statistic	0.776 (0.774 to 0.778)				
				Pseudo R ² (%)	42.6 (42.2 to 42.9)				
				QRes cohort, GP data alone, women					
				ROC statistic	0.764 (0.762 to 0.766)				
				Pseudo R ² (%)	37.3 (37.0 to 37.8)				
				QRes cohort, GP data alone, men					
				ROC statistic	0.769 (0.767 to 0.771)				
				Pseudo R ² (%)	39.5 (39.1 to 39.9)				

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
		Research Datalink (CPRD) which had linked hospital episode statistics (HES) data.							
		<p>Inclusion criteria: included all QResearch practices in England once they had been using their current EMIS system for at least one year. Patients with a valid NHS number and postcode-related Townsend deprivation score.</p> <p>Emergency admission n=132723 (9.9%) in QResearch validation cohort</p>		CPRD, HES-GP linked data, women					
				ROC statistic	0.771 (0.770 to 0.773)				
				Pseudo R ² (%)	40.5 (40.2 to 40.8)				
				CPRD cohort, HES-GP linked data, men					
				ROC statistic	0.772 (0.771 to 0.774)				
				Pseudo R ² (%)	41.9 (41.6 to 42.2)				
				CPRD cohort, GP data alone, women					
				ROC statistic	0.764 (0.763 to 0.766)				
				Pseudo R ² (%)	37.6 (37.3 to 37.9)				

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
				CPRD cohort, GP data alone, men					
				ROC statistic	0.767 (0.765 to 0.768)				
				Pseudo R ² (%)	39.2 (38.9 to 39.5)				
				CPRD cohort, HES-GP linked data, risk >68%					
				Sensitivity	6.7%				
				CPRD cohort, GP data alone, risk >66%					
				Sensitivity	6.1%				
				CPRD cohort, HES-GP linked data, risk >35%					
				Sensitivity	24.9%				
				CPRD cohort, GP data alone, risk >36%					
				Sensitivity	23.2%				
				CPRD cohort, HES-GP linked data, risk >22%					
				Sensitivity	39.4%				
				CPRD cohort, GP data alone, risk >24%					

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
				Sensitivity	37.4%				
				CPRD cohort, HES-GP linked data, risk >13%					
				Sensitivity	56.8%				
				CPRD cohort, GP data alone, risk >14%					
				Sensitivity	55.1%				
				QRes cohort, HES-GP linked data, risk >69%					
				Sensitivity	6.6%				
				QRes cohort, GP data alone, risk >57%					
				Specificity	99%				
				Sensitivity	6.0%				
				QRes cohort, GP data alone, risk >46%					
				Specificity	99%				
				Sensitivity	11%				
				QRes cohort, HES-GP linked data, risk >36%					
				Sensitivity	24.6%				
				QRes cohort, GP data alone, risk >31%					
				Specificity	97%				

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
				Sensitivity	23.4%	1 year			
				QRes cohort, HES-GP linked data, risk >23%					
				Sensitivity	39.3%				
				QRes cohort, GP data alone, risk >21%					
				Specificity	93%				
				Sensitivity	37.7%				
				QRes cohort, HES-GP linked data, risk >13%					
				Sensitivity	56.9%				
				QRes cohort, GP data alone, risk >13%					
				Specificity	84%				
				Sensitivity	55.5%				
				QRes cohort, GP data alone risk >7%					
				Sensitivity	58				
				Specificity	82				
				QRes cohort, GP data alone risk >12%					
				Sensitivity	40				

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
				Specificity	92				
				QRes cohort, GP data alone risk >18%					
				Sensitivity	26				
				Specificity	96				
				QRes cohort, GP data alone risk >28%					
				Sensitivity	13				
				Specificity	99				
				QRes cohort, GP data alone risk >36%					
				Sensitivity	7				
				Specificity	99				

Table 52: Jensen 2001⁶⁴⁰

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
Prospective	n=386	Rural, older persons in a Medicare managed-risk	Pra	Complete Pra Score:		1 year	USA	Robert Wood	Risk of bias –
				Sensitivity	52.0				

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
cohort		health plan Number of admissions: not reported	8 items: older age, male sex, self-rated health, availability of an informal caregiver, having ever had coronary artery disease, and having had a hospital admission, >6 doctor visits, or disease in the past year. A Pra risk score between 0 and 1 is assigned, with higher values indicating higher risk. A cut-off point at the 75 th percentile (0.30) was considered to represent high risk.	Specificity	71.3			Johnson Foundation	very high due to sample size/participant flow and analysis

Table 53: Mazzaglia 2007⁸²⁹

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
Population-based cohort	Total n=5396	Older adults (aged 65 and older; mean age 75.1±7.2), community-dwelling	Unnamed Included: age; sex; hospitalisations in past 6 months; ≥5 prescriptions; 'number of positive responses to screening questionnaire'	Development cohort		15 months	Italy	Agency for Regional Healthcare Services, Department of Health, Rome, Italy	Risk of bias – high due to analysis
				AUC	0.68 (0.66-0.71)				
	Development n=2470	Sample derived from random sampling of rosters of 98 PCPs		Validation cohort					
	Validation n=2926	Hospitalisations: 17.2%		AUC	0.67 (0.65-0.70)				

Table 54: Ritt 2015¹⁰²³

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
Prospective cohort	n=307	Older adults (aged 65 years or over), inpatients admitted to a geriatric ward	Clinical Frailty Scale	Unplanned hospital admission AUC	0.569 (0.502-0.636)	6 months	Germany	Robert Bosch Foundation	Risk of bias – high due to analysis
		Number of unplanned hospital admission: not reported	Frailty Phenotype	Unplanned hospital admission AUC	0.5 (0.432-0.568)				

Table 55: Schneeweiss 2001¹⁰⁸⁷

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
Population-based cohort study	n=141,611	Older adults (aged 65 years or older; mean age 75.4±6.7) with hypertension (100%), community-dwelling	Chronic Disease Score (CDS-1)	C-statistic	0.590	1 year	Canada	Drug Information Association, Pennsylvania, and Pharmacare, Ministry of Health of British Columbia. Author supported by grants from Deutsche	Risk of bias – high due to sample size/participant flow and analysis
		Female 58%	Chronic Disease Score (CDS-2)	C-statistic	0.605				
		Inclusion: all British Columbia residents aged 65 or older; filled at least one prescription for an angiotensin-converting enzyme inhibitor or calcium	Includes: sex; age; weighted medication use. Medications listed for following diseases: coronary and peripheral vascular disease; epilepsy; hypertension, HIV; TB; rheumatologic conditions; hyperlipidaemia;						

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
		channel blocker from 1995-1997 Number of emergency hospital admissions: not reported	malignancies Parkinson's disease; renal disease; ESRD; cardiac disease, CHF; diabetes; glaucoma; cystic fibrosis; liver failure; acid peptic disease; transplantation; respiratory illness; thyroid disorders; gout; Crohn's and ulcerative colitis; pain; inflammation; depression; psychotic illness; bipolar disorder; anxiety and tension					Forschungsgemeinschaft and the US Agency for Healthcare Research and Quality and by a Pharmacoeconomics Epidemiology Training and Research Grant, Harvard University, Boston MA.	
			Deyo CCI (uses ICD-9-CM codes)	C-statistic	0.601				
			Deyo CCI (calculated using ICD-9 codes from hospital discharge)	C-statistic	0.581				
			D'Hoore CCI (uses ICD-9-CM codes)	C-statistic	0.597				
			D'Hoore CCI (calculated using ICD-9 codes from hospital discharge)	C-statistic	0.578				
			Romano CCI (uses ICD-9-CM codes)	C-statistic	0.604				
			Romano CCI	C-statistic	0.582				

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
			(calculated using ICD-9 codes from hospital discharge)						
			Ghali CCI (uses ICD-9-CM codes)	C-statistic	0.577				
			Ghali CCI (calculated using ICD-9 codes from hospital discharge)	C-statistic	0.560				

Table 56: Soong 2015¹¹³⁷

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
Retrospective observational	n=20992 52	Older adults (aged 65 years or over) with acute emergency admission to any NHS provider Used English Hospital Episode Statistics (HES) data from 1/1/12 to 31/12/12, scores coded at discharge.	ED readmission (30 day)			30 days	England	National Institute for Health Research	Risk of bias – high due to analysis
			CCI, 17-item (2012 version)	AUC	0.59				
			Patients At Risk of Readmission 30-Day (PARR30)	AUC	0.7				
			18-item, 5 hospital specific variables: age; number of emergency discharges in last year, prior emergency hospital discharge in past 30 days; whether current admission was						

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
			<p>an emergency admission; deprivation band of place of residence. Plus history of 11 conditions in past 2 years: congestive heart failure; peripheral vascular disease; diabetes with chronic complications; renal disease metastatic cancer with solid tumour; other malignant cancer; moderate/severe liver disease; haemiplegia or paraplegia; dementia.</p> <p>Risk Index for Geriatric Acute Medical Admission (RIGAMA)</p> <p>30-items, history of: Ischaemic heart disease; Chronic liver disease; Cancer. Admitted with: Stroke; Pneumonia; pleural effusion; Congestive heart failure; Acute myocardial infarction. Vital signs: Respiratory rate > 20 per</p>	AUC	0.55				

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
			min; O2 saturation < 92% on room air; Systolic blood pressure < 100mmHg; Diastolic blood pressure < 60mmHg; Heart rate > 100 beats per min; Heart rate < 50 beats per min; Temperature < 35°C; Temperature > 38.5°C. Laboratory abnormalities: haemoglobin < 10 g/dl; Hematocrit < 35%; Red Distribution Width > 15%; White Cell Count > 12 per 109/l; Creatinine > 150 µmol/l; Urea > 10 mmol/l; sodium < 135 mmol/l; Sodium > 145 mmol/l; Potassium < 3.0 mmol/l; Potassium > 5.5 mmol/l; Albumin < 35 g/l; Glucose > 10 mmol/l; Glucose < 3 mmol/l; Positive troponi						
			ED readmission (90 day)			90 days			
			Cardiovascular Health Study (CHS) model	AUC	0.52				
			5 domains: nutritional						

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
			status; strength; energy; mobility; physical activity						
			Study of Osteoporotic Fractures (SOF) model	AUC	0.53				
			3-item: intentional or unintentional weight loss >5% in the past year; inability to rise from a chair five consecutive times without using the arms; self-perceived reduced energy level as described by a negative answer to the question "do you feel full of energy?"						
			Avila-Funes	AUC	0.55				
			5 domains: nutritional status; strength; energy; mobility; physical activity						
			Rothman	AUC	0.53				
			4 domains: mobility; physical activity; nutritional status;						

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
			cognition Frailty Index (FI)	AUC	0.57				
			36-items: Chronic Obstructive Pulmonary Disease; Cerebrovascular disease; Congestive heart failure; Diabetes; Dementia; Liver Disease Myocardial Infarction; Renal disease Tumour; Ulcer disease; Peripheral vascular disease; Recent Falls; Pressure sore; Polypharmacy (>3 medications every day); Do you see well; Do you have serious problems with memory; Do you feel full of energy; Weight loss >5kg in past 12 months; MMSE<24/30; Gait speed; Grip strength; Calf circumference; Mid Arm circumference; Difficulty with concentration; Sleep loss over worry						

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
			<p>Feel Depressed; Help Feeding; Help Dressing; Help Bathing; Help Grooming; Bladder incontinence; Bowel incontinence; Help Transferring; Help up/down Stairs; Help with Mobility</p> <p>Identifying Seniors at Risk (ISAR)</p> <p>6 self-report questions on: functional dependence, recent hospitalisation, impaired memory and vision, and polypharmacy. Response to these items is dichotomous (e.g. yes/no). Patients with a score of two or more are considered to be at risk.</p>	AUC	0.6				

Table 57: Susser 2008¹¹⁵⁹

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
Retro	n=520	Older adults (aged 65 years	Charlson Comorbidity	Self-report CCI		5	Canada	The author	Risk of bias

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
Prospective cohort		65 or over), ready to be discharged home from ED Male to female ratio 208:312 Secondary analysis of data from a RCT of a two-step intervention for older ED patients Inclusion criteria: 65 years of age or older, able to speak English or French, and discharged to the community Health services utilisation: not reported	Index (CCI), self-report and administrative versions	AUC (95% CI)	0.64 (0.58-0.69)	months after ED visit		was funded by a summer research bursary for health professional students from the McGill Faculty of Medicine	– high due to sample size/participant flow and analysis
				Administrative CCI AUC (95% CI)	0.65 (0.59-0.70)				

Table 58: Wallace 2013¹²⁷¹

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
Systematic review	n=8843	Community-dwelling older people (aged 65 or older). Five cohorts of participants from three studies	Prai	Hospital admissions (variation between studies in how this was reported)	69.7% (SE 2.8%)	Boult 1995, 4 years	UK, Germany, Switzerland, USA	Health Research Board of Ireland through	Prai (Pacala) Risk of bias – high due to analysis
				AUC (95% CI)		Mosley			

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
		<p>(n=8,843) were included in a meta-analysis to estimate the predictive ability of the Pra tool. A meta-analysis was performed on the cohort of participants from studies that used a score of 0.5 or greater to indicate a high risk of subsequent hospital admission, predict hospital admissions at 1-year and for whom relevant data was available.</p> <p>All studies except one used aged 65 and older or aged 70 and older as inclusion criteria.</p> <p>Hospital admissions n=2117 (25.1%)</p>		<p>Sensitivity</p> <p>Specificity</p>	<p>12% (CIs 10.5-13.6%)</p> <p>96% (CIs 95.8-96.7%)</p>	<p>2009, 1 year</p> <p>Wagner 2006</p>		<p>the HRB Centre for Primary Care Research under grant HRC/2007 1</p>	<p>Pra (Boult, Mosley) Risk of bias – high due to sample size/participant flow and analysis</p> <p>Reports that external validity was good; that the main shortcomings in relation to internal validity related to blinding, and no study specifically reported whether the outcome assessors were blind</p>

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
									to the original Pra score, though outcomes were collected from automated data sets (e.g., Medicare claims databases)

Table 59: Wallis 2015¹²⁷³

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
Retrospective observational	n=5764	Older adult (aged 75 years or over; mean age 84.3±5.9 years)	CCI	AUC	0.54 (0.52-0.56)	30 days	UK	Not stated	Risk of bias – high due to analysis
		Male/female ratio 54:56 Community-dwelling, with previous ED admission Included all emergency admissions to Cambridge	CHSA Clinical Frailty Scale 7-item	AUC	0.54 (0.52-0.56)				

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
		University Hospitals NHS Trust, aged ≥75 years between 1/8/13 and 31/7/14 ED readmission (30 days), n=759 (13.17%)							

Table 60: Widagdo 2015¹³⁰³

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments	
Retrospective cohort	n=2087	Older adults (aged 70 years or over; mean age 77±6)	Frailty phenotype	Sensitivity	9.9	3 year	Australia	US National Institute of Health, South Australian government, Flinders University, other NGOs	Risk of bias – high due to outcomes and/or sample size/participant flow	
				Specificity	93.8					
	Frailty phenotype n=1566	Male/female ratio 1:1	5-item: unintentional weight loss, low grip strength, self-rated exhaustion, low physical activity	AUC	0.52					
					Simplified frailty phenotype	Sensitivity	3.4			
	Living in care facility 3.3%	Used data from Australian Longitudinal Study of Ageing, which contains 11 waves of data from 1992-2010. Outcome data were obtained from wave 3 data.	3-item: unintentional weight loss, inability to rise from a chair 5 times without the use of arms, low energy level	AUC		0.51				
					Frailty Index n=1173	Hospitalisation - Frailty phenotype n=404 (30.1%)	Frailty Index	Sensitivity		23.8
	Prognostic Frailty Score	n=2087	Living in care facility 3.3%	Frailty Index	Specificity	88.1				

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
	n=1485	Simplified frailty phenotype n=292 (28.4%) Frailty Index n=513 (30.6%) Prognostic Frailty Score n=379 (29.8%)	39-item	AUC	0.56				
			Prognostic Frailty Score	Sensitivity	58.6				
				Specificity	58.3				
			9-items: aged ≥80 years, male, low physical activity (<4 hours per week), comorbidity, sensory deficit, calf circumference <31cm, IADL dependence, gait problem, health pessimism	AUC	0.58				

Table 61: Zekry 2012B¹³³⁹

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
Prospective cohort	n=444	Older adults (aged 75 or older), discharged from acute geriatric hospital.	CCI	Pseudo R ²	3.1	1 year	Switzerland	Swiss National Science Foundation; Swiss Foundation for Aging Research	Risk of bias – very high due to sample size/participant flow and analysis
		Random sample of patients aged 75 or older consecutively admitted to an acute geriatric hospital were selected by randomisation using computer generated	CIRS-G	Pseudo R ²	5.6				
			Rates 14 body systems on a five-point severity scale						
			ICED	Pseudo R ²	0.4				
			Based on presence and severity of 15 medical conditions and 12						

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
		randomisation table. Hospitalised once: 82 (18.5%)	physical impairments, using 2 subscales- IDS and PIS scores						
			Kaplan scale	Pseudo R ²	0.5				
			14 medical conditions, sum weight of each disease						
			GIC	Pseudo R ²	14.0				
			Classifies patients into 4 classes of increasing somatic comorbidity, based on number of diseases and severity of diseases (based on IDS)						
			Chronic Disease Score (CDS-1)	Pseudo R ²	1.7				
			30 classes of medication; 6-point scale rating, sum weight of each category						

Table 62: Zeng 2014¹⁵

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
------------	--------------------	-------------------------	-----------	------------------	--------------	---------------------	---------	-------------------	----------

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
Retrospective cohort	Validation cohort n=13163	Older adults (aged 65 or older) with multimorbidity (100% 3 or more chronic conditions). Inclusion criteria: aged 65 or older; enrolled in a health plan for at least a year; had 3 or more of 10 common chronic conditions. Development cohort responded to a survey assessing factors potentially associated with health outcomes. Validation cohort was not surveyed. Inpatient admission: not reported	Quan CCI (used ICD-10 codes) (score 1 year before)	C-statistic	0.647	1 year	USA	Agency for Healthcare Research and Quality	Risk of bias - high due to patient selection, sample size/participant flow and analysis
			Quan cumulative CCI (score over 10 years)	C-statistic	0.649	10 year			
			Quan baseline CCI (first CCI, within 10 year period)	C-statistic	0.647	10 year			
			Quan CCI trajectory: linear model (modelled using growth curve models to fit each individuals' CCI measures using available data in 10 year period)	C-statistic	0.646	10 year			
			Quan CCI trajectory: quadratic model	C-statistic	0.647	10 year			

H.2.2 Health-related quality of life

Table 63: Fortin 2005a⁴³⁴

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
Retrospective	n=238	Adults (age 18 years or over; mean age 59.0 ±14.3 years) in primary care	Cumulative Illness Rating Scale (CIRS)	Partial R ²	2.26 ^a – 15.59 ^b	6 months	Canada	Fonds de la Recherche en Sante du	Risk of bias – high due to sample

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
cohort		Male to female ratio 29:71 Used data collected on the diagnoses of chronic diseases in a group of patients who participated in a study on HRQOL. Patients were randomly selected from 980 patients who had also been selected a random for a prevalence study on multimorbidity. Inclusion criteria: not reported	Functional Comorbidity Index (FCI)	R ²	1.02 – 9.53 ^b			Quebec and Pfizer Canada	size/participant flow and analysis
			Charlson Comorbidity Index	Partial R ²	0.002 – 4.52 ^b				

(a) $p < 0.05$

(b) $p < 0.01$

Table 64: Grimmer 2014⁵¹⁶

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
Prospective cohort	Total n=148	Aged 65 years and older, living independently in the community (mean age [95% CI]: males 77.8 [75.9 – 79.7]; females 74.9 [73.4 – 76.4]) Male to female ratio 68:80	Hospital Admission Risk Profile (HARP)	Low MCS at 1 month		1 & 3 months post recruitment	Australia	CNAHS Partner contribution to the grant	Risk of bias – high due to sample size/participant flow and analysis
				Sensitivity	56.7% (44.7-68.2)				
				Specificity	44.6% (33.0-56.6)				
				AUC	0.51 (0.42-0.59)				

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
		<p>Patients presented to the ED for the management of a medical problem for which they were discharged directly from ED.</p> <p>Inclusion criteria: eligibility for the study was confirmed if they were not subsequently admitted to any hospital for any reason up to 1-week after recruitment.</p>		Low MCS at 3 months					
				Sensitivity	44.8% (32.6-57.4)				
				Specificity	57.3% (45.9-68.2)				
				AUC	0.51 (0.43-0.59)				
				Low or declining MCS over 2 months (change over time)					
				Sensitivity	56.0% (34.9-75.6)				
				Specificity	58.5% (49.3-67.3)				
				AUC	0.57 (0.48-0.65)				
				Low PCS at 1 month					
				Sensitivity	56.3% (43.3-68.6)				
				Specificity	65.5% (54.3-75.5)				
				AUC	0.61 (0.52-0.69)				
				Low PCS at 3 months					
				Sensitivity	57.2% (44.3-67.7)				
				Specificity	66.1%				

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
					(54.8-74.5)				
				AUC	0.62 (0.51-0.68)				
				Low or declining MSC scores over 2 months (change over time)					
				Sensitivity	56.3% (44.0-68.1)				
				Specificity	67.9% (56.4-78.1)				
				AUC	0.62 (0.54-0.70)				
				Low or declining PCS and MSC scores over 2 months (change over time)					
				Sensitivity	53.85 (33.4-73.4)				
				Specificity	58.5% (49.3-67.3)				
				AUC	0.56 (0.48-0.64)				

H.2.3 Admission to care facility

Table 65: Clegg 2016^{275,276}

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
Retrospective cohort	Total n=93154 1	Older adults (aged 65 to 95; mean age 75±7 years)	Electronic frailty index (eFI)	Moderate and above, internal cohort, 3 years – sensitivity 0.38, specificity 0.86		3 years	UK	Government	Risk of bias - low
	Development n=20781 4	Male to female ratio 45:55	Includes: activity limitation, anaemia, arthritis, atrial fibrillation, cerebrovascular disease, chronic kidney disease, diabetes, dizziness, dyspnoea, falls, foot problems, fragility fracture, hearing impairment, heart failure, heart valve disease, housebound, hypertension, hypotension/syncope, ischaemic heart disease, memory and cognitive problems, mobility problems, osteoporosis, Parkinsonism, peptic ulcer, peripheral vascular disease, polypharmacy, requirement for care,	Severe, internal cohort, 3 years – sensitivity 0.10, specificity 0.97					
	Internal validation n=20772 0	Development and internal validation cohort: ResearchOne database of GP practices, randomly split		Internal cohort, 3 year – C statistics 0.72, pseudo R ² 0.04					
	External validation n=51600 7	External validation cohort: THIN database of GP practices							

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
			respiratory disease, skin ulcer, sleep disturbance, social vulnerability, thyroid disease, urinary incontinence, urinary system disease, visual impairment, weight loss and anorexia. Non-weighted tool, converted to 0 to 1 scale and categories of fit, mild frailty, moderate frailty and severe frailty defined by quartiles using the 99 th centile as the upper limit.						

Table 66: Jones 2005¹⁴

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
Prosp	n=3736	Older adults (aged 65	CHSA Frailty Index	AUC	0.75	5 years	Canada	National	Risk of bias

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
Active cohort		<p>65 years or older), community-dwelling</p> <p>Female 38%</p> <p>Extracted data from the clinical examination conducted for the second wave of the Canadian Study of Health and Ageing (CSHA-2). To test predictive validity, outcomes in the third wave (CSHA-3) were evaluated.</p>	<p>Frailty Index-Comprehensive Geriatric Assessment (FI-CGA)</p> <p>Sum of a functional impairment index and CIRS.</p> <p>Included: impairment in 10 domains- cognition, mood, communication, mobility, balance, bowels, bladder, nutrition, function, social; CIRS</p>	AUC	0.66			Health Research Development Program of Canada	<p>– high due to patient selection, sample size/participant flow and analysis</p> <p>NB: length of follow-up in study is longer than specified in the protocol</p>

Table 67: Rockwood 2005¹⁰³⁴

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
Prospective cohort	n=2305	<p>Older adults (aged 65 years or older), community-dwelling</p> <p>5 year follow up of Canadian Study of Health and Aging (CSHA)-2.</p>	<p>Cumulative Illness Rating Scale (CIRS)</p> <p>Rates 14 body systems on a four-point severity scale</p>	AUC	0.62	5 years	Canada	National Health Research Development Program of Health Canada;	Risk of bias – high due to patient selection, sample size/participant flow and analysis
			<p>Modified Mini-Mental State Examination</p> <p>Examination in which a score of 77 or less indicates cognitive impairment</p>	AUC	0.69				

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
			CSHA rules-based definition of frailty	AUC	0.70			Queen Elizabeth II Research Foundation	NB: length of follow-up in study is longer than specified in the protocol
			Categorises participants as 0 (having no cognitive or functional impairment), 1 (isolated urinary incontinence), 2 (dependent in 1 ADL or having a diagnosis of CIND) or 3 (dependent in at least 2 ADLs, having mobility impairment or having a diagnosis of dementia).						
			CSHA Function Scale	AUC	0.80				
			Scores patients on each of 12 ADLs (some instrumental) as 0 (the patient is independent in carrying out this ADL), 1 (needs assistance), or 2 (is incapable).						
			CSHA Frailty Index	AUC	0.72				
			A count of 70 deficits, including the presence and severity of current diseases, ability in ADLs and physical signs from clinical and neurologic exams. To indicate severity, each deficit not restricted by its nature to 2 values (i.e., 0 or 1 for absence or presence, respectively) was assigned three (0, 0.5, or 1) or four values (0, 0.33, 0.67 or 1.0), as appropriate.						
			CSHA-3 Clinical Frailty Scale	AUC	0.75				
			Ranges from 1(robust health) to 7 (complete functional dependence on others).						

Table 68: Soong 2015¹¹³⁷

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments	
Retrospective cohort	n=20992 52	Older adults (aged 65 years or over) with acute emergency admission to any NHS provider Used English Hospital Episode Statistics (HES) data from 1/1/12 to 31/12/12, scores coded at discharge.	CCI, 17-item (2012 version)	AUC	0.62	1 year	England	National Institute for Health Research	Risk of bias – high due to analysis	
			Risk Index for Geriatric Acute Medical Admission (RIGAMA)	AUC	0.50					
			30-items, history of: Ischaemic heart disease; Chronic liver disease; Cancer. Admitted with: Stroke; Pneumonia; pleural effusion; Congestive heart failure; Acute myocardial infarction. Vital signs: Respiratory rate > 20 per min; O2 saturation < 92% on room air; Systolic blood pressure < 100mmHg; Diastolic blood pressure < 60mmHg; Heart rate > 100 beats per min; Heart rate < 50 beats per min; Temperature < 35°C; Temperature > 38.5°C. Laboratory abnormalities: haemoglobin < 10 g/dl; Hematocrit < 35%; Red Distribution Width > 15%; White Cell Count > 12 per 109/l; Creatinine > 150 µmol/l; Urea > 10 mmol/l; sodium < 135 mmol/l; Sodium > 145 mmol/l; Potassium < 3.0 mmol/l; Potassium > 5.5 mmol/l; Albumin < 35 g/l; Glucose > 10 mmol/l; Glucose < 3 mmol/l; Positive troponi							

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
			Cardiovascular Health Study (CHS) model	AUC	0.57				
			5 domains: nutritional status; strength; energy; mobility; physical activity						
			Study of Osteoporotic Fractures (SOF) model	AUC	0.44				
			3-item: intentional or unintentional weight loss >5% in the past year; inability to rise from a chair five consecutive times without using the arms; self-perceived reduced energy level as described by a negative answer to the question "do you feel full of energy?"						
			Avila-Funes	AUC	0.5				
			5 domains: nutritional status; strength; energy; mobility; physical activity						
			Rothman	AUC	0.45				
			4 domains: mobility; physical activity; nutritional status; cognition						
			Frailty Index (FI)	AUC	0.55				
			36-items: Chronic Obstructive						

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
			<p>Pulmonary Disease; Cerebrovascular disease; Congestive heart failure; Diabetes; Dementia; Liver Disease Myocardial Infarction; Renal disease Tumour; Ulcer disease; Peripheral vascular disease; Recent Falls; Pressure sore; Polypharmacy (>3 medications every day); Do you see well; Do you have serious problems with memory; Do you feel full of energy; Weight loss >5kg in past 12 months; MMSE<24/30; Gait speed; Grip strength; Calf circumference; Mid Arm circumference; Difficulty with concentration; Sleep loss over worry Feel Depressed; Help Feeding; Help Dressing; Help Bathing; Help Grooming; Bladder incontinence; Bowel incontinence; Help Transferring; Help up/down Stairs; Help with Mobility</p> <p>Identifying Seniors at Risk (ISAR)</p> <p>6 self-report questions on: functional dependence, recent hospitalisation, impaired memory and vision, and polypharmacy. Response to these items is dichotomous (e.g. yes/no). Patients with a score of 2 or more are considered to be at risk.</p>	AUC	0.65				

Table 69: Widagdo 2015¹³⁰³

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments	
Retrospective cohort	n=2087	Older adults (aged 70 years or over; mean age 77±6)	Frailty phenotype	Sensitivity	18.2	3 year	Australia	US National Institute of Health, South Australian government, Flinders University, other NGOs	Risk of bias – high due to outcomes and/or sample size/participant flow	
	Frailty phenotype n=1566 Simplified frailty phenotype n=1173 Frailty Index n=2087 Prognostic Frailty Score n=1485	Male/female ratio 1:1 Living in care facility 3.3%		Used data from Australian Longitudinal Study of Ageing, which contains 11 waves of data from 1992-2010. Outcome data were obtained from wave 3 data.	Specificity					93.4
					AUC					0.56
			Simplified frailty phenotype		Sensitivity					6.7
		Specificity		98.3						
		AUC		0.56						
		Admission to care facility - Frailty phenotype n=22 (1.7%) Simplified frailty phenotype n=15 (1.5%) Frailty Index n=31 (1.9%) Prognostic Frailty Score n=21 (1.7%)	3-item: unintentional weight loss, inability to rise from a chair 5 times without the use of arms, low energy level	Frailty Index	Sensitivity					35.5
					Specificity					85.8
					39-item					AUC

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
			Prognostic Frailty Score	Sensitivity	76.2				
				Specificity	54.8				
			9-items: aged ≥80 years, male, low physical activity (<4 hours per week), comorbidity, sensory deficit, calf circumference <31cm, IADL dependence, gait problem, health pessimism	AUC	0.66				

H.2.4 Life expectancy risk tools

Table 70: Abbatecola 2011

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
Prospective cohort	Total n=3043	Older adults (aged 70 or older; mean age 81±6 years), previously hospitalised	Hospitalised Older Patient (HOPE) index	HOPE score ≥4		2 year	Italy	Italian National Research	Risk of bias - low
				Sensitivity	95.3				
				Specificity	15.8				

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
t	Development n=1533 Validation n=1510	Male to female ratio 47:53 Development cohort: consecutively admitted patient from January 2005 to December 2006 Validation cohort: consecutively admitted patient from January 2007 to December 2008. Uses data from Hospital Network of the Italian National Research Centre on Aging (INRCA). Inclusion criteria: aged over 70 years; admitted to acute geriatric ward for unplanned admission; had complete Comprehensive Geriatric Assessment (CGA) data during hospital stay and was performed at discharge; data regarding survival after 24 months from their hospital stay; signed written informed consent (or by a relatives of critically ill or severely cognitively impaired patients)	Includes: functional status; cognitive status; depression; co-morbidity; basic and instrumental ADL; social isolation; self-perceived QoL	HOPE score ≥8 Sensitivity Specificity AUC	 75 48 0.67 (0.57-0.7)			Centre on Aging	

Table 71: Beland 2012

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
Retrospective cohort	n=1494	Older adults (aged 65 or over; mean 73.86 years), community-dwelling Male to female ratio 28:72 Used participants from longitudinal Quebec Seniors' Health Survey (used stratified population sampling with random dialling method). A random sample of participants included in the Quebec study who met the inclusion criteria was taken. Inclusion criteria: aged 65 or older; not cognitively impaired (MMSE score ≥ 22)	Geriatric Comorbidity Score (GCS) Derived from prescription claims data.	C-statistic	0.67 (0.57-0.7)	1 year	Canada	Canadian Institute of Health Research	Risk of bias – very high due to sample size/participant flow and analysis

Table 72: Bernabeu-Wittel 2011A

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
Prospective cohort	Total n=1632 Development n=757 Validation	Adults (aged 18 or older; mean age derivation 79 \pm 9, validation 78.8 \pm 9.8), with multimorbidity ('polypathological'; 2 or more chronic conditions) 75% hospitalised 17.5% outpatient	PROFUND index Includes: age; clinical (e.g. neoplasia, dementia,	AUC	0.70 (0.67-0.74)	1 year	Spain	Instituto de Salud Carlos III, Ministerio de Sanidad y	Risk of bias – high due to sample size/participant flow and analysis

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
	n n=768	<p>7.5% at home patients</p> <p>Male to female ratio 55:45</p> <p>Mean number of comorbidities derivation 3.1±1.6, validation 3.2±1.7</p> <p>Patients ≥ 4 comorbidities derivation 33%, validation 37%</p> <p>Consecutive sampling</p> <p>Inclusion criteria: polypathological patient; patient who suffers chronic diseases in two or more of the following: A. Chronic heart failure with past/present stage II dyspnea of NYHA; coronary heart disease; B. vascularities and/or autoimmune disease; chronic renal disease; C. chronic lung disease; D. chronic inflammatory bowel disease; chronic liver disease with evidence of portal hypertension; E. stroke; neurological disease with permanent motor deficit leading to severe impairment basic ADLs (Barthel index <60); neurological disease with permanent moderate-severe cognitive impairment.</p> <p>F. symptomatic peripheral artery</p>	<p>disability</p> <p>dyspnea,</p> <p>delirium in last hospital admission);</p> <p>laboratory (haemoglobin), Barthel Index;</p> <p>caregiver;</p> <p>number of hospitalisations in past 12 months</p>					Consumo, Spain	

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
		disease; diabetes with proliferate retinopathy or symptomatic neuropathy. G. chronic anaemia due to digestive-tract losses or acquired hemopathy not tributary of treatment with curative intention; solid-organ or hematological active neoplasia not tributary of treatment with curative intention H. chronic osteoarticular disease, leading to severed impairment basic ADLs							

Table 73: Boeckxstans 2015

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
Prospective cohort	n=567	Older adults (aged 80-101 years; mean age 84.7±3.7), community-dwelling Male to female ratio 37:63 37.6% reported 5 or more diseases, range 1-16 diseases. Including: hypertension 66%; osteoarthritis 57.1% Participants visited GP over 3 week	Cumulative Illness Rating Scale (CIRS) Rates 14 body systems on a four-point severity scale	Sensitivity	67.2	3 year	Belgium	Fondation Louvain	Risk of bias – high due to sample size/participant flow
				Specificity	53.2				
				AUC	0.61 (0.56-0.67)				

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
		<p>period or</p> <p>Part of BELFRAIL (BF_{c80+}) study.</p> <p>Inclusion: all or first 3 consecutive people who visited GP over a 3 week period</p> <p>Exclusion criteria: known severe dementia; in palliative care; medical urgency</p>							

Table 74: Boulton 1993

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
Longitudinal cohort	n=5876	<p>Older adults (aged 70 years or older); community-dwelling</p> <p>A subsample of a multistage probability sample of all non-institutionalised U.S. civilians who were 70 years or older.</p> <p>Male to female ratio 42.5/53.5</p> <p>Data for analyses was</p>	<p>Pra (weighted score of 8 items: age, sex, self-perceived health, number of hospital admissions in previous year, number of physician visits in previous year, presence</p>	Sensitivity	60.49	4 years	USA	<p>National Institute on Aging, The Minnesota Medical Foundation, The University of Minnesota Centre for Urban and Regional</p>	<p>Risk of bias – high due to analysis</p>
				Specificity	100				

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
		<p>obtained from the Longitudinal Study of Aging (LSOA). Split sample with second half used to validate score derived from first half.</p> <p>Coronary artery disease 16.5%, Cerebrovascular disease 17.7%, diabetes 10.2%, hypertension 44.7%, cancer 12.5% arthritis or rheumatism 54.1%.</p> <p>Exclusion criteria: data from participants whose Medicare hospitalised records were not available.</p>	of diabetes mellitus, presence of coronary heart disease, and availability of a caregiver)					Affairs, and the Alfred P. Sloan Foundation.	

Table 75: Chan 2012

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
Prospective cohort	Total n=1120 Derivation n=585 Validation n=535	Older adults (aged 86-90 years; mean age derivation 85.6±7.7, validation 86.5±7.4), resident in care facility Condition(s) (derivation/validation): Dementia 72%/75% Cerebrovascular disease 39%/38.7% Diabetes 28.2%/27.4% Ischemic heart disease 21.1%/16.3% Congestive heart failure 17.1%/15.6% Chronic renal impairment 7.3%/10.8% Chronic pulmonary disease 10.2%/12.7% Peripheral vascular disease 4.5%/2.4% Chronic liver disease 0.4%/0.5% Male to female ratio 33:67	Unnamed Included: age; Barthel Index; number hospitalisations in previous year	AUC	0.742 (0.703-0.788)	2 year	Hong Kong, China	None stated	Risk of bias – high due to patient selection and analysis

Table 76: Chan 2014A

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
Retrospective cohort	n=2050	Older adults (mean age 80.7±7.1 years) 61.5% community-dwelling 38.5% resident in care facility Male to female ratio 40:60 Hypertension 65.5% Stroke 32.6% Diabetes 31.8% Dementia 19.7% Renal impairment 16.5% Ischemic heart disease 14.9% COPD 10% Congestive heart failure 9% Peripheral vascular disease 4.1% Tumour without metastasis 1.9% Metastatic solid tumour 1.3%	CCI, 1987	Overall	0.68 (0.64-0.72)	1 year	Hong Kong, China	None stated	Risk of bias – high due to sample size/participant flow and analysis
				AUC					
				Community-dwelling (n=1262)	0.67 (0.59-0.75)				
				AUC					
Resident in care facility (n=788)	0.69 (0.63-0.74)								

Table 77: Clegg 2016^{275,276}

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
Retrospective cohort	Total n=93154	Older adults (aged 65 to 95; mean age 75±7 years)	Electronic frailty index (eFI)	Moderate and above, internal cohort, 3 years – sensitivity 0.37, specificity 0.88		3 years	UK	Government	Risk of bias - low
	Develop	Male to female ratio	Includes: activity limitation, anaemia,	Moderate and above, external					

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
	ment n=20781 4 Internal validation n n=20772 0 External validation n n=51600 7	45:55 Development and internal validation cohort: ResearchOne database of GP practices, randomly split External validation cohort: THIN database of GP practices	arthritis, atrial fibrillation, cerebrovascular disease, chronic kidney disease, diabetes, dizziness, dyspnoea, falls, foot problems, fragility fracture, hearing impairment, heart failure, heart valve disease, housebound, hypertension, hypotension/syncope, ischaemic heart disease, memory and cognitive problems, mobility problems, osteoporosis, Parkinsonism, peptic ulcer, peripheral vascular disease, polypharmacy, requirement for care, respiratory disease, skin ulcer, sleep disturbance, social vulnerability, thyroid disease, urinary incontinence, urinary system disease, visual impairment, weight loss and anorexia.	cohort, 3 years – sensitivity 0.43, specificity 0.82 Severe, internal cohort, 3 years – sensitivity 0.10, specificity 0.98 Severe, external cohort, 3 years – sensitivity 0.13, specificity 0.97 Internal cohort, 3 year – C statistics 0.70, pseudo R ² 0.06 External cohort, 3 year – C statistics 0.75, pseudo R ² 0.02					

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
			Non-weighted tool, converted to 0 to 1 scale and categories of fit, mild frailty, moderate frailty and severe frailty defined by quartiles using the 99 th centile as the upper limit.						

Table 78: Daniels 2012

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
Prospective cohort	n=532	Older adults (aged 70 or older), community-dwelling Age 70-74: 36.3% Age 75-79: 36.3% Age ≥80: 27.4% Male/female ratio 4:6 Education none/primary: 35.7% Income ≤900: 18.7% Disability, Groningen Activity and	Groningen Frailty Indicator 15 items, focused on loss of functioning in 4 domains: physical (9 items), cognitive (1 item), social (3 items), psychological (2 items)	Sensitivity	73 (44-91)	1 year	The Netherlands	Stichting Innovatie Alliantie and Zuyd University of Applied Sciences	Risk of bias – high due to sample size/participant flow
				Specificity	54 (50-58)				
				AUC	64 (50-77)				
				PPV	4 (2-8)				
			NPV	98 (96-99)					
			Dutch Tilburg	Sensitivity	67 (39-87)				

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
		Restriction Scale (GARS): mean 24.9±9.3 Groningen Frailty Indicator (≥4): 46.3% Dutch Tilburg Frailty Indicator (≥5): 40.2% Sherbook Postal Questionnaire (≥2): 59.1% Inclusion criteria: aged 70 years or older; people living in Limburg and Utrecht in the Netherlands, identified from panels of 4 GPs between November 2008 and April 2009 Mortality 2.8%	Frailty Indicator 2 subscales: socio-demographic, life event and chronic disease data (10 items); level of frailty – physical (8 items), social (3 items), psychological factors (4 items) Sherbook Postal Questionnaire 6 items: physical (4 items); social (1 item); cognitive (1 item)	Specificity AUC PPV NPV Sensitivity Specificity AUC PPV NPV	61 (56-65) 64 (50-78) 5 (2-8) 98 (96-99) 71 (42-90) 41 (37-46) 56 (42-71) 3 (1-6) 98 (94-98)				

Table 79: Diez-Manglano 2015³⁵⁷

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
prospective obser	n=465 (333 internal)	Adults (mean age 80.9±8.9) with multimorbidity (polypathological), inpatients	PROFUND index	Internal medicine AUC	0.725 (0.67 – 0.781)	1 year	Spain	Not stated	Risk of bias – high due to analysis

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
observational	medicine, 132 acute geriatric unit)	<p>Male/female ratio 45:55</p> <p>Living in nursing home 23.5%</p> <p>Mean number of drugs 8.2±3.4</p> <p>Mean Charlson Index 3.8±2.1</p> <p>Mean admissions in past 12 months 2±1.3</p> <p>Inclusion criteria: polypathological inpatients from internal medicine departments and acute geriatric unit who attended consecutively between 1st March and 30th June 2011.</p> <p>A polypathological patient was defined as person who meets at least one criterion from two different categories: CATEGORY A A.1. Heart failure which in a situation of clinical stability has been in class II of the NYHAa scale (symptoms with ordinary physical activity) A.2. Ischemic heart disease (angina or infarction)</p>	Includes: age; clinical (e.g. neoplasia, dementia, disability, dyspnea, delirium in last hospital admission); laboratory (haemoglobin), Barthel Index; caregiver; number of hospitalisations in past 12 months	Geriatrics AUC	0.546 (0.448-0.644)				

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
		<p>CATEGORY B</p> <p>B.1. Vasculitis and systemic autoimmune diseases</p> <p>B.2. Chronic renal disease defined by elevated levels of creatinine (>1.4 mg/dl in men, >1.3 mg/dl in women) or proteinuria, sustained for 3 months</p> <p>CATEGORY C</p> <p>C.1. Chronic lung disease which in a situation of clinical stability has scored grade 2 on the MRCcdyspnea scale), or FEV1<65%, ó SatO2 ≤ 90%</p> <p>CATEGORY D</p> <p>D.1. Chronic inflammatory bowel disease</p> <p>D.2. Chronic liver disease with evidence of hepatocellular insufficiency or portal hypertension</p> <p>CATEGORY E</p> <p>E.1. Stroke.</p> <p>E.2. Neurological disease with permanent motor deficit causing impairment for basic activities of daily living (Barthel index under 60)</p> <p>E.3. Neurological disease with permanent cognitive impairment, at least moderate (5 or more errors on Pfeiffer)</p>							

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
		<p>CATEGORY F: F.1. Symptomatic peripheral artery disease F.2. Diabetes mellitus with proliferative retinopathy or symptomatic neuropathy</p> <p>CATEGORY G: G.1. Chronic anaemia due to digestive loss or acquired hemopathy non-subsidiary of healing treatment presenting Hb< 10 g/dl in two determinations more than three months apart G.2. Solid or active hematologic neoplasia non-subsidiary of healing treatment</p> <p>CATEGORY H: H.1. Chronic osteoarticular disease leading by itself to an impairment for basic activities of daily living (Barthel index under 60)</p> <p>Exclusion criteria: death during hospitalisation</p> <p>Reason for split internal medicine and geriatric population: not stated</p> <p>Mortality n=179 (38.5%)</p>							

Table 80: Jones 2005

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
Prospective cohort	n=3736	Older adults (aged 65 or older), community-dwelling	CHSA Frailty Index (FI)	AUC	0.70	5 year	Canada	National Health Research Development Program of Canada	Risk of bias – high due to patient selection, sample size/participant flow and analysis
		Female 38%	70-item						
		Used data from CSHA-2, which conducted clinical examinations in clinics, care facility and patients' homes, and CSHA-3, which follow-up participants' status.	FI-CGA	AUC	0.67				
			Sum of a functional impairment index and CIRS.						
			Included: impairment in 10 domains- cognition, mood, communication, mobility, balance, bowels, bladder, nutrition, function, social; CIRS						

Table 81: Martinez-Velilla 2014

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments						
Prospective cohort	n=122	Older adults (75 years or older; mean age 85.4±5.4), hospitalised Female 56.6% In care facility 21% Mild cognitive impairment 48.2% Severe cognitive impairment 12.3% Inclusion criteria: aged 75 years or older consecutively admitted to an acute geriatric ward of a tertiary hospital; CGA	CCI, 1987	Pseudo R ²	7	5 year	Spain	None stated	Risk of bias – high due to sample size/participant flow and analysis						
				AUC	0.64 (0.53-0.75)										
			CIRS, geriatric adaption (CIRS-G)	Pseudo R ²	2.4										
				AUC	0.54 (0.42-0.66)										
			Index of Coexistent Disease (ICED)	Pseudo R ²	4.5										
				AUC	0.56 (0.45-0.67)										
										Based on presence and severity of 19 medical conditions and 11 physical impairments,					

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
			using 2 subscales- IDS and Functional Severity (FS) scores						
			Geriatric Index of Comorbidity (GIC)	Pseudo R ²	16.1				
			Classifies patients into 4 classes of increasing somatic comorbidity, based on number of diseases and severity of diseases (based on Greenfield's IDS)	AUC	0.66 (0.56-0.76)				
				BISEP	Pseudo R ²	17.2			
			Included: high risk diagnoses; albumin ≤3.5; creatinine >1.5; dementia;	AUC	0.73 (0.63-0.82)				

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
			walking impairment						
			Prognostic Index (PI)	Pseudo R ²	20.9				
			Includes: male sex; number of ADLs at discharge; congestive; cancer; creatine; albumin	AUC	0.72 (0.62-0.83)				

Table 82: Mazzaglia 2007

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
Prospective cohort	Total n=5396 Development n=2470 Validation n=2926	Older adults (aged 65 and older; mean age 75), community-dwelling Sample derived from random sampling of rosters of 98 PCPs	Unnamed 7-item questionnaire . Included: age; sex; hospitalisations in past 6 months; ≥5 prescriptions; 'number of positive responses to screening questionnaire'	AUC	0.75 (0.73-0.78)	15 months	Italy	Agency for Regional Healthcare Services, Department of Health, Rome, Italy	Risk of bias – high due to analysis

Table 83: Min 2009

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
Prospective cohort	508	Older adults (aged 75 years or older; mean 81.3), community-dwelling Male/female ratio 37:63 Baseline Short Functional Survey score (range 0-5): mean 4 VES-13 score (range 0-10): mean Inclusion criteria: aged 75 years or over; one or more positive answers to screening questions – how you fallen 2 or more times in past year? Have you fallen and hurt yourself or needed to see a doctor in the past year? Are you afraid that you will fall due to balance or walking problems? Have you had a problem with urinary incontinence that is bothersome enough that you would like to know how it can be treated? And 3 item recall tests where subject responds yes/no	13-Item Vulnerable Elders Survey (VES-13) Includes: age; self-rated health; limitations in physical capability (stooping, kneeling, bending; limitations in lifting or carrying objects up to 10 pounds); reaching; extending arms above shoulder level; limitations in writing, handling or grasping small objects; limitations in walking a	Sensitivity (≥2)	92	Mean 4.5 years	USA	Agency for Healthcare Research and Quality; National Institute on Aging; NIA/American Federation on Aging Research; Reynolds Foundation; UCLA Older Americans Independence Center	Risk of bias - low
				Specificity (≥2)	37				
				Sensitivity (≥3)	86				
				Specificity (≥3)	54				
				Sensitivity (≥4)	69				
				Specificity (≥4)	69				
				Sensitivity (≥5)	60				
				Specificity (≥5)	75				
				Sensitivity (≥6)	51				
				Specificity (≥6)	80				
				Sensitivity (≥7)	45				
				Specificity (≥7)	81				
				Sensitivity (≥8)	32				
				Specificity (≥8)	91				
Sensitivity (≥9)	17								
Specificity (≥9)	99								
Sensitivity (10)	7								
Specificity (10)	99								
AUC	0.75 (0.71-0.8)								

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
			quarter mile; limitations in performing heavy housework; IADL disability in shopping; IADL disability in managing money; ADL disability in walking across the room; IADL disability in doing light housework; ADL disability in bathing or showering						

Table 84: Ng 2012

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
Prospective cohort	n=97258	Older adults (aged 65 or older; mean age 76.1 years), community-dwelling	VES-13	AUC	0.77	2 years	USA		Risk of bias – very high due to patient selection,
			VES-13, score model	AUC	0.74				

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
		<p>Random sample of Medicare beneficiaries. Survey with telephone follow-up</p> <p>Inclusion: aged 65 or older; completed survey; with data available on health and functional status in 2005 and on death status in the following 2 year period</p> <p>Mortality n=7433 (7.6%)</p>	Items scored on 0-10 scale, rather than dichotomous yes/no						analysis

Table 85: Pilotto 2008

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
Prospective cohort	<p>Total n=1695</p> <p>Development cohort n=838</p> <p>Validation cohort n=857</p>	<p>Older adults (aged 65-100; mean age development cohort 79.2±7.2, validation 78.3±7.1), hospitalised</p> <p>Inclusion criteria: all patients aged 65 or older consecutively admitted to the Geriatric Unit of a hospital in Italy due to acute disease or relapse of a chronic disease; ability to provide informed consent or availability of a proxy for informed consent and willingness to participate in the study; complete CGA during</p>	<p>Multidimensional Prognostic Index (MPI)</p> <p>Defines 3 levels of risk based on clinical, functional, cognitive, nutritional and social</p>	AUC	0.751 (0.70-0.80)	1 year	Italy	Ministero della Salute, IRCCS Research Programme	Risk of bias – high due to analysis

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
		hospitalisation	parameters						

Table 86: Radley 2008

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
Prospective cohort	n=43811	Older adults (aged 65-99; 85% aged 75 or older), hospitalised with hip fracture Female 77% 'Non-Black' 96% 20% sample of the 1998-2000 MedPar and Part B evaluation and management claims files	Romano CCI Used ICD-9-CM codes to assign indicator flags for common chronic conditions; addition of MI to CCI	C-statistic	0.72	1 year	USA	National Institute on Aging. National Institute for Arthritis, Musculo skeletal and Skin	Risk of bias – high due to analysis

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
		<p>Inclusion: aged 65-99; Medicare enrollees eligible for Medicare parts A and B at time of index fracture; index fracture was defined as first hospitalisation in 1999 with primary diagnosis of hip fracture or any hospitalisation in 1999 with evidence of surgical hip fracture repair</p> <p>Exclusion: enrolled in a Medicare health maintenance organisation</p>	<p>Clinical Classification Software (CCS)</p> <p>Classifies ICD-9-CM codes into 259 categories</p>	C-statistic	0.76			Diseases	

Table 87: Rockwood 2005

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
Prospective cohort	n=2305	<p>Older adults (aged 65 years or older), community-dwelling or living in a care facility</p> <p>5 year follow up of Canadian Study of Health and Aging (CSHA)-2.</p>	Cumulative Illness Rating Scale (CIRS)	AUC	0.58	5 years	Canada	National Health Research Development Program of Health Canada; Queen Elizabeth II	Risk of bias – high due to patient selection, sample size/participant flow and analysis
			CSHA-3 Clinical Frailty Scale	AUC	0.7				

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
			7 item					Research Foundation	
			CSHA- 3 Frailty Index	AUC	0.69				
			Counts 70 clinical deficits, including functionality, cognitive impairment, chronic conditions including features of mental illness						
			CSHA Function scale	AUC	0.68				
			Scores the patient on 12 ADLs/IADLs as either 0 (patient is independent in carrying out this ADL), 1 (needs						

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
			assistance) or 2 (is incapable)						
			CSHA rules-based definition of frailty	AUC	0.66				
			Categorises subjects as 0 (having no cognitive or functional impairment), 1 (isolated urinary incontinence), 2 (dependent on 1 ADL or having a diagnosis of cognitive impairment without dementia), 3 (dependent in at least 2 ADLs, having a mobility impairment						

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
			or having a diagnosis of dementia)						
			Modified Mini-Mental State Examination (3MS)	AUC	0.64				
			Score of 77 or less indicates cognitive impairment						

Table 88: Sancarolo 2011

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
Prospective cohort	n=4412	Older adults (aged 65-100; mean age 78.1±7.1 years), hospitalised Female 51.8% Inclusion: aged 65 or older; admitted to geriatric unit of hospital due to acute disease or relapse of chronic disease; complete CGA during hospitalisation; ability to provide informed consent or availability of proxy consent	MPI Defines 3 levels of risk based on clinical, functional, cognitive, nutritional and social parameters	AUC	0.7173 (0.6970-0.7375)	1 year	Italy	Ministero della Salute, Italy; IRCCS Research Programme; National Institute of Aging,	Risk of bias – high due to analysis

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
								Baltimore, USA	

Table 89: Sancarolo 2012

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
Prospective cohort	n=654	Older adults (aged 66-99; mean age 79.34±6.5), hospitalised TIA 100% Hypertension 62% Dyslipidemia 32% Atrial fibrillation 13.1% Ischemic heart disease 6.9% Peripheral vascular disease 2% HF 1.8% Women 53.2% Admitted to geriatric care unit of one hospital in Italy, due to acute disease or relapse of chronic disease Inclusion: aged 65 years or older; diagnosis of TIA; ability to provide consent or availability of proxy consent; completed CGA performed during hospitalisation	MPI Defines 3 levels of risk based on clinical, functional, cognitive, nutritional and social parameters	AUC	0.751 (0.697-0.806)	1 year	Italy	Ministero della Salute, IRCCS Research Programme	Risk of bias – high due to analysis
				C-statistic	0.749 (0.698-0.801)				

Table 90: Schneeweiss 2001

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
Prospective cohort	n=141161	Older adults (aged 65 years or older; mean age 75.4±6.7) with hypertension (100%), community-dwelling Female 58% Inclusion: all British Columbia residents aged 65 or older; filled at least one prescription for an angiotensin-converting enzyme inhibitor or calcium channel blocker from 1995-1997	CDS-1 Medications listed for following diseases: coronary and peripheral vascular disease; epilepsy; hypertension, HIV; TB; rheumatologic conditions; hyperlipidaemia; malignancies Parkinson's disease; renal disease; ESRD; cardiac disease, CHF; diabetes; glaucoma; cystic fibrosis; liver failure; acid peptic disease; transplantation; respiratory	C-statistic	0.659	1 year	Canada	Drug Information Association, Pennsylvania. Pharmicare, Ministry of Health of British Columbia	Risk of bias – high due to sample size/participant flow and analysis

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
			illness; thyroid disorders; gout; Crohn's and ulcerative colitis; pain; inflammation; depression; psychotic illness; bipolar disorder; anxiety and tension						
			CDS-2 Includes: sex; age; weighted medication use. Medications listed for following diseases: coronary and peripheral vascular disease; epilepsy; hypertension, HIV; TB; rheumatologic conditions; hyperlipidaemi	C-statistic	0.663				

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
			a; malignancies Parkinson's disease; renal disease; ESRD; cardiac disease, CHF; diabetes; glaucoma; cystic fibrosis; liver failure; acid peptic disease; transplantation; respiratory illness; thyroid disorders; gout; Crohn's and ulcerative colitis; pain; inflammation; depression; psychotic illness; bipolar disorder; anxiety and tension						
			Deyo CCI (uses ICD-9-CM codes)	C-statistic	0.694				

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
			Deyo CCI (calculated using ICD-9 codes from hospital discharge)	C-statistic	0.656				
			D'Hoore CCI (uses ICD-9-CM codes)	C-statistic	0.675				
			D'Hoore CCI (calculated using ICD-9 codes from hospital discharge)	C-statistic	0.651				
			Romano CCI (uses ICD-9-CM codes)	C-statistic	0.696				
			Romano CCI (calculated using ICD-9 codes from hospital discharge)	C-statistic	0.657				
			Ghali CCI (uses ICD-9-CM codes)	C-statistic	0.649				
			Ghali CCI (calculated using ICD-9	C-statistic	0.618				

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
			codes from hospital discharge)						

Table 91: Widagdo 2015¹³⁰³

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
Retrospective longitudinal	n=2087	Older adults (aged 70 years or over; mean age 77±6)	Frailty phenotype 5-item: unintentional weight loss, low grip strength, self-rated exhaustion (assessed using 2 questions from the Centre of Epidemiologic Studies Depression (CES-D) Scale, low physical activity (assessed using a	Sensitivity	20.9	3 year	Australia	US National Institute of Health, South Australian government, Flinders University, other NGOs	Risk of bias – high due to outcome and/or sample size/participant flow
	Frailty phenotype n=1566 Simplified frailty phenotype n=1173	Male/female ratio 1:1		AUC	0.57				
		Living in care facility 3.3%		Used data from Australian Longitudinal Study of Ageing, which contains 11 waves of data from 1992-2010. Outcome data were obtained from wave 3 data.					
Frailty Index n=2087 Prognostic Frailty Score n=1485	Mortality - Frailty phenotype n=205 (13.1%) Simplified frailty phenotype n=122 (10.4%) Frailty Index n=346 (16.6%) Prognostic Frailty Score n=188 (12.7%)								

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
			question on walking for exercise or recreation in past 2 weeks and slow walking time)						
			Simplified frailty phenotype	Sensitivity	4.9				
				Specificity	98.3				
				AUC	0.52				
			3-item: unintentional weight loss, inability to rise from a chair 5 times without the use of arms, low energy level						
			Frailty Index	Sensitivity	34.4				
				Specificity	85.8				
				AUC	0.60				
			39-variables: Live alone , Self-rated health, Arthritis, Asthma, History of heart attack, Hypertension,						

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
			Migraine, Parkinson’s disease, History of stroke, Thyroid disease, Ear/nose/throat problem, Mental disorder, Genito-urinary problem, Diabetes, Cancer, Chest pain, Constipation, Dental problem, Sleep problem, Spinal problem, Hearing difficulty, Eye trouble, Skin problem, Hands shaking problem, Stooping/crouching/kneeling						

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
			problem, Difficulty with bathing, Difficulty with personal grooming, Difficulty with dressing Difficulty with eating, Difficulty with toileting, Difficulty with going out, Difficulty with moving around, Difficulty with laundry/linen, Difficulty with housework, Difficulty with preparing meal, Difficulty with using telephone, Difficulty with managing money,						

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
			Difficulty with using public transport, Difficulty with shopping						
			Prognostic Frailty Score	Sensitivity	77.1				
				Specificity	54.7				
			9-items: aged ≥80 years, male, low physical activity (<4 hours per week), comorbidity, sensory deficit, calf circumference <31cm, IADL dependence, gait problem, health pessimism	AUC	0.66				

Table 92: Zekry 2012B

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
------------	--------------------	-------------------------	-----------	------------------	--------------	---------------------	---------	-------------------	----------

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
Prospective cohort	n=496	Older adults (aged 75 or older), hospitalised and discharged Random sample of patients aged 75 or older consecutively admitted to an acute geriatric hospital were selected by randomisation using computer generated randomisation table. Exclusion: mortality before hospital discharge	CCI, 1987	Pseudo R ²	1.9	1 year	Switzerland	Swiss National Science Foundation; Swiss Foundation for Aging Research	Risk of bias – very high due to sample size/participant flow and analysis
			CIRS-G Rates 14 body systems on a five-point severity scale	Pseudo R ²	9.3				
			ICED Based on presence and severity of 19 medical conditions and 11 physical impairments, using 2 subscales- IDS and Functional Severity (FS) scores	Pseudo R ²	2.0				
			Kaplan scale 14 medical conditions, sum weight of each disease	Pseudo R ²	4.1				

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
			GIC	Pseudo R ²	8.8				
			Classifies patients into 4 classes of increasing somatic comorbidity, based on number of diseases and severity of diseases (based on IDS)						
			CDS-1	Pseudo R ²	0.2				
			Medications listed for following diseases: coronary and peripheral vascular disease; epilepsy; hypertension, HIV; TB; rheumatologic conditions; hyperlipidaemia;						

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
			malignancies Parkinson’s disease; renal disease; ESRD; cardiac disease, CHF; diabetes; glaucoma; cystic fibrosis; liver failure; acid peptic disease; transplanta tion; respiratory illness; thyroid disorders; gout; Crohn’s and ulcerative colitis; pain; inflammation; depression; psychotic illness; bipolar disorder; anxiety and tension						

Table 93: Zeng 2014

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
Retrospective cohort	Total n=1414	Older adults (aged 65 or older) with multimorbidity (100% 3 or more chronic conditions).	Quan CCI (used ICD-10 codes) (score 1 year before)	C-statistic	0.799	1 year	USA	Agency for Healthcare Research and Quality	Risk of bias – very high due to patient selection and analysis
	Development cohort n=961	Inclusion criteria: aged 65 or older; enrolled in a health plan for at least a year; had 3 or more of 10 common chronic conditions. Development cohort responded to a survey assessing factors potentially associated with health outcomes. Validation cohort was not surveyed.	Quan cumulative CCI (score over 10 years)	C-statistic	0.782	10 year			
	Validation cohort n=13163		Quan baseline CCI (first CCI, within 10 year period)	C-statistic	0.770	10 year			

Study type	Number of patients	Patient characteristics	Risk tool	Outcome measures	Effect sizes	Length of follow-up	Country	Source of funding	Comments
			Quan CCI trajectory: linear model (modelled using growth curve models to fit each individuals' CCI measures using available data in 10 year period)	C-statistic	0.77	10 year			

H.2.5 Polypharmacy: unplanned hospital admissions

Table 94: Pozzi 2010⁹⁸⁹

Reference	Pozzi 2010 ⁹⁸⁹
Study type and analysis	Prospective cohort study Cox proportional hazard regression models
Number of participants and characteristics	n=788 Italy Older adults (aged 65 years or over; mean age 73±6.8) Community-dwelling M/F ratio: 43:57 Inclusion criteria: aged ≥65 years; community-dwelling; recorded in the City Registry Office of Dicomano, Italy

Reference	Pozzi 2010 ⁹⁸⁹
	Exclusion criteria: living in a care facility
	Recruitment/selection of patients: not stated
Prognostic variable(s)	Polypharmacy (≥5 drugs)
Outcomes and effect sizes	Hospitalisation (4-8 years) n= 634 (80.5%) Polypharmacy (≥5 drugs) – hospitalisation (4-8 years): unadjusted HR 1 (0.78 – 1.28)
Comments	Study attrition not reported.
Risk of bias	Low

Table 95: Spector 2013¹¹⁴¹

Reference	Spector 2013 ¹¹⁴¹
Study type and analysis	Retrospective cohort study Fine and Grey competing risks proportional hazards regressions. This method estimates the effect of risk factors on the sub hazard function accounting for the presence of competing risks.
Number of participants and characteristics	n=62 745 USA Older adults (aged 65 years or over; 46% over 85) Living in care facility M/F ratio: 31:69 Comorbid conditions diabetes 32% congestive heart failure 25% asthma or COPD 21% cardiac dysrhythmia 18% peripheral vascular disease 10%

Reference	Spector 2013 ¹¹⁴¹
	<p>renal disease 9%</p> <p>Inclusion criteria: long-stay care facility residents (stay 90 days or longer) Exclusion criteria: end-stage disease; received hospice; had 'do not hospitalise' order</p> <p>Recruitment/selection of patients: Main source of data was the Nursing Home Stay File, a sample of residents in 10% nursing homes in the US (2006-2008). The Nursing Home Stay File links a subset of Minimum Data Set (MDS) assessment data to inpatient claims data for both short and long-stay nursing home residents. New admissions between 10/1/06 and 7/1/2008 who remained in nursing home for at least 90 days were identified. As they only had data on hospitalisation until the end of 2008, for residents admitted on 7/1/2008 hospital data was only collected for 3 months.</p>
Prognostic variable(s)	<p>Polypharmacy (5-9 drugs) Polypharmacy (10-14 drugs) Polypharmacy (≥15 drugs)</p>
Outcomes and effect sizes	<p>Ambulatory care sensitive conditions (n=6165) – conditions where hospitalisation could be avoided when good outpatient care is provided</p> <p>Polypharmacy (5-9 drugs) – hospitalisation (3 – 25 months): sub hazard risk ratio 1.099 (0.963 – 1.254) Polypharmacy (10-14 drugs) – hospitalisation (3 – 25 months): sub hazard risk ratio 1.241 (1.088 – 1.417) Polypharmacy (≥15 drugs) – hospitalisation (3 – 25 months): sub hazard risk ratio 1.411 (1.224 – 1.626)</p> <p>Additional nursing home sensitive avoidable conditions (n=7595) – conditions where hospitalisation could be avoided when good nursing home patient care is provided</p> <p>Polypharmacy (5-9 drugs) – hospitalisation (3 – 25 months): sub hazard risk ratio 1.192 (1.068 – 1.330) Polypharmacy (10-14 drugs) – hospitalisation (3 – 25 months): sub hazard risk ratio 1.329 (1.189 – 1.486) Polypharmacy (≥15 drugs) – hospitalisation (3 – 25 months): sub hazard risk ratio 1.423 (1.261 – 1.607)</p> <p>Nursing home 'unavoidable' conditions (n=9320) – conditions where hospitalisation could not be avoided</p> <p>Polypharmacy (5-9 drugs) – hospitalisation (3 – 25 months): sub hazard risk ratio 1.206 (1.091 – 1.332) Polypharmacy (10-14 drugs) – hospitalisation (3 – 25 months): sub hazard risk ratio 1.388 (1.253 – 1.537) Polypharmacy (≥15 drugs) – hospitalisation (3 – 25 months): sub hazard risk ratio 1.376 (1.231 – 1.538)</p>
Comments	<p>Concerns about outcome measurement; categorisation of hospitalisations into ambulatory care sensitive, nursing home sensitive and 'unavoidable' nursing home hospitalisation not clearly defined, may not be a valid definition of outcome. Study attrition not reported</p>

Reference	Spector 2013¹¹⁴¹
Risk of bias	Low

H.2.6 Polypharmacy: health-related quality of life

None.

H.2.7 Polypharmacy: admission to care facilities

Table 96: Zuckerman 2006

Reference	Zuckerman 2006¹³⁵²
Study type and analysis	Retrospective cohort study Continuous time proportional hazards model for interval-censored data
Number of participants and characteristics	n= 487 383 USA Older adults (aged 65 years or over; 7.9% over 85) Community-dwelling M/F ratio: 45:55 Comorbid conditions Dementia 2.9% Depression 2.1% Inclusion criteria: aged 65 years or over; privately insured covered by employer-sponsored Medicare supplemental benefit plans by at least 1 year Exclusion criteria: previous nursing home admission; without prescription coverage; periods in observation period with no supplemental insurance or no prescription drug coverage Recruitment/selection of patients: MarketScan Medicare Supplemental and Coordination of Benefits database, produced by Thomson Medstat. A cohort was assembled from 3 years (2000 – 2002) of MarketScan data.

Reference	Zuckerman 2006¹³⁵²
Prognostic variable(s)	Polypharmacy (≥13 drugs)
Outcomes and effect sizes	Polypharmacy (≥13 drugs) – admission to care facility (2 years): unadjusted RR 3.31 (3.11 – 3.52)
Comments	None
Risk of bias	Low

H.2.8 Polypharmacy: mortality

Table 97: Ahmad 2005

Reference	Ahmad 2005¹⁴
Study type and analysis	Retrospective cohort study Cox Regression with a Genetic Algorithm
Number of participants and characteristics	n= 1042 England Older adults (aged 65 years or over; mean 75.21) Community-dwelling M/F ratio: not reported Inclusion criteria: aged 65 years and over; living within the survey areas Exclusion criteria: living in care facility Recruitment/selection of patients: Nottingham Longitudinal Study of Activity and Aging. Using electoral ward-level statistics from the 1981 census, three areas of greater Nottingham were combined to provide a study population whose demographic composition (as regards age, sex, social class, ethnicity and proportion of elderly people living alone) reflected the average national pattern for England and Wales. With the consent and co-operation of these general practitioners, Nottinghamshire Family Practitioner Committee age-sex lists were used to identify all patients aged 65 years and over within the survey areas. A total of 8409 elderly people were identified from which 1299 eligible individuals (those alive and still living at the address provided) were randomly selected for interview.

Reference	Ahmad 2005¹⁴
Prognostic variable(s)	Number of drugs (continuous)
Outcomes and effect sizes	Mortality (15 year) n= 741 (71%) Number of drugs (continuous) – mortality (15 year): unadjusted HR 1.177 (1.129 – 1.226)
Comments	Study response rate and attrition not reported
Risk of bias	Low

Table 98: Espino 2006

Reference	Espino 2006⁴⁰⁸
Study type and analysis	Longitudinal study Cox proportional hazards regression models
Number of participants and characteristics	n=3050 USA Older adults (aged 65-99) Community-dwelling M/F ratio: 42:58 Inclusion criteria: adults aged 65-99 years; Mexican American Exclusion criteria: none stated Recruitment/selection of patients: Hispanic Establish Populations for Epidemiologic Studies of the Elderly (EPESE). Probability sampling was used to represent the Mexican American older adult population residing in Texas, New Mexico, Colorado, Arizona and California.
Prognostic variable(s)	Polypharmacy (≥5 drugs)
Outcomes and effect sizes	Mortality (8 year) n= 950 (30.8%)

Reference	Espino 2006⁴⁰⁸
	Polypharmacy (≥5 drugs) - mortality (8 year): unadjusted HR 1.51 (1.28 – 1.8)
Comments	Study response rate and attrition not reported
Risk of bias	Low

Table 99: Gnjudic 2012

Reference	Gnjudic 2012⁴⁹⁴
Study type and analysis	Prospective cohort study Logistic regression model Receiver operating characteristics (ROC) curve analyses were used to calculate the area under the curve (AUC)
Number of participants and characteristics	n=1705 Australia Older males (aged 70 years or over) Community-dwelling Mean number of comorbidities 1.8±1.5 Inclusion criteria: aged 70 years or older; living in specific study area in Sydney, Australia Exclusion criteria: living in care facility Recruitment/selection of patients: Australian Electoral Roll was chosen as a sampling frame. Invitation letter were sent to 3627 men and 3005 men responded. 2815 eligible men were contacted and 1511 (54%) participated in the study. An additional 194 men volunteered independently of the invitation letter.
Prognostic variable(s)	Polypharmacy (≥5 drugs) Number of drugs (continuous)
Outcomes and effect sizes	Mortality (6 years) n=305 (17.9%) Polypharmacy (≥5 drugs) – mortality (6 years): sensitivity 0.51, specificity 0.65 (AUC 0.61)

Reference	Gnjidic 2012⁴⁹⁴
	Number of drugs (continuous) – mortality (6 years): unadjusted OR 1.15 (1.11 – 1.2)
Comments	Study response rate and attrition not reported. Baseline characteristics of participants not fully reported.
Risk of bias	Low

Table 100: Gomez 2015

Reference	Gomez 2015⁵⁰⁰
Study type and analysis	Prospective cohort study Cox proportional hazards model
Number of participants and characteristics	n=5052 Spain Older adults (aged 65 years or over) Community-dwelling Comorbidity index means (SD) ranging from 0.6 (1.2) in 0 drug group to 2.4 (1.9) in the polypharmacy group. Inclusion criteria: aged 65 years or older; living in specific study area in Spain Recruitment/selection of patients: Data from the Neurological Disorders in Central Spain study, survey area of 3 communities, lists of residents from population registers. 6395 adults were mailed surveys, 5914 were deemed eligible for screening, 5278 were screened, the remainder declined, could not be located or had died. Of the 5278 screened, 217 were excluded as they had no data on daily drugs and 9 were excluded because they had missing data on death status.
Prognostic variable(s)	Polypharmacy (≥ 6 drugs) Number of drugs (continuous)
Outcomes and effect sizes	Mortality (median follow-up 6.5 years) n=2550 (50.5%)

Reference	Gomez 2015⁵⁰⁰
	Polypharmacy (≥6 drugs) vs no medication – mortality (6.5 years): unadjusted HR 2.78 (2.36-3.27) Number of drugs (continuous) – mortality (6.5 years): unadjusted HR 1.16 (1.14-1.18)
Comments	Baseline characteristics of participants not fully reported.
Risk of bias	Low

Table 101: Jyrkka 2009

Reference	Jyrkka 2009⁶⁶⁷
Study type and analysis	Prospective cohort study Cox proportional hazards model
Number of participants and characteristics	n= 601 (first cohort n=601, second cohort n=339) Finland Older adults (aged 75 years or older) Community-dwelling or living in care facility <u>First cohort (1998-2002):</u> Aged 85 years or older 28% Living in care facility 13% M/F ratio: 26:74 <u>Second cohort (2003-2009):</u> Aged 85 years or older 50% Living in care facility 14% M/F ratio: 25:75 Inclusion criteria: aged ≥75 years; living in city of Kupio, Finland at the time of recruitment on 1 January 1998 Exclusion criteria: none stated

Reference	Jyrkka 2009⁶⁶⁷
	Recruitment/selection of patients: participants were randomly selected from all eligible inhabitants. Participation rate 86% (n=15 died before examination; 84 refused to participate). At follow up in 2003, 262 participants had been lost (n=233 died, n=29 refused to participate or could not be contacted)
Prognostic variable(s)	Polypharmacy (6-9 drugs) Polypharmacy (≥ 10 drugs)
Outcomes and effect sizes	<u>First cohort:</u> Mortality n=221 (37%) Polypharmacy (6-9 drugs) – mortality (4 years): unadjusted HR 1.3 (0.92 – 1.83) Polypharmacy (≥ 10 drugs) – mortality (4 years): unadjusted HR 2.53 (1.83 – 3.48) <u>Second cohort:</u> Mortality n=137 (40%) Polypharmacy (6-9 drugs) – mortality (4 years): unadjusted HR 1.95 (1.22 – 3.12) Polypharmacy (≥ 10 drugs) – mortality (4 years): unadjusted HR 3.71 (2.33 – 5.9)
Comments	Baseline characteristics of participants not fully reported.
Risk of bias	Low

Table 102: Krause 2007

Reference	Krause 2007⁷¹²
Study type and analysis	Prospective cohort study Cox proportional hazards regression
Number of participants and characteristics	n= 5888 USA Older adults (aged 65 years or over) Community-dwelling M/F ratio: not stated

Reference	Krause 2007 ⁷¹²
	<p>Inclusion criteria: 65 years or over at the time of examination; were expected to remain in the area for the next three years; were able to give informed consent and did not require a proxy respondent at baseline.</p> <p>Exclusion criteria: living in care facility; wheelchair-bound in the home at baseline or were receiving hospice treatment; radiation therapy or chemotherapy for cancer</p> <p>Recruitment/selection of patients: Cardiovascular Health Study. Recruited from 4 US communities</p>
Prognostic variable(s)	Number of drug classes (continuous)
Outcomes and effect sizes	Number of drug classes (continuous) - mortality (8 year): unadjusted HR 1.19 (1.15 – 1.22)
Comments	Study response rate and attrition not reported.
Risk of bias	Very high due to study participation, study attrition, prognostic factor measurement

Table 103: Md Yusof 2010

Reference	Md Yusof 2010 ⁸⁴²
Study type and analysis	<p>Prognostic cohort study</p> <p>Cox regression method</p>
Number of participants and characteristics	<p>n=113</p> <p>England</p> <p>Older adults (aged 64 years or over)</p> <p>Community-dwelling</p> <p>M/F ratio: 43:57</p> <p>Inclusion criteria: aged 64 years or over; lived independently; able to travel for routine medical assessment at Age and Cognitive Performance Research Centre (ACPRC)</p> <p>Exclusion criteria: none stated</p>

Reference	Md Yusof 2010 ⁸⁴²
	Recruitment/selection of patients: data were obtained from the ACPRC volunteer panel, a group of over 6000 older adults across Greater Manchester. Volunteers were invited to take part in the study.
Prognostic variable(s)	Number of drugs (continuous)
Outcomes and effect sizes	Mortality (7 years) n=20 (17.7%) Number of drugs (continuous) - Beta coefficient: 0.231; Exp(β coefficient) = 1.26
Comments	Inclusion/exclusion criteria not adequately described.
Risk of bias	Low

Table 104: Pozzi 2010

Reference	Pozzi 2010 ⁹⁸⁹
Study type and analysis	Prospective cohort study Cox proportional hazard regression model
Number of participants and characteristics	n=788 Italy Older adults (aged 65 years or over; mean age 73±6.8) Community-dwelling M/F ratio: 43:57 Inclusion criteria: aged ≥65 years; community-dwelling; recorded in the City Registry Office of Dicomano, Italy Exclusion criteria: living in a care facility Recruitment/selection of patients: study enrolled entire community-dwelling elderly population recorded in the City Registry Office 1995 and 1999

Reference	Pozzi 2010 ⁹⁸⁹
Prognostic variable(s)	Polypharmacy (≥5 drugs)
Outcomes and effect sizes	Mortality (4-8 years) n= 271 (34.4%) Polypharmacy (≥5 drugs) – mortality (4-8 years): unadjusted HR 2.21 (1.69 – 2.91)
Comments	Study attrition not reported.
Risk of bias	Low

Table 105: Richardson 2011

Reference	Richardson 2011 ¹⁰¹⁸
Study type and analysis	Prospective cohort study Survival analysis: Cox proportional hazard regression model
Number of participants and characteristics	n=12423 England and Wales Older adults (aged 65 years or over; 10% aged over 85) Community-dwelling (96%) or living in care facility (4%) M/F ratio: 37:63 Inclusion criteria: aged 65 years or over; primary care physician in one of the participating centre in Newcastle, Nottingham, Oxford, Cambridgeshire or Gwynedd Exclusion criteria: none stated Recruitment/selection of patients: population was derived from patient lists of primary care physicians in specific urban and rural areas and included people living in care facilities. Samples were stratified to recruit 2500 participants at each centre and equal numbers of those aged 65-74 years and ≥75 years. The overall response rate was 82%
Prognostic	Polypharmacy (≥ 5 drugs)

Reference	Richardson 2011¹⁰¹⁸
variable(s)	
Outcomes and effect sizes	Mortality (18 years) n=9225 (75%) Polypharmacy (≥ 5 drugs) - mortality (18 years), men: unadjusted HR 2 (1.82 – 2.19) Polypharmacy (≥ 5 drugs) - mortality (18 years), women: unadjusted HR 1.79 (1.67 – 1.93)
Comments	Study response rate and attrition not reported.
Risk of bias	Low

Table 106: Wang 2015

Reference	Wang 2015^{1018,1280}
Study type and analysis	Prospective cohort study Survival analysis: logistic regression
Number of participants and characteristics	n=1562 China Older adults (aged 80 years or over; mean age 85.2, range 80-104) Community-dwelling M/F ratio: not reported Inclusion criteria: aged 80 years or over; leaders of Chinese People’s Liberation Army, stable clinical status Exclusion criteria: advanced disease (cancer or non-cancer), initial estimate of life expectancy <3 months, Recruitment/selection of patients: population was derived the geriatric outpatient clinic on routine check-up in the South Building of Chinese PLA hospital in 2009.
Prognostic variable(s)	Polypharmacy (continuous)
Outcomes and effect sizes	Mortality (5 years) number of deaths not reported

Reference	Wang 2015^{1018,1280}
	Polypharmacy (continuous) - mortality (5 years): unadjusted OR 1.19 (1.12 – 1.23)
Comments	Study response rate and attrition not reported.
Risk of bias	Low

H.3 Frailty

Table 107: Auyeung 2014

Study	Auyeung 2014
Study type	Prospective cohort
Number of studies (number of participants)	1 (4000)
Country and setting	Hong Kong
Funding	Funded by the Jockey Club Charities Trust, the S H Ho Centre for gerontology and geriatrics, the Chinese University of Hong Kong, and the Hong Kong Research Grant Council
Duration of study	3 years
Age, gender, ethnicity	Age: Older adults (mean age 72 years, SD = 5.15). Gender: 2000 male, 2000 female. Ethnicity: Chinese
Patient characteristics	Community dwelling older adults recruited as part of a study on bone density in older Chinese adults. People were excluded if they were unable to walk without the assistance of another person, had had a bilateral hip replacement, were not competent to give informed consent, and had medical conditions that would make it unlikely that they would survive the duration of the study (3 years). Population was stratified by age; ages 65-69 years, 70-74 years, and 75 years and over
Index test	<ul style="list-style-type: none"> • BMI ≤ 18.5 • Physical activity as assessed with the Physical activity scale for the elderly (PASE; range 0-361); threshold for frailty defined as being in the lowest quintile of sample • Grip strength assessed using a dynamometer twice on each side, and maximum reading used; threshold for frailty defined as being in the lowest quintile of sample • Walking speed (m/s) over 6m distance at normal pace; threshold for frailty defined as being in the lowest quintile of

Study	Auyeung 2014	
	sample <ul style="list-style-type: none"> Self-reported exhaustion (yes/no) 	
Reference standard	Modified Fried's frailty criteria (shrinking defined as BMI <18.5; self-reported exhaustion; weakness defined as grip strength in the lowest quintile of sample; low physical activity defined as the lowest quintile in the sample on a questionnaire; slow walking speed defined as being in the lowest quintile of sample. Frailty defined as the presence of 3 or more deficits.	
Target condition	Frailty	
Results:	<u>BMI < 18.5 - Males</u>	<u>BMI < 18.5 - Females</u>
Sensitivity	31.7	22.2
Specificity	95.7	95.9
Area under the curve	0.637	<u>0.591</u>
Results:	<u>Self-reported exhaustion - Males</u>	<u>Self-reported exhaustion - Females</u>
Sensitivity	38.5	28.3
Specificity	95.5	95.1
Area under the curve	0.670	0.617
Results:	<u>Grip strength ≤28 kg – Males</u>	<u>Grip strength ≤18 kg – Females</u>
Sensitivity	89.5	84.5
Specificity	80.6	81.9
Area under the curve	0.862	0.844

Study	Auyeung 2014	
Results:	<u>Walking speed ≤0.89 m/s – Males</u>	<u>Walking speed ≤0.78 m/s – Females</u>
Sensitivity	82.7	91.9
Specificity	83.1	84.5
Area under the curve	0.826	0.880
Results:	<u>PASE ≤56.4 – Males</u>	<u>PASE ≤58.8– Females</u>
Sensitivity	83.7	82.8
Specificity	83.5	84.7
Area under the curve	0.849	0.857
General limitations (according to QUADAS 2)	Unclear if blinding of index test/reference standard; general concerns about reference standard; slight deviation from usual reference standard (uses BMI to assess unintentional weight loss); composite reference standard including index test; thresholds determined from within study sample	

Table 108: Boxer 2008a

Study	Boxer 2008a
Study type	Prospective cohort
Number of studies (number of participants)	1 (60)
Country and setting	USA; outpatient
Funding	Supported by the General Clinical Research Center

Study	Boxer 2008a
Duration of study	
Age, gender, ethnicity	Age: Older adults (mean age 77-78 years, SD = 9 - 12). Gender: 43 male, 17 female. Ethnicity: not reported
Patient characteristics	<p>Older adults with congestive heart failure and an ejection fraction $\leq 40\%$ within the preceding year, recruited from the University of Connecticut Health Center Heart Failure Center. Exclusion criteria were intended to exclude people with serious end-stage disease of other organ systems, disorders that greatly affected ambulation, and hormonal therapy known to affect muscle function. Exclusion criteria were; metastatic, active or advanced cancer; active chemotherapy, radiation treatment, or hormonal therapy; systemic rheumatologic or connective tissue disorders; consumption of >3 alcoholic drinks per day; use of androgen, oestrogen, dehydroepiandrosterone, or hormone receptor antagonists in the preceding year; or the presence of advanced liver disease, renal disease requiring dialysis, Parkinson's disease, an inability to ambulate, or a myocardial infarction within 3-months before the study.</p> <p>Heart failure class of participants (as determined with New York Heart Association distinctions) were as follows; class I (1%), class II (57%), class III (37%) and class IV (5%). Mean ejection fraction = 29% (SD = 8). The reference standard identified 16 participants (27%) as frail.</p>
Index test	6-minute walking test: participants were permitted to use a walker or cane as required while the observer recorded symptoms such as chest pain, shortness of breath, and leg pain. Low endurance was defined as walking ≤ 300 m
Reference standard	Modified Fried's frailty criteria (shrinking defined as unintentional weight loss of 4.5kg or more in the last year; exhaustion defined as responses to 2 questions from the Center for Epidemiological Studies Depression Scale; weak grip strength; low physical activity as assessed using Physical activity scale for the elderly (PASE); slow walking speed on an 8-foot walk. Frailty defined as the presence of 3 or more deficits.
Target condition	Frailty
Results:	
TP	15
FP	11
FN	1
TN	33
Sensitivity	0.94
Specificity	0.75

Study	Boxer 2008a
PPV	0.58
NPV	0.97
Positive likelihood ratio	3.75
Negative likelihood ratio	0.08
General limitations (according to QUADAS 2)	Unclear if blinding of index test/reference standard; only applicable to older adults with heart failure and no significant organ failure, unclear if MM; small sample size; general concerns about reference standard; composite reference standard including index test; unclear thresholds for some items of reference standard

Table 109: Castell 2013

Study	Castell 2013
Study type	Cross-sectional cohort
Number of studies (number of participants)	1 (1327)
Country and setting	Spain: community
Funding	Funded by the Ministry of Health, Spain, and RETICEF (Red Temática de Investigación Cooperativa en Envejecimiento y Fragilidad)
Duration of study	
Age, gender, ethnicity	Age: Older adults ≥ 65 years (mean age 75.4 years, SD = 7.4; range = 65 – 104 years). Gender: 619 male, 708 female. Ethnicity: not reported
Patient characteristics	Older adults living in 2 urban neighbourhoods in northern Madrid. A random sample of participants, stratified by sex and 5-year age groups, was recruited from primary health care centres. 41% of the sample was from a low SES background, 20.2% lived alone, 33.8% (N = 461) participants were diagnosed with ≥2 comorbid diseases, 10.5% of participants were disabled, 55.7% used ≥ 5 medications, and 15.6% had cognitive decline. The reference standard identified in 11.2% (148/1325) participants.
Index test	Walking speed: Participants were asked to walk 3 meters at usual pace.
Reference standard	Modified Fried's frailty criteria (shrinking defined as unintentional weight loss of 5kg or more in the last year or more than 3

Study	Castell 2013
	kg in the last 3-months; exhaustion defined as responses of ‘frequently or ‘always’ to either of the questions “I felt that everything I did was an effort” and “I could not get going” for the last week; weakness measured using grip strength in the lowest quintile adjusted by BMI (cut off points were for men: BMI ≤24 and grip strength <18.5 kg; BMI 24 – 28 and grip strength < 20 kg; BMI >28 and grip strength <22 kg. For women: BMI ≤29 and grip strength <11 kg; BMI >29 and grip strength <12 kg); slowness defined in the same way as the index test; low physical activity as assessed using the Longitudinal Ageing Study Amsterdam (LASA) Physical Activity Questionnaire (LAPAQ), which is used to record daily physical activity and physical exercise. Cut-offs were the same as those proposed by Fried; <383 kcal/week for men and <270 kcal/week for women). Frailty was defined as impairment in 3 or more domains.
Target condition	Frailty
Results: TP FP FN TN Sensitivity Specificity	<u>Threshold = 0.8 m/s</u> 147 418 1 759 0.99 0.64
General limitations (according to QUADAS 2)	Unclear if blinding of index test/reference standard; composite reference standard which included factors related to index test; general concerns about reference standard; pop^ not MM although 55% taking ≥5 medications; multiple thresholds tested

Table 110: Da Cmara 2013

Study	Da Cmara 2013
Study type	Cross-sectional cohort
Number of studies (number of participants)	1 (124)
Country and setting	Canada and Brazil: community
Funding	Funded by the National Council for Scientific and Technological Development
Duration of study	2-months
Age, gender, ethnicity	Age: Older adults (mean age 69.48 years, SD = 2.95; range = 65 – 74 years). Gender: 51 male, 73 female. Ethnicity: not reported
Patient characteristics	Older adults living in the community recruited as part of a larger study to increase knowledge about the sex-/gender-mobility gap. Participants were recruited from 2 sites; Saint Bruno (Québec, Canada) and in Santa Cruz (Brazil). These sites were selected as they represent communities from different socioeconomic backgrounds. Inclusion criteria were adults aged between 65-74 years, free of severe activity of daily living (ADL) disability (defined as the inability to carry out any of the following activities; bathing, getting out of bed, eating, grooming, or using the toilet). At Santa Cruz, a random sample of adults was selected from municipal rolls and stratified by mobility (inability to walk a mile or climb 1 flight of stairs) and sex. Adults were recruited in Saint Bruno through advertisements in local newspapers and shops. Mean BMI (SD) at Santa Cruz site = 26.32 (4.06) and at Saint Bruno = 29.34 (6.62). Proportion of participants at Santa Cruz site = 40.6% and at Saint Bruno = 26.7%. According to the reference standard, 19.4% of the total sample were frail, and 50% of the sample were pre-frail. A higher proportion of participants at the Santa Cruz site were identified as frail (28.1%, as compared with 10% at Saint Bruno).
Index test	The Short Physical Performance Battery: includes tests of gait, balance, and chair stand, with scores for each component assessed on a 0 – 4 scale; with 0 representing inability to perform the test and 4 indicates the best performance. For balance, participants are asked to maintain their feet side by side, semi-tandem and tandem positions for 10 seconds each. For gait, a 4-m walk at the participants’ usual pace was timed. For the chair stand test, participants were asked to stand up and sit down 5 times as quickly as possible.
Reference standard	Modified Fried’s frailty criteria (shrinking defined as unintentional weight loss of 5kg or more in the last year; exhaustion defined as responses of ‘occasionally’ or ‘most of the time’ to either of the questions “I felt that everything I did was an effort” and “I could not get going in the last week”; weakness defined based on thresholds defined by Fried, and adjusted to age and sex; low physical activity defined as being in the lowest gender-specific quintile on the short form from the International Physical Activity Questionnaire (cut offs were 299.54 kcal/week for men and 208.82 Kcal/week for women)). Frailty was defined as impairment in 3 or more domains, and pre-frailty was defined as impairment in 1 or 2 domains.

Study	Da Cmara 2013		
Target condition	Frailty		
Results:	<u>Total sample</u> Threshold = 9, as derived from the best trade-off between sensitivity and specificity	<u>Santa Cruz (Brazil)</u> Threshold = 9, as derived from the best trade-off between sensitivity and specificity	<u>Saint Bruno (Canada)</u> Threshold = 9, as derived from the best trade-off between sensitivity and specificity
Sensitivity	0.92	0.81	0.92
Specificity	0.54	0.52	0.80
Area under the curve	0.78 (CI = 0.69 – 0.86)	0.67 (CI = 0.49 – 0.84)	0.81 (CI = 0.70 – 0.92)
General limitations (according to QUADAS 2)	Unclear if blinding of index test/reference standard; general concerns about reference standard; composite reference standard including factors related to index test; Threshold determined based on lowest quintile of study population; 1 item of reference standard had internal threshold (quintile of study pop [^]); 50% of study sample had 2 or more comorbidities, this was higher (67%) in Saint Bruno cohort than in the Santa Cruz cohort (47%); incomplete data for pre-frailty; differences between Canada and Brazil samples, with no clear explanation		

Table 111: Dent 2012

Study	Dent 2012
Study type	Prospective cohort
Number of studies (number of participants)	1 (100)
Country and setting	Australia
Funding	Study authors have received funding from industry, government and academic sources
Duration of study	

Study	Dent 2012
Age, gender, ethnicity	Age: Older adults (mean age 85.2 years, SD = 6.1). Gender: 25 male, 75 female. Ethnicity: not reported
Patient characteristics	Inpatient older adults admitted to the geriatric evaluation and management unit (GEMU) with acute illness. People spent a mean of 6 days in hospital prior to admission to GEMU, and a mean of 14.8 days in GEMU
Index test	Mini-nutritional assessment (short form) (BMI measurements and first 6 items of the MNA on food intake, weight loss, mobility, psychological problems, and dementia); scores assessed on a scale 0-30. Malnourishment defined as scores of <8
Reference standard	Modified Fried's frailty criteria (shrinking defined as unintentional weight loss of 4.5kg or more in the last year; exhaustion defined as responses to the questions "I felt that everything I did was an effort" and "I could not get going in the last week"; weakness defined as grip strength <30kg for males and <18 kg for females; low physical activity defined as yes to all 3 items assessing physical activity; slow walking speed defined as >30s or unable to complete 6m. Frailty defined as the presence of 3 or more deficits.
Target condition	Frailty
Results:	
	<u>Standard threshold = ≤7</u>
Sensitivity	0.636
Specificity	0.794
PPV	0.857
NPV	0.529
	<u>Threshold based on maximum Youden Index = ≤8</u>
Sensitivity	0.803
Specificity	0.765
PPV	0.869
NPV	0.667
Area under the curve	0.802

Study	Dent 2012
General limitations (according to QUADAS 2)	Unclear if blinding of index test/reference standard; general concerns about reference standard; composite reference standard including factor related to index test; in patients with acute illness and unclear if MM

Table 112: Dibari 2014

Study	Dibari 2014
Study type	Prospective cohort
Number of studies (number of participants)	1 (1037)
Country and setting	Italy: community
Funding	Supported by the Italian Ministry of Health
Duration of study	
Age, gender, ethnicity	Age: Older adults ≥70 years. Gender: not reported. Ethnicity: not reported
Patient characteristics	A subgroup of older adults recruited as part of a wider study to develop screening programs for identifying frailty in the population. Participants who were in long-term care services for the disabled were excluded. Participants received a copy of the postal questionnaire (index test) through the post. The participants included in the analysis were those who also consented to a Comprehensive Geriatric Assessment (CGA) in their homes, irrespective of the result of the postal questionnaire. According to the reference standard, 380 participants (36.6%) were identified as frail.
Index test	A postal questionnaire consisting of 1 disability item and 10 frailty items, all of which required a yes/no response. Frailty items were derived from the Sherbrooke Postal Questionnaire (SPG), which identifies people at risk of losing their autonomy on the basis of not living alone, taking multiple drugs daily, using assistive walking devices, and having hearing, vision, or memory problems. The version used in this study has been adapted and validated elsewhere. The questionnaire is designed to be self-completed by older adults with limited literacy. Frailty was defined as scoring positive on 4 frailty items and responded no to the disability item, indicating non-disabled.
Reference standard	Fried's phenotype: Frailty was assessed using a CGA and in accordance with Fried's phenotype model. Study staff, which included trained nurses and social workers, performed the CGA in participants' homes. Frailty was defined as impairment in ≥3 domains (unintentional weight loss of 5kg in the previous year; poor muscle strength; slow walking speed; exhaustion when performing common chores; and 30minutes/day or less of moderate intensity physical activity. Poor muscle strength, slow walking speed and exhaustion were all inferred from a score <3 on the repeated chair standing of the SPPB, a score <4

Study	Dibari 2014
	on the 4-m walk test of the SPPB, and an answer of 'No' on the geriatric depression scale item (GDS) 'do you feel full of energy?', respectively).
Target condition	Frailty
Results:	<u>Pre-specified threshold = 4 items. The best compromise between sensitivity and specificity was identified as a threshold of 5 items.</u>
	<u>Threshold 4 frailty items</u>
Sensitivity	0.93
Specificity	0.27
	<u>Threshold 5 frailty items</u>
Sensitivity	0.71
Specificity	0.58
	<u>Threshold 5 frailty items</u>
PPV	49.1%
NPV	77.2%
Area under the curve	0.695
General limitations (according to QUADAS 2)	Unclear if blinding of reference standard; general concerns about reference standard; composite reference standard but no obvious overlap with index test; multiple thresholds tested, with pre-determined (4) and best (5) reported; unclear if population is MM; unclear time interval between index test and reference standard

Table 113: Hoogendijk 2013

Study	Hoogendijk 2013
Study type	Cross-sectional cohort
Number of studies (number of participants)	1 (102)

Study	Hoogendijk 2013
Country and setting	Netherlands: Primary care
Funding	Supported by The Netherlands Organization for Health Research and Development (ZonMw): Dutch National Care for the Elderly Program
Duration of study	
Age, gender, ethnicity	Age: Older adults (>65 years; mean age 78.6 years, range 65-96 years). Gender: 44 male, 58 female. Ethnicity: not reported
Patient characteristics	A subpopulation of older adult people of a primary care practice in Amsterdam who were enrolled in a larger study (the Identification of Frail Elderly Study in the Netherlands). People were selected using unclear method and stratified by age, sex and GFI score. Three groups were formed; non frail (GFI <2), some frailty (GFI 2 or 3), and moderate to severe frailty (GFI ≥4), leading to oversampling of older adults with frailty. According to Fried's criteria, 11.6% of participants were identified as frail. Mean number of chronic diseases = 2.9 (SD = 1.9); mean number of prescribed medicine = 4.1 (SD = 3.2); mean MMSE (0-30) = 26.1 (SD = 2.2); mean mobility limitations (0-4) = 0.3 (SD = 0.6).
Index test	<ul style="list-style-type: none"> • Clinical judgement of the GP: GPs were asked 'would you consider this patient to be frail, if frailty is defined as a loss of resources in several domains of functioning (physical, psychological, social), increasing the risk of adverse outcomes?' (yes/no). • Self-rating: people were asked the question 'how would you rate your health status on a scale from 0 to 10?'. A cut off point of 6 or lower was chosen to indicate frailty. • Polypharmacy: electronic medical records were used to derive the number of medicine prescriptions for each person. A cut off point of 5 or more medications with different Anatomic Therapeutic Chemical classification system codes prescribed over the last 6 months was chosen to indicate moderate to major polypharmacy • GFI: frailty was defined as a score of ≥4 • PRISMA7: frailty was defined as a score of ≥3
Reference standard	Fried's frailty criteria: frailty was defined as impairment in 3 or more domains (weight loss, self-reported exhaustion, weakness, slow walking speed, and low physical activity)
Target condition	Frailty

Study	Hoogendijk 2013				
Results:	<u>Clinical judgement</u>	<u>Self-rating</u>	<u>Polypharmacy</u>	<u>GFI</u>	<u>PRISMA7</u>
Sensitivity	0.70	0.85	0.70	0.57	0.86
Specificity	0.77	0.73	0.73	0.72	0.83
Area under the curve	0.73	0.79	0.71	0.64	0.85
General limitations (according to QUADAS 2)	Unclear if blinding of index test/reference standard; unclear selection process; sample stratified to include greater proportion of individuals with frailty according to 1 of the index tests; general concerns about reference standard				

Table 114: Nunes 2015

Study	Nunes 2015
Study type	Cross-sectional cohort
Number of studies (number of participants)	1 (433)
Country and setting	Brazil
Funding	Funded through a master's fellowship award (Fundação de Amparo à Pesquisa do Estado de São Paulo)
Duration of study	
Age, gender, ethnicity	Age: Older adults (>75 years; mean age 85.7 years, SD = 5.1). Gender: 150 male, 283 female. Ethnicity: not reported
Patient characteristics	Older adults living in the community who were recruited as part of a large multi-centre survey several years' earlier (original sample N = 2143) and re-interviewed as part of a subproject to identify the determining factors of frailty. A majority of the sample were multimorbid (63.5%), 37% were identified as frail by the reference standard. Cognitive decline was identified in 26.1% of the sample, depression in 18.5%, the mean level of education was <3 years, 47.3% expressed experiencing difficulty with ≥1 basic activity of daily living, 65.8% expressed experiencing difficulty with ≥1 instrumental activity of daily living.
Index test	Self-report questionnaire derived earlier in the multi-centre survey and validated with this population. Questionnaire contains 6 items related to the domains of the Fried phenotype model:

Study	Nunes 2015
	<ul style="list-style-type: none"> • Weight loss: frailty defined as a loss of >3kg. ‘In the last 12months, did you lose weight without going on any diet? If yes, how many kilograms did you lose? Between 1kg and 3kg, or more than 3kg?’ • Decreased strength: ‘In the last 12months, do you feel weaker or think your strength has decreased? Yes/no’. • Decreased walking speed: ‘Do you think that you are walking more slowly than you did 12-months ago? Yes/no’. • Low physical activity: ‘do you think that you are currently performing less physical activity than you did 12-months ago? Yes/No’. • Self-reported fatigue (2 items): In the past week, how often did you feel that you could not perform daily activities (you started something but could not finish)? Never or rarely (less than 1 day); a few times (1-2 days); sometimes (3-4 days), most of the time?’ ‘In the past week, how often did the performance of your routine activities require a major effort? Never or rarely (less than 1 day); a few times (1-2 days); sometimes (3-4 days), most of the time?’ <p>Frailty was defined as scoring positive for 3 or more of the above domains. Unclear from the report whether the questionnaire was completed through interview or was completed by the person independently.</p>
Reference standard	<p>Fried’s frailty criteria. Frailty was defined as impairment in 3 or more domains (mobility assessed using the Short Physical Performance Battery Assessing Lower Extremity Function, adjusted for sex and height, with impairment defined as being in the highest 20% of the sample; strength assessed using grip strength, stratified by sex and BMI, impairment defined as being in the lowest 20% of the cohort; fatigue assessed according to self-reported exhaustion on 2 questions (how often in the last week did you feel (1) everything was an effort or (2) you could not get going?), with impairment defined as having experienced a symptom sometimes or most of the time during the past week; physical activity limitation was assessed with the International Physical Activity Questionnaire (IPAQ), stratified by sex, with impairment defined as a score in the lowest quartile of the sample; nutrition assessed as any weight loss > 3 kg in the 1 year between surveys).</p>
Target condition	Frailty
<p>Results:</p> <p>Sensitivity</p> <p>Specificity</p>	<p>0.632</p> <p>0.716</p>

Study	Nunes 2015
General limitations (according to QUADAS 2)	No blinding of the results to each test (reference standard and index test performed in the same assessment, by the same interviewer); unclear selection process; general concerns about reference standard

Table 115: Purser 2006

Study	Purser 2006
Study type	Prospective cohort
Number of studies (number of participants)	1 (309)
Country and setting	USA
Funding	Funded by Doris Duke Foundation; Claude D. Pepper Older American's Independence Center
Duration of study	
Age, gender, ethnicity	Age: Older adults (mean age 77 years, SD = 5). Gender: 216 male, 93 female. Ethnicity: "Minority" = 15.9%
Patient characteristics	Inpatient older adults with significant coronary artery disease. Mean number of comorbidities = 3.8 (SD = 1.6): diabetes mellitus (36.6%), hypertension (80.3%), hyperlipidemia (75.4%), congestive heart failure (29.4%), COPD (16.8%), cerebrovascular disease (19.1%), myocardial infarction (41.7%), depression (24.9%). Prevalence of frailty was 27% according to Fried's frailty criteria and 63% according to CUMULATIVE DEFICIT MODEL deficit model
Index test	Grip strength: no pre-determined threshold; threshold chosen based on AUC curve Gait speed (15 feet): no pre-determined threshold; threshold chosen based on AUC curve 30-second chair stand test: no pre-determined threshold; threshold chosen based on AUC curve
Reference standard	Two reference standards used: <ul style="list-style-type: none"> Fried's frailty criteria. Frailty was defined as impairment in 3 or more domains (mobility assessed as time to walk 4.6m, with impairment defined as being in the lowest 20% of same-gender/height community dwelling older adults; strength assessed using grip strength, impairment defined as being in the lowest 20% of a community based cohort; endurance assessed according to self-reported exhaustion on 2 questions (how often in the last week did you feel (1) everything was an effort or (2) you could not get

Study	Purser 2006		
	<p>going?), with impairment defined as having experienced a symptom on 3 or more days during the past week; physical activity limitation was assessed with the physical function subscale from the Medical Outcomes Study Short Form, with impairment defined as a score in the lowest quartile for sex; nutritional status, assessed as patient-reported unintentional weight loss > 10 pounds).</p> <ul style="list-style-type: none"> Cumulative deficit model: Self-reported impairments in 1 or more domains (mobility, ADLs, incontinence, cognitive impairment), as indicated by a score of 1 or more on a scale of 0-3 for each domain. 		
Target condition	Frailty		
<p>Results:</p> <p>Sensitivity (optimal threshold, extracted from plots)</p> <p>Specificity (optimal threshold, extracted from plots)</p> <p>Area under the curve</p>	<p>Grip strength (Fried as reference standard)</p> <p>0.72 (threshold = 25kg)</p> <p>0.72 (threshold = 25kg)</p> <p>0.83</p>	<p>Gait speed (Fried as reference standard)</p> <p>0.82 (threshold = 0.65 m/s)</p> <p>0.82 (threshold = 0.65 m/s)</p> <p>0.89</p>	<p>30-second chair stand test (Fried as reference standard)</p> <p>0.79 (threshold = 7 stands)</p> <p>0.79 (threshold = 7 stands)</p> <p>0.78</p>
General limitations (according to QUADAS 2)	Unclear if blinding of index test/reference standard; thresholds determined on study sample, general concerns about reference standard; composite reference standard that includes factors overlapping with index tests		
<p>Results:</p> <p>Area under the curve</p>	<p>Grip strength (Cumulative deficit model as reference standard)</p> <p>0.66</p>	<p>Gait speed (Cumulative deficit model as reference standard)</p> <p>0.70</p>	<p>30-second chair stand test (Cumulative deficit model as reference standard)</p> <p>0.57</p>

Study	Purser 2006
General limitations (according to QUADAS 2)	Unclear if blinding of index test/reference standard; general concerns about reference standard; composite reference standard that includes factors overlapping with index tests; outcome reporting

Table 116: Savva 2013

Study	Savva 2013
Study type	Cross-sectional cohort
Number of studies (number of participants)	1 (1814)
Country and setting	Ireland; community
Funding	Supported by Irish life, the Department for Health and Children, and The Atlantic Philanthropies
Duration of study	
Age, gender, ethnicity	Age: Older adults >65 years (median age 70 years, range = 65-93 years). Gender: 889 male, 925 female. Ethnicity: not reported
Patient characteristics	A subgroup of older adults living in the community who were recruited as part of The Irish Longitudinal Study on Ageing (TILDA) and attended a health centre assessment as part of the study. The reference standard identified 81 participants (4.5%) as frail and 716 participants (39.5%) as pre-frail.
Index test	Timed up and go test (TUG): participants were asked to stand from a seated position, walk 3m at their usual pace, turn around, walk back to the chair, and sit down. Walking aids were permitted where required.
Reference standard	Fried's model of frailty, frailty defined as impairment in 3 or more domains, with thresholds for impairment derived from population specific cut-points; weight loss >4.5kg, grip strength (20.5kg for men with BMI<24, 21.5kg for men with BMI 24-26, 23kg for men with BMI > 26; 11.5kg for women with BMI <23, 13 kg for women with BMIA >23), physical activity (international physical activity questionnaire <868 kcal/week for men, <309 kcal/week for women); walking speed 4.88m (109.7 cm/s for men less than 173cm, 116.7 cm/s for men taller than 173cm; 100.7 cm/s for those less than 159 cm and 108.4 cm/s for those taller than 159cm); exhaustion (a response of sometimes or often to the items 'I could not get going' and 'I felt that everything I did was an effort)
Target condition	Frailty

Study	Savva 2013
Results:	<u>Frailty</u>
Sensitivity	8 seconds = 0.97 9 seconds = 0.95 10 seconds = 0.93 11 seconds = 0.80 12 seconds = 0.72
Specificity	8 seconds = 0.18 9 seconds = 0.42 10 seconds = 0.62 11 seconds = 0.78 12 seconds = 0.86
Area under the curve	0.87
General limitations (according to QUADAS 2)	Unclear if blinding of index test/reference standard; no pre-determined thresholds for index tests; study population thresholds were used for reference standard; general concerns about reference test

Table 117: Schoon 2014

Study	Schoon 2014
Study type	Cross-sectional cohort
Number of studies (number of participants)	1 (593)
Country and setting	Netherlands
Funding	Funded by the National Programme for Elderly Care, which is coordinated and sponsored by ZonMw (Netherlands), organisation of health research and development

Study	Schoon 2014		
Duration of study			
Age, gender, ethnicity	Age: Older adults (mean age 76.8 years, range = 70-92 years). Gender: 260 male, 333 female. Ethnicity: not reported		
Patient characteristics	Older adults living in the community recruited as part of a study to validate the Two-step Older Persons Screening study (TOS-study). Six general practitioners recruited patients from their practices, which were located in urban (2 practices), suburban (1 practice), and rural (3 practices) areas in the Netherlands. People were excluded if they were too ill to be screened, were receiving treatment from a geriatrician, or had received a comprehensive geriatric assessment in the past 3-months. People were excluded from a specific test if they could not perform it independently or safely. 10% of participants were identified as frail by the reference standard, and 43% of the sample were identified as pre-frail.		
Index test	<ul style="list-style-type: none"> Gait speed 4m (thresholds; 0.76 m/s (based on Fried); 0.80 m/s, 0.90 m/s) Maximum step length (mean of 3 successful steps, corrected for leg length) Chair lift – time to rise from a chair x5 without arms 		
Reference standard	Two reference standards used <ul style="list-style-type: none"> Cumulative deficit model: Frailty assessed using the frailty index (Mitniski, Mogilner & Rockwood 2001); range 0-1, representing the ratio of number of deficits present from a 45-item list included in a CGA; higher=more frail. Frailty identified as a score ≥ 0.25 Frailty phenotype – Fried; frailty assessed as impairment on 3 or more domains (5% weight loss, self-reported exhaustion (2 items) LASA physical activity questionnaire < 393 kcal/week for men and < 280 kcal/week for women, < 0.76 m/s gait speed), weak handgrip < 30 kg males and < 18 kg females). 		
Target condition	Frailty		
Results:	<u>Gait speed (Cumulative deficit model as reference standard)</u>	<u>Maximum step length (Cumulative deficit model as reference standard)</u>	<u>Chair lift (Cumulative deficit model as reference standard)</u>
Area under the curve	0.81 (CI = 0.76 – 0.85) N = 518	0.77 (CI = 0.72 – 0.81) N = 547	0.76 (CI = 0.71 – 0.80) N = 540
General limitations (according to QUADAS 2)	AUC only reported; no thresholds reported for some index tests; general concerns about reference standard; 9% of participants were not able to complete chair stand and excluded from analysis; unclear if MM; prevalence rate only reported for 1 reference test and evidence suggests different prevalence rates between reference standards		

Study	Schoon 2014		
Results:	<u>Gait speed (Fried as reference standard)</u>	<u>Maximum step length (Fried as reference standard)</u>	<u>Chair lift (Fried as reference standard)</u>
Sensitivity	0.90 (threshold = 0.76 m/s) 0.85 (threshold = 0.80 m/s) 0.61 (threshold = 0.90 m/s)	Not reported	Not reported
Specificity	0.76 (threshold = 0.76 m/s) 0.91 (threshold = 0.80 m/s) 0.96 (threshold = 0.90 m/s)	Not reported	Not reported
Area under the curve	0.92 (CI = 0.87 – 0.96) N = 518	0.84 (CI = 0.77 – 0.90) N = 547	0.81 (CI = 0.75 – 0.88) N = 540
General limitations (according to QUADAS 2)	AUC only reported for some index tests; no thresholds reported for some index tests; multiple thresholds tested for 1 index test; general concerns about reference standard; 9% of participants were not able to complete chair stand and excluded from analysis; unclear if MM; prevalence rate only reported for 1 reference test and evidence suggests different prevalence rates between reference standards; overlap between the reference standard and 1 of the index tests		

Table 118: Smets 2014

Study	Smets 2014
Study type	Prospective cohort
Number of studies (number of participants)	1 (290)
Country and setting	Netherlands: General practice
Funding	Funded by VLK (de Vlaamse Lig tegen Kanker) and Interreg IV Gensregio Vlaanderen – Netherlands.
Duration of study	6-months

Study	Smets 2014
Age, gender, ethnicity	Age: Older adults (≥70 years; median age 78 years; range = 70 – 97 years). Gender: 105 male, 185 female. Ethnicity: not reported
Patient characteristics	Older adult people recruited through general practices in Belgium and the Netherlands. Exclusion criteria were the inability to speak Dutch, a formal diagnosis of dementia, a previous diagnosis of invasive cancer (except non-melanoma of the skin), current diagnosis of cancer, being too ill to participate or life expectancy shorter than 6-months (based on judgement of the attending doctor). No participants were currently residing in a nursing home.
Index test	<ul style="list-style-type: none"> • Abbreviated Comprehensive Geriatric Assessment (aCGA): 15 questions covering 3 domains (functional status, impairment defined as a score ≥1 from 7 items on ADL and IADL; cognitive status, impairment defined as a score ≤6 from 4 items from the MMSE; and depression, impairment indicated by a score ≥ 2 from 4 items from the GDS-15). Frailty defined as impairment in ≥1 • VES-13: 13 questions covering age, self-rated health status, physical fitness and need for assistance with activities. Maximum score = 10; frailty defined as a score ≥3 • GFI: 15 questions covering mobility, physical fitness, assistance needed with toileting and shopping, poor hearing and vision, medicine use, complaints about memory and depression. Maximum score = 15 points; frailty defined as ≥ 4 • G8: 8 questions about age, functional status, cognitive status, nutrition and medication use. Maximum score = 17 points; frailty defined as scores ≤ 14. The specific questions used in the G8 were not used – items were instead assessed using similar questions asked at different parts of the interview
Reference standard	Full Comprehensive Geriatric Assessment (CGA): impairments in 2 or more domains (functional status, as defined by a problem on at least 2 items from the activities of daily living (ADL) or instrumental activities of daily living (IADL) scale; cognition, as indicated by a score of ≤ 23 on the MMSE; depression, as indicated by a score of ≥ 8 on the GDS-15; nutritional status, as indicated by a decline in food intake in the previous week or if participants had lost at least 1 kg in weight over the last 3-months; and medication use, as indicated by a score of >3 drugs).
Target condition	Frailty

Study	Smets 2014			
Results:	<u>aCGA (≥1 domain)</u>	<u>VES-13 (≥3)</u>	<u>GFI (≥4)</u>	<u>G8 (≤14)</u>
Sensitivity	0.87	0.82	0.74	0.75
Specificity	0.64	0.79	0.73	0.69
PPV	0.70	0.78	0.72	0.70
NPV	0.84	0.82	0.75	0.75
General limitations (according to QUADAS 2)	Unclear method of recruitment; high rate of missing data; unclear blinding of index test/reference standard; composite reference standard with factors overlapping 1 of the index tests; general concerns about reference standard.			

Table 119: Tribess 2012, Tribess 2013

Study	Tribess 2012, Tribess 2013
Study type	Cross-sectional cohort
Number of studies (number of participants)	1 (624)
Country and setting	Brazil; community
Funding	Funded by Fundação de Amparo à Pesquisa do Estado de Minas Gerais
Duration of study	
Age, gender, ethnicity	Age: Older adults (mean age 71.08 years, range = 60-96 years). Gender: 218 male, 406 female. Ethnicity: not reported
Patient characteristics	Older adults living in the community who were recruited as part of the Population Study of Physical Activity and Aging study. 95.3% self-reported having 1 or more 'disease' (unspecified); 19.9% of participants were identified as frail according to the reference standard. 72.7% of participants were retired, 40.3% of participants had a maximum of 2 years' education and 19.1% were illiterate. 16.7% of participants were identified as having mild to moderate cognitive impairment.

Study	Tribess 2012, Tribess 2013	
Index test	<ul style="list-style-type: none"> Physical activity – International physical activity questionnaire (IPAQ) adapted for elderly (work, transportation, housework/leisure) Age 	
Reference standard	Modified Fried frailty criteria; impairments in 3 or more domains (decreased handgrip strength in the dominant hand, adjusted by gender and BMI; weight loss >5% of body weight; reports of exhaustion (1 item); incapacity to rise from chair 5 times without arms; <150 min/week physical activity; Brazilian; TRIBESS2012)	
Target condition	Frailty	
Results:	<u>Physical activity (N = 622)</u>	<u>Age (N = 624)</u>
Sensitivity	Males (threshold 140 minutes/week) = 0.977; Females (threshold 145 minutes/week) = 0.844	Males (threshold 67 years) = 0.977; Females (threshold 72 years) = 0.844
Specificity	Males (threshold 140 minutes/week) = 0.731; Females (threshold 145 minutes/week) = 0.814	Males (threshold 67 years) = 0.320; Females (threshold 72 years) = 0.814
Area under the curve	Males = 0.90 (CI 0.86 – 0.94); Females = 0.86 (CI 0.85 – 0.92) Overall 0.89 (CI 0.86 – 0.91)	Males = 0.59 (CI 0.52 – 0.66); Females = 0.72 (CI 0.67 – 0.76)
General limitations (according to QUADAS 2)	Unclear if blinding of index test/reference standard; no pre-determined thresholds; unclear if sample is a multimorbid population; general concerns about reference standard; overlap between reference standard and 1 of the index tests	

H.4 Delivering an approach to care that takes account of multimorbidity

H.4.1 Treatment burden

Table 120: Gibbons 2013⁴⁸¹

Reference	Patient characteristics	Questionnaire	Performance	Comments
Gibbons 2013 ⁴⁸¹	<p>n=610</p> <p>Age, years (mean ± SD) 70±10</p> <p>Gender (M:F): 49:51</p> <p>Number of exemplar conditions (mean ± SD) 2.3±0.8</p> <p>Number of total conditions (mean ± SD) 7.3±3.2</p> <p>Patients with 2-5 comorbidities 34.2%</p> <p>Patients with 6-10 comorbidities 50.2%</p> <p>Patients with 11+ comorbidities 15.6%</p> <p>Disease burden score (mean ± SD) 23.5±12.5</p>	<p><u>Treatment Burden subscale</u></p> <p>6 items. All items were rated and scored on a 4-point scale from 1 'strongly disagree' to 4 'strongly agree'.</p> <ol style="list-style-type: none"> 1. Taking medications for each of my conditions has caused me problems 2. Having more than one condition makes my treatments less effective 3. It is difficult to take all of the medications the way I am supposed to 4. Having more than one condition makes it difficult to get the best available treatment 5. I don't like mixing medications for different conditions 6. I feel so overwhelmed by the treatment for one condition that it is hard to manage any others 	<p><u>Construct validity</u></p> <p>Tested by cross-sectional Spearman's Rho correlations between MULTIPLEs scales and the following external measures: the Brief Illness Perception Questionnaire (bIPQ), the Health Education Impact Questionnaire (heiQ), and the Hospital Anxiety and Depression Scales (HADS). As bIPQ was designed for use with single conditions and not multimorbidity, patients were asked to nominate the condition they felt was most disabling and complete the bIPQ in relation to that condition</p> <p>Brief Illness Perception Questionnaire construct (Spearman's Rho)</p> <ul style="list-style-type: none"> • Impact of illness (0.32) • Timeline of illness (not reported) • Perceived control of illness (-0.16) • Efficacy of treatment (-0.16) • Experience of symptoms (0.25) • Concern (0.28) • Understanding of illness (-0.11) • Emotional affect (0.44) • Total (0.26) <p>HADS construct (Spearman's Rho)</p>	<p>Source of funding: NIHR School for Primary Care Research</p> <p>Evidence of floor/ceiling effect >40% missing data from responders</p> <p>Responsiveness: not assessed</p> <p>Interpreta</p>

	<p>Diabetes 45% Depression 41% Osteoarthritis 52% Chronic obstructive pulmonary disease 35% Coronary heart disease 50%</p> <p>Patients that completed the questionnaire who were identified from Quality and Outcomes Framework registers as having two or more of the following 'exemplar' conditions: diabetes, depression, osteoarthritis, chronic obstructive pulmonary disease, coronary heart disease.</p> <p>Patients were still included if they had other long term conditions in addition to the above conditions.</p> <p>Patients with terminal illness or severe and enduring mental health problems were excluded.</p> <p>40 excluded as they did</p>		<ul style="list-style-type: none"> Anxiety (0.49) Depression (0.5) Psychological distress (0.52) <p><u>Test-Retest reliability</u> Assessed comparing scores obtained as baseline and at one month follow up using a random sample of 40% baseline completers (n=244)</p> <p>Spearman's Rho=0.63</p> <p><u>Fit to Rasch model</u> Overall scale fit to the Rasch model is indicated by a non-significant summary Chi-square statistic.</p> <p>$\chi^2 = 27.25$ (p=0.7)</p> <p><u>Internal reliability</u> PSI = 0.7 Cronbach's alpha = 0.9</p> <p>Factor analysis – exploratory with oblique rotation (individual item factor loadings (communalities)) Hard to manage other conditions 0.84 Difficult to get best treatment 0.65 Don't like mixing medications 0.64 Difficult to take all medicines 0.63 Makes treatment less effective 0.63 I take advice for some conditions more than others 0.59 Medication has caused me problems 0.51</p> <p>Eigenvalue 2.386</p> <p>Unidimensionality: t-test 1.2%</p>	<p>bility: not assessed</p>
--	--	--	---	-----------------------------

<p>not recognise that they had 2 of the long term conditions that made up their definition of multimorbidity. 9 excluded because questionnaire not sufficiently completed</p>	<p><u>Activity Limitation subscale</u></p> <p>3 items. All items were rated and scored on a 6-point scale from 0 'strongly disagree' to 6 'strongly agree'.</p> <ol style="list-style-type: none"> 1. Time spend managing my condition has made it more difficult to carry out my usual activities 2. Time spent managing my conditions has reduced my social life 3. Spending time managing my conditions has limited my activities 	<p><u>Construct validity</u></p> <p>Brief Illness Perception Questionnaire construct (Spearman's Rho)</p> <ul style="list-style-type: none"> • Impact of illness (0.45) • Timeline of illness (not reported) • Perceived control of illness (-0.19) • Efficacy of treatment (-0.17) • Experience of symptoms (0.38) • Concern (0.35) • Understanding of illness (not reported) • Emotional affect (0.46) • Total (0.37) <p>HADS construct (Spearman's Rho)</p> <ul style="list-style-type: none"> • Anxiety (0.52) • Depression (0.53) • Psychological distress (0.55) <p><u>Test-Retest reliability</u> Spearman's Rho=0.6</p> <p><u>Fit to Rasch model</u> The three-items Activity Limitations scale showed reasonable fit to the Rasch model ($\chi^2(9)=13.73$, $p=0.13$). However category thresholds were distorted for all three items. Model fit was improved following rescoring in the same manner as the Treatment Burden scale including excellent dimensionality, absence of differential item functioning and local dependency and reliability.</p> <p>Fit after rescoring: $\chi^2=8.9$, $p=0.44$</p>
---	---	---

			<p><u>Internal reliability</u></p> <p>PSI = 0.65 Cronbach's alpha = 0.8</p> <p>Factor analysis – exploratory with oblique rotation (individual item factor loading (communalities))</p> <p>Managing conditions reduced my social life 0.79 Difficult to carry out usual activities 0.63 Time managing has limited my activities 0.59</p> <p>Eigenvalue 1.51</p> <p>Unidimensionality: t-test 29%</p>	
--	--	--	---	--

Table 121: Tran 2012¹²¹³

Reference	Patient characteristics	Questionnaire	Performance	Comments
Tran 2012 ¹²¹³	<p>n=502</p> <p>Age, years (mean± SD) 59.3± 17</p> <p>Gender (M:F): 47:53</p> <p>Inpatients 51.2% Paris, France</p> <p>Presence of daily symptoms 62.6%</p>	<p><u>Treatment Burden Questionnaire 2012 (French version)</u></p> <p>Aims to measure the extent to which healthcare impacts on the functioning and wellbeing of people with chronic condition(s), apart from specific treatment side effects.</p> <p>7 constructs (13 items) assessing the extent to which patients believed each item caused them 'burden'. All items were rated and scored on a 10-point</p>	<p><u>Construct validity</u></p> <p>Hypothesis: negative correlation between treatment burden and treatment satisfaction.</p> <p>Treatment Satisfaction Questionnaire for Medication (TSQM)</p> <p>TSQM global rs= -0.41 TSMQ convenience rs= -0.53 TSMQ efficacy rs= -0.26 TSMQ side effects score* rs=-0.52</p> <p>*Calculated only for patients experiencing side effects</p>	<p>Source of funding: Partly funded by INSERM U738, Paris, France</p> <p>Responsiveness: not assessed</p>

Reference	Patient characteristics	Questionnaire	Performance	Comments
	<p>Need for assistance 26.4%</p> <p>Need for specific organisation for daily care 67.3%</p> <p>Need for self-monitoring 33.47%</p> <p>Presence of side effects 36.3%</p> <p>Main chronic condition:</p> <p>Diabetes 16.5%</p> <p>Rheumatologic diseases 12%</p> <p>High blood pressure and dyslipidemia 9%</p> <p>Systemic diseases 8.8%</p> <p>Pulmonary disease (other than asthma) 8.1%</p> <p>Heart diseases 7.5%</p> <p>Asthma 7.5%</p> <p>Cancers and haematological malignancy 6.9%</p> <p>HIV infection 3.9%</p> <p>Arterial or venous thrombosis 3.5%</p> <p>Other diseases 16.3%</p> <p>Consecutive patients from 6 teaching hospitals of the Assistance-Publique Hopitaux de Paris and 8 general practitioner clinics in Paris</p>	<p>scale ranging from 0 'no burden' to 10 'considerable burden')</p> <p>Items in TBQ (translated from French to English):</p> <p>1. Medication:</p> <p>1a. Taste, shape or size of your tablets and/or inconvenience caused by your injections (e.g. pain, bleeding, scars)</p> <p>1b. Number of times you have to take your medication daily</p> <p>1c. Things you do to remind yourself to take your daily medication and/or to manage your treatment when not at home</p> <p>1d. Specific conditions when taking your medication (e.g. taking it at a specific time of day or meal, not being able to do certain things after taking them like driving or lying down)</p> <p>2. Assessments/ appointments:</p> <p>2a. Lab tests and other exams (frequency, time spent and inconvenience of these exams)</p> <p>2b. Self-monitoring (e.g. taking your blood pressure or measuring your blood sugar yourself: frequency, time spent and inconvenience of this surveillance)</p> <p>2c. Doctors' visits (frequency and time spent for visits)</p> <p>2d. Arrange appointments and</p>	<p><u>Test-Retest reliability</u></p> <p>Retests obtained for 211 patients (n=211, 42%). Patients completed a baseline test and a retest at 2 weeks (n=182) or 1 month (n=29). Agreement considered acceptable with ICC > 0.6</p> <p>ICC 0.76 (95% CI 0.67 to 0.83)</p> <p><u>Internal reliability</u></p> <p>Cronbach's alpha = 0.89</p>	

Reference	Patient characteristics	Questionnaire	Performance	Comments
		<p>schedule doctors' visits and lab tests</p> <p>3. How would you rate the burden associated with taking care of paperwork from health insurance agencies, welfare organisations, hospitals and/or social care?</p> <p>4. How would you rate the constraints associated with your diet (e.g. not being able to eat certain foods)?</p> <p>5. How would you rate the burden associated with the recommendations from your doctors to practise regular physical exercises?</p> <p>6. What is the impact of your healthcare on your social relationships (e.g. need for assistance, being ashamed to take your medication in front of people)?</p> <p>7. 'Frequent healthcare reminds me of my health problems'</p>		

Table 122: Tran 2014¹²¹²

Reference	Patient characteristics	Questionnaire	Performance	Comments
Tran 2014 ¹²¹²	<p>n=610</p> <p>Age, years (mean ± SD) 51.5 ± 12.4</p>	<p><u>Treatment Burden Questionnaire 2014 (English version)</u></p> <p>Aims to measure the 'work' of being a person with chronic condition(s) (i.e.</p>	<p><u>Construct validity</u></p> <p>Tested by confirming four pre-specified hypotheses:</p> <p>1. Quality of life</p> <p>Measured by the PatientsLikeMe Quality of Life (PLMQOL) scale. The</p>	<p>Source of funding: Partly funded by</p>

Reference	Patient characteristics	Questionnaire	Performance	Comments
	<p>Gender (M:F): 23:77</p> <p>USA 57.5%; UK 8.7%; Canada 8.4%; Australia/New Zealand 3.4%; Other/missing 22%</p> <p>Treatments (mean ± SD) Tablets and pills/day 8.5 ± 6.4 Injections/week 1.4 ± 4.6 Drug administration(s)/day 3.0 ± 2.0 Number of different doctors the patient sees 3.0 ± 2.3 Appointments/month 2.9 ± 2.9 Hospitalizations/year 0.5 ± 1.7</p> <p>Presence of an informal caregiver 45.9%</p> <p>Most common location for medical consultations: public hospital 10.3%; private hospital 3.3%; general practice clinic 47.7%; specialist clinic</p>	<p>challenges associated with everything patients have to do to take care of themselves) and its effect on quality of life.</p> <p>15 items assessing the extent to which patients believed each item caused them problems. All items rated and scored on a 10-point scale ranging from 0 'not a problem' to 10 'large problem'.</p> <ol style="list-style-type: none"> 1. Taste, shape or size of your tablets and/or the annoyances caused by your injections (e.g., pain, bleeding, bruising or scars) 2. Number of times you should take your medication daily 3. Efforts you make not to forget to take your medications (e.g., managing your treatment when you are away from home, preparing and using pillboxes) 4. Necessary precautions when taking your medication (e.g., taking them at specific times of the day or meals, not being able to do certain things after taking medications such as driving or lying down) 5. Lab tests and other exams (e.g., blood tests or radiology): frequency, time spent and associated nuisances or inconveniences 	<p>PLMQOL scale is a validated 24-item questionnaire assessing physical, mental, and social quality of life. PLMQOL scores range from 0 to 100 for each domain (higher scores indicating better quality of life) and are summed for a global assessment of quality of life.</p> <p>Hypothesis: negative correlation between treatment burden (as measured by the TBQ global score) and quality of life.</p> <p>Result: Construct validity showed a significant moderate negative correlation between the TBQ global score and PLMQOL score ($r_s = -0.50$; $P < 0.0001$). Correlation coefficients ranged from $r_s = -0.39$ ($P < 0.0001$) for physical quality of life to $r_s = -0.50$ ($P < 0.0001$) for mental quality of life, indicating that patients with high TBQ score had low quality of life.</p> <ol style="list-style-type: none"> 2. Adherence to medication Measured by Morisky's Medication Adherence Scale 8 (MMAS-8), a validated eight-item questionnaire, with scores ranging from 0 to 8. High adherence is a score of 8; medium adherence, 6 to 7; and low adherence, less than 6. Hypothesis: the greater the treatment burden, the lower the adherence to treatment. Results: High/moderate adherence (mean ± SD) 37.7 ± 27.5; Low adherence v 61.8 ± 30.5 3. Patient's knowledge of their conditions and treatments Assessed by the following two questions: 1) 'Do you think you have sufficient knowledge about your conditions (e.g., symptoms, disease progression)?'; 2) 'Do you think you have sufficient knowledge about your treatments (e.g., possible side effects, expected benefits, other treatment options)?'. Answers were rated on a five-step scale: 'very sufficient', 'sufficient', 'average', 'insufficient' and 'very insufficient'. 	<p>INSERM U738, Paris, France</p> <p>Cronbach's alpha stated as to be calculated in methods but not reported in results</p> <p>Responsive ness: not assessed</p>

Reference	Patient characteristics	Questionnaire	Performance	Comments
	<p>36.7%</p> <p>Duration of oldest chronic condition, years: <5, 29.8%</p> <p>5 to 10, 35.6%; >10, 33.6%</p> <p>Number of chronic conditions (mean ± SD) 2.9 ± 1.9</p> <p>Conditions:</p> <p>Neurologic disease 45.4%</p> <p>Psychiatric disease 41%</p> <p>Rheumatologic disease 33.3%</p> <p>High blood pressure 25.6%</p> <p>Gastrointestinal disease 21.1%</p> <p>Endocrine disorder (other than diabetes) 19.8%</p> <p>Lung disease 15.2%</p> <p>Vision problems 13.6%</p> <p>Fibromyalgia 12.9%</p> <p>Skin disease 11.6%</p> <p>Hearing problem 8%</p> <p>Diabetes 7.4%</p> <p>Kidney disease 6.2%</p> <p>Heart disease 5.6%</p> <p>Cancer or malignant blood disease 5.1%</p>	<p>6. Self-monitoring (e.g., taking your blood pressure or checking your blood sugar): frequency, time spent and associated nuisances or inconveniences</p> <p>7. Doctor visits and other appointments: frequency and time spent for these visits and difficulties finding healthcare providers</p> <p>8. Difficulties you could have in your relationships with healthcare providers (e.g., feeling not listened to enough or not taken seriously)</p> <p>9. Arranging medical appointments and/or transportation (doctors' visits, lab tests and other exams) and reorganizing your schedule around these appointments</p> <p>10. Administrative burden related to healthcare (e.g., all you have to do for hospitalizations, insurance reimbursements and/or obtaining social services)</p> <p>11. Financial burden associated with your healthcare (e.g., out-of-pocket expenses or expenses not covered by insurance)</p> <p>12. Burden related to dietary changes (e.g., avoiding certain foods or alcohol, having to quit smoking)</p> <p>13. Burden related to doctors' recommendations to practice physical activity (e.g., walking, jogging,</p>	<p>Hypothesis: the greater the patient's knowledge of their conditions and treatments, the lower treatment burden</p> <p>Results patient's knowledge of their conditions (mean ± SD)</p> <ul style="list-style-type: none"> Sufficient knowledge 49.3 ± 30.7 Insufficient knowledge 63.0 ± 31.6 <p>Results patient's knowledge of their treatments (mean ± SD)</p> <ul style="list-style-type: none"> Sufficient knowledge 47.8 ± 30.4 Insufficient knowledge 62.3 ± 31.3 <p>4. Clinical variables</p> <p>Hypothesis: positive correlation between treatment burden and the specified clinical variables:</p> <p>1) number of conditions (mean ± SD)</p> <ul style="list-style-type: none"> 1 (n=181) 44.3±29.1 2-3 (n=234) 49.7±29 >4 (n=195) 65.4±33 <p>2) drug administration</p> <ul style="list-style-type: none"> No. of tablets and pills/day rs=0.2 No. of injections/week rs=0.11 No. of drug administrations/day rs=0.25 <p>3) medical follow-up</p> <ul style="list-style-type: none"> No. of different doctors the patient regularly sees rs=0.21 No. of appointments/month rs=0.25 No. of hospitalization/year rs=0.11 	

Reference	Patient characteristics	Questionnaire	Performance	Comments
	Infectious disease 3.1% Stroke or cerebrovascular disease 2.8% Used an internet platform, the Open Research Exchange, to recruit patients on PatientsLikeMe (PLM), an online network where 200,000 voluntary participants with chronic conditions share data about their treatment, conditions, and symptoms. Members of PLM join the site with the expectation that they will be participating in research.	swimming) 14. How does your healthcare impact your relationships with others (e.g., being dependent on others and feeling like a burden to them, being embarrassed to take your medications in public) 15. 'The need for medical healthcare on a regular basis reminds me of my health problems'		

H.4.2 Ranking

None.

H.4.3 Stopping antihypertensive treatment

Table 123: Freis 1975⁴⁴⁸

Study	Veterans Admission Cooperative Study on morbidity trial: Freis 1975 ⁴⁴⁸
Study type	RCT (patient randomised; parallel)
Number of studies (number of participants)	1 (n=86)

Study	Veterans Admission Cooperative Study on morbidity trial: Freis 1975 ⁴⁴⁸
Countries and setting	Conducted in USA
Line of therapy	Primary prevention (excluded participants with major cardiovascular events)
Duration of study	Follow up (post intervention): 72 weeks
Method of assessment of guideline condition	Unclear method of assessment/diagnosis
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Diastolic blood pressures of 3 preceding visits measured 90 mm Hg or less; no diastolic blood pressures above 95 mm Hg were recorded during the 3 visits; average of all diastolic blood pressures during preceding months was 95 mm Hg or less
Exclusion criteria	Patients who had major cardiovascular complications in the past (for example stroke, myocardial infarction, congestive heart failure, renal failure); patients who exhibited violations of pill counts on more than 2 visits during the preceding year; patients who had been transferred to drugs other than the hydrochlorothiazide-reserpine-hydralazine combination
Recruitment/selection of patients	Participants recruited from Veterans Administration Cooperative Study on morbidity whose blood pressure had been controlled at normotensive levels for a period of two years or longer. Participants who met the inclusion criteria for this study were enrolled.
Age, gender and ethnicity	Age: average 52.2 (placebo), 52.8 (continuers). Gender (M:F): 1:0. Ethnicity: 42 described as “white”, 44 described as “black”.
Further population details	1. Age: unclear (adults average age intervention 52.2 years, control 52.8 years). 2. Multimorbidity: no multimorbidity reported. 3. Reason for stopping: not stated (allocated to stopping group)
Extra comments	Male veterans hospitalised prior to treatment. Treated patients whose blood pressure has been at normotensive levels for 2 years or longer. Systolic blood pressure before trial (mm Hg, mean): placebo 171, continuers 171. Diastolic blood pressure before trial (mm Hg, mean): placebo 108.8, continuers 111.6. Severity scores (0-4, mean): Optic fundi - placebo 1.1, continuers 1.1; cardiac - placebo 0.7, continuers 0.8; CNS - placebo 0.4, continuers 0.6; renal - placebo 0.3, continuers 0.6.
Indirectness of population	No serious indirectness
Interventions	(n=60) Intervention 1: antihypertensives – stopping. Replacement of hydrochlorothiazide, reserpine or hydralazine with placebo. Patients were informed they may be transferred to inert tablets but would be replaced on active treatment if the hypertension became re-established. Duration 72 weeks. Concurrent medication/care: placebo used in addition to discontinuing antihypertensives.

Study	Veterans Admission Cooperative Study on morbidity trial: Freis 1975⁴⁴⁸
	(n=26) Intervention 2: antihypertensives - continuing. Continuation of: hydrochlorothiazide, reserpine or hydralazine. Duration 72 weeks. Concurrent medication/care: none stated.
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: STOPPING versus CONTINUING	
Protocol outcome 1: cardiovascular mortality - Actual outcome: cardiovascular mortality at 72 weeks; group 1: 1/60, group 2: 0/26; risk of bias: high; indirectness of outcome: no indirectness	
Protocol outcome 2: non-fatal myocardial infarction - Actual outcome: non-fatal congestive heart failure at 72 weeks; group 1: 3/60, group 2: 0/26; risk of bias: high; indirectness of outcome: serious indirectness - Actual outcome: atrial fibrillation at 72 weeks; group 1: 1/60, group 2: 0/26; risk of bias: high; indirectness of outcome: serious indirectness - Actual outcome: Right bundle block at 72 weeks; group 1: 1/60, group 2: 0/26; risk of bias: high; indirectness of outcome: serious indirectness	
Protocol outcome 3: blood pressure - Actual outcome: return to hypertension (% patients attaining diastolic blood pressure of 95 mm Hg or higher) at 55 weeks; placebo 86% (52/60); continuers 12% (3/26). N.B. These figures taken from graph in paper; risk of bias: high; indirectness of outcome: no indirectness	
Protocol outcomes not reported by the study	Quality of life; all-cause mortality; stroke; admission to care facility; hospitalisation; falls

Table 124: Greenberg 1986⁵⁰⁹

Study	Medical Research Council trial of treatment of mild hypertension trial: Greenberg 1986⁵⁰⁹
Study type	RCT (patient randomised; parallel)
Number of studies (number of participants)	1 (n=1620) At 2 year follow up: n=396 (24.4%)
Countries and setting	Conducted in England, United Kingdom
Line of therapy	Primary prevention (excluded participants with stroke or myocardial infarction during phase I)
Duration of study	Follow up (post intervention): 2 years
Method of assessment of guideline condition	Unclear method of assessment/diagnosis
Stratum	Overall

Study	Medical Research Council trial of treatment of mild hypertension trial: Greenberg 1986 ⁵⁰⁹
Subgroup analysis within study	Not stratified but pre-specified: males/females
Inclusion criteria	Participated in phase I of MRC trial of treatment of mild hypertension
Exclusion criteria	No longer taking drugs from phase I of the trial; had stroke or myocardial infarction during phase I; blood pressure at re-randomisation exceeded 109 mm Hg diastolic or 200 mm Hg systolic; GPs were unwilling for them to take part; unable to attend necessary frequent follow up visits
Recruitment/selection of patients	Consenting patients from phase I of the trial
Age, gender and ethnicity	Age – range: 35-64. Gender (M:F): 1418:1347. Ethnicity: not reported
Further population details	1. Age: adults (<65). 2. Multimorbidity: no multimorbidity reported. 3. Reason for stopping: not stated (allocated to stopping group)
Indirectness of population	No serious indirectness
Interventions	(n=783) Intervention 1: antihypertensives – stopping. Discontinuation of bendrofluazide (5-10mg daily), propranolol (80-240mg daily). Duration 2 years. Concurrent medication/care: none stated. (n=837) Intervention 2: antihypertensives – continuing. Continuation of bendrofluazide (5-10mg daily), propranolol (80-240mg daily). Duration 2 years. Concurrent medication/care: none stated.
Funding	Equipment/drugs provided by industry (Imperial Chemical Industries Ltd, Flockhart and Co Ltd, Ciba Laboratories, Mark Sharp and Dohme Ltd)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: STOPPING versus CONTINUING	
Protocol outcome 1: blood pressure - Actual outcome: patients with diastolic blood pressure below 90 mm Hg at 2 years; group 1: 57/129, group 2: 147/204; risk of bias: high; indirectness of outcome: no indirectness	
Protocol outcomes not reported by the study	Quality of life; all-cause mortality; cardiovascular mortality; stroke; non-fatal myocardial infarction; admission to care facility; hospitalisation; falls

Table 125: Maland 1983⁸⁰¹

Study	The National Hypertension Detection and Follow-up Program (HDFP): Withdrawal study trial: Maland 1983 ⁸⁰¹
Study type	RCT (patient randomised; parallel)
Number of studies (number of participants)	(n=62)

Study	The National Hypertension Detection and Follow-up Program (HDFP): Withdrawal study trial: Maland 1983 ⁸⁰¹
Countries and setting	Conducted in USA
Line of therapy	Primary prevention (excluded participants with major cardiovascular events)
Duration of study	Follow up (post intervention): 1 year
Method of assessment of guideline condition	Unclear method of assessment/diagnosis
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Patients who participated in the HDFP trial and demonstrated an average diastolic blood pressure (DBP) of ≤ 90 mm Hg and no DBP >95 mm Hg at 3 consecutive appointments, demonstrated an average DBP of ≤ 90 mm Hg for all appointments in the preceding 12 months, and used on diuretic antihypertensive medication in the preceding 12-months
Exclusion criteria	Patients with a history of major cardiovascular events such as stroke, myocardial infarction, transient ischaemic attack, congestive heart failure, renal failure, and severe angina pectoris. Patients demonstrating less than 80% or more than 110% use of prescribed medication, as indicated by valid count of unused medication on more than 2 occasions in the preceding 12 months. Patients unable or unwilling to attend clinic at least once every 4- to 6-weeks.
Recruitment/selection of patients	Patients recruited from the HDFP trial who met study inclusion criteria and provided consent to participate in a further trial on withdrawal
Age, gender and ethnicity	Age: >30 years; mean age 60.3 years; 60% of patients aged 60 years and over. Gender (M:F): 1:1. Ethnicity: 98% of patients described as "non-black", 2% "black"
Further population details	1. Age: Adults (60% <60). 2. Multimorbidity: no multimorbidity reported. 3. Reason for stopping: not stated (allocated to stopping group).
Indirectness of population	No serious indirectness
Interventions	(n=31) Intervention 1: antihypertensives – stopping. Placebo medication, physically identical to the patient's previous hypertensive medication. Duration 1 year. Concurrent medication/care: no patients were taking potassium supplements, uricosuric drugs, or allopurinol. (n=31) Intervention 2: antihypertensives – continuing. Patients continued on the same hypertension medication they had received during the HDFP trial; 87% were taking chlorthalidone, 11% were taking hydrothiazide, and 2% were taking triamterene. All patients had been taking this medication for at least 12 months prior to the withdrawal trial. Duration >2 years. Concurrent medication/care: no patients were taking potassium supplements, uricosuric drugs, or allopurinol.

Study	The National Hypertension Detection and Follow-up Program (HDFP): Withdrawal study trial: Maland 1983⁸⁰¹
Funding	Other (study partly funded by the Montana State Heart Association)
<p>RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: STOPPING versus CONTINUING</p> <p>Protocol outcome 1: cardiovascular mortality - Actual outcome: mortality due to cardiac arrest at 1 year; group 1: 0/31, group 2: 1/31; risk of bias: high; indirectness of outcome: no indirectness</p> <p>Protocol outcome 2: stroke - Actual outcome: transient ischaemic attack at 1 year; group 1: 0/31, group 2: 1/31; risk of bias: high; indirectness of outcome: no indirectness</p> <p>Protocol outcome 3: non-fatal myocardial infarction - Actual outcome: non-fatal myocardial infarction at 1 year; group 1: 1/31, group 2: 0/31; risk of bias: high; indirectness of outcome: no indirectness</p> <p>Protocol outcome 4: blood pressure - Actual outcome: number of patients reverting to elevated blood pressure at up to 1 year; group 1: 9/29, group 2: 1/30; risk of bias: high; indirectness of outcome: no indirectness</p>	
Protocol outcomes not reported by the study	Quality of life; all-cause mortality; admission to care facility; hospitalisation; falls

H.4.4 Stopping drugs for osteoporosis

Table 126: Black 2006 (Ensrud 2004)

Study (subsidiary papers)	Black 2006 ¹⁴² (Ensrud 2004 ⁴⁰³)
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=1099)
Countries and setting	Conducted in USA; Setting: Secondary care
Line of therapy	Unclear
Duration of study	Intervention time: 5 years
Method of assessment of guideline condition	--
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	For the FIT study, postmenopausal women aged 55 to 81 years with low femoral neck BMD (<0.68 g/cm ²) were eligible to participate. Women were randomized to alendronate, 5 mg/d for 2 years and 10 mg/d thereafter (n = 3236), or placebo (n=3223). One year of alendronate, 10 mg/d, was offered at no cost to all participants at the end of FIT. Women assigned to receive alendronate during FIT who completed at least 3 years of treatment during the trial and subsequent open-label period were eligible for the current FLEX study.
Exclusion criteria	Women whose total hip BMD at FLEX baseline was less than 0.515 g/cm ² (T score <-3.5) ¹⁰ or whose total hip BMD was lower than at FIT baseline. Documented abnormalities of the oesophagus (e.g., stricture, achalasia, Barrett's oesophagus); diagnosis of dysphagia, esophagitis, gastritis, or peptic ulcer disease within the past 3 months that was not adequately controlled with medical management (e.g., H ₂ antagonists or proton-pump inhibitors); upper gastrointestinal bleed or myocardial infarction during the previous 3 months; severe malabsorption syndrome; or impaired renal function (serum creatinine >2.0 mg/dl).

Recruitment/selection of patients	10 US clinical centres that participated in the Fracture Intervention Trial (FIT).
Age, gender and ethnicity	Age - Mean (SD): Placebo: 73.7 (5.9); alendronate 5mg/day: 72.7 (5.7); alendronate 10mg/day: 72.9 (5.5) years. Gender (M:F): 100% women. Ethnicity: White: placebo: 421 (96.3%); alendronate 5mg/day: 322 (97.9%); alendronate 10mg/day: 327 (98.2%); the rest described as "other"
Further population details	1. Age: Overall 2. Menopause: Post-menopause
Indirectness of population	No indirectness
Interventions	<p>(n=329) Intervention 1: Bisphosphonates (continuing) - Alendronate. Alendronate 5mg/day. Duration 5 years. Concurrent medication/care: All participants were strongly encouraged to take a daily supplement containing calcium (500 mg) and vitamin D (250 IU).</p> <p>(n=333) Intervention 2: Bisphosphonates (continuing) - Alendronate. Alendronate 10mg/day. Duration 5 years. Concurrent medication/care: All participants were strongly encouraged to take a daily supplement containing calcium (500 mg) and vitamin D (250 IU).</p> <p>(n=437) Intervention 3: Placebo. Placebo. Duration 5 years. Concurrent medication/care: All participants were strongly encouraged to take a daily supplement containing calcium (500 mg) and vitamin D (250 IU).</p>
Funding	Study funded by industry (Merck & Co)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ALENDRONATE 5MG/DAY versus PLACEBO

Protocol outcome 1: Fracture

- Actual outcome: Clinical vertebral fractures (combined alendronate 5 and 10mg/day groups) at 5 years; Group 1: 16/662, Group 2: 23/437; Risk of bias: Low;

Indirectness of outcome: No indirectness

- Actual outcome: Morphometric vertebral fractures (combined alendronate 5 and 10mg/day groups) at 5 years; Group 1: 60/662, Group 2: 46/437; Risk of bias: Low;

Indirectness of outcome: No indirectness

- Actual outcome: Non-spine clinical fractures (combined alendronate 5 and 10mg/day groups) at 5 years; Group 1: 125/662, Group 2: 83/437; Risk of bias: Low;

Indirectness of outcome: No indirectness

Protocol outcome 2: Discontinuation of drugs due to side effects

- Actual outcome: Discontinuation due to side effects (combined alendronate 5 and 10mg/day groups) at 3 years; Group 1: 69/662, Group 2: 50/437; Risk of bias: Low; Indirectness of outcome: No indirectness

Protocol outcome 3: Hospitalisation

- Actual outcome: Hospitalisation due to side effects (combined alendronate 5 and 10mg/day groups) at 3 years; Group 1: 183/662, Group 2: 125/437; Risk of bias: Low; Indirectness of outcome: No indirectness

Protocol outcomes not reported by the study

Quality of life; Atypical fracture; Falls; Functional outcomes; Pain; GI bleed; Admission to care facility

Table 127: Black 2012

Study	Black 2012 ¹⁴⁰
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=1233)
Countries and setting	Conducted in Multiple countries; Setting: Secondary care
Line of therapy	Unclear
Duration of study	Intervention time: 3 years
Method of assessment of guideline condition	--
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	This trial was an extension of the HORIZON-PFT; osteoporotic women were randomly assigned to annual intravenous ZOL 5mg or placebo and followed for 3 years. In this extension, only women in the intervention condition who had received treatment with ZOL for 3 years were eligible.
Exclusion criteria	Exclusions included major protocol violations during the core study, aged >93 years, and specific bone-active medication use.
Recruitment/selection of patients	This trial was an extension of the HORIZON-PFT
Age, gender and ethnicity	Age - Mean (SD): 75.5 (4.9) years. Gender (M:F): 100% women. Ethnicity: Not stated
Further population details	1. Age: Not applicable / Not stated / Unclear 2. Menopause: Post-menopause

Indirectness of population	No indirectness
Interventions	<p>(n=616) Intervention 1: Bisphosphonates (continuing) - Zolendronate. Zolendronic acid 5mg intravenous infusion once a year for 3 years. Duration 3 years. Concurrent medication/care: All patients received daily oral calcium (1000 to 1500 mg) and vitamin D (400 to 1200 IU).</p> <p>(n=617) Intervention 2: Placebo. Placebo. Duration 3 years. Concurrent medication/care: All patients received daily oral calcium (1000 to 1500 mg) and vitamin D (400 to 1200 IU).</p>
Funding	Study funded by industry (Novartis Pharma AG, Basel Switzerland)
<p>RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ZOLENDRONATE versus PLACEBO</p> <p>Protocol outcome 1: Fracture</p> <ul style="list-style-type: none"> - Actual outcome: Morphometric vertebral fracture at 3 years; Group 1: 14/469, Group 2: 30/486; Risk of bias: High; Indirectness of outcome: No indirectness - Actual outcome: Non-vertebral fracture at 3 years; Group 1: 38/469, Group 2: 37/486; Risk of bias: High; Indirectness of outcome: No indirectness - Actual outcome: Vertebral fracture at 3 years; HR 0.55 (0.16 to 1.89); Risk of bias: High; Indirectness of outcome: No indirectness <p>Protocol outcome 2: Atypical fracture</p> <ul style="list-style-type: none"> - Actual outcome: Atypical femur fracture at 3 years; Group 1: 0/469, Group 2: 0/486; Risk of bias: High; Indirectness of outcome: No indirectness <p>Protocol outcome 3: Discontinuation of drugs due to side effects</p> <ul style="list-style-type: none"> - Actual outcome: Discontinuing due to adverse event at 3 years; Group 1: 14/613, Group 2: 11/616; Risk of bias: Low; Indirectness of outcome: No indirectness 	
Protocol outcomes not reported by the study	Quality of life; Falls; Functional outcomes; Pain; GI bleed; Hospitalisation; Admission to care facility

Table 128: Black 2015

Study	Black 2015 ¹⁴¹
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	(n=190)
Countries and setting	Conducted in Multiple countries; Setting: Secondary care
Line of therapy	Unclear
Duration of study	Intervention + follow up: 6 years
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	This trial was an extension of the HORIZON-PFT; osteoporotic women were randomly assigned to annual intravenous ZOL 5mg or placebo and followed for 6 years. In this extension, women in the intervention condition who had received treatment with ZOL for 6 years were eligible.
Exclusion criteria	Exclusions included major protocol violations during the core study, aged >93 years, and specific bone-active medication use.
Recruitment/selection of patients	This trial was an extension of the HORIZON-PFT
Age, gender and ethnicity	Age - Mean (SD): 78 years (4.71/4.85). Gender (M:F): 100% women. Ethnicity: Not reported

Further population details	1. Age: Adults aged >65 years (All adults >70 years). 2. Menopause: Post-menopause
Extra comments	. A total of 451 women completed the previous extension of the trial, however 325 women chose not to participate in this second extension prior to randomisation (114 based on own or physician's decision; 21 did not fulfil the inclusion criteria).
Indirectness of population	No indirectness
Interventions	(n=95) Intervention 1: Bisphosphonates (continuing) - Zolendronate. Zolendronic acid 5mg intravenous infusion once a year for 3 years. Duration 3 years. Concurrent medication/care: All patients received daily oral calcium (1000 to 1500 mg) and vitamin D (400 to 1200 IU). (n=95) Intervention 2: Placebo. Placebo. Duration 3 years. Concurrent medication/care: All patients received daily oral calcium (1000 to 1500 mg) and vitamin D (400 to 1200 IU).
Funding	Study funded by industry (funded by Novartis Pharma AG)
<p>RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ZOLENDRONATE versus PLACEBO</p> <p>Protocol outcome 1: Fracture - Actual outcome: Morphometric vertebral fracture at 3 years; OR 0.611 (95%CI 0.135 to 2.767) (p value 0.461); Risk of bias: High; Indirectness of outcome: No indirectness - Actual outcome: Clinical fractures at 3 years; HR 1.11 (95%CI 0.45 to 2.73) Reported; Risk of bias: Low; Indirectness of outcome: No indirectness</p>	
Protocol outcomes not reported by the study	Quality of life; Atypical fracture; Falls; Functional outcomes; Discontinuation of drugs due to side effects; Pain; GI bleed; Hospitalisation; Admission to care facility

Table 129: Michalska 2006

Study	Michalska 2006 ⁸⁵⁵
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=66)
Countries and setting	Conducted in Czech Republic; Setting: Secondary care
Line of therapy	Unclear
Duration of study	Intervention time: 2 years
Method of assessment of guideline condition	--
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Ambulatory postmenopausal women, 50–80 years of age, and previous treatment with alendronate (10 mg/d) for more than 3 yr. All patients filled their prescription regularly and were reportedly compliant.
Exclusion criteria	Subjects were excluded from the study for any of the following reasons: bone disorders other than primary osteoporosis, endocrine and malignant diseases, uterine and ovarian abnormalities, clinically severe postmenopausal symptoms that required oestrogen therapy, a history of thromboembolic disorders, severe chronic diseases, or treatment with any agent that might influence bone turnover.
Recruitment/selection of patients	The study participants were recruited from ambulatory women in the authors' clinic.
Age, gender and ethnicity	Age - Mean (SD): Alendronate 65.4 (6.8); placebo 64.5 (6.3) years. Gender (M:F): 100% women. Ethnicity: Not stated

Further population details	1. Age: 2. Menopause: Post-menopause
Indirectness of population	No indirectness
Interventions	(n=33) Intervention 1: Bisphosphonates (continuing) - Alendronate. Alendronate 10mg/day. Duration 2 years. Concurrent medication/care: All patients received supplemental calcium (500 mg/d) and vitamin D (800 IU/d). (n=33) Intervention 2: Placebo. Placebo (double blind) for the first year then no treatment (open label) for the second years. Duration 2 years. Concurrent medication/care: All patients received supplemental calcium (500 mg/d) and vitamin D (800 IU/d).
Funding	Equipment / drugs provided by industry (Eli Lilly & Co Indianapolis)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ALENDRONATE versus PLACEBO	
Protocol outcome 1: Fracture - Actual outcome: Non-vertebral fractures at 2 years; Group 1: 1/33, Group 2: 2/33; Risk of bias: High; Indirectness of outcome: No indirectness	
Protocol outcome 2: Discontinuation of drugs due to side effects - Actual outcome: Discontinuation due to side effects at 2 years; Group 1: 2/33, Group 2: 0/33; Risk of bias: Very high; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Quality of life; Atypical fracture; Falls; Functional outcomes; Pain; GI bleed; Hospitalisation; Admission to care facility

Table 130: Miller 1997

Study	Miller 1997 ⁸⁵⁸
Study type	RCT (Patient randomised; Parallel)

Number of studies (number of participants)	(n=193)
Countries and setting	Conducted in United Kingdom
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 2 years
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Secondary prevention: Participants were recruited into phase I of the trial (6-7 years previously) with post-menopausal osteoporosis, manifesting as between 1-4 vertebral fractures
Subgroup analysis within study	Not stratified but pre-specified: Length of etidronate therapy
Inclusion criteria	Women with post-menopausal osteoporosis, manifesting as between 1-4 vertebral fractures, recruited as part of a RCT to compare intermittent cyclical etidronate regimen with a calcium placebo. This analysis included those participants who had completed the first stage of the trial in addition to an open-label phase (etidronate or calcium placebo). For the purposes of the efficacy analyses, only participants who had received open-label Etidronate in the previous year were included. The safety analyses included all participants, including 4 participants (2 in each group) who had not received etidronate in the previous year (open-label calcium only), but had received etidronate in the 2 years prior to this (blinded). [*note for team: all participants therefore had received etidronate for at least 1 year. Some participants (unclear n) had received etidronate for 3 years before this, so total 4 years. 4 participants in the safety analysis had received etidronate for 2 years, with a 1 year break before the trial).
Exclusion criteria	Having received any other treatment for osteoporosis (including oestrogen) prior to phase I of the trial
Age, gender and ethnicity	Age - Mean (SD): 70.4 years (SD not reported). Gender (M:F): 100% female. Ethnicity: Caucasian and Asian
Further population details	1. Age: Adults aged >65 years (Mean age = 70.4 years, no range given. All participants were post-menopause). 2. Menopause: Post-menopause (Post-menopause).
Indirectness of population	No indirectness

Interventions	<p>(n=93) Intervention 1: Bisphosphonates (continuing) - Etidronate. Participants were randomised to receive blinded treatment with phosphate 2g or corresponding placebo for 3 days, followed by etidronate 400mg or placebo daily for 14 days, and then elemental calcium 500mg (as calcium carbonate) daily for 74 days. Treatment cycles were repeated every 91 days for the initial 3-year period. In the third year, participants were offered the opportunity remain on blinded treatment or to receive open-label calcium. Following this study, participants were enrolled on an open-label, follow-up study during which all participants received treatment cycles of etidronate 400mg daily for 14 days, followed by elemental calcium 500mg for 76 days. This cycle was repeated every 90 days. After 2 years, participants were offered the opportunity to enter the current study. Participants were stratified to ensure equal groups in each group received either etidronate or placebo in the original (phase I) study. Participants in this group were randomised to receive intermittent cyclical therapy with etidronate (400mg/day) for 14 days, followed by 76 days of elemental calcium (500mg/day) for 8 cycles over a period of 2 years. . Duration 2 years. Concurrent medication/care: Not described</p> <p>(n=100) Intervention 2: Stopping. Participants were randomised to receive blinded treatment with phosphate 2g or corresponding placebo for 3 days, followed by etidronate 400mg or placebo daily for 14 days, and then elemental calcium 500mg (as calcium carbonate) daily for 74 days. Treatment cycles were repeated every 91 days for the initial 3-year period. In the third year, participants were offered the opportunity remain on blinded treatment or to receive open-label calcium. Following this study, participants were enrolled on an open-label, follow-up study during which all participants received treatment cycles of etidronate 400mg daily for 14 days, followed by elemental calcium 500mg for 76 days. This cycle was repeated every 90 days. After 2 years, participants were offered the opportunity to enter the current study. Participants were stratified to ensure equal groups in each group received either etidronate or placebo in the original (phase I) study. Participants in this group were randomised to receive intermittent cyclical therapy with placebo for 14 days, followed by 76 days of elemental calcium (500mg/day) for 8 cycles over a period of 2 years. . Duration 2 years. Concurrent medication/care: Not described</p>
Funding	Study funded by industry (Medications provided by Industry)
<p>RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ETIDRONATE versus STOPPING</p> <p>Protocol outcome 1: Fracture - Actual outcome for Secondary prevention: Non-vertebral fracture (patients with fracture) at 104 weeks; Group 1: 14/76, Group 2: 14/90; Risk of bias: High; Indirectness of outcome: No indirectness</p> <p>Protocol outcome 2: Discontinuation of drugs due to side effects</p>	

- Actual outcome for Secondary prevention: Withdrawal from trial due to adverse experiences or intercurrent illness at 104 weeks; Group 1: 9/93, Group 2: 6/100; Risk of bias: High; Indirectness of outcome: Serious indirectness

Protocol outcomes not reported by the study

Quality of life; Atypical fracture; Falls; Functional outcomes; Pain; GI bleed; Hospitalisation; Admission to care facility

H.4.5 Stopping statins

Table 131: Kutner 2015

Study	Kutner 2015 ⁷²²
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=381)
Countries and setting	Conducted in USA; community
Line of therapy	Not applicable
Duration of study	Intervention + follow up: Median follow-up 18 weeks, IQR 8-36 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Mean number of non-statin medications 11.6 (SD 5.0)
Stratum	Overall (mixed primary and secondary prevention)
Subgroup analysis within study	Not applicable
Inclusion criteria	English speaking adults older than or currently 18 years of age, receiving a statin for 3 months or longer for primary or secondary prevention of cardiovascular disease, diagnosis of "advanced, life-limiting illness" determined by at least 1 physician indicating he or she "would not be surprised if the patient died in the next year", life expectancy of >1 month and recent deterioration in functional status with a reduction in the Australia-Modified Karnofsky Performance status scale score to less than 80% in the previous 3 months. Patients were either cognitively intact or represented by a legally authorised English-speaking person.
Exclusion criteria	Physician opinion that the patient had active CVD requiring ongoing therapy with statin medications, symptoms of myositis/deranged LFTs or other contraindications to stopping statin therapy
Recruitment/selection of patients	Enrolled from 15 Palliative Care Research Cooperative Group member sites after relevant institutional review board approval
Age, gender and ethnicity	Age - Mean (SD): 74.1 (11.6). Gender (M:F): 210 male/171 female. Ethnicity: 82.7% white, 14.2% black, 2.6% other, 0.5% multiple
Further population details	1. Age: 65 yrs or over (Mean age 74.1). 2. MM: > 50% (Mean number of drugs (excluding statins) ~11). 3. Reason for stopping: Not applicable / Not stated / Unclear
Indirectness of population	No indirectness
Interventions	(n=189) Intervention 1: Statins - Stopping. Discontinued statins at time of randomisation. Duration: Median follow-up 18 weeks. Concurrent medication/care: Usual care

	(n=192) Intervention 2: Statins - Continuing. No change to statin therapy. Duration: Median follow-up 18 weeks. Concurrent medication/care: Usual care
Funding	Academic or government funding (National Institute of Nursing Research)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: STOPPING versus CONTINUING	
<p>Protocol outcome 1: Quality of life - Actual outcome: MacGill Quality of life - Total (mean of subscales) at Mean AUC difference at 20 weeks; MD 0.26 (95%CI 0.02 to 0.5) MacGill Quality of life 0-10 High is good outcome; Risk of bias: High; Indirectness of outcome: No indirectness</p> <p>Protocol outcome 2: All-cause mortality - Actual outcome: All-cause mortality at Median follow-up 18 weeks, IQR 8-36 weeks; HR 0.95 (95%CI 0.7 to 1.29) Calculated – from Kaplan-Meier curve + numbers at risk; Risk of bias: High; Indirectness of outcome: No indirectness</p> <p>Protocol outcome 3: Non-fatal MI - Actual outcome: Cardiovascular-related event (new cardiovascular event or invasive cardiovascular procedure with hospital or emergency department admission) at end of follow-up) at Median follow-up 18 weeks, IQR 8-36 weeks; Group 1: 13/182, Group 2: 11/189; Risk of bias: High; Indirectness of outcome: Serious indirectness</p>	
Protocol outcomes not reported by the study	CV mortality; Stroke; Institutionalisation; Myalgia; Hospitalisation

H.5 Interventions

H.5.1 Models of care

H.5.1.1 Models of Care review

Table 132: Alkema 2007

Study	Alkema 2007 ³²
Study type	RCT (patient randomised; parallel)
Number of studies (number of participants)	1 (n=781)
Countries and setting	Conducted in USA; setting: community
Line of therapy	Adjunctive to current care
Duration of study	Intervention + follow up: 12-month intervention and 12-month post intervention study period
Method of assessment of guideline condition	Partially adequate method of assessment/diagnosis: number of conditions unclear
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	A member of one of the four contracted medical groups, aged 65 or older, enrolment in the Medicare managed care plan for at least one year, and scored four or more (scale of 0-11) on the health care utilisation algorithm.
Exclusion criteria	Nursing home residents and those enrolled in similar studies were excluded
Recruitment/selection of patients	A health care utilisation algorithm was created to identify participants who had multiple needs based on health care utilisation in the previous year. Participants were followed from March 2000 to June 2003 using the health plan's administrative utilisation and retention data to evaluate characteristics associated with mortality.
Age, gender and ethnicity	Age - mean (SD): Intervention: 82.98 (7.12). Control: 83.66 (7.36). Gender (M:F): 271/510. Ethnicity: not stated
Further population details	1. Age: aged 65 or older. 2. Deprivation: not stated. 3. Ethnicity: not stated. 4. Number of conditions: not stated. 5. Type of condition: cancer: intervention n=91, control n=89; COPD & pneumonia: intervention n= 141, control n=132; diabetes: intervention n=81, control n=65; heart disease: intervention n=231, control n=231; hypertension: intervention n=263, control n= 255.
Indirectness of population	Serious indirectness: older adult
Interventions	(n=377) Intervention 1: Case management. The CA Program offered telephone-based care management to older adults with high health care utilisation enrolled in a Medicare managed care health plan. Duration 12 months.

Study	Alkema 2007³²
	<p>Concurrent medication/care: The Care Advocate Program (CA Program) bridged medical and social care delivery systems using telephone-based care management to coordinate health and long-term care services for chronically ill older adults. Part of the Program for Elders in Managed Care Initiative, the CA Program was designed to improve care for managed care members by helping them link to non-insured home- and community-based services (HCBS) and reconnect with health plan services when needed. Social work care managers called "care advocates" geographically located in and employed by 2 community-based social service agencies. Standardised instruments and protocols and monthly coordination meetings were used to ensure uniformity across sites. The term "care advocate" was used to denote the role of educator, consultant, and coach. Care advocates completed an 83-item psychological and functional assessment with participants, used to discuss options and link participants to HCBS (HCBS referral types included in-home care, nutrition, home safety, transportation, non-insured adaptive equipment, and supportive services). Care advocates also referred participants back to their medical group via the primary care physician to access insured services (such as specialist referrals and durable medical equipment). Participants received a call within 1 week of assessment and monthly follow-up calls during the 12 month intervention period to monitor progress. Care advocates encouraged willing and able participants and family members to contact suggested HCBS providers to make their own care arrangements. Upon completion of the study period, participants received additional community referrals to ensure ethical termination.</p> <p>(n=404) Intervention 2: Standard care. Usual care. Duration 12 months. Concurrent medication/care: the control group received "usual and customary care" from the health plan, which included medical group case management services designed to triage and address members' health-related issues, and facilitate access to insured health plan services (for example, insured durable medical equipment).</p>
Funding	Other (Grant from the California Healthcare Foundation as part of The Program for Elders in Managed Care)
<p>RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: CASE MANAGEMENT versus STANDARD CARE</p> <p>Protocol outcome 1: Mortality - Actual outcome: Mortality - died during total study at 24 months (12 months intervention/12 months post intervention); group 1: 51/377, group 2: 90/404; risk of bias: very high; indirectness of outcome: serious indirectness</p>	
Protocol outcomes not reported by the study	Health-related quality of life; functional outcomes (mobility, activities of daily living); patient and carer satisfaction; length of hospital stay; unscheduled care; continuity of care; admission to care facility; patient/carer treatment burden

Table 133: Beck 1997¹⁰⁹

Study	Beck 1997 ¹⁰⁹
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=321)
Countries and setting	Conducted in USA; Setting: USA, community
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 12 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: >65 and had a chronic illness inclusion criteria
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	>65, had a chronic illness (heart/lung/joint or diabetes), high healthcare utilisation patterns in preceding 12 months
Exclusion criteria	None
Recruitment/selection of patients	Identified on administrative databases, sent postal survey and those who consented were selected
Age, gender and ethnicity	Age - Range of means: 72-75. Gender (M:F): 31:69. Ethnicity:
Further population details	1. Age: >65 years 2. Deprivation: Not applicable / Not stated / Unclear 3. Ethnicity: Not applicable / Not stated / Unclear 4. Number of conditions: Not applicable / Not stated / Unclear 5. Type of condition: Not applicable / Not stated / Unclear
Indirectness of population	No indirectness
Interventions	(n=160) Intervention 1: A combination of above. Patients were invited to monthly group visits at the Cooperative Healthcare Clinic. Group visits involved a 30 minute talk by a member of the MDT on a relevant topic, breaks in which nurses took blood pressures and doctors circulated addressing individual concerns of patients and 30 minutes set aside at the end of the talk for patients to get one-to-one visits with the physician. Duration 12 months. Concurrent medication/care: Usual care (n=161) Intervention 2: Standard care. Nil. Duration 12 months. Concurrent medication/care: Usual care
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: GROUP VISIT versus USUAL CARE	
Protocol outcome 1: Mortality	

Study	Beck 1997 ¹⁰⁹
	- Actual outcome: Mortality at 12 months; Group 1: 5/160, Group 2: 9/161; Risk of bias: Low; Indirectness of outcome: No indirectness
	Protocol outcome 2: Unscheduled care
	- Actual outcome: Urgent care visits per patient at 12 months; Group 1: mean 0.24 (SD 0.73); n=160, Group 2: mean 0.3 (SD 0.81); n=161; Risk of bias: High; Indirectness of outcome: No indirectness
	- Actual outcome: Emergency care centre visits per patient at 12 months; Group 1: mean 0.41 (SD 0.87); n=160, Group 2: mean 0.67 (SD 1.62); n=161; Risk of bias: High; Indirectness of outcome: No indirectness
	Protocol outcome 3: Admission to care facility
	- Actual outcome: Proportion of patients hospitalised at 12 months; Group 1: mean 0.22 (SD 0.33); n=160, Group 2: mean 0.29 (SD 0.33); n=161; Risk of bias: High; Indirectness of outcome: No indirectness
	"
Protocol outcomes not reported by the study	Health-related quality of life ; Functional outcomes (mobility, activities of daily living) ; Patient & carer satisfaction ; Length of hospital stay ; Continuity of care ; Patient/carers treatment burden ; to be deleted

Table 134: Berglund 2015¹²²

Study	Berglund 2015 ¹²²
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=161)
Countries and setting	Conducted in Sweden; Setting: Sweden, patients presenting at ED but living in own home
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 12 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: >65
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Living in own home, visited ED, aged >80 OR 65-79 with need for assistance in at least one ADL and a minimum of one chronic illness
Exclusion criteria	Severe acute illness, dementia, severe cognitive impairment, palliative care
Recruitment/selection of patients	Invited to participate by registered nurses at the ED

Study	Berglund 2015 ¹²²
Age, gender and ethnicity	Age - Other: >65, mean not reported. Gender (M:F): 72:89. Ethnicity:
Further population details	1. Age: >65 years 2. Deprivation: Not applicable / Not stated / Unclear 3. Ethnicity: Not applicable / Not stated / Unclear 4. Number of conditions: Not applicable / Not stated / Unclear 5. Type of condition: Not applicable / Not stated / Unclear
Indirectness of population	No indirectness
Interventions	<p>(n=85) Intervention 1: Provider continuity. Nurse with geriatric expertise made assessment of health/social care need at ED, assessment transferred to ward if patient transferred to ward, also sent to municipal MDT (nurse, social worker, physiotherapist, OT), case manager co-ordinated planning for discharge, case manager contacted relatives to offer support and advice, care-planning meeting after discharge organised in patient's own home with MDT, within 1 week after care-planning meeting older person contacted by case manager and plan for follow-up made, after 6 months a new care-planning meeting could be held if needed. Duration 12 months. Concurrent medication/care: Usual care</p> <p>(n=76) Intervention 2: Standard care. Usual care - some discharge planning in hospital, no meeting or proactive contact after discharge. Duration 12 months. Concurrent medication/care: Nil else</p>
Funding	Academic or government funding
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: CONTINUUM OF CARE versus STANDARD CARE	
Protocol outcome 1: Mortality - Actual outcome: Mortality at 12 months; Group 1: 14/83, Group 2: 9/76; Risk of bias: High; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Health-related quality of life ; Functional outcomes (mobility, activities of daily living) ; Patient & carer satisfaction ; Length of hospital stay ; Unscheduled care ; Continuity of care ; Admission to care facility ; Patient/carer treatment burden ; to be deleted

Table 135: Bouman 2008¹⁷¹

Study	Bouman 2008 ¹⁷¹
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=330)

Study	Bouman 2008 ¹⁷¹
Countries and setting	Conducted in Netherlands; Setting: Community, Netherlands
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 18 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Living at home, age 70-84
Exclusion criteria	Patients who self-rated health status as "moderate or good", already receiving home nursing care, on waiting list for care home admission
Recruitment/selection of patients	Postal survey to patients living at home in certain area of Netherlands, ages 70-84
Age, gender and ethnicity	Age - Mean (SD): 76 (3.7). Gender (M:F): 40:60. Ethnicity: Not stated
Further population details	1. Age: >65 years 2. Deprivation: Not applicable / Not stated / Unclear 3. Ethnicity: Not applicable / Not stated / Unclear 4. Number of conditions: Not applicable / Not stated / Unclear 5. Type of condition: Not applicable / Not stated / Unclear
Indirectness of population	No indirectness
Interventions	<p>(n=160) Intervention 1: CGA. Program of eight home visits, with telephone follow-up over 18 month period, visited by trained home nurses, visits included multidimensional geriatric assessment with advice and referral to professional and community services. Differentiated from other CGA studies as each patient had formulaic pattern of follow-up as opposed to individualised treatment plan on back of CGA. Duration 18 months. Concurrent medication/care: Usual care</p> <p>Further details: 1. Post-CGA intervention: CGA + various</p> <p>(n=170) Intervention 2: Standard care. Usual care, participants could apply for all available care but no structured follow-up. Duration 18 months. Concurrent medication/care: Nil else</p> <p>Further details: 1. Post-CGA intervention: Not applicable / Not stated / Unclear</p>
Funding	Academic or government funding

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: HOME VISITING PROGRAM versus STANDARD CARE

Study	Bouman 2008 ¹⁷¹
Protocol outcome 1: Mortality - Actual outcome: Mortality at 24 months; Group 1: 29/160, Group 2: 23/170; Risk of bias: High; Indirectness of outcome: No indirectness	
Protocol outcome 2: Length of hospital stay - Actual outcome: Bed days per patient at 24 months; Group 1: mean 8.14 (SD 18.14); n=160, Group 2: mean 8.54 (SD 17.99); n=170; Risk of bias: High; Indirectness of outcome: No indirectness	
Protocol outcome 3: Unscheduled care - Actual outcome: Hospital admissions at 24 months; Group 1: 80/160, Group 2: 71/170; Risk of bias: High; Indirectness of outcome: No indirectness	
Protocol outcome 4: Admission to care facility - Actual outcome: Nursing home admissions at 24 months; Group 1: 10/160, Group 2: 11/170; Risk of bias: High; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Health-related quality of life ; Functional outcomes (mobility, activities of daily living) ; Patient & carer satisfaction ; Continuity of care ; Patient/carers treatment burden ; to be deleted

Table 136: Coburn 2008^{168,169,179}

Study	Health Quality Partners (HQP) programme, nested within Medicare Coordinated Care Demonstration trial: Coburn 2012 ²⁷⁷
Study type	RCT (patient randomised; parallel)
Number of studies (number of participants)	2 (n=1736)
Countries and setting	Conducted in USA; setting: Eastern Pennsylvania
Line of therapy	Unclear
Duration of study	Follow up (post intervention): mean 4.2 years
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Overall
Subgroup analysis within study	Stratified then randomised: risk strata (high, moderate, low, very low). Determined by geriatric-related risks using the Sutter Health questionnaire, individuals scoring above 3 on the Sutter instrument were classified as high risk, individuals scoring at or below 3 on the Sutter instrument were classified as moderate, low or very low according to a 'disease-specific risk assessment developed by Health Quality Partners (HQP)'. Individuals in very low and low risk categories were excluded.

Study	Health Quality Partners (HQP) programme, nested within Medicare Coordinated Care Demonstration trial: Coburn 2012 ²⁷⁷
Inclusion criteria	65 years or older; with heart failure, CHD, asthma, diabetes, hypertension or hyperlipidaemia; receiving care at primary care practice agreeing to work with the HQP programme.
Exclusion criteria	Dementia; end stage renal disease; schizophrenia; active cancer (except skin) in prior 5 years; life expectancy less than 6 months; current or imminent residence in long-term care facility. Assessment of risk classified as low or very low according to a 'disease-specific risk assessment developed by HQP'.
Recruitment/selection of patients	Randomised into HQP programme from MCCD
Age, gender and ethnicity	Age - mean (SD): 74.8 (6.5). Gender (M:F): 39:61. Ethnicity: not reported
Further population details	1. Age: aged 65 years and over. 2. Deprivation: not stated. 3. Ethnicity: not stated. 4. Number of conditions: all participants mean 3.8 (SD 1.9). 5. Type of condition: not stated.
Extra comments	Age group, years: 65-69 (29%), 70-74 (25%), 75-79 (24%), 80-84 (15%), 85+ (7%). Perceived health: excellent (18%), good (65%), fair (15%), poor (2%). Depressed in prior 3 months 14%. Living alone 31%. Fall in prior year 22%. Limited mobility 9%. ADL score (mean±SD): 0.8±2.1. IADL score (mean±SD): 1.1±2.4. Chronic conditions (mean±SD): 3.8±1.9.
Indirectness of population	Serious indirectness: older adult
Interventions	<p>(n=873) Intervention 1: Case management and care plan. HQP programme. Individualised plan developed by nurse case manager, based on: the patient's self-identified primary concerns and unmet needs; findings from their initial and on-going assessments; and the patient's motivational stage of change. The interventions typically incorporated into care plan include: education, symptom monitoring, medication reconciliation, counselling for adherence, help identifying, arranging and monitoring community and social service referrals. Group interventions directly provided by nurse case managers included: structured lifestyle and behaviour change programs for weight loss, weight loss maintenance, exercise classes and a balance and mobility programme for fall prevention</p> <p>Concurrent medication/care: High risk people undertook a CGA ('high risk' on the Sutter Health Questionnaire (SHQ)): multidimensional in-home assessment of physical assessment (HQP), IADL, Mini-Mental State Exam, Clock Drawing Test, Geriatric Depression Screen-Short Form, Nutritional Risk Assessment (NSI), violence screening (HQP), alcohol abuse using CAGE Questionnaire, behavioural and caregiver assessment, home environment safety checklist, Numeric Pain Scale, sleep, incontinence, immunisations and preventative screenings, psychological support needs (HQP).</p> <p>(n=863) Intervention 2: Standard care. Usual care. Duration mean 4.2 years. Concurrent medication/care: none stated</p>
Funding	Academic or government funding (Health Quality Partners, provided by the US Centres for Medicare and Medicare Services [CMS])

Study	Health Quality Partners (HQP) programme, nested within Medicare Coordinated Care Demonstration trial: Coburn 2012²⁷⁷
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: CASE MANAGEMENT versus STANDARD CARE	
Protocol outcome 1: Mortality - Actual outcome: Mortality, adjusted (HR) at 4.2 years; HR 0.73 (95% CI 0.55 to 0.98) reported; risk of bias: very high; indirectness of outcome: no indirectness	
Protocol outcomes not reported by the study	Health-related quality of life; functional outcomes (mobility, activities of daily living); patient and carer satisfaction; length of hospital stay; unscheduled care; continuity of care; admission to care facility; patient/carer treatment burden

Table 137: Courtney 2009²⁹⁹

Study	Courtney 2009²⁹⁹
Study type	RCT (patient randomised; parallel)
Number of studies (number of participants)	1 (n=122)
Countries and setting	Conducted in Australia
Line of therapy	Adjunctive to current care
Duration of study	Intervention + follow up: 24 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Patients with risk factors for readmission: patients aged 65 years and over admitted with a medical condition and at least one risk factor (that is, aged 75 years and over, multiple admissions in previous 6-months, multiple comorbidities, lives alone, lacking social support, poor self-rating of health, moderate to severe functional impairment, history of depression).
Exclusion criteria	Factors that would undermine patients' ability to participate in the intervention: patients requiring home oxygen, patients unable to walk independently for 3 meters (with/without walking aids), patients with neurological or cognitive deficit or disease.
Recruitment/selection of patients	Participants recruited within 72 hours of admission to medical wards at a tertiary referral hospital in Brisbane, Australia.

Study	Courtney 2009 ²⁹⁹
Age, gender and ethnicity	Age - mean (SD): 78.8 (years (6.9). Gender (M:F): 46/76. Ethnicity: not reported
Further population details	1. Age: >65 years . 2. Deprivation: not stated. 3. Ethnicity: not stated. 4. Number of conditions (median, range): intervention: 5 (0-8); control: 4 (1-12). 5. Type of condition: not stated.
Extra comments	Intervention aimed at an older adult population who are at known risk of readmission but relatively healthy and able to live independently. Population conditions included cardiac (78%), orthopaedic (48%), respiratory (49%), gastrointestinal (40%), and endocrine disease (38%). Mean duration of hospital stay = 4.6 days (SD = 2.92).
Indirectness of population	Serious indirectness: older adult
Interventions	<p>(n=64) Intervention 1: A combination of above. Older hospitalised patients' discharge planning and in-home follow-up protocol (OHP-DP protocol). Within 72 hours of admission a registered nurse (RN) and physiotherapist undertook a comprehensive patient assessment and developed a goal-directed, individualised care plan in consultation with the patient, health professionals, family and caregivers. The care plan included:</p> <ul style="list-style-type: none"> * An individually tailored exercise program prescribed by the physiotherapies including: muscle stretching, balance training, walking for endurance and muscle strengthening using resistance exercises. * The nurse visited daily during participants' hospital stay to address concerns, facilitate the exercise program and oversee discharge planning. The nurse developed a transitional care plan while the patients was in hospital, which covered the areas of functional ability and need for assistance with activities of daily living; post-discharge treatments and follow-up care; social support; chronic disease management plans and information; medication information; community services; and assistance with the exercise program. The nurse and physiotherapist combined their visits when planning, explaining and demonstrating the exercise program to ensure continuity when the nurse continued to facilitate the exercise program during extended hospital stays and at home. Written guidelines were provided on post-discharge management, including diagrams and specific instructions for their exercise program. * Within 48 hours of discharge, the nurse undertook a home visit to assess availability of support; address transitional concerns; provide advice and support; and ensure the exercise program could be safely undertaken at home. Extra home visits were provided if required. Weekly telephone calls were provided for 4 weeks followed by monthly follow-up for further 5-months. The nurse was also available for contact between 9am - 5pm weekdays. During the telephone follow-ups, feedback was sought on issues identified in hospital or during the home visit; general health; level of support available; management of treatment regimens; health promotion activities; any new problems or concerns; levels of adherence with the exercise program, and progress with the exercise plan and goals. These were adjusted to reflect progress or difficulties, and advice, information, positive feedback and support were offered. Duration in hospital + 6-months post-discharge. Concurrent medication/care: usual care. <p>(n=64) Intervention 2: Standard care. Discharge planning and rehabilitation advice normally provided. If in-home follow-up was necessary, this was organised in the routine way (for example referral to community health services).</p>

Study	Courtney 2009²⁹⁹
	Duration in hospital + 6-months post-discharge. Concurrent medication/care: usual care.
Funding	Academic or government funding (Funded by an Australian Research Council Discovery Project Grant)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: CASE MANAGEMENT + CARE PLAN versus STANDARD CARE	
<p>Protocol outcome 1: Health-related quality of life</p> <p>- Actual outcome: SF-12 (v2; physical component) at 6-months; other: $\eta p^2 = 0.50$ (p-value <.001); risk of bias: high; indirectness of outcome: no indirectness</p> <p>- Actual outcome: SF-12 (v2; mental component) at 6-months; mean $\eta p^2 = 0.19$ (p-value <.001); risk of bias: high; indirectness of outcome: no indirectness</p> <p>Protocol outcome 2: Unscheduled care</p> <p>- Actual outcome: Emergency hospital readmissions at 6-months; OR 0.14 (95%CI 0.04 to 0.44) (p-value .001); risk of bias: high; indirectness of outcome: no indirectness</p> <p>- Actual outcome: Emergency GP visits at 6-months; group 1: 15/58, group 2: 43/64; risk of bias: very high; indirectness of outcome: no indirectness</p>	
Protocol outcomes not reported by the study	Mortality; functional outcomes (mobility, activities of daily living); patient and carer satisfaction; length of hospital stay; continuity of care; admission to care facility; patient/carers treatment burden

Table 138: Eklund 2013³⁹⁴

Study	Eklund 2013³⁹⁴
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=181)
Countries and setting	Conducted in Sweden; Setting: Community (identified at ED presentation)
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 12 months
Method of assessment of guideline condition	Inadequate method of assessment/diagnosis: >65
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Define
Exclusion criteria	Define
Recruitment/selection of patients	Recruited in ED

Study	Eklund 2013 ³⁹⁴
Age, gender and ethnicity	Age - Other: Mean not reported, either older than 80 or between 65-79 with at least one chronic condition and one ADL dependency. Gender (M:F): Define. Ethnicity: Not stated
Further population details	1. Age: >65 years 2. Deprivation: Not applicable / Not stated / Unclear 3. Ethnicity: Not applicable / Not stated / Unclear 4. Number of conditions: Not applicable / Not stated / Unclear 5. Type of condition: Not applicable / Not stated / Unclear
Indirectness of population	Serious indirectness
Interventions	<p>(n=89) Intervention 1: A combination of above. Collaboration between a nurse with geriatric competence at the emergency department, the hospital wards and a multi-professional team in the community. Participants underwent geriatric assessment by nurse with geriatric competence, during admission followed by care co-ordination, care-planning and home follow-up. Focus of intervention was on creating a continuum of care.. Duration 12 months. Concurrent medication/care: Usual care Further details: 1. Post-CGA intervention: Not applicable / Not stated / Unclear</p> <p>(n=92) Intervention 2: Standard care. Standard care including a routine assessment and care planning by community team following discharge from hospital, possibly including rehabilitation if required.. Duration 12 months. Concurrent medication/care: Usual care Further details: 1. Post-CGA intervention:</p>
Funding	Funding not stated
<p>RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: INTERVENTION versus USUAL CARE</p> <p>Protocol outcome 1: Mortality - Actual outcome: Mortality at 12 months; Group 1: 30/85, Group 2: 18/76; Risk of bias: Very high; Indirectness of outcome: No indirectness</p> <p>Protocol outcome 2: Functional outcomes (mobility, activities of daily living) - Actual outcome: ADL - number of people improving ADL score at 12 months; Group 1: 33/85, Group 2: 18/76; Risk of bias: Very high; Indirectness of outcome: No indirectness - Actual outcome: ADL - number of people with worsening ADL score at 12 months; Group 1: 32/85, Group 2: 36/76; Risk of bias: Very high; Indirectness of outcome: No indirectness</p>	
Protocol outcomes not reported by the study	Health-related quality of life ; Patient & carer satisfaction ; Length of hospital stay ; Unscheduled care ; Continuity of

Study	Eklund 2013³⁹⁴
	care ; Admission to care facility ; Patient/carer treatment burden ; to be deleted

Table 139: EII 2010³⁹⁷

Study	EII 2010³⁹⁷
Study type	RCT (patient randomised; parallel)
Number of studies (number of participants)	1 (n=387)
Countries and setting	Conducted in USA
Line of therapy	Unclear
Duration of study	Follow up (post intervention): 18 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Endorsed one of two cardinal depression symptoms more than half to days to nearly every day and scored ≥ 10 on the PHQ-9 indicating a high likelihood of clinically significant depression. Provided written informed consent.
Exclusion criteria	Acute suicidal ideation, score of ≥ 8 on the Alcohol Use Disorders Test alcohol assessment, recent lithium/antipsychotic medication use, inability to speak English or Spanish.
Recruitment/selection of patients	Trained study recruiters identified diabetic patients from medical charts. Patients provided verbal consent to depression symptom screening.
Age, gender and ethnicity	Age - other: all ≥ 18 . Aged ≥ 50 years: 75.1% intervention, 69.1% comparison. Gender (M:F): 1:4. Ethnicity: 96.5% Hispanic.
Further population details	1. Age: Aged ≥ 50 years. 2. Deprivation: low SES (low income). 3. Ethnicity: 96.5% Hispanic. 4. Number of conditions: patients with 2 conditions. 5. Type of condition: physical with mental health.
Indirectness of population	Serious indirectness: older adult
Interventions	(n=193) Intervention 1: Collaborative care. Multifaceted Diabetes and Depression Programme: problem solving therapy; monthly telephone with diabetes depression clinical specialists (DDCS) follow up symptom monitoring, treatment maintenance, and relapse prevention; care and service system navigation by DDCS and an assistant patient navigator. Psychiatrist and principal investigator provided weekly telephone DDCS supervision and if requested provided PCP antidepressant medication telephone consultation. Duration 12 month. Concurrent medication/care: none stated.

Study	Eli 2010³⁹⁷
	(n=194) Intervention 2: Standard care. Enhanced usual care. Duration 12 months. Concurrent medication/care: given patient- and family-focused depression education pamphlets and a community, financial, social services, transportation and child care resource list. Primary care physicians were informed of patient depression diagnoses and study participation and could prescribe antidepressant medications or refer patients to community mental health care. Patients could seek mental health treatment.
Funding	Academic or government funding (NIMH)
<p>RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: COLLABORATIVE CARE versus STANDARD CARE</p> <p>Protocol outcome 1: Health-related quality of life - Actual outcome: Health-related quality of life - SF12 physical component (18 months) at 18 months; MD; risk of bias: very high; indirectness of outcome: no indirectness - Actual outcome: Health-related quality of life - SF12 mental component (18 months) at 18 months; MD; risk of bias: very high; indirectness of outcome: no indirectness</p> <p>Protocol outcome 2: Functional outcomes (mobility, activities of daily living) - Actual outcome: Functional outcome - Sheehan Disability Scale of functional impairment (12 months) at 12 months; MD; risk of bias: very high; indirectness of outcome: no indirectness - Actual outcome: Functional outcome - Sheehan Disability Scale of functional impairment (18 months) at 18 months; MD; risk of bias: very high; indirectness of outcome: no indirectness</p>	
Protocol outcomes not reported by the study	Mortality; patient and carer satisfaction; length of hospital stay; unscheduled care; continuity of care; admission to care facility; patient/carer treatment burden

Table 140: Hogg 2009⁵⁹⁵

Study	Anticipatory and Preventive Team Care (APTCare) trial: Hogg 2009⁵⁹⁵
Study type	RCT (patient randomised; parallel)
Number of studies (number of participants)	1 (n=241)
Countries and setting	Conducted in Canada; setting: primary care
Line of therapy	Adjunctive to current care

Study	Anticipatory and Preventive Team Care (APTCare) trial: Hogg 2009 ⁵⁹⁵
Duration of study	Intervention + follow up: 12-18 months (mean 14.9 months)
Method of assessment of guideline condition	Partially adequate method of assessment/diagnosis: mean number of chronic conditions from table (intervention: 2.7/control: 2.3). Conditions not specified.
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	50 years of age or older, roistered in the practice, and considered by their family physicians to be good candidates to benefit from additional medical resources and at risk of functional decline, physical deterioration, or experiencing an event requiring emergency services. There were no restrictions on diagnoses.
Exclusion criteria	Substantial cognitive impairment, language or cultural barriers, life expectancy less than 6 months, and plans to move or to be away for more than 6 weeks during the study period.
Recruitment/selection of patients	The study was conducted in a family health network in a rural area of Ottawa, Canada. Patients within the family health network were allocated to either the intervention or the control arm. Recruitment of patients took place between October 2004 and March 2005. Not further information on recruitment or selection of patients.
Age, gender and ethnicity	Age - other: Intervention: 69.6 years. Control: 72.8 years (no range or SD provided). Gender (M:F): 103/138. Ethnicity: not specified
Further population details	1. Age: Aged ≥50 years. 2. Deprivation: not stated. 3. Ethnicity: first language English: intervention 92%, control 93%. 4. Number of conditions (mean): intervention 2.7, control 2.4. 5. Type of condition: not stated.
Indirectness of population	Serious indirectness: older adult
Interventions	<p>(n=120) Intervention 1: Case management. The intervention consisted of care provided by a multi-disciplinary team. One pharmacist and 3 nurse practitioners (NPs) were added to a family practice. The pharmacist and the NPs delivered care in patients' home or by telephone. Both performed comprehensive chart reviews and home visits for each patient at the start of the study. Pharmacist then conducted a medication management review and worked directly with the patients and in collaboration with the NPs and family physicians to address issues and new drug-related problems as they arose. Each patient's NP developed an individualised care plan in collaboration with the patient and in consultation with the pharmacist and the patient's family physician. The care plan identified the patient's active health issues and outlined the management goals that the patient and the team of providers would work toward over the course of the intervention. Duration 15 months. Concurrent medication/care: intervention patients took part in the Anticipatory and Prevention Team Care (APTCare) trial.</p> <p>(n=121) Intervention 2: Standard care. Control patients received usual care from their family physicians. Duration 15 months. Concurrent medication/care: no further information provided.</p>

Study	Anticipatory and Preventive Team Care (APTCare) trial: Hogg 2009 ⁵⁹⁵
Funding	Academic or government funding (physicians in the practice were remunerated by the publicly funded Medicare system through a blended payment formula of capitation [principally], fee-for-service, and incentives). Funding for this research was provided by the Ontario Ministry of Health and Long-Term Care Primary Health Care Transition Fund.
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: CASE MANAGEMENT versus STANDARD CARE	
<p>Protocol outcome 1: Health-related quality of life</p> <ul style="list-style-type: none"> - Actual outcome: SF-36 physical component at 15 months; MD 1.6 (95%CI -0.8 to 4.1) SF-36 1-100 top=high is good outcome; risk of bias: high; indirectness of outcome: no indirectness - Actual outcome: SF-36 mental component at 15 months; MD -1.1 (95%CI -3.7 to 1.6) SF-36 1-100 top=high is good outcome; risk of bias: high; indirectness of outcome: no indirectness - Actual outcome: Health related Quality of Life total number of unhealthy days in last 30 days at 15 months; risk of bias: high; indirectness of outcome: no indirectness <p>Protocol outcome 2: Mortality</p> <ul style="list-style-type: none"> - Actual outcome: Mortality at 15 months; group 1: 3/120, group 2: 0/121; risk of bias: high; indirectness of outcome: no indirectness <p>Protocol outcome 3: Unscheduled care</p> <ul style="list-style-type: none"> - Actual outcome: Unscheduled care - average number of ED visits at 15 months; MD -0.10 (95%CI -0.38 to 0.18); risk of bias: high; indirectness of outcome: no indirectness <p>Protocol outcome 4: Patient/carer treatment burden</p> <ul style="list-style-type: none"> - Actual outcome: Caregiver burden at 15 months; risk of bias: high; indirectness of outcome: no indirectness 	
Protocol outcomes not reported by the study	Functional outcomes (mobility, activities of daily living); patient & carer satisfaction; length of hospital stay; continuity of care; admission to care facility

Table 141: Metzelthin 2013⁸⁵⁴

Study	Metzelthin 2013 ⁸⁵⁴
Study type	RCT (Cluster randomised; Parallel)
Number of studies (number of participants)	1 (n=346)

Study	Metzelthin 2013 ⁸⁵⁴
Countries and setting	Conducted in Netherlands; Setting: Community
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 2 years
Method of assessment of guideline condition	Inadequate method of assessment/diagnosis: People over the age of 70
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Community dwelling, frail, people over the age 70
Exclusion criteria	Terminally ill, confined to bed, severe cognitive or psychological impairment, unable to communicate in Dutch
Recruitment/selection of patients	All people meeting criteria in included GP centres were sent postal survey
Age, gender and ethnicity	Age - Range of means: 76.8-77.49. Gender (M:F): 42:58. Ethnicity:
Further population details	1. Age: >65 years 2. Deprivation: Not applicable / Not stated / Unclear 3. Ethnicity: Not applicable / Not stated / Unclear 4. Number of conditions: Not applicable / Not stated / Unclear 5. Type of condition: Not applicable / Not stated / Unclear
Indirectness of population	Serious indirectness
Interventions	<p>(n=193) Intervention 1: A combination of above. People received an in home multidimensional assessment by a practice nurse, GP and practice nurse discussed the assessment and the need for other assessments, preliminary treatment plan formulated by GP and practice nurse with or without an MDT meeting, second home visit by practice nurse to formulate final treatment plan with person, practice nurse also acts as case manager to regularly review achievement of goals and need for additional support. Duration 2 years. Concurrent medication/care: 1Usual care Further details: 1. Post-CGA intervention: Not applicable / Not stated / Unclear</p> <p>(n=153) Intervention 2: Standard care. Usual care. Duration 2 years. Concurrent medication/care: Usual care, no further details provided Further details: 1. Post-CGA intervention:</p>
Funding	Academic or government funding
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: INTERVENTION versus CONTROL	
<p>Protocol outcome 1: Functional outcomes (mobility, activities of daily living)</p> <p>- Actual outcome: Groningen Activity Restriction Scale - ADL subscale at 2 years; MD 0.77 (95%CI -0.05 to 1.59); Risk of bias: Very high; Indirectness of outcome: No</p>	

Study	Metzelthin 2013 ⁸⁵⁴
indirectness - Actual outcome: Groningen Activity Restriction Scale - IADL subscale at 2 years; MD 0.40 (95%CI -0.54 to 1.34); Risk of bias: Very high; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Health-related quality of life ; Mortality ; Patient & carer satisfaction ; Length of hospital stay ; Unscheduled care ; Continuity of care ; Admission to care facility ; Patient/carers treatment burden ; to be deleted

Table 142: Naylor 2004⁸⁹⁶

Study	Naylor 2004 ⁸⁹⁶
Study type	RCT (patient randomised; parallel)
Number of studies (number of participants)	1 (n=239)
Countries and setting	Conducted in USA; setting: six Philadelphia academic and community hospitals
Line of therapy	Adjunctive to current care
Duration of study	Intervention + follow up: 3 month intervention + follow-up through 52 weeks post index hospital discharge
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: mean number of health conditions: intervention, n=6.4 (2.5); control, n=6.4 (2.0)
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Eligible patients had to speak English, be alert and oriented, be reachable by telephone after discharge, and reside within a 60-mile radius service area of the admitting hospital
Exclusion criteria	Elders with end-stage renal disease were excluded because of their access to unique Medicare services
Recruitment/selection of patients	All patients aged 65 and older admitted to study hospitals from their home between February 1997 and January 2001 with a diagnosis of heart failure
Age, gender and ethnicity	Age - mean (SD): intervention: 76.4 (6.9); control: 75.6 (6.5). Gender (M:F): 102/137. Ethnicity: African American, n=86; White, n=153.
Further population details	1. Age: aged 65 years and older. 2. Deprivation: income < 10,000 dollars: intervention 29%, control 37%; 10,000-19,999: intervention 26%, control 27%; more than 20,000: intervention 15%, control 17%. 3. Ethnicity: African American: intervention 34%, control 38%; White: intervention 66%, control 62%. 4. Number of conditions (mean, SD):

Study	Naylor 2004⁸⁹⁶
	intervention 6.4 (2.5), control 6.4 (2). 5. Type of condition: heart failure.
Indirectness of population	Serious indirectness: older adult
Interventions	<p>(n=121) Intervention 1: Standard care. Control group patients received care routine for the admitting hospital, including site-specific heart failure patient management and discharge planning critical paths and, if referred, standard home agency care consisting of comprehensive skilled home health services. Duration 3 month intervention/12 month follow-up. Concurrent medication/care: standards of care for all study hospitals include institutional policies to guide, document, and evaluate discharge planning. The attending physician was responsible for determining the discharge date, and the primary nurse, discharge planner, and physical collaborated in the design and implementation of the discharge plan; including: liaison nurses to facilitate referrals to home care, availability of comprehensive, intermittent skilled home care services in patients' residences 7 days per weeks; and on-call registered nurse available 24 hours per day.</p> <p>(n=118) Intervention 2: Collaborative care. A 3-month APN-directed discharge planning and home follow-up protocol. Duration 3 month intervention/12 month follow-up. Concurrent medication/care: in collaboration with patients' physicians, 3 APNs (advanced practice nurses) implemented an intervention extending from index hospital admission through 3 months after the index hospital discharge. The intervention included all of the following components: (1) a standardised orientation and training programme guided by a multidisciplinary team of heart failure experts to prepare APNs to address the unique needs of older adults and their caregivers throughout an acute episode of heart failure; (2) use of Cost Model of APN Transitional Care, including identification of patients' and caregivers' goals, individualised plans of care developed and implemented by APNs in collaboration with patients' physicians, educational and behavioural strategies to address patients' and caregivers' learning needs, continuity of care and care coordination across settings, and the use of expert nurses to deliver and manage clinical services to high-risk patient groups; (3) APN implementation of an evidence-based protocol, guided by national heart failure guidelines and designed for this patient group and their caregivers with a unique focus on comprehensive management of needs and therapies associated with an acute episode of heart failure complicated by multiple comorbid conditions. The protocol consisted of an initial APN visit within 24 hours of index hospital admission, and daily visits during the hospitalisation, weekly visits during the first month, bimonthly visits during the second and third months, additional APN visits based on patients' needs and APN telephone availability 7 days per week. If a patient was hospitalised for any reason during the intervention period, the APN resumed daily visits. APNs had access to multidisciplinary team members for challenging cases. After patients were discharged to their home, APNs conducted targeted assessments to identify changes in patients' health status.</p>
Funding	Academic or government funding (National Institute for Nursing Research, National Institutes of Health funded this study)

Study	Naylor 2004 ⁸⁹⁶
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: COLLABORATIVE CARE versus STANDARD CARE	
<p>Protocol outcome 1: Health-related quality of life - Actual outcome: Quality of life - Minnesota Living with Heart Failure Questionnaire (total score) at 12 months; group 1: mean 2.8 (SD 1.8); n=75, group 2: mean 2.6 (SD 1.7); n=74; The Minnesota Living with Heart Failure Questionnaire 0-105 top=high is poor outcome; risk of bias: high; indirectness of outcome: no indirectness</p>	
<p>Protocol outcome 2: Mortality - Actual outcome: Mortality at 12 months; group 1: 11/118, group 2: 13/121; risk of bias: high; indirectness of outcome: no indirectness</p>	
<p>Protocol outcome 3: Functional outcomes (mobility, activities of daily living) - Actual outcome: Functional outcome - Functional Status Score at 12 months; group 1: mean 3.1 (SD 1.5); n=76, group 2: mean 2.9 (SD 1.6); n=71; The Enforced Social Dependency Scale 12-72 top=high is poor outcome; risk of bias: high; indirectness of outcome: no indirectness</p>	
<p>Protocol outcome 4: Patient & carer satisfaction - Actual outcome: Patient & carer satisfaction - patient satisfaction at 6 weeks; group 1: mean 83.1 (SD 9.6); n=92, risk of bias: high; indirectness of outcome: no indirectness</p>	
Protocol outcomes not reported by the study	Length of hospital stay; unscheduled care; continuity of care; admission to care facility; patient/carers treatment burden

Table 143: Sandberg 2015¹⁰⁷⁶

Study	Sandberg 2015 ¹⁰⁷⁶
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=153)
Countries and setting	Conducted in Sweden; Setting: Sweden, community
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 12 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: >65 inclusion criteria, range for "health complaints" 2-23
Stratum	Overall
Subgroup analysis within study	Not applicable

Study	Sandberg 2015 ¹⁰⁷⁶
Inclusion criteria	Live in ordinary home (i.e. not nursing or sheltered housing), >65 years old, dependent in at least two ADLs, admitted to hospital at least twice/had at least four visits to outpatients/primary care in previous 12 months
Exclusion criteria	Not able to communicate verbally, cognitive impairments, special accommodation
Recruitment/selection of patients	Patients were screened at hospital clinics and contacted based on their demographics from the primary care records
Age, gender and ethnicity	Age - Range of means: 81.4-81.6. Gender (M:F): 51/102. Ethnicity:
Further population details	1. Age: >65 years 2. Deprivation: Not applicable / Not stated / Unclear 3. Ethnicity: Not applicable / Not stated / Unclear 4. Number of conditions: Not applicable / Not stated / Unclear 5. Type of condition: Not applicable / Not stated / Unclear
Indirectness of population	No indirectness
Interventions	(n=80) Intervention 1: Case management. Patients received traditional case management with assessment, co-ordination, home visits and telephone calls. Patients also received general information about the healthcare system and specific information about their needs. Case managers either had nursing or physiotherapy backgrounds. Monthly visits (over 12 months) took place in the patients' own homes. Each visit lasted ~1 hour and the contents of the visits depended on the individual's care plan. The first visit involved a CGA to inform a care plan to be used for subsequent visits.. Duration 12 months. Concurrent medication/care: Usual care Further details: 1. Post-CGA intervention: CGA + long-term care plan (n=73) Intervention 2: Standard care. Usual care. Duration 12 months. Concurrent medication/care: Usual care Further details: 1. Post-CGA intervention:
Funding	Academic or government funding

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: CASE MANAGEMENT versus STANDARD CARE

Protocol outcome 1: Mortality

- Actual outcome: Mortality at 12 months; Group 1: 10/80, Group 2: 3/73; Risk of bias: High; Indirectness of outcome: No indirectness

Protocol outcome 2: Length of hospital stay

- Actual outcome: Total length of inpatient stays at 12 months; Group 1: mean 4.6 (SD 15.42); n=80, Group 2: mean 4.05 (SD 11.71); n=73; Risk of bias: High; Indirectness of outcome: No indirectness

Protocol outcome 3: Unscheduled care

Study	Sandberg 2015 ¹⁰⁷⁶
	- Actual outcome: Hospital admissions per patient at 12 months; Group 1: mean 0.49 (SD 0.81); n=80, Group 2: mean 0.48 (SD 0.84); n=73; Risk of bias: Very high; Indirectness of outcome: No indirectness
Protocol outcomes not reported by the study	Health-related quality of life ; Functional outcomes (mobility, activities of daily living) ; Patient & carer satisfaction ; Continuity of care ; Admission to care facility ; Patient/carer treatment burden ; to be deleted

Table 144: Slaets 1997¹¹²⁶

Study	Slaets 1997 ¹¹²⁶
Study type	RCT (patient randomised; parallel)
Number of studies (number of participants)	1 (n=237)
Countries and setting	Conducted in Netherlands; setting: hospital
Line of therapy	Adjunctive to current care
Duration of study	Intervention time: length of stay in hospital: intervention 19.7 days; control 24.8 days
Method of assessment of guideline condition	Partially adequate method of assessment/diagnosis: >75 years
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Patients must be 75 years old or older and have been referred to the department of general medicine.
Exclusion criteria	Patients admitted for day treatment were excluded
Recruitment/selection of patients	Data collected at the Leyenburg Hospital in The Hague, a teaching hospital. The study was carried out in two units located on different floors of the hospital.
Age, gender and ethnicity	Age - mean (SD): 82.8 (5.0). Gender (M:F): 29.5%/70.5%. Ethnicity: not stated
Further population details	1. Age: over 75 years old. 2. Deprivation: not stated. 3. Ethnicity: not stated. 4. Number of conditions: not stated. 5. Type of condition: Main diagnostic groups were similar in both groups: cancer 10.7% intervention, 14.4% usual care; congestive heart failure 41.4% and 41.2%; chronic lung disease 7.0% and 4.1%; pneumonia 12.1% and 10.3%; gastrointestinal bleeding or gastrointestinal problems 20.0% and 16.5%; and diabetes or other endocrinological problems 28.6% and 26.8%.
Indirectness of population	Serious indirectness: older adult
Interventions	(n=97) Intervention 1: Standard care. Usual care consisted of services provided by physicians and nurses in another general medical unit in the same hospital but on a different floor. The staff of the usual care unit, including the

Study	Slaets 1997¹¹²⁶
	<p>attending physicians and resident physicians, were not involved in the care of the patient in the intervention unit. The data collected in the usual care unit for the study were kept hidden from the staff. Duration: unclear. Concurrent medication/care: note that due to financial restrictions the collection of data in the usual care unit was limited to 100 consecutive admissions. Three patients were admitted for day treatment, so 97 were included in the trial for the usual care group.</p> <p>(n=140) Intervention 2: Integrated care. Psychogeriatric intervention, consisting of multidisciplinary joint treatment by a psychogeriatric team. The intervention consisted of multidisciplinary joint treatment by geriatric team in addition to the usual care. The main purpose of the intervention was to obtain the optimal level of physical functioning in basic ADL functioning and mobility. To achieve that goal a team of experts was formed: a geriatrician, a specialised geriatric liaison nurse, and a physiotherapist. Furthermore, the staff-to-patient ration was increased by three nurses in the intervention unit. The geriatrician was the leader of the geriatric team. The main task of the team was assessment on admission, generating and implementing the treatment plans, and planning and management of discharge. Apart from meetings, the geriatrician spent about 2 hours per day in direct contact with the patients or their family. Together with the physiotherapist and the liaison nurse, he made an integrated assessment of every new admission. The physiotherapist was responsible for assessing the patient's level of daily functioning and mobility and implementing procedures with nursing staff for the prevention of increased disability and for rehabilitation therapy. The specific task of the liaison nurse was to communicate all the relevant information to all members of staff involved in treatment of the patient. He was also responsible for communication with the primary care health care system. Duration: unclear. Concurrent medication/care: the procedure was as follows: a weekly multidisciplinary meeting was held, attended by the geriatric team, the nurses, social worker, dietician, psychiatrist, and other occasionally invited consultants. The geriatrician was present at the weekly ward rounds with the attending physician and the two resident physicians. In addition, the geriatric team had their own ward rounds every week. The geriatric team, the nursing staff, and the resident physicians were considered to be crucial in making an integrated assessment and in the implementation of the geriatric treatment plans.</p>
Funding	Other (no mention of funding source)
<p>RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: INTEGRATED CARE versus STANDARD CARE</p> <p>Protocol outcome 1: Mortality - Actual outcome: Mortality - number of patients died in hospital at unclear; group 1: 18/140, group 2: 5/97; risk of bias: high; indirectness of outcome: serious indirectness</p>	

Study	Slaets 1997¹¹²⁶
Protocol outcome 2: Unscheduled care - Actual outcome: Hospital readmission within 6 months; group 1: 24/140, group 2:29/97; risk of bias: high; indirectness of outcome: serious indirectness	
Protocol outcomes not reported by the study	Health-related quality of life; functional outcomes (mobility, activities of daily living); patient and carer satisfaction; length of hospital stay; unscheduled care; continuity of care; admission to care facility; patient/carer treatment burden

Table 145: Sommers 2010

Study	Senior Care Connections trial: Sommers 2000¹¹³⁵
Study type	RCT (Cluster randomised; Parallel)
Number of studies (number of participants)	1 (n=543)
Countries and setting	Conducted in USA; Setting: Primary care
Line of therapy	Mixed line
Duration of study	Intervention + follow up: 24 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Under treatment for at least 2 chronic conditions (conditions not specified)
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Objective was to define a group of patients who were community dwelling but had difficulties in living independently: (1) Demographic factors: one or more visits with primary care physician, age 65 years or older, spoke English; (2) Functional status: independent in activities of daily living (walking, toileting, feeding), unable to carry out at least 1 instrumental activity of daily living; (3) Health status: under treatment for at least 2 chronic conditions (stable or unstable - if stable, having at least 1 health risk factor).
Exclusion criteria	Not terminally ill, not residing in a nursing home, not under therapy for metastatic disease, Alzheimer disease, or related dementias.
Recruitment/selection of patients	30 primary care physicians (PCP) from San Francisco Bay area were invited to participate, 18 with sufficient patients to recruit accepted. PCPs were randomised to intervention or control. Before randomisation, each physician met with coordinator and used criteria to select at least 35 patients from list of those having been seen in their office during past 2 months. After physician randomisation, all patients received a questionnaire. During 6-month study enrolment, as intervention patients came into the office for their appointments, the PCP determined whether they still met study

Study	Senior Care Connections trial: Sommers 2000 ¹¹³⁵
	criteria and, if so, described the SCC and introduced to nurse/social worker. To obtain an identifiable patient cohort, each PCP extended participation to patients not originally sent the first questionnaire but who were seen in the office during the enrolment period and met criteria. No new patients were added to the control arm.
Age, gender and ethnicity	Age - Mean (SD): 77.03 (6.608). Gender (M:F): Control: 33%/67%. Intervention: 30%/70%. Ethnicity: Control 80% white / Intervention 84% white
Further population details	1. Age: Mean (SD): 77.03 (6.608). 2. Deprivation: Not stated. 3. Ethnicity: white: intervention 84%, control 80%. 4. Number of conditions: cancer: intervention 13%, control 11%; respiratory disease: intervention 23%, control 17%; gastrointestinal tract disease: intervention 18%, control 17%; hypertension: intervention 48%, control 45%; heart disease: intervention 14%, control 18%; diabetes: intervention 15%, control 21%; stroke: intervention 12%, control 10%. 5. Type of condition: Not stated.
Indirectness of population	Serious indirectness: older adult
Interventions	<p>(n=383) Intervention 1: Case management. Senior Care Connections (SCC) intervention required collaboration among a primary care physician, nurse with geriatrics training, and a clinical social-worker. Home visit assessment followed by team discussion and development of a risk reduction plan and treatment targets. Throughout the intervention, the team met with trainers to learn team building skills and strategies for coaching patients in chronic disease self-management. The SCC intervention focused on a set of defined activities for each intervention patient. The nurse or social worker visited the patient in the home (noted health concerns, completed patient functional assessment, etc.). Using this data and the PCP knowledge, the team discussed the patients' health status and generated frailty and health risk scores. A risk reduction plan was discussed with the patient and his/her family to set target objectives and plan treatment by means of chronic disease self-management strategies. Nurse/social worker monitored the patient's health status between office visits through telephone calls, home visits or office/hospital visits at least once every 6 weeks. PCP/nurse/social worker met at least monthly to review patient's status and revise care plans.. Duration 24 months. Concurrent medication/care: All patients received a questionnaire. Patients were asked for demographic data and were queried about daily habits, use of support services, chronic conditions, and self-efficacy for health-related behaviours. Physical functioning was assessed and perceived health status measured. Checklists were used to assess nutritional habits, recent symptoms, and social activities, and a list of current medications was requested.</p> <p>(n=351) Intervention 2: Standard care. Controls received usual care from their primary care physician. Controls physicians did not re-review patients as they came in for office visits during enrolment period and no new patients were added. Duration 24 months. Concurrent medication/care: All patients received a questionnaire. Patients were asked for demographic data and were queried about daily habits, use of support services, chronic conditions, and self-efficacy for health-related behaviours. Physical functioning was assessed and perceived health status measured. Checklists were used to assess nutritional habits, recent symptoms, and social activities, and a list of current</p>

Study	Senior Care Connections trial: Sommers 2000 ¹¹³⁵
	medications was requested.
Funding	Other (Supported by a grant from the John A. Hartford Foundation, New York, NY (as part of their Generalist Physician Imitative Program), to the California Pacific Medical Centre, San Francisco, with support from Alta Bates Medical Centre, Berkeley, Calif, and Marin General Hospital, Corte Madera, Calif.)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: CASE MANAGEMENT versus STANDARD CARE	
Protocol outcome 1: Mortality - Actual outcome: Mortality at 24 months; Group 1: 24/280, Group 2: 26/263; Risk of bias: Very high; Indirectness of outcome: No indirectness	
Protocol outcome 2: Unscheduled care - Actual outcome: Unscheduled care - hospital admissions per year at 24 months; OR 0.63 (95%CI 0.41 to 0.96); Risk of bias: Very high; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Patient & carer satisfaction ; Length of hospital stay ; Continuity of care ; Admission to care facility ; Patient/carers treatment burden ; to be deleted

H.5.1.2 Models of care with a self-management component

Table 146: Behm 2014¹¹²

Study (subsidiary papers)	Behm 2014 ¹¹²
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=459)
Countries and setting	Conducted in Sweden; Setting: Community
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 2 years
Method of assessment of guideline condition	Inadequate method of assessment/diagnosis: 80 years or older
Stratum	Overall
Subgroup analysis within study	Not applicable

Study (subsidiary papers)	Behm 2014 ¹¹²
Inclusion criteria	Participants must live in their ordinary housing, not dependent on home help or care, independent of help from another person in ADL and without overt cognitive impairment
Exclusion criteria	None stated
Age, gender and ethnicity	Age - Range of means: 85-86. Gender (M:F): Define. Ethnicity:
Further population details	1. Age: >65 years 2. Deprivation: Not applicable / Not stated / Unclear 3. Ethnicity: Not applicable / Not stated / Unclear 4. Number of conditions: Not applicable / Not stated / Unclear 5. Type of condition: Not applicable / Not stated / Unclear
Indirectness of population	Serious indirectness
Interventions	<p>(n=174) Intervention 1: A combination of above. Single home visit made by either a nurse, physiotherapist, social worker or occupational therapist. Participant given verbal and written information on what the urban district provides in terms of meeting places, activities, physical training for seniors, help and support available from professional organisations and volunteers. Visitor also identified falls risks and advice given on how to prevent falls. Visit lasted between 1.5 and 2 hours.. Duration 24 months. Concurrent medication/care: Usual care Further details: 1. Post-CGA intervention: Not applicable / Not stated / Unclear</p> <p>(n=171) Intervention 2: A combination of above. Four weekly meetings, no more than six participants in each group, each lasting ~2hrs, focus on information about aging process and consequences and provision of tools/strategies for solving problems that can arise in the home environment. Follow-up home visit two to three weeks after group meetings completed. Group meetings were multi-professional and multi-dimensional, led either by occupational therapist, nurse, physiotherapist or social worker.. Duration 24 months. Concurrent medication/care: Usual care Further details: 1. Post-CGA intervention: Not applicable / Not stated / Unclear</p> <p>(n=114) Intervention 3: Standard care. Usual care, access to ordinary range of services in municipality (e.g. meals on wheels, help with ADLs). Duration 24 months. Concurrent medication/care: Usual care Further details: 1. Post-CGA intervention:</p>
Funding	Funding not stated
"	
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: INTERVENTION 1 (SINGLE HOME VISIT) versus STANDARD CARE	
Protocol outcome 1: Health-related quality of life	
- Actual outcome: Participants declining in self-rated health as per SF-36 at 24 months; OR 0.64 (95%CI 0.38 to 1.07); Risk of bias: High; Indirectness of outcome: No indirectness	

Study (subsidiary papers)	Behm 2014 ¹¹²
	<p>- Actual outcome: Participants declining in satisfaction with physical health at 24 months; OR 0.43 (95%CI 0.22 to 0.84); Risk of bias: High; Indirectness of outcome: No indirectness</p> <p>- Actual outcome: Participants declining in satisfaction with psychological health at 24 months; OR 0.30 (95%CI 0.16 to 0.56); Risk of bias: High; Indirectness of outcome: No indirectness</p> <p>RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: INTERVENTION 2 (GROUP MEETINGS) versus STANDARD CARE</p> <p>Protocol outcome 1: Health-related quality of life</p> <p>- Actual outcome: Participants declining in self-rated health as per SF-36 at 24 months; OR 0.95 (95%CI 0.57 to 1.57); Risk of bias: High; Indirectness of outcome: No indirectness</p> <p>- Actual outcome: Participants declining in satisfaction with physical health at 24 months; OR 0.28 (95%CI 0.14 to 0.59); Risk of bias: High; Indirectness of outcome: No indirectness</p> <p>- Actual outcome: Participants declining in satisfaction with psychological health at 24 months; OR 0.40 (95%CI 0.22 to 0.72); Risk of bias: High; Indirectness of outcome: No indirectness</p> <p>"</p>
Protocol outcomes not reported by the study	Mortality ; Functional outcomes (mobility, activities of daily living) ; Patient & carer satisfaction ; Length of hospital stay ; Unscheduled care ; Continuity of care ; Admission to care facility ; Patient/carer treatment burden ; to be deleted

Table 147: Boulton 2008^{168,169,179}

Study (subsidiary papers)	Guided Care trial: Boulton 2008 ¹⁶⁸ (Boulton 2011 ¹⁶⁹ , Boyd 2010 ¹⁷⁹ , Boulton 2013 ¹⁷⁰)
Study type	RCT (cluster randomised; parallel)
Number of studies (number of participants)	1 (n=904)
Countries and setting	Conducted in USA; setting: primary care, mid-Atlantic region of the United States. Primary care practices in 3 health care delivery systems in the Baltimore-Washington DC area.
Line of therapy	Adjunctive to current care
Duration of study	Intervention + follow up: paper states 12 month intervention. Participants followed-up at 6 months.
Method of assessment of guideline condition	Partially adequate method of assessment/diagnosis: mean number of self-reported conditions: intervention 4.3 (0-13) /control 4.3 (0-12). Conditions not specified.
Stratum	Overall

Study (subsidiary papers)	Guided Care trial: Boulton 2008 ¹⁶⁸ (Boulton 2011 ¹⁶⁹ , Boyd 2010 ¹⁷⁹ , Boulton 2013 ¹⁷⁰)
Subgroup analysis within study	Not applicable
Inclusion criteria	Patients 65 years old or older, require upper quartile of risk for using health services heavily during the coming year according to their scores on the hierarchical condition category predictive model, which is based on diagnoses on health insurance claims submitted during the previous year. Patients had to be covered by insurance.
Exclusion criteria	Patients who were interviewed in their home for eligibility were considered ineligible if they did not have a telephone, did not speak English, were planning extended travel during the following 2.5 years, or failed a brief cognitive screen and did not have a proxy.
Recruitment/selection of patients	Primary care practices were eligible if they cared for at least 400 patients who were 65 years old or older (N=8). Nurses were recruited for the GCN role. Patient recruitment was a multistage process. High risk patients (based on their hierarchical condition category predictive model score) received introductory letters, offering them the opportunity to 'opt-out'. Those that did not receive a telephone call were offered an in-home meeting. Professional interviewers visited the home of those who accepted to screen potential participants for eligibility.
Age, gender and ethnicity	Age - mean (range): intervention: 77.2 (66-106). Control: 78.1 (66-96). Gender (M:F): 409/495. Ethnicity: intervention: Caucasian 51.1%, African American 45.6%, other 3.3%. Control: Caucasian 48.9%, African American 46.3%, other, 4.8%.
Further population details	1. Age: 65 years old or older. 2. Deprivation: some money left over at the end of the month: intervention 57.9%, control 51.1%; just enough money left over at the end of the month: intervention 32.8%, control 34.2%; not enough money left over at the end of the month: intervention 9.3%, control 14.7%. 3. Ethnicity: white: intervention 51.5%, control 48.95; African American: intervention 45.6%, control 46.3%. 4. Number of conditions (mean, range): intervention 4.3 (0-13), control 4.3 (0-12). 5. Type of condition: not stated.
Indirectness of population	Serious indirectness: older adult
Interventions	<p>(n=419) Intervention 1: Standard care. Teams of 2-5 physicians and their at-risk older patients were randomised to guide care intervention. 'Guided Care' programme included home-based assessment, individual management plan, coaching for self-management with monthly monitoring and coordination of care provision. Duration 12 months. Concurrent medication/care: all baseline interviews were conducted face-to-face, and all follow-up interviews (6 months after each patient's start date) were conducted by telephone. Baseline interviews were carried out using computer-assisted interviewing technology. All primary care physicians were surveyed anonymously at baseline and approximately 1 year later. Each week of the intervention, GCNs received the names and contact information of additional consented patients. Each GCN scheduled and conducted in-home assessments of, on average, two patients per week until a case load of 50-60 patients was developed.</p> <p>(n=485) Intervention 2: Case management. Teams of 2-5 physicians and their at-risk older patients were randomised</p>

Study (subsidiary papers)	Guided Care trial: Boulton 2008 ¹⁶⁸ (Boulton 2011 ¹⁶⁹ , Boyd 2010 ¹⁷⁹ , Boulton 2013 ¹⁷⁰)
	to guide care intervention. Duration 12 months. Concurrent medication/care: all baseline interviews were conducted face-to-face, and all follow-up interviews (6 months after each patient's start date) were conducted by telephone. Baseline interviews were carried out using computer-assisted interviewing technology. All primary care physicians were surveyed anonymously at baseline and approximately 1 year later. Each week of the intervention, GCNs received the names and contact information of additional consented patients. Each GCN scheduled and conducted in-home assessments of, on average, two patients per week until a case load of 50-60 patients was developed.
Funding	Other (supported by John A. Hartford Foundation, the Agency for Healthcare Research and Quality, the National Institute on Aging, the Jacob and Valeria Langeloth Foundation, Kaiser-Permanente Mid-Atlantic, John Hopkins HealthCare, and the Roger C. Lipiz Centre for Integrated Health Care.)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: CASE MANAGEMENT versus STANDARD CARE

Protocol outcome 1: Health-related quality of life

- Actual outcome: SF-36 physical (Boulton 2013) at 32 months; Adjusted MD = -1.31 (95%CI -3.02, 0.41); Risk of bias: High; Indirectness of outcome: No indirectness
- Actual outcome: SF-36 mental (Boulton 2013) at 32 months; Adjusted MD = 1.05 (95%CI -1.08, 3.12); Risk of bias: High; Indirectness of outcome: No indirectness

Protocol outcome 2: Mortality

- Actual outcome: Mortality (Boulton 2008) at 6 months; Group 1: 28/485, Group 2: 24/419; Risk of bias: Very high; Indirectness of outcome: No indirectness
- Actual outcome: Mortality (Boulton 2013) at 32 months; OR 0.88 (95%CI 0.59 to 1.31); Risk of bias: High; Indirectness of outcome: No indirectness

Protocol outcome 3: Patient & carer satisfaction

- Actual outcome: 'Very satisfied' with regular health care (Boulton 2013) at 32 months; OR 1.50 (95%CI 0.77 to 2.82); Risk of bias: High; Indirectness of outcome: No indirectness
- Actual outcome: Patient assessment of chronic illness care (PACIC; Boulton 2013) at 32 months; Adjusted MD = 0.27 (95%CI 0.08, 0.45); Risk of bias: High; Indirectness of outcome: No indirectness

Protocol outcome 4: Unscheduled care

- Actual outcome: Unscheduled care - emergency department visits (Boulton 2011) at 6-8 months; OR 1.04 (95%CI 0.81 to 1.34); Risk of bias: Very high; Indirectness of outcome: No indirectness

Protocol outcome 5: Continuity of care

- Actual outcome: Primary care assessment survey integration subscale (management continuity; Boulton 2013) at 32 months; Adjusted MD 2.79 (95%CI -0.97 to 6.6); Risk of bias: High; Indirectness of outcome: No indirectness

Study (subsidiary papers)	Guided Care trial: Boulton 2008 ¹⁶⁸ (Boulton 2011 ¹⁶⁹ , Boyd 2010 ¹⁷⁹ , Boulton 2013 ¹⁷⁰)
- Actual outcome: Primary care assessment survey communication subscale (management continuity; Boulton 2013) at 32 months; Adjusted MD = -1.31 (95%CI -3.02, 0.41); Risk of bias: High; Indirectness of outcome: No indirectness - Actual outcome: Access to doctor's appointment 'same day' when sick (provider continuity; Boulton 2013) at 32 months; OR 1.20 (95%CI 0.65 to 2.29); Risk of bias: High; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Functional outcomes (mobility, activities of daily living); length of hospital stay; admission to care facility; patient/carer treatment burden

Table 148: Chow 2014²⁶³

Study	Chow 2014 ²⁶³
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=281)
Countries and setting	Conducted in Hong Kong (China); Setting: Recruited from 1700 bed, acute, general, regional hospital in Hong Kong
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 12 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Inclusion >65, majority had 2 or more chronic conditions
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	>65, admitted with a diagnosis related to chronic respiratory, cardiac, diabetic or renal disease
Exclusion criteria	MMSE <20, discharged to institutional care, unable to communicate, terminally ill
Recruitment/selection of patients	Eligible patients were recruited and consented from the ward
Age, gender and ethnicity	Age - Mean (range): 76.5 (60-95). Gender (M:F): 134:147. Ethnicity: Hong Kong
Further population details	1. Age: >65 years 2. Deprivation: Not applicable / Not stated / Unclear 3. Ethnicity: Asian >80% 4. Number of conditions: Not applicable / Not stated / Unclear 5. Type of condition: Not applicable / Not stated / Unclear
Indirectness of population	No indirectness

Study	Chow 2014 ²⁶³
Interventions	<p>(n=96) Intervention 1: Case management. A nurse case manager (NCM) carried out a pre-hospital discharge assessment using the Omaha system (involves problem classification, interventions and problem rating). Patients received weekly visits for 4 weeks after discharge. Patients were encouraged to make decisions and take action to monitor their condition. Interventions were tailor made for patients. NCM made a home visit in the first week, in the second week the NCM called the patients to monitor and support them, in the third week nursing students visited the patient and in the fourth week the NCM made a final telephone call to remind them about adhering to positive behaviours.. Duration 4 weeks. Concurrent medication/care: Usual care Further details: 1. Post-CGA intervention: Not applicable / Not stated / Unclear</p> <p>(n=108) Intervention 2: Case management. A nurse case manager (NCM) carried out a pre-hospital discharge assessment using the Omaha system (involves problem classification, interventions and problem rating). Patients received weekly visits for 4 weeks after discharge. Patients were encouraged to make decisions and take action to monitor their condition. Interventions were tailor made for patients. The NCM made a first telephone call based on the patient's needs identified at assessment, nursing students called the patient in the second and third week post-discharge. Patients were referred to the goals and interventions developed by the NCM during the assessment. In the fourth week the NCM made a final phone call.. Duration 4 weeks. Concurrent medication/care: Usual care Further details: 1. Post-CGA intervention: Not applicable / Not stated / Unclear</p> <p>(n=108) Intervention 3: Standard care. Placebo phone calls made twice in the 4 weeks, 5 minute calls only about social topics (for example, weather, television programmes, leisure activities). Duration 4 weeks. Concurrent medication/care: Usual care Further details: 1. Post-CGA intervention:</p>
Funding	Academic or government funding
<p>RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: VISIT CASE MANAGEMENT versus PHONE CASE MANAGEMENT</p> <p>Protocol outcome 1: Health-related quality of life - Actual outcome: SF-36 mental component at 12 weeks; Group 1: mean 55.5 (SD 6.5); n=87, Group 2: mean 54.8 (SD 11); n=96; Risk of bias: High; Indirectness of outcome: No indirectness - Actual outcome: SF-36 physical component at 12 weeks; Group 1: mean 42.4 (SD 7.4); n=87, Group 2: mean 42.6 (SD 7.6); n=96; Risk of bias: High; Indirectness of outcome: No indirectness</p> <p>RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: VISIT CASE MANAGEMENT versus STANDARD CARE</p>	

Study	Chow 2014 ²⁶³
<p>Protocol outcome 1: Health-related quality of life</p> <p>- Actual outcome: SF-36 physical component at 12 weeks; Group 1: mean 42.4 (SD 7.4); n=87, Group 2: mean 39.3 (SD 7.3); n=98; Risk of bias: High; Indirectness of outcome: No indirectness</p> <p>- Actual outcome: SF-36 mental component at 12 weeks; Group 1: mean 55.5 (SD 6.5); n=87, Group 2: mean 53.6 (SD 7.9); n=98; Risk of bias: High; Indirectness of outcome: No indirectness</p> <p>RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: PHONE CASE MANAGEMENT versus STANDARD CARE</p> <p>Protocol outcome 1: Health-related quality of life</p> <p>- Actual outcome: SF-36 physical component at 12 weeks; Group 1: mean 42.6 (SD 7.6); n=96, Group 2: mean 39.3 (SD 7.3); n=98; SF-36 0-100 Top=High is good outcome; Risk of bias: High; Indirectness of outcome: No indirectness</p> <p>- Actual outcome: SF-36 mental component at 12 weeks; Group 1: mean 54.8 (SD 11); n=96, Group 2: mean 53.6 (SD 7.9); n=98; Risk of bias: High; Indirectness of outcome: No indirectness</p>	
Protocol outcomes not reported by the study	Mortality ; Functional outcomes (mobility, activities of daily living) ; Patient & carer satisfaction ; Length of hospital stay ; Unscheduled care ; Continuity of care ; Admission to care facility ; Patient/carer treatment burden ; to be deleted

Table 149: Gitlin 2006^{168,169,179}

Study (subsidiary papers)	ABLE programme trial: Gitlin 2006 ⁴⁹¹ (Gitlin 2009 ⁴⁸⁹ , Gitlin 2006 ⁴⁹⁰)
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=319)
Countries and setting	Conducted in USA
Line of therapy	Mixed line
Duration of study	Intervention + follow up: Intervention: 12 months. Follow-up: 48 months.
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Mean number of health conditions: interventions, 7.1 / control, 6.7. 84% arthritis, 71% hypertension, 43% cataracts or macular degeneration, 39% cardiovascular problems, 23% diabetes mellitus.
Stratum	Overall

Study (subsidiary papers)	ABLE programme trial: Gitlin 2006⁴⁹¹ (Gitlin 2009⁴⁸⁹, Gitlin 2006⁴⁹⁰)
Subgroup analysis within study	Not applicable
Inclusion criteria	All participants were aged 70 or older, cognitively intact (Mini Mental State Examination (MMSE) score 423 on a scale ranging from 0 to 30) and English speaking, were not receiving home care, and reported the need for help or difficulties with two IADLs (instrumental activities of daily living) or one or more ADLs (activities of daily living)
Exclusion criteria	None specified
Recruitment/selection of patients	Participants were recruited from an area agency on aging, media announcements, and posters at senior housing and community settings
Age, gender and ethnicity	Age - Mean (SD): 79 (5.925). Gender (M:F): 58/261. Ethnicity: Intervention: white 53.1%, African American 45.0%, other 1.9%. Control: white 52.2%, African American 45.9%, other 1.9%.
Further population details	1. Age: aged 70 and older 2. Deprivation: Not stated. 3. Ethnicity: Not stated. 4. Number of conditions: 84% arthritis, 71% hypertension, 43% cataracts or macular degeneration, 39% cardiovascular problems, 235 diabetes mellitus. 5. Type of conditions: Not stated.
Indirectness of population	Serious indirectness: older adult
Interventions	<p>(n=159) Intervention 1: Standard care. Participants assigned to the no-treatment control group did not receive any intervention contact. At the conclusion of the 12-month follow-up interview, control participants were provided with educational materials on home safety and safe performance techniques. Duration 12 months. Concurrent medication/care: No more information provided.</p> <p>(n=160) Intervention 2: Self-management programmes - Self-management programmes. Multicomponent home intervention (the ABLE programme) delivered by occupational therapist (5 contacts, 4x face-to-face for 90 minutes and 1x 20 minute telephone contact) and physical therapist (90 minutes), aimed at reducing functional difficulties; over 6 months, followed by 6 month follow-up and 3 telephone contacts and final home visit. Due to considerable variability in home environments and functional difficulties, specific control-orientated strategies were individualised to the needs of participants, although the intervention was standardised in that each participant received 4 treatment components (education and problem-solving; home modification; energy conserving techniques; and balance, muscle strengthening, and fall-recovery techniques) for specific targeted functional areas. Duration 12 months. Concurrent medication/care: Intervention goal was to compensate for declining abilities by training in the use of control-enhancing strategies including cognitive (problem-solving, reframing), behavioural (pace self, sit instead of stand to perform tasks), and environmental (grab bars) modifications. Occupational therapists (OTs) initially met with participants and conducted a semi structured clinical interview to identify and prioritise problem areas. For each targeted area, an OT observed the participant's performance for safety, efficiency, and difficulty and presence of environmental barriers. In subsequent sessions, the OT engaged the participant in problem solving to identify</p>

Study (subsidiary papers)	ABLE programme trial: Gitlin 2006⁴⁹¹ (Gitlin 2009⁴⁸⁹, Gitlin 2006⁴⁹⁰)
	behavioural and environmental contributors to performance difficulties. Specific strategies were derived and equipment options provided. In the fourth session, the physical therapist (PT) provided balance and muscle strengthening and fall-recovery techniques. In the fifth session (telephone), the OT reinforced strategy use; and in the sixth session, the OT reviewed problem solving, refined strategy use, and provided education and resources to address future needs for environmental adjustments. Before the sixth contact, home modifications (grab bars, rails, raised toilet seats) were installed. Over the following 6 months, OTs conducted 3 telephone calls to reinforce the use of intervention-derived strategies and generalise these strategies to new problem areas. A final home visit was conducted to obtain closure. Interventionists were licensed therapists with 1 or more years of home care experience, having received 35 hours of training. Treatment intervention was monitored and maintained in supervision meetings held every other week in which cases were systematically presented. Interventionists also submitted taped treatment sessions for review
Funding	Academic or government funding (National Institute on Aging grant)
<p>RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: SELF-MANGEMENT versus STANDARD CARE</p> <p>Protocol outcome 1: Mortality</p> <ul style="list-style-type: none"> - Actual outcome: Mortality at 4 years from study entry; HR 0.76 (95%CI 0.48 to 1.2) Calculated – from logrank P-value; Risk of bias: Low; Indirectness of outcome: No indirectness - Actual outcome: Mortality at 2 years from study entry; HR 0.4 (95%CI 0.18 to 0.86) Calculated – from logrank P-value; Risk of bias: Low; Indirectness of outcome: No indirectness - Actual outcome: Mortality at 3 years from study entry; HR 0.74 (95%CI 0.44 to 1.24) Calculated – from logrank P-value; Risk of bias: Low; Indirectness of outcome: No indirectness <p>Protocol outcome 2: Functional outcomes (mobility, activities of daily living)</p> <ul style="list-style-type: none"> - Actual outcome: ADL (mean difficulty across 6 items: dressing above waist, dressing below waist, grooming, bathing/showering, toileting, feeding) at 6 months; Risk of bias: High; Indirectness of outcome: No indirectness - Actual outcome: Mobility (mean difficulty across 6 items: getting in/out of car, walking indoors, walking one block, climbing one flight of stairs, moving in/out chair, moving in/out of bed) at 6 months; Risk of bias: High; Indirectness of outcome: No indirectness - Actual outcome: IADL (mean difficulty across 6 items: light housework, shopping, preparing meals, managing money, telephone use, taking medications) at 6 months; Risk of bias: High; Indirectness of outcome: No indirectness <p>Protocol outcome 3: Patient self-efficacy</p> <ul style="list-style-type: none"> - Actual outcome: Functional self-efficacy (mean confidence in managing difficulties across 17 items: ADLs, IADLs and mobility) at 6 months; Risk of bias: High; 	

Study (subsidiary papers)	ABLE programme trial: Gitlin 2006⁴⁹¹ (Gitlin 2009⁴⁸⁹, Gitlin 2006⁴⁹⁰)
Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Health-related quality of life; Patient and carer satisfaction; Unplanned hospital admissions; Length of hospital stay; Continuity metrics; Patient/carers treatment burden

Table 150: Katon 2010^{168,169,179}

Study (subsidiary papers)	Katon 2010⁶⁷⁷ (Mcgregor 2011⁸³⁹, Ludman 2013⁷⁸⁹, Von korff 2011¹²⁶⁰)
Study type	RCT (patient randomised; parallel)
Number of studies (number of participants)	1 (n=214)
Countries and setting	Conducted in USA; setting: primary care
Line of therapy	Mixed line
Duration of study	Intervention time: 12 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: patients with diagnoses of diabetes, coronary heart disease, or both and coexisting depression
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Diagnoses of diabetes, coronary heart disease, or both according to the International Classification of Disease, 9 th Revision, or Current Procedural Terminology codes for coronary-artery interventions. Patients had one or more measures of poor disease control within the previous 12 months, including: blood pressure above 140/90 mm Hg (based on two blood-pressure readings as separate visits within 12 months), a low-density lipoprotein cholesterol level above 130 milligrams per deciliter, or a glycated hemoglobin level of 8.5% or higher. Patients were ambulatory, spoke English, and planned to be enrolled in a health-maintenance-organisation (HMO) plan for 12 months. PHQ-2 score 3 or higher and PHQ-9 score 10 or higher.
Exclusion criteria	Terminal illness, residence in a long-term care facility, severe hearing loss, planned bariatric surgery within 3 months, pregnancy or breast feeding, on-going psychiatric care, bipolar disorder or schizophrenia, use of antipsychotic or mood-stabiliser medication, and observed mental confusion suggesting dementia.
Recruitment/selection of patients	Patients and primary care physicians in 14 primary care clinics in the Group Health Cooperative in Washington State participated. Patients identified from electronic medical records. Eligible patients were assigned to a treatment group with the use of a permuted-block design, with randomly selected block sizes of 4, 6, and 8 patients.
Age, gender and ethnicity	Age - mean (SD): 56.84 (11.35). Gender (M:F): 108/112. Ethnicity: Non-white or Hispanic: intervention, 25%; control,

Study (subsidiary papers)	Katon 2010⁶⁷⁷ (Mcgregor 2011⁸³⁹, Ludman 2013⁷⁸⁹, Von korff 2011¹²⁶⁰)
	22%.
Further population details	1. Age: mean (SD): 56.84 (11.35). 2. Deprivation: part-time or full-time employment: intervention 53%, control 59%; retired: intervention 34%, control 26%; unemployed or disabled: intervention 10%, control 13%; homemaker: intervention 3%, control 2%. 3. Ethnicity: non-white or Hispanic: intervention 25%, control 22%. 4. Number of conditions: not stated. 5. Type of condition: poorly controlled diabetes, coronary heart disease, or both and co-existing depression.
Indirectness of population	Serious indirectness: older adult
Interventions	<p>(n=108) Intervention 1: Standard care. Controls received "enhanced usual care", that is, after randomisation, patients in the usual-care group received usual care and were advised to consult with their primary care physician to receive care for depression and for diabetes, coronary heart disease, or both. With patient's permission, primary care physicians were notified about depression and poor control of medical disease and received laboratory test results at baseline, 6 months, and 12 months. Duration 12 months. Concurrent medication/care: eligible patients received the Patient Health Questionnaire-2 (PHQ-2) depression screening by mail or telephone. Patients with a PHQ-2 score of 3 or more completed the PHQ-9 by telephone interview. In structured visits in each patient's primary care clinic every 2 to 3 weeks, nurses monitored the patient's progress.</p> <p>(n=106) Intervention 2: Collaborative care. Primary care-based, care-management intervention for multiple conditions. Intervention group involved a medically supervised nurse, working with each patient's primary care physician, providing guideline-based, collaborative care management, with the goal of controlling risk factors associated with multiple diseases. Duration 12 months. Concurrent medication/care: registered nurses with experience in diabetes education collaborated with primary care physicians to implement the 12-month intervention, aimed to manage depression and improved glycaemic, blood-pressure and lipid control by integrating a treat-to-target program for diabetes and coronary heart disease with collaborative care for depression. The intervention combined support for self-care with pharmacotherapy to control depression, hyperglycaemia, hypertension, and hyperlipidaemia. Using motivational and encouraging coaching, nurses helped patients solve problems and set goals for improved medication adherence and self-care. Eligible patients received the Patient Health Questionnaire-2 (PHQ-2) depression screening by mail or telephone. Patients with a PHQ-2 score of 3 or more completed the PHQ-9 by telephone interview. In structured visits in each patient's primary care clinic every 2 to 3 weeks, nurses monitored the patient's progress. Treatment protocols guided adjustments of commonly used medicines in patients who did not achieve specific goals. Once a patient achieved targeted levels, a maintenance plan was developed. Nurses then followed up patients with telephone calls every 4 weeks. Patients with disease control that worsened were offered follow-up visits or telephone calls and protocol-based intensification of treatment regimens. Nurses received weekly supervision, to review new cases and patient progress. Supervising physicians recommended initial choices and changes in medications tailored to the patient's history and clinical response. The nurse communicated recommended</p>

Study (subsidiary papers)	Katon 2010⁶⁷⁷ (Mcgregor 2011⁸³⁹, Ludman 2013⁷⁸⁹, Von korff 2011¹²⁶⁰)
	medication changes to the primary care physician responsible for medication management.
Funding	Other (supported by grants from the Services Division of the National Institute of Mental Health and by institutional support from Group Health Cooperative. Multiple other sources of support notes, included author support from Pfizer; author receiving payment for a manuscript from Prescott Medical, lecture fees from HealthSTAR Communications, travel fees from World Psychiatry Association, and a grant from John A. Hartford Foundation; author grant pending with Johnson & Johnson; etc.)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: COLLABORATIVE CARE versus STANDARD CARE	
<p>Protocol outcome 1: Health-related quality of life</p> <p>- Actual outcome: Health-related quality of life - quality of life score, over the previous month (Katon 2010) at 12 months; group 1: mean 6 (SD 2.2); n=106, risk of bias: very high; indirectness of outcome: no indirectness</p> <p>- Actual outcome: Health-related quality of life - global quality of life rating (Von Korff 2012) at 12 months; group 1: mean 6 (SD 2.2); n=92, group 2: mean 5.2 (SD 1.9); n=92; global quality of life rating 0-10 top=high is good outcome; risk of bias: very high; indirectness of outcome: no indirectness</p>	
<p>Protocol outcome 2: Mortality</p> <p>- Actual outcome: Mortality (Katon 2010) at 12 months; group 1: 1/106, group 2: 2/108; risk of bias: very high; indirectness of outcome: no indirectness</p>	
<p>Protocol outcome 3: Functional outcomes (mobility, activities of daily living)</p> <p>- Actual outcome: Functional outcomes - Sheehan social role disability scale (Von Korff 2012) at 12 months; group 1: mean 3.8 (SD 3); n=92, group 2: mean 4.5 (SD 2.9); n=92; Sheehan social role disability scale 0-10 top=high is poor outcome; risk of bias: very high; indirectness of outcome: no indirectness</p> <p>- Actual outcome: Functional outcomes - WHODAS-2 activities of daily living (Von Korff 2012) at 12 months; group 1: mean 12.9 (SD 10); n=92, group 2: mean 12.9 (SD 11.2); n=92; WHODAS-2 activities of daily living 0-4 top=high is poor outcome; risk of bias: very high; indirectness of outcome: no indirectness</p>	
<p>Protocol outcome 4: Patient & carer satisfaction (as assessed by the number of patients satisfied with care for diabetes, heart disease or both)</p> <p>- Actual outcome: Patient/Carer satisfaction - satisfaction with care of diabetes, heart disease, or both (Katon 2010) at 12 months; group 1: 79/92, group 2: 62/88; risk of bias: very high; indirectness of outcome: no indirectness</p>	
<p>Protocol outcome 5: Unscheduled care</p> <p>- Actual outcome: Unscheduled care - proportion hospitalised (had at least one hospitalisation) (Katon 2010) at 12 months; group 1: 27/106, group 2: 23/108; risk of bias: very high; indirectness of outcome: no indirectness</p>	
Protocol outcomes not reported by the study	Length of hospital stay; continuity of care; admission to care facility; patient/carers treatment burden

Table 151: Legrain 2011⁷⁵²

Study	Optimisation of Medication in AGEd (OMAGE) trial: Legrain 2011 ⁷⁵²
Study type	RCT (patient randomised; parallel)
Number of studies (number of participants)	1 (n=665)
Countries and setting	Conducted in France; setting: acute geriatric units of 5 university affiliated hospitals and 1 private clinic in Paris, France.
Line of therapy	Not applicable
Duration of study	Follow up (post intervention): 6 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Aged 70 or older admitted to participating acute geriatric unit
Exclusion criteria	Expected length of stay less than 5 days; poor chance of survival at 3 months (according to clinical judgement of the senior geriatrician in charge); receiving palliative care; previous participation in OMAGE study; inclusion in another therapeutic trial, not French speaking, impossible to follow up (for example lived in foreign country), absence of any health insurance (required by French law on clinical trials).
Recruitment/selection of patients	Admitted to participating acute geriatric unit
Age, gender and ethnicity	Age - mean (SD): 86.4 (6.3). Gender (M:F): 38:64. Ethnicity: not stated.
Further population details	1. Age: >65 years 2. Deprivation: not stated. 3. Ethnicity: not stated. 4. Number of conditions: Patients with 3 conditions (number of chronic diseases, mean (SD): 3.29 (1.64)). 5. Type of condition: physical multimorbidity only.
Extra comments	Living alone - intervention 47%, control 47.1%. Nursing home resident - intervention 18%, control 20%. Home help - intervention 67.5%, control 79.1%. Nurse at home - intervention 25.2%, control 20%. Help with planning medication - intervention 47.7%, control 52.7%. Help with taking medication - intervention 35.2%, control 39.6%.
Indirectness of population	Serious indirectness: older adult
Interventions	(n=317) Intervention 1: Case management. Case manager sets up care plan only. Comprehensive chronic treatment review: intervention-dedicated geriatrician performed an in-depth reconciliation of all medications (including over the counter medications) from all available sources; history of iatrogenic illness and adherence problems assessed; performed a standardised review of all chronic diagnoses for each participant to assess whether diagnoses were evidence based or needed further investigations; screened for major depression (4-item Geriatric Depression Scale); screened for protein energy malnutrition; chronic diseases and medications were investigated to identify suboptimal prescribing; on detecting suboptimal prescribing refinements were proposed; recommendations were made based

Study	Optimisation of Medication in AGEd (OMAGE) trial: Legrain 2011 ⁷⁵²
	<p>on: (1) opinion of usual prescriber on considered treatment changes (for example GP), (2) participant's health priorities, determined according to the corresponding education programme. (3) Education on self-management of disease: assessed participant's health priorities (preferences, values, treatment burden), (4) structured sessions - participant's health problems and the links between them, education on detecting drug related problems and managing these situations themselves or by mobilising resources (for example GP), drug management and self-follow-up criteria. Transition of care communication: healthcare professionals (for example GPs) were contacted after participant's admission as soon as changes in chronic treatment were considered to obtain agreement and discharge GPs received report. Duration: not stated. Concurrent medication/care: usual care.</p> <p>(n=348) Intervention 2: Standard care. Standard care from the acute geriatric unit; care includes a rehabilitation component in addition to acute care. Duration: not stated. Concurrent medication/care: none stated.</p>
Funding	Academic or government funding (French Ministry of Health)
<p>RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: CASE MANAGEMENT versus STANDARD CARE</p> <p>Protocol outcome 1: Mortality - Actual outcome: Mortality at 6 months; group 1: 56/317, group 2: 65/317; risk of bias: high; indirectness of outcome: no indirectness</p> <p>Protocol outcome 2: Unscheduled care - Actual outcome: Unscheduled care – emergency department visit at 6 months; group 1: 19/317, group 2: 22/348; risk of bias: high; indirectness of outcome: no indirectness - Actual outcome: Unscheduled care - readmission to acute geriatric unit at 6 months; group 1: 103/317, group 2: 133/348; risk of bias: high; indirectness of outcome: no indirectness</p>	
Protocol outcomes not reported by the study	Health-related quality of life; functional outcomes (mobility, activities of daily living); patient and carer satisfaction; length of hospital stay; continuity of care; admission to care facility; patient/carers treatment burden

H.5.2 Holistic assessment

H.5.2.1 Holistic assessment inpatient ward

Table 152: Applegate 1990

Study	Applegate 1990
Study type	RCT (randomised; parallel)
Number of studies (number of participants)	1 (n=155)
Countries and setting	Conducted in USA; setting: community rehabilitation hospital
Line of therapy	Adjunctive to current care
Duration of study	Intervention: 6-12 months.
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Mean age 78.8 years.
Stratum	CGA inpatient - ward
Subgroup analysis within study	Not applicable
Inclusion criteria	Functionally impaired elderly patients who were recovering from acute medical or surgical illnesses; and were considered at risk for nursing home placement, to have potentially reversible functional impairment, or both. In addition: age 65 or older, loss of independence in more than 1 activity of daily living, willingness to participate in a randomised study and give signed informed consent, and access to a primary physician willing to resume care of the patient at discharge. *a few patients under the age of 65 were considered if they met all criteria*
Exclusion criteria	Excluded if they had medical problems that were unstable or required continued short-term monitoring, if their survival was estimated to be less than 6 months, if they had serious chronic mental impairment, or if a nursing home placement was considered inevitable.
Recruitment/selection of patients	Patients were selected from all patients referred to the geriatric assessment unit of the Baptist Memorial Hospital by physicians or social-work personnel.
Age, gender and ethnicity	Age - mean (SD): Intervention: 79.4 (7.0). Control: 78.1 (7.6). Gender (M:F): Intervention: 79.5% female. Control: 74.0% female. Ethnicity: Intervention: 84.6% white. Control: 84.3% white.
Further population details	1. Age: age 65 years or older. 2. Deprivation: not stated. 3. Ethnicity: white: intervention 84.6%, control 84.3%. 4. Number of conditions: not stated. 5. Type of condition: not stated.
Indirectness of population	Serious indirectness: older adult
Interventions	(n=78) Intervention 1: CGA. The geriatric assessment unit was a 10-bed unit in a rehabilitation hospital that occupies a

Study	Applegate 1990
	<p>separate building within the hospital complex. Within the unit, emphasis was placed equally on interdisciplinary assessment of the problems of the patients and on rehabilitation. The objective was to improve health and functional status sufficiently that patients at risk of admission to care facility could avoid placement in nursing home. An interdisciplinary assessment of medical, social and physiological function was completed within 72 hours of admission by team physicians, rehabilitation nurses, physical therapists, occupational therapists, psychologists, social workers, nutritionists, and specialist in speech therapy and audiology. Particular attention was paid to problems common in frail, hospitalised older persons. After the assessments were completed, the team determined at the first of a series of weekly meetings whether a patient was a candidate for a specific treatment, rehabilitation, or both. If medical treatment was required, the patients was either treated in the unit or returned to the care of the referring physician. Any patient with a defect in vision, hearing or speech was referred to the appropriate therapist. If the patient needed rehabilitative care, a rehabilitation plan with specific goals was developed, and the patient's progress was re-evaluated weekly. When patients reached their rehabilitation goals or attained a stable level of function, they were discharged without any subsequent services from the geriatric-assessment-unit team.</p> <p>(n=77) Intervention 2: Standard care. Usual care. Duration 6 months. Neither the staff members of the geriatric assessment unit nor the investigators in the study were involved in the care of the patients in the control group after randomisation. The controls received usual care provided by their physicians. The patients in the control group received a wide range of services after discharge from the acute care hospital, including home care in and care in other rehabilitation units. Care would compare favourably with national norms.</p>
Funding	Other (Grant from the Robert Wood Johnson Foundation)
<p>RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: CGA versus STANDARD CARE</p> <p>Protocol outcome 1: Mortality - Actual outcome: Mortality, up to 6 months; group 1: 8/78, group 2: 16/77; risk of bias: low; Indirectness of outcome: No indirectness</p> <p>Protocol outcome 2: Mortality - Actual outcome: Mortality, end of follow-up; group 1: 16/78, group 2: 19/77; risk of bias: low; Indirectness of outcome: No indirectness</p> <p>Protocol outcome 3: Admission to care facility - Actual outcome: Admission to care facility, up to 6 months; group 1: 8/78, group 2: 14/77; risk of bias: low; Indirectness of outcome: No indirectness</p> <p>Protocol outcome 4: Admission to care facility</p>	

Study	Applegate 1990
	- Actual outcome: Admission to care facility, end of follow-up; group 1: 7/78, group 2: 15/77; risk of bias: low; Indirectness of outcome: No indirectness
	Protocol outcome 5: Functional outcome - Actual outcome: Activities of daily living (at 6 months); group 1: 1.1 (1.9)/78, group 2: 0.64 (2.3)/77; risk of bias: low; Indirectness of outcome: No indirectness
Protocol outcomes not reported by the study	Patient and carer satisfaction; length of hospital stay; unscheduled care; continuity of care; patient/carer treatment burden

Table 153: Asplund 2000

Study	Asplund 2000
Study type	RCT (randomised; parallel)
Number of studies (number of participants)	1 (n=413)
Countries and setting	Conducted in Sweden; setting: hospital
Line of therapy	Adjunctive to current care
Duration of study	Intervention and follow-up: 3 months.
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: ≥70 years.
Stratum	CGA inpatient - ward
Subgroup analysis within study	Not applicable
Inclusion criteria	Older patients with acute medical illness. Patients ages 70 years and over.
Exclusion criteria	Patients who required treatment in specialised units, such as the intensive care unit, coronary care unit, or acute stroke unit, or required treatment in 1 of the designated subspecialties, such as in a renal unit, were excluded.
Recruitment/selection of patients	Patients admitted acutely to the University Hospital for medical ailments during the study period were considered for inclusion in the study.
Age, gender and ethnicity	Age - mean (95% CL): Intervention: 80.9 (78.1 to 81.9). Control: 81.0 (80.3 to 81.8). Gender (M:F): 162/25. Ethnicity: not stated.
Further population details	1. Age: aged 70 years and older. 2. Deprivation: not stated. 3. Ethnicity: not stated. 4. Number of conditions: not stated 5. Type of condition: not stated.
Indirectness of population	Serious indirectness: older adult
Interventions	(n=190) Intervention 1: CGA. Duration 3 months. Acute geriatrics-based ward (AGW). The geriatric approach followed

Study	Asplund 2000
	<p>the principles outlined by the Nordic Working Group on Geriatric Assessment and Rehabilitation. Staffing of the ward was designed to optimise the conditions for treatment, nursing, early rehabilitation, and planning of care for older, acutely ill patients. The staff was recruited from geriatric, medical and surgical departments. The AGW had 11 beds and shared facilities with a surgical ward. There was a 1-week education period for the staff with emphasis on the principles of interdisciplinary and geriatric working forms and on ethical issues.</p> <p>(n=223) Intervention 2: Standard care. Usual care. Duration 3 months. General medical wards (MWs). The MWs (2) each had 30 beds. Both were mixed wards in which acutely ill patients from the local hospital catchment area constituted the majority of patients. Small stroke units, each caring for, on average, 6 to 8 patients, were in operation on both wards. In addition, 1 of the wards provided tertiary in-hospital care for patients with endocrine disorders and the other for patients with gastroenterological disorders.</p>
Funding	Other (study supported by the Vasterbotten County Council and by grants from Vardalstiftelsen and King Gustaf V's and Queen Victoria's Foundation)
<p>RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: CGA versus STANDARD CARE</p> <p>Protocol outcome 1: Mortality - Actual outcome: Mortality, up to 6 months; group 1: 21/190, group 2: 17/223; risk of bias: very high; blinding, incomplete outcome data; Indirectness of outcome: No indirectness</p> <p>Protocol outcome 2: Mortality - Actual outcome: Mortality, end of follow-up; group 1: 21/190, group 2: 12/226; risk of bias: very high; blinding, incomplete outcome data; Indirectness of outcome: No indirectness</p> <p>Protocol outcome 3: Admission to care facility - Actual outcome: Admission to care facility, up to 6 months; group 1: 48/169 group 2: 72/206; risk of bias: very high; blinding, incomplete outcome data; Indirectness of outcome: No indirectness</p> <p>Protocol outcome 4: Admission to care facility - Actual outcome: Admission to care facility, end of follow-up; group 1: 48/169 group 2: 72/206; risk of bias: very high; blinding, incomplete outcome data; Indirectness of outcome: No indirectness</p> <p>Protocol outcome 5: Length of stay</p>	

Study	Asplund 2000
- Actual outcome: Length of stay (at 3 months); group 1: 5.9 (5.7)/190, group 2: 7.3(5.7)/223; risk of bias: very high; blinding, incomplete outcome data; Indirectness of outcome: No indirectness	
Protocol outcome 6: Unscheduled care - Actual outcome: Readmissions (at 3 months); group 1: 61/182, group 2: 79/217; risk of bias: very high; blinding, incomplete outcome data; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Functional outcomes; patient and carer satisfaction; care; continuity of care; patient/carers treatment burden

Table 154: Cohen 2002

Study	Cohen 2002
Study type	RCT (randomised; parallel)
Number of studies (number of participants)	1 (n=1388)
Countries and setting	Conducted in USA; setting: hospital (and outpatient follow-up)
Line of therapy	Adjunctive to current care
Duration of study	Intervention and follow-up: 12 months.
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: ≥65 years.
Stratum	Overall
Subgroup analysis within study	CGA inpatient - ward
Inclusion criteria	An age of at least 65 years, hospitalised on a medical or surgical ward, an expected length of stay of at least 2 days, and a frail condition.
Exclusion criteria	Admitted from a nursing home, were already receiving care at an outpatient clinic for geriatric evaluation and management, had previously been hospitalised in an inpatient unit for geriatric evaluation and management, were currently enrolled in another clinical trial, had a severe disabling disease or terminal condition or severe dementia, did not speak English, lacked access to a telephone for follow-up, or were unwilling or unable to return for follow-up clinic visits.
Recruitment/selection of patients	Hospitalised at Veterans Affairs medical centres.
Age, gender and ethnicity	Age - mean: 74.2. Gender (M:F): 1355/33. Ethnicity: White, not Hispanic, n=1004; Black, not Hispanic, n=346; Other, n=38.

Study	Cohen 2002
Further population details	1. Age: aged 65 years of age or older. 2. Deprivation: not stated. 3. Ethnicity: white, not Hispanic: 72%; black, not Hispanic: 25%; other 3%. 4. Number of conditions: not stated. 5. Type of condition: not stated.
Indirectness of population	Serious indirectness: older adult
Interventions	<p>*Patients were randomly assigned to receive either usual care in an inpatient geriatric unit (GEMU) or usual inpatient care (UCIP), followed by either care at an outpatient geriatric clinic (GEMC) or usual outpatient care (UCOP):</p> <p>GEMU-UCOP: 348 GEMU-GEMC: 346 UCIP-UCOP: 348 UCIP-GEMC: 346</p> <p>Intervention 1: CGA. Duration 12 months. The inpatient and outpatients intervention teams, each consisting of a geriatrician, a social worker, and a nurse, followed their standard protocols for geriatric evaluation and management, with specific instructions to complete the history taking and physical examination, including screening for geriatric syndromes such as incontinence or falls; develop a list of problems; assess the patient's functional, cognitive, affective, and nutritional status; evaluate the caregiver's capabilities; and assess the patient's social situation. A plan of care was developed, and the team on the geriatric evaluation and management unit met at least twice a week to discuss the plan. Preventative and management services were coordinated to address the problems identified.</p> <p>Intervention 2: Standard care. Usual care. Duration 12 months. Patients assigned to receive usual care received all appropriate hospital services except for those provided by the team on the geriatric evaluation and management unit. Outpatients assigned to receive usual care were provided with at least 1 follow-up appointment in an appropriate clinic.</p>
Funding	Other (supported by the Department of Veterans Affairs Cooperative Studies Program)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: CGA versus STANDARD CARE

Protocol outcome 1: Health-related Quality of Life (SF-36)

- Actual outcome: Health-related quality of life, 12 months; GEMC/UCOP;

physical functioning, group 1: 6.8 (9.7)/692, group 2: 4.5 (7.2)/696; risk of bias: low; Indirectness of outcome: No indirectness;

physical limitations, group 1: 31.3 (24.1)/692, group 2: 32.5 (29.2)/696; risk of bias: low; Indirectness of outcome: No indirectness;

emotional limitations, group 1: 22.1 (9.2)/692, group 2: 20.2 (8.0)/696; risk of bias: low; Indirectness of outcome: No indirectness;

bodily pain, group 1: 21.9 (10.2)/692, group 2: 22.9 (9.6)/696; risk of bias: low; Indirectness of outcome: No indirectness;

Study	Cohen 2002
	<p>energy, group 1: 5.4 (3.6)/692, group 2: 1.0 (3.2)/696; risk of bias: low; Indirectness of outcome: No indirectness; mental health, group 1: 6.3 (5.7)/692, group 2: 0.8 (1.5)/696; risk of bias: low; Indirectness of outcome: No indirectness; social activity, group 1: 18.3 (16.0)/692, group 2: 16.4 (13.8)/696; risk of bias: low; Indirectness of outcome: No indirectness; general health, group 1: -4.4 (-5.5)/692, group 2: -8.2 (-7.1)/696; risk of bias: low; Indirectness of outcome: No indirectness.</p> <p>Protocol outcome 2: Mortality - Actual outcome: Mortality, up to 6 months; GEMC; group 1: 58/346, group 2: 52/346; risk of bias: low; Indirectness of outcome: No indirectness</p> <p>Protocol outcome 3: Mortality - Actual outcome: Mortality, up to 6 months; UCOP; group 1: 46/348, group 2: 46/348; risk of bias: low; Indirectness of outcome: No indirectness</p> <p>Protocol outcome 4: Mortality - Actual outcome: Mortality, end of follow-up; GEMC; group 1: 79/346, group 2: 73/346; risk of bias: low; Indirectness of outcome: No indirectness</p> <p>Protocol outcome 5: Mortality - Actual outcome: Mortality, end of follow-up; UCOP; group 1: 71/348, group 2: 74/348; risk of bias: low; Indirectness of outcome: No indirectness</p> <p>Protocol outcome 6: Admission to care facility - Actual outcome: Admission to care facility, end of follow-up; GEMC; group 1: 67/346, group 2: 88/346; risk of bias: low; Indirectness of outcome: No indirectness</p> <p>Protocol outcome 7: Admission to care facility - Actual outcome: Admission to care facility, end of follow-up; UCOP; group 1: 60/348, group 2: 89/348; risk of bias: low; Indirectness of outcome: No indirectness</p> <p>Protocol outcome 8: Length of stay - Actual outcome: Length of stay (at 12 months); GEMC; group 1: 23.8 (25.3)/346, group 2: 14.8 (23.3)/346; risk of bias: low; Indirectness of outcome: No indirectness</p> <p>Protocol outcome 9: Length of stay - Actual outcome: Length of stay (at 12 months); UCOP; group 1: 22.7 (27.9)/348, group 2: 15.2 (23.8)/348; risk of bias: low; Indirectness of outcome: No indirectness</p>
Protocol outcomes not reported by the study	Functional outcomes; patient and carer satisfaction; unscheduled care; continuity of care; patient/carers treatment burden

Table 155: Collard 1985

Study	Collard 1985
Study type	RCT (randomised; parallel)
Number of studies (number of participants)	1 (n=695)
Countries and setting	Conducted in USA; setting: community hospital
Line of therapy	Adjunctive to current care
Duration of study	Intervention and follow-up: 6 months.
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: ≥65 years.
Stratum	CGA inpatient - ward
Subgroup analysis within study	Not applicable
Inclusion criteria	At least 65 years old, to have a predicted length of stay of at least 48 hours, and to be in the care of a participating physician.
Exclusion criteria	None reported.
Recruitment/selection of patients	Two hospitals treating predominantly adult medical/surgical patients.
Age, gender and ethnicity	Age - mean: intervention 77.7; control: 77.4. Gender (M:F): 205/327. Ethnicity: not stated.
Further population details	1. Age: aged 65 years and over. 2. Deprivation: not stated. 3. Ethnicity: not stated. 4. Number of conditions: not stated. 5. Type of condition: not stated.
Indirectness of population	Serious indirectness: older adult
Interventions	(n=190) Intervention 1: CGA. Duration 6 months. Ten beds in existing space at each hospital were designated a Geriatric Special Care Unit (GSCU). Patients on the GSCU are cared for by registered nurses and nursing assistants selected from existing hospital staff and trained to participate in the project. Nursing care on the GSCU is delivered under a primary nursing model. The 2 GSCUs share a full-time social worker, and each has a medical director appointed from the hospital's medical staff. Within a short time of admission to the GSCU, a detailed assessment of each patient is performed by the primary nurse who coordinated the patient's hospital care. In cases of elective admissions, the patient is assessed at home. On the basis of the assessment, an individualised nursing care plan is developed for each patient. The care plan emphasises maximum patient independence. Patients are encouraged to perform as much as possible, their own activities of daily living, to wear their own clothing, to dine in communal area, and to participate in an exercise program. Discharge planning begins at admission. A projected length of stay, based on national diagnosis-related group norms, is identified and displayed on the front of the patient's record. All members of the patient care team (primary nurse, social worker, physicians, physical therapist, occupational therapist, medical director) attend interdisciplinary conferences twice a week as they work. Shortly after discharge,

Study	Collard 1985
	<p>the primary nurse calls the patient at home to see how well they are adjusting. Approximately 3 weeks after discharge, the primary nurse visits the patient at home to ascertain their progress and to identify problems that might have arisen since the patient left the hospital.</p> <p>(n=190) Intervention 2: Standard care. Usual care. Duration 6 months. Usual care patients received care on 1 of the traditional medical/surgical units.</p>
Funding	Other (grant from the John A. Hartford Foundation)
<p>RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: CGA versus STANDARD CARE</p> <p>Protocol outcome 1: Mortality - Actual outcome: Mortality, up to 6 months; group 1: 8/218, group 2: 39/477; risk of bias: low; Indirectness of outcome: No indirectness</p> <p>Protocol outcome 2: Mortality - Actual outcome: Mortality, end of follow-up; group 1: 8/218, group 2: 39/477; risk of bias: low ; Indirectness of outcome: No indirectness</p> <p>Protocol outcome 3: Admission to care facility - Actual outcome: Admission to care facility, up to 6 months; group 1: 47/218, group 2: 119/477; risk of bias: low; Indirectness of outcome: No indirectness</p> <p>Protocol outcome 4: Admission to care facility - Actual outcome: Admission to care facility, end of follow-up; group 1: 47/218, group 2: 119/477; risk of bias: low; Indirectness of outcome: No indirectness</p>	
Protocol outcomes not reported by the study	Functional outcome; patient and carer satisfaction; length of hospital stay; unscheduled care; continuity of care; patient/carers treatment burden

Table 156: Counsell 2000

Study	Counsell 2000
Study type	RCT (randomised; parallel)
Number of studies (number of participants)	1 (n=1531)
Countries and setting	Conducted in USA; setting: community teaching hospital

Study	Counsell 2000
Line of therapy	Adjunctive to current care
Duration of study	Intervention and follow-up: 12 months.
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: ≥70 years.
Stratum	CGA inpatient - ward
Subgroup analysis within study	Not applicable
Inclusion criteria	Community-dwelling persons aged 70 or older, admitted to a medicine or family practice service.
Exclusion criteria	Transferred from a nursing facility or another hospital, required speciality unit admission (for example, intensive care, coronary care, telemetry, or oncology), were admitted electively, had a length of stay less than 2 days, or had been previously enrolled in the study.
Recruitment/selection of patients	No information provided.
Age, gender and ethnicity	Age – mean (SD): intervention 80.0 (7); control: 79.0 (7). Gender (M:F): 605/926. Ethnicity: white, n=1348; black, n=183.
Further population details	1. Age: aged 70 or older. 2. Deprivation: less than 10,000: intervention 35%, control 33%; 10,000-19,999: intervention 35%, control 37%; more than 20,000: intervention 305, control 30%. 3. Ethnicity: not stated. 4. Number of conditions: not stated. 5. Type of condition: congestive heart failure: intervention 305, control 285; chronic lung disease; intervention 27%, control 21%; cerebrovascular disease: intervention 21%; control 22%; dementia: intervention 16%, control 18%; myocardial infarction: intervention 17%, control 17%; cancer: intervention 9%; control 7%.
Indirectness of population	Serious indirectness: older adult
Interventions	<p>(n=767) Intervention 1: CGA. Duration 12 months. Acute Care for Elders (ACE) intervention. Intervention implemented on a 34-bed unit that was renovated to provide the prepared environment of ACE. Daily interdisciplinary team rounds were conducted by the geriatrician medical director and a geriatric clinical nurse specialist. Suggestions by the interdisciplinary team were recorded and communicated to the attending physician. Nursing care plans for fall risk assessment, mobility, self-care, skin integrity, nutrition, continence, confusion, depression, and anxiety, which had been modified for the intervention from those used routinely on usual care units, were implemented when appropriate. Medications of potential risk to older patients were identified by the medical director, who recommended alternatives. Hospital records were reviewed. Process measures included use of the 9 nursing care plans aimed at preventing disability, time from admission to initiation of discharge planning, social work consultation, orders for bed rest, physical therapy consults, use of urinary catheters, and application of physical restraints.</p> <p>(n=764) Intervention 2: Standard care. Usual care. Duration 12 months. Usual care, no other information provided.</p>
Funding	Other (supported by a grant from the Summa Health System Foundation)

Study	Counsell 2000
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: CGA versus STANDARD CARE	
Protocol outcome 1: Mortality - Actual outcome: Mortality, up to 6 months; group 1: 173/767, group 2: 172/764; risk of bias: high; blinding; Indirectness of outcome: No indirectness	
Protocol outcome 2: Mortality - Actual outcome: Mortality, end of follow-up; group 1: 241/767, group 2: 223/764; risk of bias: high; blinding; Indirectness of outcome: No indirectness	
Protocol outcome 3: Admission to care facility - Actual outcome: Admission to care facility, up to 6 months; group 1: 58/767, group 2: 61/764; risk of bias: high; blinding; Indirectness of outcome: No indirectness	
Protocol outcome 4: Admission to care facility - Actual outcome: Admission to care facility, end of follow-up; group 1: 52/767, group 2: 56/764; risk of bias: high; blinding; Indirectness of outcome: No indirectness	
Protocol outcome 5: Unscheduled care - Actual outcome: Readmission, 12 months; group 1: 161/767, group 2: 138/764; risk of bias: high; blinding; Indirectness of outcome: No indirectness	
Protocol outcome 6: Patient & carer satisfaction - Actual outcome: Patient & carer satisfaction (caregiver), at discharge; group 1: 62 (9)/160, group 2: 59 (10)/173; risk of bias: high; blinding; Indirectness of outcome: No indirectness	
Protocol outcome 7: Patient & carer satisfaction - Actual outcome: Patient & carer satisfaction (patient), 1 month; group 1: 75 (16)/480, group 2: 72 (17)/478; risk of bias: high; blinding; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Functional outcome; length of hospital stay; continuity of care; patient/carer treatment burden

Table 157: Fretwell 1990

Study	Fretwell 1990
Study type	RCT (randomised; parallel)

Study	Fretwell 1990
Number of studies (number of participants)	1 (n=436)
Countries and setting	Conducted in USA; setting: teaching hospital
Line of therapy	Adjunctive to current care
Duration of study	Intervention and follow-up: 12 months.
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: ≥75 years.
Stratum	CGA inpatient - ward
Subgroup analysis within study	Not applicable
Inclusion criteria	Eligible if their physician had given consent for all of his or her patients to participate, if they were at least 75 years of age, were not on protocol treatment, and, on admission, did not require coronary or intensive care. Patients also become eligible when ready to transfer out of the intensive or coronary-care units.
Exclusion criteria	No information provided.
Recruitment/selection of patients	No information provided.
Age, gender and ethnicity	Age – mean (SD): intervention 83.5 (5.3); control: 83.0 (5.7). Gender (M:F): intervention: 71.5% female, control: 71.6% female. Ethnicity: intervention: 96.8% white, control: 100% white.
Further population details	1. Age: aged 75 years and over. 2. Deprivation: not stated. 3. Ethnicity: white: intervention 96.8%, control 100%. 4. Number of conditions: not stated. 5. Type of condition: not stated.
Indirectness of population	Serious indirectness: older adult
Interventions	(n=221) Intervention 1: CGA. Duration 12 months. The philosophy of the Senior Care Unit (SCU) was to integrate a psychosocial and functional orientation to care within the traditional model of patient management. Intervention patients admitted to the SCU, a regular 18-bed medical ward. Activities on the unit that distinguished it from the control unit include: (1) a functional assessment by nurses within their routine admission evaluations of older patients; (2) 4-month rotations of experienced nurses as coordinators of the geriatric assessment team; and (3) 3 clinical-team meetings and 1 administrative team meetings per week. Patients were evaluated by the geriatric assessment team, which included a physician specialising in geriatric medicine, the nurse coordinator, a physical therapist, a clinical pharmacist, a dietician, and a social worker. The screening functional assessment was administered by the patient's primary nurse and reviewed within 24 hours of admission by the nurse coordinator. During the next 48 hours, each patient was evaluated by all members of the team who, approximately 72 hours after randomisation, participated in an interdisciplinary team conference facilitated by the nurse coordinator. The team systematically reviewed medical diagnosis, medications, and problems in 6 areas of concern (nutrition, continence, cognition, emotion, mobility, and social support). Individualised care plan was developed. Consultation recommendations were then placed in each patients chart. Intervention patients were treated directly by all members

Study	Fretwell 1990
	<p>of the team except the geriatrician. Before the patient discharge, an updated care plan was prepared. The nurse coordinator provided telephone follow-up for a 2-month interval. Follow-up telephone calls were made weekly for 1 month and once 2 months after discharge. After each contact, a written summary of the follow-up status was sent to the attending physician, other team members, and staff nurses.</p> <p>(n=215) Intervention 2: Standard care. Usual care. Duration 12 months. Control patients were housed on traditional medical and surgical floors and received the standard medical care of the hospital. A small number of control patients had consultation assessments by geriatricians but they did not receive the organised team intervention or follow-up that was provided for the treatment patients.</p>
Funding	Other (supported in part by the National Institute of Aging, Geriatric Medicine Academic Award; the Robert Wood Johnson Foundation, “enhancing hospital care for the older patient”; and the National Centre for Health Services Research and Health Care Technology Assessment “post-doctoral health services research training program in gerontology and geriatrics” grant)
<p>RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: CGA versus STANDARD CARE</p> <p>Protocol outcome 1: Mortality - Actual outcome: Mortality, up to 6 months; group 1: 47/221, group 2: 38/215; risk of bias: high; blinding; Indirectness of outcome: No indirectness</p> <p>Protocol outcome 2: Mortality - Actual outcome: Mortality, end of follow-up; group 1: 57/221, group 2: 47/215; risk of bias: high; blinding; Indirectness of outcome: No indirectness</p> <p>Protocol outcome 3: Admission to care facility - Actual outcome: Admission to care facility, up to 6 months; group 1: 70/221, group 2: 85/215; risk of bias: high; blinding; Indirectness of outcome: No indirectness</p> <p>Protocol outcome 4: Admission to care facility - Actual outcome: Admission to care facility, end of follow-up; group 1: 70/221, group 2: 85/215; risk of bias: high; blinding; Indirectness of outcome: No indirectness</p> <p>Protocol outcome 5: Length of stay - Actual outcome: Length of stay, at discharge; group 1: 11.6 (12.2)/221, group 2: 12.8 (15.8)/215; risk of bias: high; blinding; Indirectness of outcome: No indirectness</p> <p>Protocol outcome 6: Carer treatment burden</p>	

Study	Fretwell 1990
	- Actual outcome: carers with self-reported poor health, at 3 months; adjusted OR 0.51 (0.29 to 0.90); risk of bias high; blinding; Indirectness of outcome: No indirectness
	- Actual outcome: carers with self-reported emotional health, at 3 months; adjusted OR 0.77 (0.49 to 1.21); risk of bias high; blinding; Indirectness of outcome: No indirectness
Protocol outcomes not reported by the study	Functional outcome; patient & carer satisfaction; unscheduled care (readmissions); continuity of care

Table 158: Harris 1991

Study	Harris 1991
Study type	RCT (randomised; parallel)
Number of studies (number of participants)	1 (n=267)
Countries and setting	Conducted in Australia; setting: emergency department
Line of therapy	Adjunctive to current care
Duration of study	Intervention and follow-up: 12 months.
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: ≥70 years.
Stratum	CGA inpatient - ward
Subgroup analysis within study	Not applicable
Inclusion criteria	1). 70 years of age and over; 2). were non-elective admissions; 3). were not re-admits (that is, they had no previous medical unit involvement in the 7 years before presentation; 4). lived in Southern Health Region of the Adelaide metropolitan area; 5). did not reside in a nursing home.
Exclusion criteria	No information provided.
Recruitment/selection of patients	Patients were referred to the Centre's Emergency Department. Study cases were identified each morning by reference to triage lists and the relevant medical notes were tagged.
Age, gender and ethnicity	Age – mean (SEM): intervention 79.1 (0.6); control: 77.9 (0.4). Gender (M:F%): intervention: 34/66%, control: 40/66%. Ethnicity: intervention: not stated.
Further population details	1. Age: 70 years and over. 2. Deprivation: not stated. 3. Ethnicity: not stated. 4. Number of conditions: not stated. 5. Type of condition: circulatory system: 49.5% (intervention), 46.5% (control); respiratory system: 10.3% (intervention), 17.1% control; digestive system: 5.2% (intervention), 3.5% (control).

Study	Harris 1991
Indirectness of population	Serious indirectness: older adult
Interventions	<p>(n=97) Intervention 1: CGA. Duration 12 months. The Geriatric Assessment Units (GAUs), 14-bed centre is 1 of 8 medical units, each of which practices general medicine together with a speciality interest. It has higher level of nursing staff and dedicated physiotherapy, occupational therapy, and social work time. All 8 medical units participate in a roster which involved each unit being responsible for all medical admissions through the Emergency Department for a 24-hour period. Each unit has access to allied health professionals and all units undertake discharge planning. The GAU has no long term nursing or rehabilitation beds under its direct control. On the day of discharge, a multidimensional questionnaire was administered by trained research assistants. Follow-up interviews with patients at their place of residence were arranged at 3, 6, 9, and 12 months after discharge.</p> <p>(n=170) Intervention 2: Standard care. Usual care. Duration 12 months. Usual care patients admitted to 1 of 2 general medical units (GMUs). No other information provided.</p>
Funding	Academic or government funding (the Department of Community Services and Health, Canberra).

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: CGA versus STANDARD CARE

Protocol outcome 1: Mortality

- Actual outcome: Mortality, up to 6 months; group 1: 15/97, group 2: 36/170; risk of bias: very high; allocation concealment, blinding; Indirectness of outcome: No indirectness

Protocol outcome 2: Mortality

- Actual outcome: Mortality, end of follow-up; group 1: 22/97, group 2: 49/170; risk of bias: very high; allocation concealment, blinding; Indirectness of outcome: No indirectness

Protocol outcome 3: Functional outcome

- Actual outcome: Activities of daily living, at 12 months; group 1: 11.5 (4.9)/97, group 2: 11 (5.2)/170; risk of bias: very high; allocation concealment, blinding; Indirectness of outcome: No indirectness

Protocol outcome 4: Length of stay

- Actual outcome: Length of stay, at discharge; group 1: 10.9 (7.9)/97, group 2: 9.8 (7.8)/170; risk of bias: very high; allocation concealment, blinding; Indirectness of outcome: No indirectness

Study	Harris 1991
Protocol outcomes not reported by the study	Patient & carer satisfaction; unscheduled care (readmissions); continuity of care; admission to care facility; patient/carer treatment burden

Table 159: Harvey 2014

Study	Residential Care Intervention Program in the Elderly (RECIPE) trial: Harvey 2014 ⁵⁵¹
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=116)
Countries and setting	Conducted in Australia
Line of therapy	Adjunctive to current care
Duration of study	Intervention time: 6 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Aged 65 years and older
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Patients aged 65 years or older admitted to hospital from residential care facilities in outer Melbourne, Australia
Exclusion criteria	Less than 65 years of age, were not living permanently in residential care facilities, had already been enrolled, had non-medical primary diagnoses, were expected to die during their index admission, lived outside the health service catchment area, exhibited severe behavioural disturbance, or consent was not obtained for study participation
Recruitment/selection of patients	Patients were recruited during their acute hospital stay
Age, gender and ethnicity	Age - Mean (SD): intervention: 83.8 (7), control: 86.7 (7). Gender (M:F): 43/73. Ethnicity: Australian born - intervention: 34 (60%), control: 38 (64%).
Further population details	1. Age: aged 65 years or older 2. Deprivation: Not stated. 3. Ethnicity: Australian born: intervention 60%, control 64%. 4. Number of conditions: intervention: 7.7 (SD 2.7), control: 5.7 (SD 2.5) 5. Type of condition: severe dementia: intervention 47%, control 50%; heart failure: 12%, control 7%; COPD: intervention 4%, control 2%.
Indirectness of population	Serious indirectness: older adult
Interventions	(n=57) Intervention 1: CGA - CGA (team). Geriatrician-led outreach service. Patients were recruited during their acute hospital stay and followed up at the residential care facility (RCF) for 6 months. The intervention group received a post-discharge home visit within 96 hours, at which a comprehensive geriatric assessment was performed and a care

Study	Residential Care Intervention Program in the Elderly (RECIPE) trial: Harvey 2014⁵⁵¹
	<p>plan developed. Patients and their families were also offered further meetings to discuss Advanced Care Planning and document Advanced Directives.. Duration 6 months. Concurrent medication/care: The RECIPE team comprised 2 part-time geriatricians and an aged care nurse consultant. All intervention group patients were reviewed in the RCF within 4 days of discharge. At the first visit, a comprehensive assessment and a tailored care plan was developed. Appropriate services were provided and patients were offered further visits for review of intercurrent illness if required. The service also provided education and support to RCF staff and the patients' primary care physician. Further details: 1. Post-CGA intervention: CGA + short-term care plan</p> <p>(n=59) Intervention 2: Standard care. The usual care group was managed by the treating medical unit according to standard hospital protocols and received standard discharge planning, with follow-up at the residential care facility by their primary care physician service. Duration 6 months. Concurrent medication/care: No other information provided Further details: 1. Post-CGA intervention: Not applicable / Not stated / Unclear</p>
Funding	Academic or government funding (Department of Health (Victoria), Australia through the Northern Alliance Hospital Admission Risk Program)
<p>RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: CGA (TEAM) versus STANDARD CARE</p> <p>Protocol outcome 1: Mortality - Actual outcome: Mortality at 6 months; Group 1: 22/57, Group 2: 22/59; Risk of bias: High; Indirectness of outcome: No indirectness</p> <p>Protocol outcome 2: Patient & carer satisfaction - Actual outcome: Patient & carer satisfaction - family/resident satisfaction at 6 months; Group 1: 19/20, Group 2: 14/24; Risk of bias: High; Indirectness of outcome: No indirectness</p> <p>Protocol outcome 3: Unscheduled care - Actual outcome: Unscheduled care - emergency department presentations at 6 months; Group 1: 19/57, Group 2: 28/59; Risk of bias: High; Indirectness of outcome: No indirectness - Actual outcome: Unscheduled care - readmission rate at 6 months; Group 1: 22/57, Group 2: 20/59; Risk of bias: High; Indirectness of outcome: No indirectness</p>	
Protocol outcomes not reported by the study	Health-related quality of life; Functional outcomes (mobility, activities of daily living) ; Length of hospital stay ; Continuity of care ; Admission to care facility ; Patient/carers treatment burden ; to be deleted

Table 160: Kay 1992

Study	Kay 1992
Study type	RCT (randomised; parallel)
Number of studies (number of participants)	1 (n=59)
Countries and setting	Conducted in Canada; setting: acute care community hospital
Line of therapy	Adjunctive to current care
Duration of study	Intervention and follow-up: unclear – follow-up measures taken at time of discharge or 4 weeks after baseline measures, whichever came first.
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: ≥70years.
Stratum	CGA inpatient - ward
Subgroup analysis within study	Not applicable
Inclusion criteria	Over the age of 70; medically stable; possible acute confusion but not known chronic confusion; some form of functional impairment with rehabilitation potential (for example, incontinence); multiple geriatric problems (for example, medical, social, emotional).
Exclusion criteria	None reported.
Recruitment/selection of patients	Elderly patients in the hospital were recruited for the study and randomly assigned.
Age, gender and ethnicity	Age – mean: intervention 81.4; control: 81.9. Gender (M:F): 26/33. Ethnicity: not stated.
Further population details	1. Age: over age 70. 2. Deprivation: not stated. 3. Ethnicity: not stated. 4. Number of conditions: intervention, 2.8 (0-5); control, 2.5 (1-6). 5. Type of condition: not stated.
Indirectness of population	Serious indirectness: older adult
Interventions	<p>(n=30) Intervention 1: CGA. Duration: unclear. The Geriatric Assessment Unit (GAU) committee designed a multidisciplinary assessment tool to collect the patient data required to develop the plan of care. The primary nurse was responsible, in collaboration with the multidisciplinary team, for decisions regarding care and care-planning and was accountable for the outcomes of that plan. Weekly team meetings, to evaluate client progress towards set goals and to formulate discharge plans, were facilitated by the primary nurse. Assessments of physical, cognitive and ADL functioning, as well as monitoring of medications, morale and discharge positions. All patients referred to the GAU were assessed by the consulting physician to the GAU project.</p> <p>(n=29) Intervention 2: Standard care. Usual care. Duration: unclear. Those assigned to the control group were evaluated according to the research instrument; however, they did not move to the GAU and their care remained the same.</p>

Study	Kay 1992
Funding	Funding not stated.
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: CGA versus STANDARD CARE	
Protocol outcome 1: Mortality - Actual outcome: Mortality, up to 6 months; group 1: 2/30, group 2: 0/29; risk of bias: high; blinding; Indirectness of outcome: No indirectness	
Protocol outcome 2: Mortality - Actual outcome: Mortality, end of follow-up; group 1: 8/30, group 2: 8/29; risk of bias: high; blinding; Indirectness of outcome: No indirectness	
Protocol outcome 3: Admission of care facility - Actual outcome: Admission to care facility, up to 6 months; group 1: 12/30, group 2: 12/29; risk of bias: high; blinding; Indirectness of outcome: No indirectness	
Protocol outcome 4: Admission of care facility - Actual outcome: Admission to care facility, end of follow-up; group 1: 12/30, group 2: 12/29; risk of bias: high; blinding; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Functional outcome, patient & carer satisfaction; length of hospital stay, unscheduled care (readmissions); continuity of care; patient/carers treatment burden

Table 161: Landefeld 1995

Study	Landefeld 1995
Study type	RCT (randomised; parallel)
Number of studies (number of participants)	1 (n=651)
Countries and setting	Conducted in USA; setting: teaching hospital
Line of therapy	Adjunctive to current care
Duration of study	Intervention and follow-up: unclear (discharge from hospital).
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: ≥70years.
Stratum	CGA inpatient - ward
Subgroup analysis within study	Not applicable

Study	Landefeld 1995
Inclusion criteria	Aged 70 years or older, admitted for general medical care.
Exclusion criteria	Patients who were admitted to a speciality unit (for example, intensive care, cardiology-telemetry, or oncology) were ineligible.
Recruitment/selection of patients	No information.
Age, gender and ethnicity	Age – mean (SD): intervention 80.2 (6.9); control: 80.1 (6.6). Gender (M:F): 216/435. Ethnicity: intervention: white 59%, black 41%; control: white 60%, black 40%.
Further population details	1. Age: 70 years of age or older. 2. Deprivation: not stated. 3. Ethnicity: white: 59% intervention, 60% control; black: 41% intervention, 40% control. 4. Number of conditions: Charlson comorbidity score: intervention 2.3 (2.3), control 2.3 (2.2). 5. Type of condition: congestive heart failure: intervention 26%, control 23%; cancer: intervention 23%, control 21%; chronic lung disease: intervention 22%, control 20%; myocardial infarction: intervention 17%, control 21%; cerebrovascular disease: intervention 12%, control 18%; dementia: intervention 10%, control 13%.
Indirectness of population	Serious indirectness: older adult
Interventions	<p>(n=327) Intervention 1: CGA. Duration: unclear, at discharge. Special unit designed to help older persons maintain or achieve independence in self-care activities. In both the intervention and usual care units, each patient was assigned a primary nurse, 2 resident physicians, and an attending physician. The intervention and usual care units had the same hospital-supported staff-to-patient ratios and used the same hospital-wide support services (for example, social work, physical therapy, and nutrition). Under the leadership of the medical and nursing directors, the primary nurse assigned to each patient in the intervention group was responsible for assessing the patient’s specific needs daily and implementing protocols for the prevention of disability and for rehabilitation.</p> <p>(n=324) Intervention 2: Standard care. Usual care. Duration: unclear, at discharge. Usual care consisted of services provided by physicians and nurses in other acute care medical units. The staff of the intervention unit was not involved in the care of the patients receiving usual care, and none of the 4 elements of the program were implemented in usual care units.</p>
Funding	Other (John A. Hartford Foundation and the National Institute of Aging).
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: CGA versus STANDARD CARE	
Protocol outcome 1: Mortality - Actual outcome: Mortality, up to 6 months; group 1: 24/327, group 2: 24/324; risk of bias: low; Indirectness of outcome: No indirectness	

Study	Landefeld 1995
Protocol outcome 2: Mortality	- Actual outcome: Mortality, end of follow-up; group 1: 42/327, group 2: 40/324; risk of bias: low; Indirectness of outcome: No indirectness
Protocol outcome 3: Admission of care facility	- Actual outcome: Admission to care facility, up to 6 months; group 1: 43/327, group 2: 67/327; low; Indirectness of outcome: No indirectness
Protocol outcome 4: Admission of care facility	- Actual outcome: Admission to care facility, end of follow-up; group 1: 67/327, group 2: 90/324; low; Indirectness of outcome: No indirectness
Protocol outcome 5: Unscheduled care	- Actual outcome: Readmissions, unclear, discharge from hospital; group 1: 104/327, group 2: 109/324; low; Indirectness of outcome: No indirectness
Protocol outcome 6: Length of stay	- Actual outcome: Length of stay, unclear, discharge from hospital; group 1: 11.6, group 2: 12.8; risk of bias: low; Indirectness of outcome: No indirectness
Protocol outcome 7: Functional outcomes	- Actual outcome: Participants improving in ADL, unclear, discharge from hospital; group 1: 111/326, group 2: 78/324; risk of bias: low; Indirectness of outcome: No indirectness
Protocol outcome 7: Functional outcomes	- Actual outcome: Participants worsening in ADL, unclear, discharge from hospital; group 1: 52/326, group 2: 68/324; risk of bias: low; Indirectness of outcome: No indirectness
Protocol outcomes not reported by the study	Patient & carer satisfaction; continuity of care; patient/carers treatment burden

Table 162: Nikolaus 1999⁹⁰⁶

Study	GEM-HIT trial: Nikolaus 1999 ⁹⁰⁶
Study type	RCT (patient randomised; parallel)
Number of studies (number of participants)	(n=545)

Study	GEM-HIT trial: Nikolaus 1999 ⁹⁰⁶
Countries and setting	Conducted in Germany
Line of therapy	Adjunctive to current care
Duration of study	Intervention + follow up 12 months
Method of assessment of guideline condition	Unclear method of assessment/diagnosis: elderly population >65 years
Stratum	CGA inpatient - ward
Subgroup analysis within study	Not applicable
Inclusion criteria	Elderly people who lived at home before admission to hospital, had multiple chronic conditions or functional deterioration after convalescence or were at risk for a nursing home placement
Exclusion criteria	Patients with a terminal illness or severe dementia, patients who lived too far away (>15 km) for the home intervention team to make visits
Recruitment/selection of patients	Elderly patients with acute disease admitted to the geriatric centre in the participating hospital
Age, gender and ethnicity	Age - other: mean = 81.4 years. Gender (M:F): 145/400. Ethnicity: not reported.
Further population details	1. Age: >65 years (> 65 years). 2. Deprivation: not stated. 3. Ethnicity: not stated. 4. Number of conditions: not stated. 5. Type of condition: not stated.
Indirectness of population	Serious indirectness: older adult
Interventions	<p>(n=179) Intervention 1: Care plan. Comprehensive Geriatric Assessment (CGA) and additional in-hospital and post-discharge follow-up treatment by an interdisciplinary home intervention team. The CGA was carried out once patients were in a stable medical condition. Duration Assessment at discharge. Concurrent medication/care: usual care</p> <p>(n=181) Intervention 2: Care plan. Comprehensive Geriatric Assessment (CGA) and additional in-hospital and post-discharge follow-up treatment by an interdisciplinary home intervention team. The CGA was carried out once patients were in a stable medical condition. The home intervention team consisted of 3 nurses, a physiotherapist, an occupational therapist, a social worker and a secretary. The team worked closely with hospital staff and the primary care physician. While the patient was in hospital the team gave them additional treatment (such as additional training in washing, eating dressing, and/or walking). One home visit was carried out during the hospital stay to evaluate the patient's home (for example safety hazards) and to prescribe technical aids when necessary. After discharge, the team provided treatment (such as physiotherapy/occupational therapy), which home services could not or could not immediately provide for as long as necessary (twice a week, up to twice a day, for a minimum of 30 minutes). At least 1 visit was made to check whether recommendations were being implemented, home care continued and technical aids used, and to identify any new problems. Duration: mean = 7.6 days (range = 1 – 41 days). Concurrent medication/care: usual care.</p>

Study	GEM-HIT trial: Nikolaus 1999⁹⁰⁶
	(n=185) Intervention 3: Standard care. Assessment of activities of daily living and cognition, followed by usual care at home. Duration Assessment at discharge. Concurrent medication/care: usual care.
Funding	Academic or government funding (funded by Sozialministerium Baden-Wuttemberg)
<p>RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: CGA ASSESSMENT versus USUAL CARE</p> <p>Protocol outcome 1: Mortality – plus ESD - Actual outcome: Mortality, end of follow-up; group 1: 33/181, group 2: 16/92; risk of bias: low; Indirectness of outcome: No indirectness</p> <p>Protocol outcome 2: Mortality - WARD - Actual outcome: Mortality, end of follow-up; group 1: 30/179, group 2: 16/93; risk of bias: low; Indirectness of outcome: No indirectness</p> <p>Protocol outcome 3: Admission of care facility – plus ESD - Actual outcome: Admission to care facility, end of follow-up; group 1: 30/181, group 2: 21/92; risk of bias: low; Indirectness of outcome: No indirectness</p> <p>Protocol outcome 4: Admission of care facility - WARD - Actual outcome: Admission to care facility, end of follow-up; group 1: 35/179, group 2: 21/93; risk of bias: low; Indirectness of outcome: No indirectness</p> <p>Protocol outcome 5: Functional outcome – plus ESD - Actual outcome: Activities of daily living; group 1: 91.8 (14.4)/181, group 2: 91.1 (15.9)/92; risk of bias: low; Indirectness of outcome: No indirectness</p> <p>Protocol outcome 6: Functional outcome – WARD - Actual outcome: Activities of daily living; group 1: 92.6 (14.3)/179, group 2: 91.1 (15.9)/93; risk of bias: low; Indirectness of outcome: No indirectness</p> <p>Protocol outcome 7: Length of stay – plus ESD - Actual outcome: Length of stay; group 1: 33.5 (21.5)/181, group 2: 42.7 (20.4)/93; risk of bias: low; Indirectness of outcome: No indirectness</p> <p>Protocol outcome 8: Length of stay – WARD - Actual outcome: Length of stay; group 1: 40.7 (24.1)/179, group 2: 42.7 (20.4)/92; risk of bias: low; Indirectness of outcome: No indirectness</p>	

Study	GEM-HIT trial: Nikolaus 1999 ⁹⁰⁶
Protocol outcome 9: Unscheduled care - Actual outcome: Readmission; group 1: 64/179, group 2: 33/93; risk of bias: low; Indirectness of outcome: No indirectness	
Protocol outcome 10: Unscheduled care - Actual outcome: Readmission; group 1: 59/181, group 2: 32/92; risk of bias: low; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Patient and carer satisfaction; continuity of care; patient/carer treatment burden

Table 163: Rubenstein 1984

Study	Rubenstein 1984
Study type	RCT (randomised; parallel)
Number of studies (number of participants)	1 (n=123)
Countries and setting	Conducted in USA; setting: Veterans Administered Medical Centre.
Line of therapy	Adjunctive to current care
Duration of study	Intervention and follow-up: 24 months.
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: ≥65 years.
Stratum	CGA inpatient - ward
Subgroup analysis within study	Not applicable
Inclusion criteria	To be included, a patient was required to be at least 65 years of age and have a persistent medical, functional, or psychosocial problem that interfered with his or her discharge home.
Exclusion criteria	The following groups of patients were excluded: those with well-diagnosed severe dementia or another disabling disease (for example, multiple sclerosis or end-stage cirrhosis) resistant to further medical management who could perform no more than 3 activities of daily living, and who had no social support system that might be capable of preventing a nursing-home placement, those in the terminal phases of severe medical disorders (for example, malignant conditions or end-stage heart failure resistant to medical management), and those on the verge of discharge who were functioning well and would definitely return to the community without the need of support services or extended care.
Recruitment/selection of patients	The names of all patients aged 65 years or over who were admitted to the acute-care services of the Sepulveda Veterans Administration Medical Centre were recorded daily and screened for eligibility. Eligible patients were

Study	Rubenstein 1984
	approached on the acute-care ward, after stabilisation of their acute problems, to ascertain their interest in participating in the study.
Age, gender and ethnicity	Age – mean (SEM): intervention 78.8 (0.95); control: 77.1 (1.11). Gender (M:F%): intervention, 95.2% male; control, 96.7% male. Ethnicity: intervention, 93.7% white; control, 96.7% white.
Further population details	1. Age: over 65 years old. 2. Deprivation: not stated. 3. Ethnicity: white: intervention 93.7%, control 96.7%. 4. Number of conditions: intervention 4.48 (0.27), control 4.45 (0.26). 5. Type of condition: not stated.
Indirectness of population	Serious indirectness: older adult)
Interventions	<p>(n=63) Intervention 1: CGA. Duration: 24 months. Innovative geriatric evaluation unit intended to provide diagnostic assessment, therapy, rehabilitation and placement. Patients assigned to the geriatric evaluation unit were admitted there as soon as possible after assignment, usually within 48 hours. The acute-care services at the hospital consist of 3 acute-care mixed medical wards, 2 intensive-care units, a coronary-care unit, 2 medical-speciality wards, and 5 surgical wards. Consultative and other hospital services available to patients in the control group were identical to services on the unit. Patients discharged from the unit usually received follow-up care in the geriatric medical outpatient clinic.</p> <p>(n=60) Intervention 2: Standard care. Usual care. Duration: 24 months. Those assigned to the control group followed a natural course through the acute-care services of the hospital and were discharged to their homes or placed in long-term care facilities in the usual manner by acute-service personnel. Patients discharged from the unit usually received follow-up care in the geriatric medical outpatient clinic, whereas control patients were eligible to use all other outpatient services.</p>
Funding	Other (supported by the Health Services Research and Development Service of the Veterans Administration).
<p>RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: CGA versus STANDARD CARE</p> <p>Protocol outcome 1: Mortality - Actual outcome: Mortality, up to 6 months; group 1: 9/63, group 2: 9/60; risk of bias: high; blinding; Indirectness of outcome: No indirectness</p> <p>Protocol outcome 2: Mortality - Actual outcome: Mortality, end of follow-up; group 1: 15/63, group 2: 29/60; risk of bias: high; blinding; Indirectness of outcome: No indirectness</p> <p>Protocol outcome 3: Admission of care facility</p>	

Study	Rubenstein 1984
	- Actual outcome: Admission to care facility, up to 6 months; group 1: 8/63, group 2: 19/60; risk of bias: high; blinding; Indirectness of outcome: No indirectness
	Protocol outcome 4: Admission of care facility - Actual outcome: Admission to care facility, end of follow-up; group 1: 13/63, group 2: 9/60; risk of bias: high; blinding; Indirectness of outcome: No indirectness
	Protocol outcome 5: Unscheduled care - Actual outcome: Readmission, unclear; group 1: 22/63, group 2: 30/60; risk of bias: high; blinding; Indirectness of outcome: No indirectness
	Protocol outcome 6: Functional outcome - Actual outcome: Independent in at least 2 ADL at 24 months; group 1: 28/63, group 2: 20/60; risk of bias: high; blinding; Indirectness of outcome: No indirectness
Protocol outcomes not reported by the study	Patient & carer satisfaction; length of hospital stay; continuity of care; patient/carer treatment burden

Table 164: Saltvedt 2002

Study	Saltvedt 2002
Study type	RCT (randomised; parallel)
Number of studies (number of participants)	1 (n=254)
Countries and setting	Conducted in Norway; setting: community hospital.
Line of therapy	Adjunctive to current care
Duration of study	Intervention and follow-up: 12 months.
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: ≥75 years.
Stratum	CGA inpatient - ward
Subgroup analysis within study	Not applicable
Inclusion criteria	Eligible patients had to meet at least 1 of the inclusion criteria, used to target frail patients: chronic disability, acute impairment of single activity of daily living, mild/moderate dementia, confusion, depression, imbalance/dizziness, falls, impaired mobility, urinary incontinence, malnutrition, polypharmacy, vision or hearing impairment, social problems, or prolonged bed rest. Briefly, they should not be in need of specific treatment offered by the section to which they were already admitted and should be suitable for transfer to the GEMU.
Exclusion criteria	Patients with acute stroke were only included if the Stroke Unit was full. Nursing home patients and those previously

Study	Saltvedt 2002
	fully independent and who seemed to recover quickly from the acute illness were not included, nor were patients for whom discharge was planned within 3 days. Other exclusion criteria were cancer with metastasis, other disease with expected survival less than 6 months, and known severe dementia before admission to hospital.
Recruitment/selection of patients	Patients from the city of Trondheim admitted acutely to the Department of Internal Medicine were screened for enrolment in the study.
Age, gender and ethnicity	Age – mean (SD): intervention 81.8 (4.8); control: 82.4 (5.2). Gender (M:F): 89/165. Ethnicity: not reported.
Further population details	1. Age: aged 75 and older. 2. Deprivation: not stated. 3. Ethnicity: not stated. 4. Number of conditions: not stated. 5. Type of condition: heart disease: intervention 36%, control 46%; cerebrovascular disease: intervention 19%, control 135; endocrine disease: intervention 16%, control 13%; airway disease: intervention 14%, control 7%; cancer: 12%, control 9%.
Indirectness of population	Serious indirectness: older adult
Interventions	<p>(n=127) Intervention 1: CGA. Duration: 12 months. Patients allocated to the geriatric evaluation and management unit (GEMU) were transferred on the day of inclusion. In the GEMU, the treatment strategy emphasised interdisciplinary assessment of all relevant disorders, prevention of complications and iatrogenic conditions, early mobilisation/rehabilitation, and comprehensive discharge planning. The staff of the GEMU consisted of 1 geriatrician and 1 (occasionally 2) resident. The number of nurses was comparable with that of other medical wards (MWs), although some of these nurses also had formal training in geriatric nursing. In addition, the GEMU had 2 occupational therapists and 1 physiotherapist. During the study period, a nurse was assigned to organise the study, recruit patients, and perform assessments during the index stay and follow-up. A social worker, a dentist, and other medical specialists were consulted when necessary. The physical environment in the GEMU was comparable with that in other MWs, apart from the additional combined dinning/activity-room. In the GEMU, comprehensive assessment of all relevant illnesses and disabilities was emphasised, as was prevention of complications and iatrogenic conditions. An interdisciplinary approach was employed, with close collaboration between all disciplines involved. Meetings were arranged twice a week to report assessments, set goals, discuss problems, and plan discharge. When necessary, relevant rehabilitation measures were initiated. If further rehabilitation was indicated, patients were referred to specialist rehabilitation facilities. In the GEMU, meetings were arranged to discuss necessary arrangements after discharge; patients, their family members, and representatives from the home services and the staff of the GEMU were invited. If necessary, an occupational therapist visited the patients at home to assess the need for adjustments. After patients were discharged from hospital, the GPs were responsible for the medical treatment of patients in both groups.</p> <p>(n=127) Intervention 2: Standard care. Usual care. Duration: 12 months. The control group received treatment as usual from the Department of Internal Medicine. Patients in the MWs were treated according to the general routines</p>

Study	Saltvedt 2002
	<p>for the Department of Internal Medicine. Residents and specialists in internal medicine and different subspecialties were responsible for the care provided. Physiotherapy and occupational therapy were normally given when prescribed by the doctor, with each occupational therapist and physiotherapist serving several wards. In the MW, home care nurses were telephoned to discuss arrangements after discharge if the hospital staff found it necessary. After patients were discharged from hospital, the GPs were responsible for the medical treatment of patients in both groups.</p>
Funding	Academic or government funding (supported by the Norwegian Ministry of Health and Social Affairs and the Research Council of Norway).
<p>RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: CGA versus STANDARD CARE</p> <p>Protocol outcome 1: Mortality - Actual outcome: Mortality, up to 6 months; group 1: 15/127, group 2: 34/127; risk of bias: low; Indirectness of outcome: No indirectness</p> <p>Protocol outcome 2: Mortality - Actual outcome: Mortality, end of follow-up; group 1: 35/127, group 2: 43/127; risk of bias: low; Indirectness of outcome: No indirectness</p> <p>Protocol outcome 3: Admission of care facility - Actual outcome: Admission to care facility, up to 6 months; group 1: 11/127, group 2: 14/127; risk of bias: low; Indirectness of outcome: No indirectness</p> <p>Protocol outcome 4: Admission of care facility - Actual outcome: Admission to care facility, end of follow-up; group 1: 16/127, group 2: 16/127; risk of bias: low; Indirectness of outcome: No indirectness</p> <p>Protocol outcome 5: Length of stay - Actual outcome: Length of stay, unclear, 12 months; group 1: 21.2 (16.2)/127, group 2: 12.2 (15)/127; risk of bias: low; Indirectness of outcome: No indirectness</p> <p>Protocol outcome 6: Unscheduled care - Actual outcome: Readmission, unclear, 12 months; group 1: 51/127, group 2: 51/127; risk of bias: low; Indirectness of outcome: No indirectness</p> <p>Protocol outcome 7: Functional outcome - Actual outcome: Dependence in ADL, Barthel <12, at 12 months; group 1: 18/72, group 2: 14/61; risk of bias: low; Indirectness of outcome: No indirectness</p>	

Study	Saltvedt 2002
Protocol outcome 8: Functional outcome - Actual outcome: Dependence in IADL, Lawton <4, at 12 months; group 1: 32/72, group 2: 26/59; risk of bias: low; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Patient & carer satisfaction; continuity of care; patient/carers treatment burden

Table 165: Shamian 1984

Study	Shamian 1984
Study type	RCT (randomised; parallel)
Number of studies (number of participants)	1 (n=36)
Countries and setting	Conducted in Canada; setting: University teaching hospital.
Line of therapy	Adjunctive to current care
Duration of study	Intervention and follow-up: intervention, 9 weeks, follow-up 30 days after transfer back to original ward (approximately 90 days after initial assessment).
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: ≥65 years.
Stratum	CGA inpatient - ward
Subgroup analysis within study	Not applicable
Inclusion criteria	All identified patients met the following criteria: they were over 65 years of age; they were medically stable and with no acute illness at the time of initial evaluation; and they were not on high priority lists for transfer either to the existing geriatric unit within the hospital or to a chronic care facility elsewhere.
Exclusion criteria	None reported.
Recruitment/selection of patients	A review of 110 geriatric patients in the institution by the geriatric unit revealed that there were 36 patients who would qualify for study entry.
Age, gender and ethnicity	Age – mean: not reported. Gender (M:F): 14/12. Ethnicity: Catholic, n=5; Jewish, n=29; other, n=2.
Further population details	1. Age: over 65 years of age. 2. Deprivation: not stated. 3. Ethnicity: not stated. 4. Number of conditions: not stated. 5. Type of condition: not stated.
Indirectness of population	Serious indirectness: older adult
Interventions	(n=20) Intervention 1: CGA. Duration: 90 days after initial assessment. The experimental group patients were relocated for 9 weeks, following which they were moved back to the nursing units of origin. During the period of

Study	Shamian 1984
	<p>relocation, the patients fell under the care of a different health care team. In each case the patients was relocated from a unit with an acute medical or surgical focus to a unit where the focus was geriatric medicine. All experimental and control patients underwent 4 evaluations within 30-day interval and were observed for 90 days. All 4 evaluations included data on: mortality and morbidity; activities of daily living; and, medication management. At zero time, all experimental and control patients were evaluated on their original units. Following the initial evaluation, the experimental patients were transferred to the temporary unit, which was staffed by a geriatrician, a head nurse who was a geriatrics specialist, and a nursing staff which included both experienced geriatrics nurses and newly hired nursing staff. There was no occupational therapist or physiotherapist assigned to the unit, although these professionals were available as consultants from the regular geriatrics unit, and all subjects retained their previous social workers. Care was based on the multidisciplinary team approach used on the established geriatrics unit. The participants were transferred back to their units of origin and their care was reassigned to the medical and nursing staff of those units.</p> <p>(n=16) Intervention 2: Standard care. Usual care. Duration: 90 days after initial assessment. The control group patients remained in their original units. All experimental and control patients underwent 4 evaluations within 30-day interval and were observed for 90 days. All 4 evaluations included data on: mortality and morbidity; activities of daily living; and, medication management. At zero time, all experimental and control patients were evaluated on their original units. Patients in the control remained on their units and received the same care as they had received prior to entrance in the study.</p>
Funding	Other (partially funded by the Sir Mortimer B. Davis – Jewish General Hospital).
<p>RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: CGA versus STANDARD CARE</p> <p>Protocol outcome 1: Mortality - Actual outcome: Mortality, up to 6 months; group 1: 1/20, group 2: 1/16; risk of bias: very high; blinding, incomplete outcome data; Indirectness of outcome: No indirectness</p> <p>Protocol outcome 2: Mortality - Actual outcome: Mortality, end of follow-up; group 1: 1/20, group 2: 1/16; risk of bias: very high; blinding, incomplete outcome data; Indirectness of outcome: No indirectness</p>	
Protocol outcomes not reported by the study	Functional outcome, patient & carer satisfaction; length of hospital stay; unscheduled care; continuity of care;

Study	Shamian 1984
	admission to care facility (admission to care facility); patient/carer treatment burden

Table 166: White 1994

Study	White 1994
Study type	RCT (randomised; parallel)
Number of studies (number of participants)	1 (n=40)
Countries and setting	Conducted in USA; setting: large urban university hospital.
Line of therapy	Adjunctive to current care
Duration of study	Intervention and follow-up: unclear, 30 days after discharge.
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: ≥65 years.
Stratum	CGA inpatient - ward
Subgroup analysis within study	Not applicable
Inclusion criteria	In general, medically stable elderly patients at risk for functional decline or with rehabilitation potential were accepted on the service. Age 65 years of age and older. Medically stable. Priority given to patients with a potential for maintaining or improving their current physical, psychological, and functional status.
Exclusion criteria	Do not resuscitate, imminently terminal patients will not be accepted.
Recruitment/selection of patients	Forty consecutive geriatric service consult patients received a formal evaluation.
Age, gender and ethnicity	Age – mean: intervention 73.9; control: 79.2. Gender (M:F): not reported. Ethnicity: not reported.
Further population details	1. Age: aged 65>. 2. Deprivation: not stated. 3. Ethnicity: not stated. 4. Number of conditions: not stated. 5. Type of condition: not stated.
Indirectness of population	Serious indirectness: older adult
Interventions	(n=20) Intervention 1: CGA. Duration: unclear, 30 days after discharge. An interdisciplinary geriatric team was developed consisting of a medical director/geriatrician, a gerontological nurse practitioner, a social worker, a dietician, a pharmacist, and an occupational therapist. A physical therapist and speech therapist saw selected patients. The service was nurse-managed, with the philosophy of care encompassing a shift in focus from acute illness-driven care to restorative, functional-based care. The service comprised of 6 beds. The geriatric service performed consultations imitated by attending or resident physicians, social workers, and rehabilitation and nursing staff. The appropriateness for geriatric service was made jointly by the geriatrician and nurse practitioner. Patients in the study group experienced a change in attending physician, transfer from a teaching, resident-managed service to a

Study	White 1994
	<p>non-teaching, nurse-managed service. All patients, experimental and control, were screened by a registered dietician as a routine component of their hospital stay. Every patient in the experimental group was evaluated by each geriatric team member during interdisciplinary rounds and team meetings. Discharge planning was a major focus of the geriatric service, with optimal post-hospital placement a goal. Caregiver education was also of prime importance.</p> <p>(n=20) Intervention 2: Standard care. Usual care. Duration: unclear, 30 days after discharge. The control group patients received only a formal consultation with recommendations from the geriatric service. These patients remained with their original attending and resident physicians and received their care in the usual manner. Control patients were seen in consultation by the geriatrician and the nurse practitioner. Recommendations related to care were made in writing. Patients were monitored by the nurse practitioner 4 outcome, but no attempt was made to enforce recommendations made during the initial consultation.</p>
Funding	Funding not stated.
<p>RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: CGA versus STANDARD CARE</p> <p>Protocol outcome 1: Mortality - Actual outcome: Mortality, up to 6 months; group 1: 0/20, group 2: 0/20; risk of bias: high; blinding; Indirectness of outcome: No indirectness</p> <p>Protocol outcome 2: Mortality - Actual outcome: Mortality, end of follow-up; group 1: 0/20, group 2: 0/20; risk of bias: high; blinding; Indirectness of outcome: No indirectness</p> <p>Protocol outcome 3: Admission of care facility - Actual outcome: Admission to care facility, up to 6 months; group 1: 6/20, group 2: 13/20; risk of bias: high; blinding; Indirectness of outcome: No indirectness</p> <p>Protocol outcome 4: Admission of care facility - Actual outcome: Admission to care facility, end of follow-up; group 1: 6/20, group 2: 13/20; risk of bias: high; blinding; Indirectness of outcome: No indirectness</p> <p>Protocol outcome 5: Unscheduled care - Actual outcome: Readmission, unclear, 30 days after discharge; group 1: 7/20, group 2: 4/20; risk of bias: high; blinding; Indirectness of outcome: No indirectness</p>	
Protocol outcomes not reported by the study	Functional outcome, patient & carer satisfaction; length of hospital stay; continuity of care; patient/carers treatment

Study	White 1994
	burden

H.5.2.2 Holistic assessment inpatient team

Table 167: Atfeld 2013

Study	Atfeld 2013³⁹
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=720)
Countries and setting	Conducted in USA; Setting: Hospital
Line of therapy	Adjunctive to current care
Duration of study	Intervention + follow up: Mean intervention: 5.8 days. Follow-up: 30 days.
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: 65 years and older
Stratum	CGA inpatient (team)
Subgroup analysis within study	Not applicable
Inclusion criteria	Patients eligible for inclusion in the study were those 65 years and older admitted for an inpatient hospitalisation at the study hospital between June 2009 and January 2010 and discharged home with 7 or more medication and at least 1 of the following criteria documented: lives alone; is without a support system for care post discharge; has a high risk for falls, has at least 1 previous inpatient admission to the study hospital in the 12 months prior to the current admission; is without a source of emotional support; has an in-depth psychosocial need
Exclusion criteria	Patients unable to effectively communicate in English, discharged to a skilled nursing or home institutional care facility, or those involved in another transitional care intervention were excluded
Recruitment/selection of patients	A flyer briefly describing the project and indicating that patients might receive a post-discharge telephone call inviting them to participate was distributed to every patients admitted to the acute hospital
Age, gender and ethnicity	Age - Mean (SD): 74.5 (6.9). Gender (M:F): Not stated. Ethnicity: White: 352 (49.25); African American: 326 (45.6%); All other categories: 37 (5.2%)
Further population details	1. Age: aged 65>. Deprivation: Not stated 3. Ethnicity: white: 49.0% intervention, 44.9% control; African American: 46.2% intervention, 49.4% control. 4. Number of conditions: Not stated 5. Type of condition: Not stated.
Indirectness of population	Serious indirectness: older adult
Interventions	(n=360) Intervention 1: CGA - CGA (team). Intervention participants received the telephone-based Enhanced

Study	Altfeld 2013 ³⁹
	<p>Discharge Planning (EDPP) assessment and an individualised plan following program protocols to address identified transitional care needs. The model involved the creation of a personalised intervention plan addressing both psychosocial and health issues, including connecting older adults to community resources, and collaborating with health care professional such as the discharge planning team, home health providers, and the physicians. Duration 30 days. Concurrent medication/care: EDPP is a social work-based telephone intervention developed at an urban medical centre for discharged medical and surgical inpatients over the age of 65 judged to be at risk for post-hospital medical or psychosocial complications. Referrals are generated through an automated daily report of hospital discharges utilising risk criteria. The social workers work collaboratively with the entirety of the interdisciplinary team involved in a particular patient’s care. The EDPP intervention began with a review of a referred patient, for relevant medical and psychosocial information. The intervention was not rigidly scripted so that it could be most responsive to patients identified needs. However, critical elements of the interview included confirmation of the plan for follow-up medical care, transportation plans, medication problems and adherence, knowledge of ‘red flags’, and receipt of services such as home health, ordered at discharge. The EDPP worker confirmed the post-discharge plan of care and identified potential problem areas that required additional assessment. The EDPP work contacted patients or caregivers by telephone within 2 working days of discharge to ass the patients’ post-discharge adjustment and needs. The EDPP worker administered the baseline survey to consenting patients at the end of the first telephone contact. The EDPP worked followed up with service providers; and determined if patients had obtained medications ordered at discharge, had made an appointment for outpatient follow-up with the physician, and had transportation for the visit. Workers also assessed for needs that may have emerged only after discharge, both concrete (such as home delivered meals) and psychological (such as anxiety). Cases were closed once the EDPP worker confirmed that a plan was in place to meet patient needs, both health and psychological. Prior to terminating the intervention, patients and caregivers were made aware of the option to connect back with EDPP workers for assistance in the future. A follow-up survey phone call was completed 30 days after hospital discharge</p> <p>Further details: 1. Post-CGA intervention: CGA + short-term care plan</p> <p>(n=360) Intervention 2: Standard care. The usual care group received conventional care given all patients discharged from the medical centre which did not include any post-discharge contact between hospital staff and patients or caregivers. Duration 30 days. Concurrent medication/care: The usual care group did not receive a baseline survey to ensure the usual care group received only conventional care in the 30-day post-discharge interval. The patients in the usual group were contacted by telephone 30 days after discharge to administer the follow-up survey. At the conclusion of the follow-up telephone call, usual care group participants were given information regarding the hospital-based older adult resource centre</p> <p>Further details: 1. Post-CGA intervention:</p>

Study	Altfeld 2013 ³⁹
Funding	Academic or government funding (Rush University Medical Center Department on Health and Aging. Support for data analysis was provided by New York Academy of Medicine.)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: CGA (TEAM) versus STANDARD CARE	
Protocol outcome 1: Mortality - Actual outcome: Mortality at 30 days; Group 1: 14/455, Group 2: 20/451; Risk of bias: High; Indirectness of outcome: No indirectness	
Protocol outcome 2: Unscheduled care - Actual outcome: Unscheduled care - readmission within 30 days at 30 days; OR 1.11 (95%CI 0.76 to 1.62); Risk of bias: High; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Health-related quality of life ; Functional outcomes (mobility, activities of daily living) ; Patient & carer satisfaction ; Length of hospital stay ; Continuity of care ; Admission to care facility ; Patient/carer treatment burden ; to be deleted
Protocol outcomes not reported by the study	Health-related quality of life; Functional outcomes (mobility, activities of daily living); Patient & carer satisfaction; Length of hospital stay; Continuity of care; Admission to care facility; Patient/carer treatment burden

Table 168: Edmans 2013

Study	Edmans 2013 ³⁸⁵
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=433)
Countries and setting	Conducted in UK; Setting: 2 teaching hospitals
Line of therapy	Adjunctive to current care
Duration of study	Intervention + follow up: Follow-up at 90 days
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Mean age - Intervention: 83.1 (6.7). Control: 82.8 (7.0).
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Patients were eligible is they were discharged from an acute medical unit within 72 hours of attending hospital, were aged 70 or over, and were identified as being at heightened risk of future health problems (defined by a score of at least 2/6 on the Identification of Seniors At Risk tool).
Exclusion criteria	Not being resident in the hospital catchment area, lacking mental capacity to give informed consent and without a

Study	Edmans 2013 ³⁸⁵
	consultee, any exceptional reason cited by acute medical unit staff why patients should not be recruited, and participation in other related studies.
Recruitment/selection of patients	Trained researchers embedded in the acute medical units recruited participants.
Age, gender and ethnicity	Age - Mean (SD): Intervention: 83.1 (6.7). Control: 82.8 (7.0). Gender (M:F): 159/274. Ethnicity: intervention, n=211 (98%) white; control, n=206 (95%) white.
Further population details	1. Age: aged 70> 2. Deprivation: Not stated 3. Ethnicity: white: 98% intervention, 95% control. 4. Number of conditions: Charlson comorbidity score: intervention 1 (1-2), control 1 (0-2). 5. Type of condition: Not stated.
Indirectness of population	Serious indirectness: older adult
Interventions	<p>(n=217) Intervention 1: Standard care. Usual care on the acute medical units before recruitment for both the control and intervention groups comprised assessment and treatment by a consultant physician and attending medical team. Some patients were referred to a multidisciplinary team (physiotherapist, occupational therapist, nurse). Patients' general practitioners were responsible for all aftercare. Patients in the control group received no additional intervention over and above usual care. Further details: 1. Post-CGA intervention: Not applicable / Not stated / Unclear</p> <p>(n=216) Intervention 2: CGA - CGA (team). Intervention: usual care plus interface geriatrician. Usual care on the acute medical units before recruitment for both the control and intervention groups comprised assessment and treatment by a consultant physician and attending medical team. Some patients were referred to a multidisciplinary team (physiotherapist, occupational therapist, nurse). The AMIGOS protocol expected all participants randomised to the intervention to be seen by a geriatrician with community experience on the acute medical unit before returning home. Patients in the intervention group were assessed before discharge from the acute medical unit by 1 of 12 geriatricians, who aimed to coordinate the delivery of whatever additional immediate care or aftercare they deemed necessary. The geriatrician took whatever steps he or she thought were required on the basis of the assessment. Such care could include a review of diagnosis; a drug review; further assessment at home or in a clinic or by recommending admission rather than discharge; advanced care planning; or liaison with primary care, intermediate care, and specialist community services. It was anticipated that most patients would require some sort of additional input from the interface geriatric on the acute medical unit leading to some further intervention, and that most would also require follow-up for more detailed assessment, or monitoring the compliance with and response to advice given. The interface geriatricians from both centres met monthly to discuss their experiences and cases. The intervention was expected to be complete within 1 month of randomisation. All geriatricians completed logs of their intervention. Further details: 1. Post-CGA intervention: CGA + short-term care plan</p>
Funding	Academic or government funding (this article present independent research funded by the National Institute for

Study	Edmans 2013 ³⁸⁵
	Health Research (NIHR) under its Programme Grants for Applied Research funding scheme).
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: CGA (TEAM) versus STANDARD CARE	
Protocol outcome 1: Health-related quality of life - Actual outcome: EQ-5D at 90 days; Group 1: 0.45 (0.32)/139, Group 2: 0.45 (0.32)/146; Risk of bias: High; Indirectness of outcome: No indirectness	
Protocol outcome 2: Mortality - Actual outcome: Mortality at 90 days; Group 1: 12/217, Group 2: 14/216 [HR 1.22 (0.57 to 2.65; p=0.61)]; Risk of bias: High; Indirectness of outcome: No indirectness	
Protocol outcome 3: Admission to Care Facility - Actual outcome: Admission to care facility at 90 days; Group 1: 4/156, Group 2: 5/153 [adjusted OR 1.31 (0.34 to 4.97; p=0.69)]; Risk of bias: High; Indirectness of outcome: No indirectness	
Protocol outcome 4: Functional outcome - Actual outcome: Activities of daily living (Barthel ADL ≥ 17) at 90 days; Group 1: 67/157, Group 2: 75/156 [OR 1.25 (0.72 to 2.17; p=0.42)]; Risk of bias: High; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Patient & carer satisfaction; Length of hospital stay; Unscheduled care; Continuity of care; Patient/carers treatment burden

Table 169: Hogan 1987

Study	Hogan 1987
Study type	RCT (randomised; parallel)
Number of studies (number of participants)	1 (n=113)
Countries and setting	Conducted in Canada; setting: tertiary referral centre
Line of therapy	Adjunctive to current care
Duration of study	Intervention and follow-up: 12 months.
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: ≥ 75 years.
Stratum	CGA inpatient - team
Subgroup analysis within study	Not applicable

Study	Hogan 1987
Inclusion criteria	Patients were included in the study if they met 1 of the following criteria: confused state, impaired mobility, falls not associated with loss of consciousness, urinary incontinence, polypharmacy, living in a nursing home or admission to an acute care hospital within the previous 3 months.
Exclusion criteria	Patients were excluded, even when they met 1 of the criteria, if they: were in intensive care unit or had suffered an acute cerebrovascular accident or if permission was refused by the patient or the attending staff physician.
Recruitment/selection of patients	Patients admitted to the Department of Medicine on an emergency basis were admitted to the study. Within 48 hours of admission, patients were interviewed by a trained assessor, who reviewed their hospital charts. The patients were specifically screened for confusional state, impaired mobility or falls, urinary incontinence and polypharmacy.
Age, gender and ethnicity	Age – mean (SD): intervention 82.2 (6.2); control: 83.3 (6.0). Gender (M:F%): intervention: 40% male, control: 25% male. Ethnicity: not stated.
Further population details	1. Age: aged 75>. 2. Deprivation: Not stated. 3. Ethnicity: Not stated. 4. Number of conditions: Not stated. 5. Type of condition: heart failure: 19% intervention, 20% control; heart disease: 9% intervention, 13% control.
Indirectness of population	Serious indirectness: older adult
Interventions	(n=57) Intervention 1: CGA. Duration 12 months. Patients in the intervention group were seen by the geriatric consultation service, which consisted of a geriatrician, a nurse, and a physiotherapist. The initial involvement of the service was a medical consultation performed by the geriatrician, who made specific recommendation to the attending staff. After this the other service members became involved, and recommendations and care came from any of them. Patients were seen daily on weekdays by at least 1 of the service members; full-team rounds were held once per week. At the time of discharge the assessor reviewed the discharge medications. (n=56) Intervention 2: Standard care. Usual care. Duration 12 months. Patients were randomly assigned to 'not receive'. No other information provided.
Funding	Academic or government funding (the Department of Medicine, Victoria General Hospital).
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: CGA versus STANDARD CARE	
Protocol outcome 1: Mortality - Actual outcome: Mortality, up to 6 months; group 1: 10/57, group 2: 17/56; risk of bias: high; allocation concealment; Indirectness of outcome: No indirectness	
Protocol outcome 2: Mortality - Actual outcome: Mortality, end of follow-up; group 1: 24/57, group 2: 25/56; risk of bias: high; allocation concealment; Indirectness of outcome: No indirectness	

Study	Hogan 1987
Protocol outcome 3: Admission of care facility - Actual outcome: Admission to care facility, up to 6 months; group 1: 23/57, group 2: 22/56; risk of bias: high; allocation concealment; Indirectness of outcome: No indirectness	
Protocol outcome 4: Admission of care facility - Actual outcome: Admission to care facility, end of follow-up; group 1: 23/57, group 2: 22/56; risk of bias: high; allocation concealment; Indirectness of outcome: No indirectness	
Protocol outcome 5: Length of stay - Actual outcome: Length of stay, unclear; group 1: 15.8 (12.7)/57, group 2: 14.2 (13.3)/56; risk of bias: high; allocation concealment; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Functional outcome, patient & carer satisfaction; unscheduled care (readmissions); continuity of care; patient/carer treatment burden

Table 170: Kircher 2007

Study	Kircher 2007
Study type	RCT (randomised; parallel)
Number of studies (number of participants)	1 (n=345, plus 90 additional patients as an external comparison group)
Countries and setting	Conducted in Germany; setting: hospital
Line of therapy	Adjunctive to current care
Duration of study	Intervention and follow-up: 12 months.
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: ≥65years.
Stratum	CGA inpatient - team
Subgroup analysis within study	Not applicable
Inclusion criteria	At least 65 years, expected length of stay of at least 8 days, of functional impairment and potential breakdown of home situation.
Exclusion criteria	Admitted from a nursing home, had previously been hospitalised in a geriatric evaluation and management inpatient unit, had a terminal condition or severe dementia, did not speak German, were living beyond a 60km radius of the

Study	Kircher 2007
	coordinating centre, would not need help at home or could not give informed consent.
Recruitment/selection of patients	Consultation service physician at each centre identified patients who met the criteria. Five hospitals with at least 3 years' experience of providing a consultation service took part in a randomisation trial (4 internal medicine and 1 psychiatry). In addition, 4 separate hospitals without consultation services formed an external, comparison group (3 medicine and 1 psychiatry).
Age, gender and ethnicity	Age – mean (SD): intervention 79.0 (6.9); control: 78.4 (6.9); comparison; 76.9 (7.5). Gender (M:F): 106/254. Ethnicity: not stated.
Further population details	1. Age: aged 65>. 2. Deprivation: Not stated. 3. Ethnicity: Not stated. 4. Number of conditions: Not stated. 5. Type of condition: Not stated.
Indirectness of population	Serious indirectness: older adult
Interventions	<p>(n=150) Intervention 1: CGA. Duration: 12 months. Patients were assessed by a research physician who collected baseline data using standardised, multidimensional assessment instruments within 3 days after randomisation. The consultation service teams comprised a social worker and physician. The geriatrician summarised problems and recommendations in a structured treatment note. Team conferences were held at least weekly, with 20 minutes spent on each new patient and 20 minutes on follow-up of previously assessed patients. Treatment was evaluated, and the implementation of recommendations was appraised. Recommendations were implemented by either the consultation team, the other staff members, the patient, the proxy or the general practitioner. When necessary, the nurse or social worker visited the patient's home together with a relative to appraise living conditions. The GP was contacted about the recommendations by the consultation service physician shortly before discharge. Community services received a detailed and structured recommendation plan and were contacted by telephone before discharge. The only additional outpatient procedure for the intervention group was a follow-up call to the patient and/or relatives by the social worker 2 weeks after discharge, who, when necessary, provided brief, limited further support in the form of a telephone consultation.</p> <p>(n=129) Intervention 2: Standard care. Usual care. Duration: 12 months. Patients received all appropriate hospital services except those provided by the consultation team.</p>
Funding	Academic or government funding (the German Research Council (DFG), the Ministry of Social Affairs Baden-Wuerttemberg and the fortune-Programme of the University Tubingen).

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: CGA versus STANDARD CARE

Study	Kircher 2007
Protocol outcome 1: Health-related Quality of Life - Actual outcome: Quality of Life Philadelphia Geriatric Centre Morale Scale at 12 months; group 1: 8 (7-9)/150, group 2: 8 (7-10)/129; risk of bias: high; outcome data; Indirectness of outcome: No indirectness	
Protocol outcome 2: Mortality - Actual outcome: Mortality, end of follow-up: 12 months; group 1: 28/150, group 2: 20/129; risk of bias: high; incomplete outcome data; Indirectness of outcome: No indirectness	
Protocol outcome 3: Admission of care facility - Actual outcome: Admission to care facility, end of follow-up; group 1: 24/150, group 2: 15/129; risk of bias: high; incomplete outcome data; Indirectness of outcome: No indirectness	
Protocol outcome 4: Unscheduled care - Actual outcome: Readmissions, 12 months; group 1: 84/150, group 2: 65/129; risk of bias: high; incomplete outcome data; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Functional outcome, patient & carer satisfaction; length of hospital stay; continuity of care; patient/carers treatment burden

Table 171: Naughton 1994

Study	Naughton 1994
Study type	RCT (randomised; parallel)
Number of studies (number of participants)	1 (n=111)
Countries and setting	Conducted in USA; setting: Private, non-profit, academic medical centre in densely populated urban area.
Line of therapy	Adjunctive to current care
Duration of study	Intervention and follow-up: unclear (assume discharge from hospital).
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: ≥70 years.
Stratum	CGA inpatient - team
Subgroup analysis within study	Not applicable
Inclusion criteria	Patients 70 years of age and older, who were admitted from emergency department to the medicine service and who did not regularly receive care from an attending internist on staff at the study hospital at the time of admission.

Study	Naughton 1994
Exclusion criteria	Patients admitted to an intensive care unit or transferred from the medical service to a surgical service (for example, general surgery, urology, gynaecology).
Recruitment/selection of patients	At the hospital, patients who did not have an internist on staff and who require admission from the emergency department to the medical service agree to accept assignment to the attending physician on call for medical admissions.
Age, gender and ethnicity	Age – mean (SD): intervention 80.1 (6.6); control: 80.1 (6.4). Gender (M:F%): intervention, 51.0% male; control, 58.3% male. Ethnicity: intervention, 60.8% white; control, 58.35 white.
Further population details	1. Age: aged 70+. 2. Deprivation: Not stated. 3. Ethnicity: white: 60.8% intervention, 58.3% control. 4. Number of conditions: 4.3 (2.2) intervention, 4.1 (2.0) control. 5. Type of condition: Not stated.
Indirectness of population	Serious indirectness: older adult
Interventions	<p>(n=51) Intervention 1: CGA. Duration: unclear, at discharge. Patients were admitted to the direct care of a team consisting of medical house staff, a social worker, and an attending geriatrician. Attending responsibility rotated monthly among the geriatricians. The geriatrician and social worker comprised the core geriatric evaluation and management (GEM) team. A nurse clinical specialist and a physical therapist joined the core team as needed. The team systematically, consistently, and routinely evaluated the patients' mental status, psychosocial condition, functional status, and medical condition to determine the medical, rehabilitative, and social needs of the patients. Information about the patients was discussed at team conferences 2 or 3 times per week. The progress of the medical condition and the plans for rehabilitation were then reviewed by the physician. Additional information was provided to the team by the nurse specialist and physical therapist at the point at which they were involved in the patient's care. Responsibility for implementing the care plan was apportioned among team members. The physician's responsibilities included treating medical conditions, adjusting medications, obtaining psychiatric consultation and treatment, systematically determining the impact of impaired mental status on treatment options and patient autonomy, and overseeing rehabilitation treatment for functional deficits. The social worker was responsible for identifying and coordinating community resources such as home care services, providing caregiver support and education, and insuring that components of a post-hospital treatment plan were in place and sufficient at the time of hospital discharge and 2 weeks later. The nurse clinical specialist was responsible for coordinating the transfer to home health care, where indicated.</p> <p>(n=60) Intervention 2: Standard care. Usual care. Duration: unclear, at discharge. Patients were given 'usual care' by medical house staff and an attending physician. The care of these patients was assigned during each attending physician's clinical teaching rotation. The services of social workers and discharge planners were available upon request.</p>

Study	Naughton 1994
Funding	Other (grant from the Northwestern Memorial Foundation).
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: CGA versus STANDARD CARE	
<p>Protocol outcome 1: Mortality - Actual outcome: Mortality, up to 6 months; group 1: 3/51, group 2: 5/60; risk of bias: very high; blinding, incomplete outcome data; Indirectness of outcome: No indirectness</p> <p>Protocol outcome 2: Mortality - Actual outcome: Mortality, end of follow-up; group 1: 3/51, group 2: 5/60; risk of bias: very high; blinding, incomplete outcome data; Indirectness of outcome: No indirectness</p> <p>Protocol outcome 3: Admission of care facility - Actual outcome: Admission to care facility, up to 6 months; group 1: 9/51, group 2: 11/60; risk of bias: very high; blinding, incomplete outcome data; Indirectness of outcome: No indirectness</p> <p>Protocol outcome 4: Admission of care facility - Actual outcome: Admission to care facility, end of follow-up; group 1: 9/51, group 2: 11/60; risk of bias: very high; blinding, incomplete outcome data; Indirectness of outcome: No indirectness</p> <p>Protocol outcome 5: Length of stay - Actual outcome: Length of stay, unclear, assume at discharge from hospital; group 1: 5.4 (5.5)/51, group 2: 7 (7)/60; risk of bias: very high; blinding, incomplete outcome data; Indirectness of outcome: No indirectness</p>	
Protocol outcomes not reported by the study	Functional outcome, patient & carer satisfaction; unscheduled care (readmissions); continuity of care; patient/carers treatment burden

Table 172: Reuben 1995

Study	Reuben 1995
Study type	RCT (multicentre randomised; parallel)
Number of studies (number of participants)	1 (n=2353)

Study	Reuben 1995
Countries and setting	Conducted in USA; setting: multicentre HMO.
Line of therapy	Adjunctive to current care
Duration of study	Intervention and follow-up: 12 months.
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: ≥65 years.
Stratum	CGA inpatient - team
Subgroup analysis within study	Not applicable
Inclusion criteria	Patients met 1 of 13 criteria for inclusion: stroke, immobility, impairment in any basic activity of daily living, malnutrition, incontinence, confusion or dementia, prolonged bed rest, falls within the previous 3 months, depression, social or family problems, unplanned readmission to the hospital within 3 months of a previous hospitalisation, a new fracture, and an age of 80 years or older.
Exclusion criteria	Patients were excluded from the study if they had been admitted to a hospice or for terminal care, were not members of the HMO's health plan, lived outside the MO's medical-service area or were usually cared for at a medical centre in the H MONTHS that was not in the study, were discharged or died before randomisation, did not speak English, or were admitted from a nursing home.
Recruitment/selection of patients	Patients who were 65 years of age or older were screened 24 to 72 hours after admission to 1 of the 4 experimental sites.
Age, gender and ethnicity	Age – mean: intervention 77.6; control: 76.7. Gender (M:F%): intervention, 56% female; control, 48% female. Ethnicity: intervention, 85% white; control, 83% white.
Further population details	1. Age: aged 80>. 2. Deprivation: Not stated. 3. Ethnicity: white: 85% intervention, 83% control. 4. Number of conditions: Not stated. 5. Type of condition: Not stated.
Indirectness of population	Serious indirectness: older adult
Interventions	(n=1261) Intervention 1: CGA. Duration: 12 months. Patients in the assessment group were interviewed and examined by a team comprising a social worker, a nurse practitioner, and a geriatric. Using standardised, multidimensional assessment instrument, the nurse practitioner recorded each patient's medical history and performed a limited physical examination, focusing on geriatric issues; the social worker assessed functional status and cognitive and emotional health, noted stressful or otherwise important events in the patient's life, and reviewed the patient's social support system, use of community services, and advance directives. After these evaluations, the nurse and social worker met with the geriatrician to present and discuss the case, and usually the entire team saw the patient together. The geriatrician summarised the geriatric problems and the team's recommendations in a structured consultation note that was sent to both the attending physician and the patient's primary care physician. Team conferences were held daily and lasted about 1 hour, with 20 minutes spent on each new patient and 20 minutes on

Study	Reuben 1995
	<p>follow-up of previously assessed patients. Recommended procedures that did not involve major changes in therapy usually were directly ordered by the geriatrician. Many of the recommendations were to be implemented after discharge. The consultation team continued to follow the assessed patients until discharge, to ensure that recommendations were implemented and to evaluate the patient's conditions. The social worker placed a follow-up telephone call to each patient 3 weeks after discharge. The charts of patients were reviewed to find out whether the team's recommendation had been carried out within 3 months after randomisation.</p> <p>(n=1016) Intervention 2: Standard care. Usual care. Duration: 12 months. Patients assigned to the control group received usual care. No other information.</p>
Funding	Other (supported by grants from the Robert Wood Johnson Foundation, by the Southern California Kaiser Permanente Medical Care Program, by a grant from the National Institute on Aging UCLA Claude D. Pepper Older Americans Independence Centre, and by the West Los Angeles and Sepulveda Veterans Affairs Medical Centres).
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: CGA versus STANDARD CARE	
<p>Protocol outcome 1: Mortality - Actual outcome: Mortality, end of follow-up; group 1: 347/1337, group 2: 258/1016; risk of bias: high; blinding; Indirectness of outcome: No indirectness</p>	
Protocol outcomes not reported by the study	Functional outcome, patient & carer satisfaction; length of hospital stay, unscheduled care (readmissions); continuity of care; admission to care facility; patient/carer treatment burden

Table 173: Rubin 1993

Study (subsidiary papers)	Rubin 1993 ¹⁰⁵¹ (Rubin 1992 ¹⁰⁵⁰)
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=196)
Countries and setting	Conducted in USA; Setting: Parkland Memorial Hospital, Dallas, Texas
Line of therapy	Unclear
Duration of study	Follow up (post intervention): 12 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Older adults (aged 70 or older); mean number of conditions: intervention 4.2±3.2, control 3.6±1.4

Study (subsidiary papers)	Rubin 1993 ¹⁰⁵¹ (Rubin 1992 ¹⁰⁵⁰)
Stratum	CGA inpatient - team
Subgroup analysis within study	Not applicable
Inclusion criteria	Aged 70 years or older; Dallas County residents admitted to medicine service; high risk of hospital readmission for inpatient treatment to stabilise acute episodes of chronic illness; good candidates for outpatient management of existing chronic conditions as an alternative to inpatient treatment
Exclusion criteria	Unable to give informed consent for example, medical instability or severe cognitive impairment; admitted to non-medicine service; known to be terminally ill upon admission; under care of private physician; judged too socially and medically stable and independent
Recruitment/selection of patients	Recruited from medicine inpatient service, admitted to emergency room. Patients at least 70 years old were consecutively screen for randomisation until 100 patients were enrolled in each group
Age, gender and ethnicity	Age - Mean (SD): Intervention 76.8 (5.8); control 76.7 (5.3). Gender (M:F): 39:61. Ethnicity: Black: intervention 61.9%; control 61.9%. White: intervention 24.7%; control 34%. Hispanic: intervention 13.4%; control 3.1%
Further population details	1. Age: >65 years (Aged 70 or older). 2. Deprivation: Not stated. 3. Ethnicity: Black: intervention 61.9%; control 61.9%. White: intervention 24.7%; control 34%. Hispanic: intervention 13.4%; control 3.1%. 4. Number of conditions: Not stated. 5. Type of condition: Not stated
Indirectness of population	Serious indirectness: older adult
Interventions	<p>(n=97) Intervention 1: CGA - CGA (ward). Comprehensive geriatric evaluation and development of a long term care plan conducted by geriatric assessment team (GAT). GAT consisted of geriatric-internist, geropsychiatrist, geriatric clinical nurse specialist and geriatric social worker. Duration 1 year. Concurrent medication/care: Discharge planning was directed by the GAT. Discharge planning consisted of making effort to contact family members while patients were still in hospital to introduce team and its purpose. GAT encouraged family participation in the care of the patient.</p> <p>Further details: 1. Post-CGA intervention: CGA + long-term care plan (Long-term outpatient comprehensive geriatric care).</p> <p>(n=97) Intervention 2: Standard care. Usual inpatient care - care for my medical team consisting of attending physician, resident intern and medical students. At discharge patients received the usual disposition and follow-up care that is arranged my medical team, usually provided in general medical clinic. No access to geriatric consultation; could not have been referred to geriatric clinic after discharge. Duration 1 year. Concurrent medication/care: None stated</p> <p>Further details: 1. Post-CGA intervention:</p>
Funding	Academic or government funding (Robert Wood Johnson Program for Hospital Initiatives in Long Term Care; Dallas

Study (subsidiary papers)	Rubin 1993 ¹⁰⁵¹ (Rubin 1992 ¹⁰⁵⁰)
	Area Agency on Aging; National Institute on Aging)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: CGA (TEAM) versus STANDARD CARE	
Protocol outcome 1: Mortality - Actual outcome: Mortality at 12 months; Group 1: 29/91, Group 2: 27/87; Risk of bias: Low; Indirectness of outcome: No indirectness	
Protocol outcome 2: Functional outcomes (mobility, activities of daily living) - Actual outcome: Katz ADL - improved at 12 months; Group 1: 18/97, Group 2: 21/97; Risk of bias: High; Indirectness of outcome: No indirectness - Actual outcome: Five-Item OARS IADL - improved at 12 months; Group 1: 18/97, Group 2: 9/97; Risk of bias: High; Indirectness of outcome: No indirectness - Actual outcome: Katz ADL - declined at 12 months; Group 1: 43/97, Group 2: 48/97; Risk of bias: High; Indirectness of outcome: No indirectness - Actual outcome: Five-Item OARS IADL - declined at 12 months; Group 1: 52/97, Group 2: 60/97; Risk of bias: High; Indirectness of outcome: No indirectness	
Protocol outcome 3: Patient/carer treatment burden - Actual outcome: 'Health troubles stand in the way of doing things a great deal' at 12 months; Group 1: 19/60, Group 2: 34/60; Risk of bias: Very high; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Health-related quality of life; Patient & carer satisfaction; Length of hospital stay; Unscheduled care; Continuity of care; Admission to care facility

Table 174: Thomas 1993

Study	Thomas 1993
Study type	RCT (randomised; parallel)
Number of studies (number of participants)	1 (n=132)
Countries and setting	Conducted in USA; setting: community hospital.
Line of therapy	Adjunctive to current care
Duration of study	Intervention and follow-up: unclear, 12 months.
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: ≥70 years.
Stratum	CGA inpatient - team
Subgroup analysis within study	Not applicable
Inclusion criteria	All patients over the age of 70 years, admitted to a community hospital were eligible for the study.

Study	Thomas 1993
Exclusion criteria	Patients were excluded for the refusal of consent, admission to the intensive care unit or coronary care unit, an obvious terminal illness, renal haemodialysis, or place of residence greater than 50 miles from the hospital.
Recruitment/selection of patients	Not reported.
Age, gender and ethnicity	Age – mean (SD): intervention 77 (5.4); control: 76 (5.4). Gender (M:F): 46/74. Ethnicity: white, n=92; black, n=18.
Further population details	1. Age: aged 70>. 2. Deprivation: Not stated. 3. Ethnicity: white: intervention, n=43, control, n=49; black: intervention, n=15, control, n=13. 4. Number of conditions: Not stated. 5. Type of condition: Not stated.
Indirectness of population	Serious indirectness: older adult
Interventions	<p>(n=62) Intervention 1: CGA. Duration: 12 months. Multi-dimensional geriatric team assessment, leading to formal recommendations to the attending physician. A standard proprietary instrument, the Functional Assessment Inventory, was used to evaluate each patient. The experimental group received individual assessments from each team members consisting of a physician, geriatric nurse specialist, home health nurse, medical social worker, dietician, pharmacist, and physical therapist. Team discussion of each patient led to formal recommendations place in the patient’s chart. An additional copy of the consultation was mailed to the attending physician’s office. The team continued to monitor progress of the experimental group.</p> <p>(n=58) Intervention 2: Standard care. Usual care. Duration: 12 months. The control group received no intervention and no subsequent visits.</p>
Funding	Funding not stated.

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: CGA versus STANDARD CARE

Protocol outcome 1: Mortality

- Actual outcome: Mortality, up to 6 months; group 1: 3/68, group 2: 12/64; risk of bias: very high; blinding, study protocol against contamination; Indirectness of outcome: No indirectness

Protocol outcome 2: Mortality

- Actual outcome: Mortality, end of follow-up; group 1: 7/68, group 2: 13/64; risk of bias: very high; blinding, study protocol against contamination; Indirectness of outcome: No indirectness

Protocol outcome 3: Functional outcome

Study	Thomas 1993
	- Actual outcome: Activities of daily living, unclear, 12 months; group 1: 14.3 (3.5)/68, group 2: 14 (3)/64; risk of bias: very high; blinding, study protocol against contamination; Indirectness of outcome: No indirectness
	Protocol outcome 4: Length of stay - Actual outcome: Length of stay, unclear, 12 months; group 1: 9 (7.5)/68, group 2: 10.1 (7.6)/64; risk of bias: very high; blinding, study protocol against contamination; Indirectness of outcome: No indirectness
Protocol outcomes not reported by the study	Patient & carer satisfaction; unscheduled care (readmissions); continuity of care; admission to care facility (admission to care facility); patient/carer treatment burden

Table 175: Trentini 2001

Study	Trentini 2001 ¹²¹⁴
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=152)
Countries and setting	Conducted in Italy; Setting: 11 hospital geriatric evaluation management units
Line of therapy	Unclear
Duration of study	Follow up (post intervention): 1 year
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Older adult (aged 65 years or older); mean number of conditions: intervention 4.2±0.2, control 3.9±0.2
Stratum	CGA inpatient - team
Subgroup analysis within study	Not applicable
Inclusion criteria	Age >75; need for frequent clinical and therapeutic contact; progressive worsening of health; lacking in care; living alone; living in an unsuitable house; high risk of going into a nursing home; 3 or more admission to hospital in last 12 months
Exclusion criteria	Age <65; terminal disease; completely bed-ridden; living in a nursing home; good health defined as no need for home care); severe disabling irreversible conditions; likely non compliance
Recruitment/selection of patients	All acute patients hospitalised for at least 10 days were screened for eligibility
Age, gender and ethnicity	Age - Mean (SD): Intervention 78.7 (SD 0.8); control 80.0 (SD 0.7). Gender (M:F): 40:60. Ethnicity: Not stated
Further population details	1. Age: >65 years (Aged 65 or older). 2. Deprivation: Not stated. 3. Ethnicity: Not stated. 4. Number of conditions: Not

Study	Trentini 2001 ¹²¹⁴
	stated. 5. Type of condition: Physical with MH (Psychiatric illness: intervention 29.1%; control 20.5%).
Extra comments	Alzheimer's/Parkinson's: intervention 26.6%; control 23.3%. Ictus/cerebrovascular disorder: intervention 41.8%; control 35.6%. Psychiatric illness: intervention 29.1%; control 20.5%. Diabetes/dythyroidism: intervention 21.5%; control 17.8%. Hypertension: intervention 29.1%; control 34.2%. Heart disease: intervention 44.3%; control 46.6%. Lower limbs arterial and venous disease: intervention 19%; control 13.7%. Pulmonary disorder: intervention 21.5%; control 20.5%. Gastrointestinal disorder: intervention 29.1%; control 24.7%. Genital and urinary disease: intervention 32.9%; control 26%.
Indirectness of population	Serious indirectness: older adult)
Interventions	<p>(n=79) Intervention 1: CGA - CGA (team). CGA (performed at end of the hospitalisation period before discharge) and CGA-based interventions (conducted after discharge). Received a complete and personalised treatment based on results of CGA and performed by the same geriatric team in the outpatient clinic or day hospital. Planned evaluations at 3, 6 and 12 months. Duration 12 months. Concurrent medication/care: Some participants received telephone consultations Further details: 1. Post-CGA intervention: CGA + various</p> <p>(n=73) Intervention 2: CGA - CGA (team). CGA (performed at end of the hospitalisation period before discharge). No personalised care plan. Entrusted to GP with standard discharge letter. Planned evaluations at 3, 6 and 12 months. Duration 12 months. Concurrent medication/care: None stated Further details: 1. Post-CGA intervention: CGA + various (No care plan).</p>
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: CGA (WARD) versus CGA (WARD)	
Protocol outcome 1: Mortality - Actual outcome: Mortality at 12 months; Group 1: 6/74, Group 2: 12/57; Risk of bias: High; Indirectness of outcome: No indirectness	
Protocol outcome 2: Admission to care facility - Actual outcome: Admission to care facility at 12 months; Group 1: 3/74, Group 2: 5/57; Risk of bias: High; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Health-related quality of life; Functional outcomes (mobility, activities of daily living); Patient & carer satisfaction; Length of hospital stay; Unscheduled care; Continuity of care; Patient/carer treatment burden

Table 176: Winograd 1993

Study	Winograd 1993
Study type	RCT (randomised; parallel)
Number of studies (number of participants)	1 (n=197)
Countries and setting	Conducted in USA; setting: tertiary care teaching hospital.
Line of therapy	Adjunctive to current care
Duration of study	Intervention and follow-up: 12 months.
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: ≥65 years.
Stratum	CGA inpatient - team
Subgroup analysis within study	Not applicable
Inclusion criteria	Participants with the following characteristics were screened for inclusion in the trial: anticipated length of stay 96 hours or more; residence within 2 hours' drive from the centre; and, not enrolled in a geriatric or rehabilitation program. Patients were considered eligible for the trial if they were functionally impaired and aged 65 years with 1 of the following validated proxy criteria for frailty: confusion, dependence in activities of daily living, polypharmacy (more than 6 medications), disabling chronic illness(es), or a stressed caregiver system.
Exclusion criteria	Patients were excluded if they were independent in all activities of daily living prior to hospital admission ('too independent'), were a permanent nursing home resident, and had a terminal illness with life expectancy of less than 6 months by report of primary physicians ('too impaired').
Recruitment/selection of patients	Patients admitted directly to intensive care units were screened after transfer to general wards. Prospective patients were entered into a log consecutively. When found eligible for the study, and after giving consent, patients were registered as entered into the study.
Age, gender and ethnicity	Age – mean (SD): intervention 75.7 (9.0); control: 76.6 (9.7). Gender (M:F): 100/0. Ethnicity: not reported.
Further population details	1. Age: aged 65>. 2. Deprivation: low income: 66.2% intervention, 69.2% control. 3. Ethnicity: Not stated. 4. Number of conditions: intervention 4.2 (0.2), control 3.9 (0.2). 5. Type of condition: diabetes and dysthyroidism: 21.5% intervention, 17.8% control; hypertension: 29.1% intervention, 34.2% control; heart disease: 44.3% intervention, 46.6% control; pulmonary disorder: 21.5% intervention, 20.5% control.
Indirectness of population	Serious indirectness: older adult
Interventions	(n=99) Intervention 1: CGA. Duration: 12 months. The consultation intervention consisted of a comprehensive functional, mental, medical, and social evaluation and recommendations by an interdisciplinary team consisting of an attending faculty geriatrician, a geriatric fellow, and internal medicine house officer, a social worker, and a clinical nurse specialist. Members of other disciplines (for example, psychology, nutrition) were available to the consult team

Study	Winograd 1993
	<p>as needed. After initial evaluation, the team met as a group to discuss the patient and formulate recommendations, Recommendations were directed primarily at 5 areas: medical issues, referral for rehabilitation, evaluation and management of geriatric syndromes, discharge planning, and psychological issues. A formal consultation note outlining recommendation was place in the patients’ charts and discussed with the primary care team. Patients were seen by physician members of the team a minimum of 3 times per week throughout the hospital stay and follow-up notes were written on at least a weekly basis.</p> <p>(n=98) Intervention 2: Standard care. Usual care. Duration: 12 months. The control group patients receive usual care and were not evaluated by the consultation team.</p>
Funding	Other (work supported in part by the National Institute on Aging Clinical Investigator Award, The Henry J. Kaiser Family Foundation Grant, and the Veterans Affairs Health Services Research and Development Administration Grant).

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: CGA versus STANDARD CARE

Protocol outcome 1: Mortality
- Actual outcome: Mortality, up to 6 months; group 1: 14/99, group 2: 6/98; risk of bias: high; blinding; Indirectness of outcome: No indirectness

Protocol outcome 2: Mortality
- Actual outcome: Mortality, end of follow-up; group 1: 41/99, group 2: 35/98; risk of bias: high; blinding; Indirectness of outcome: No indirectness

Protocol outcome 3: Admission of care facility
- Actual outcome: Admission to care facility, up to 6 months; group 1: 17/99, group 2: 18/98; risk of bias: high; blinding; Indirectness of outcome: No indirectness

Protocol outcome 4: Admission of care facility
- Actual outcome: Admission to care facility, end of follow-up; group 1: 26/99, group 2: 27/98; risk of bias: high; blinding; Indirectness of outcome: No indirectness

Protocol outcome 5: Functional outcomes
- Actual outcome: Activities of daily living, 12 months; group 1: 3.6 (2)/99, group 2: 4 (2.1)/98; risk of bias: high; blinding; Indirectness of outcome: No indirectness

Protocol outcome 6: Length of stay
- Actual outcome: Length of stay, 12 months; group 1: 24.8 (22)/99, group 2: 26.7 (33)/98; risk of bias: high; blinding; Indirectness of outcome: No indirectness

Study	Winograd 1993
Protocol outcomes not reported by the study	Patient & carer satisfaction; unscheduled care (readmissions); continuity of care; patient/carer treatment burden

H.5.2.3 Community holistic assessment

Table 177: Boorsma 2011

Study	Boorsma 2011 ¹⁶⁰
Intensity subgroup	Low
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=340)
Countries and setting	Conducted in Netherlands; Setting: Residential care facilities (n=10)
Line of therapy	Adjunctive to current care
Duration of study	Intervention + follow up: Follow-up at 6 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Mean age - Intervention: 85.8 (6.2). Control: 85.5 (8.0).
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Residential care facility residents with physical or cognitive disabilities
Exclusion criteria	Residents who were terminally ill
Recruitment/selection of patients	No information provided
Age, gender and ethnicity	Age - Mean (SD): Intervention: 85.8 (6.2). Control: 85.5 (8.0). Gender (M:F): 84:256. Ethnicity: Not stated
Further population details	1. Age: Mean (SD): Intervention: 85.8 (6.2). Control: 85.5 (8.0) 2. Deprivation: Education- primary school: intervention 58.8%, control 59.8% or less 3. Ethnicity: Not stated 4. Number of conditions: Not stated 5. Type of condition: Mix physical and mental conditions, depression: intervention 5%, control 11.8%
Indirectness of population	Serious indirectness: older adult
Interventions	(n=139) Intervention 1: Standard care. For facilities assigned to usual care, the family physician was responsible for medical care and offered it on request. There was neither coordination nor structured planning of care. Multidisciplinary meetings were mostly not attended by family physicians. Duration Follow-up at 6 months. Concurrent medication/care: No other information provided (n=201) Intervention 2: CGA - CGA (team). The intervention, inspired by the disease management model, consisted of

Study	Boorsma 2011¹⁶⁰
	<p>a geriatric assessment of functional health every 3 months. The interview consisted of a computerised assessment of functional health, activities of daily living, depression, cognition, satisfaction with care, and use of medications.. Duration Follow-up at 6 months. Concurrent medication/care: Multidisciplinary integrated care – concept focused on identification and monitoring of the functional disabilities caused by chronic diseases. Its 3 basic elements correspond to those of the disease management model: monitoring of disabilities, coordination of care and empowerment. The model of multidisciplinary integrated care used in our study comprised 5 elements. First, a geriatric multidisciplinary assessment of all residents was conducted every 3 months. The Web-based Long-term Care Facility version 9.0 of the Resident Assessment Instrument was used for this purpose. The identified problem areas guide the design of an individualised care plan that is intended to improve or maintain functional health status. Second, the care plan was discussed with the resident, the resident’s family and family physician, and adapted to personal wishes. Third, residents with complex care needs were scheduled at least twice a year for a multidisciplinary meeting. Fourth, consultation with a geriatrician or psychologist was optional for the frailest residents with complex health care problems. Fifth, data from the Web-based Resident Assessment Instrument was used to provide an overview every 3 months.</p> <p>Further details: 1. Post-CGA intervention: CGA + short-term care plan</p>
Funding	Academic or government funding (Netherlands Organisation for Health Research and Development)
<p>RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: CGA (TEAM) versus STANDARD CARE</p> <p>Protocol outcome 1: Health-related quality of life (short 12-item version Rand Health Insurance Study Questionnaire) - Actual outcome: short 12-item version Rand Health Insurance Study Questionnaire at 6 months; Group 1: 42.31 (6.04)/147, Group 2: 42.35 (6.35)/87; Risk of bias: High; Indirectness of outcome: No indirectness</p> <p>Protocol outcome 2: Mortality - Actual outcome: Mortality at 6 months; Group 1: 28/201, Group 2: 25/139; Risk of bias: High; Indirectness of outcome: No indirectness</p> <p>Protocol outcome 3: Unscheduled care - Actual outcome: Hospitalisation at 6 months; Group 1: 22/142, Group 2: 12/85; Risk of bias: High; Indirectness of outcome: No indirectness</p>	

Table 178: Brettschneider 2015

Study	Brettschneider 2015
Intensity subgroup	High
Study type	RCT (Patient randomised; Parallel)

Study	Brettschneider 2015
Number of studies (number of participants)	1 (n=304)
Countries and setting	Conducted in Germany; Setting: Community, in patients own homes
Line of therapy	Not applicable
Duration of study	Follow up (post intervention): 18 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	>80 years, residents of Leipzig or Halle, live at home or be in hospital with discharge to home planned already
Exclusion criteria	Insufficient German language skills, cognitive impairment, not able to give consent, care level >1 (if needed assistance with more than 2 activities of basic nursing more than once a day, maximum amount of care must not exceed 3 hours a day).
Recruitment/selection of patients	Recruited via GPs, hospitals and registration offices
Age, gender and ethnicity	Age - Mean (SD): 84 (3.5). Gender (M:F): 28-34:72-66. Ethnicity: Not stated
Further population details	1. Age: >65 years 2. Deprivation: Not applicable / Not stated / Unclear 3. Ethnicity: Not applicable / Not stated / Unclear 4. Number of conditions: Not applicable / Not stated / Unclear 5. Type of condition: Not applicable / Not stated / Unclear
Indirectness of population	Serious indirectness: older adult
Interventions	<p>((n=150) Intervention 1: CGA - CGA (team). First visit multidimensional geriatric assessment performed by trained personnel (nursing scientist, psychologist or sociologist) in first home visit assessing nutrition status, sight and hearing, incontinence, loss of functional muscle mass. Social activities, housing conditions, economic conditions, polypharmacy and cognitive status determined. Case conference with nursing scientist, psychologist, gerontopsychiatrist, nutritionist and social worker within 3 weeks of assessment, work out individualised recommendations based on analysis of identified self-care deficits and risk factors for institutionalisation. Second visit by same personnel who performed first visit, reported to patient on outcome of case conference, presented recommendations. Third visit 4 weeks later, adherence to recommendations evaluated, obstacles and facilitators identified, recommendations reviewed and further support offered.. Duration 4 weeks. Concurrent medication/care: Usual care (every service offered by the statutory health insurance system and utilized by the patient on his/her own initiative).</p> <p>Further details: 1. Post-CGA intervention: CGA + long-term care plan</p> <p>(n=155) Intervention 2: Standard care. Usual care (every service offered by statutory health insurance system and</p>

Study	Brettschneider 2015
	utilised at patient's own initiative). Duration 4 weeks. Concurrent medication/care: Nil else Further details: 1. Post-CGA intervention:
Funding	Academic or government funding
<p>RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: CGA (TEAM) versus STANDARD CARE</p> <p>Protocol outcome 1: Health-related quality of life at Define - Actual outcome: EQ-5D at 18 months; Group 1: mean 0.5563 (SD 0.3068); n=133, Group 2: mean 0.5503 (SD 0.3165); n=145; EQ-5D Index 0-1 Top=High is good outcome; Risk of bias: Very high; Indirectness of outcome: No indirectness</p> <p>Protocol outcome 2: Mortality at Define - Actual outcome: Deaths at 18 months; Group 1: 12/133, Group 2: 26/145; Risk of bias: High; Indirectness of outcome: No indirectness</p> <p>Protocol outcome 3: Admission to care facility at Define - Actual outcome: Nursing home admissions at 18 months; Group 1: 8/133, Group 2: 15/145; Risk of bias: High; Indirectness of outcome: No indirectness - Actual outcome: Nursing home admissions at 18 months; HR 0.55 (95%CI 0.23 to 1.3) Reported; Risk of bias: High; Indirectness of outcome: No indirectness</p> <p>Protocol outcomes not reported by the study Mortality at Define; Functional outcomes (mobility, activities of daily living) at Define; Patient & carer satisfaction at Define; Length of hospital stay at Define; Unscheduled care at Define; Continuity of care at Define; Admission to care facility at Define; Patient/carer treatment burden at Define; to be deleted at Define</p>	

Table 179: Counsell 2007

Study	Counsell 2007 ²⁹⁸
Intensity subgroup	High
Study type	RCT (Cluster randomised; Parallel)
Number of studies (number of participants)	1 (n=951)
Countries and setting	Conducted in USA
Line of therapy	Unclear

Duration of study	Intervention + follow up: 2 years
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: older adult
Stratum	Community CGA
Subgroup analysis within study	Not applicable
Inclusion criteria	Aged 65 years or older; established patient (defined as at least 1 visit to primary care clinician at same site within last 12 months; income less than 200% of the federal poverty level (defined as qualifying for Indiana Medicaid coverage or being enrolled in the county medical assistance plan
Exclusion criteria	residence in a nursing home; living with a study participant already enrolled in the trial; enrolled in another research study; receiving dialysis; severe hearing loss; English language barrier; no access to a telephone; severe cognitive impairment (defined by Short Portable Mental Status Questionnaire score ≤ 5); without an available caregiver to consent to participate
Age, gender and ethnicity	Age – Mean (SD): intervention 71.8 (5.6), control 71.6 (5.8). Gender (M:F): 24:76. Ethnicity: Black: intervention 57.6%, control 62.5%
Further population details	1. Age: >65 years (aged 65 or older). 2. Deprivation: Low SES (household income <\$10000 annually: intervention 73.4%, control 71.5%; education <12 years: intervention 62.5%, control 60%). 3. Ethnicity: Not applicable / Not stated / Unclear (Black: intervention 57.6%, control 62.5%). 4. Number of conditions: Not stated 5. Type of condition: Systematic review: mixed (Depression (PHQ-9 score ≤ 10): intervention 11.7%, control 11.4%).
Indirectness of population	Serious indirectness: older adult
Interventions	<p>(n=474) Intervention 1: CGA. GRACE intervention. The GRACE support team consisted of an advanced practise nurse and social worker, who care for low-income older adults, in collaboration with the patient's primary care physician and a geriatrics interdisciplinary team led by a geriatrician. The support team met with the patient in the home to conduct an initial CGA. The support team then presented their findings to the larger GRACE interdisciplinary team to develop an individualised care plan. Then the support team met face-to-face with the patient's primary care physician to discuss the care plan and make any modifications. The support team then implemented the plan through face-to-facer and telephone contact with patients, family members, caregivers and healthcare professionals. Each patient received a minimum of 1 home follow-up to review care plan, 1 telephone or face-to-face contact per month and a face-to-face home visit after any ED visit or hospitalisation. Duration 2 years. Concurrent medication/care: None stated</p> <p>Further details: 1. Post-CGA intervention: Comments: CGA community-dwelling</p> <p>(n=477) Intervention 2: Standard care. Usual care. Had access to all primary and speciality care services available as part of usual care. Duration 2 years. Concurrent medication/care: None stated</p>

Funding	Academic or government funding (National Institute on Aging, National Institutes of Health)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: CGA versus STANDARD CARE	
<p>Protocol outcome 1: Health-related quality of life</p> <p>- Actual outcome: SF-36 (physical component) at 2 years; Group 1: mean -1.1 (SD 8.9); n=474, Group 2: mean -1.6 (SD 8.8); n=477; Risk of bias: Low; Indirectness of outcome: No indirectness</p> <p>- Actual outcome: SF-36 (mental component) at 2 years; Group 1: mean 2.1 (SD 10.2); n=474, Group 2: mean -0.3 (SD 10.8); n=477; Risk of bias: Low; Indirectness of outcome: No indirectness</p>	
<p>Protocol outcome 2: Functional outcomes (mobility, activities of daily living)</p> <p>- Actual outcome: Basic ADL at 2 years; Group 1: mean 0.2 (SD 2.7); n=474, Group 2: mean 0.4 (SD 2.7); n=477; Risk of bias: Low; Indirectness of outcome: No indirectness</p> <p>- Actual outcome: IADL at 2 years; Group 1: mean 0.4 (SD 3.3); n=474, Group 2: mean 0.6 (SD 3.6); n=477; Risk of bias: Low; Indirectness of outcome: No indirectness</p>	
Protocol outcomes not reported by the study	Mortality; Patient & carer satisfaction; Length of hospital stay; Unscheduled care; Continuity of care; Admission to care facility; Patient/carer treatment burden

Table 180: Ekdahl 2015

Study	Ekdahl 2015
Intensity subgroup	High
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=844)
Countries and setting	Conducted in Sweden; Setting: Sweden, southeastern municipality, community
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 24 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Patients had "3 or more concomitant medical diagnoses"
Stratum	Overall

Study	Ekdahl 2015
Subgroup analysis within study	Not applicable
Inclusion criteria	Community dwelling, 75 years of age or older, received inpatient hospital care 3 or more times in the previous 12 months, 3 or more concomitant medical diagnoses
Exclusion criteria	-
Recruitment/selection of patients	Participants were identified using a care data warehouse of an administrative database maintained by the county council, patients were then contacted by letter and consented over the phone
Age, gender and ethnicity	Age - Range of means: 82.3 (4.6) - 82.7 (5.1). Gender (M:F): 193:189. Ethnicity: Not stated
Further population details	1. Age: >65 years 2. Deprivation: Not applicable / Not stated / Unclear 3. Ethnicity: Not applicable / Not stated / Unclear 4. Number of conditions: Patients with >4 conditions (Inclusion criteria required patients to have 3 or more conditions). 5. Type of condition: Not applicable / Not stated / Unclear
Extra comments	-
Indirectness of population	No indirectness
Interventions	<p>(n=208) Intervention 1: CGA. Patients were invited to receive individually tailored care and attend follow-up visits as the ambulatory geriatric unit during the study period. Initial CGA was performed based on a standardised procedure. Thereafter all care was personalized according to patients' situations and preferences, best-known evidence and practice and team members' competences. Nurses reassessed patients after 1 year and initialized home visits by HCPs if needed. The team of professionals at ambulatory geriatric unit (nurse, geriatrician, care manager, occupational therapist, physiotherapist, dietician) planned care during team meetings, the common goal was increasing quality of life. Care manager contacted patients and informed them of available forms of support from municipality service. Intensity of follow-up ranged from few contacts per year to daily/weekly visits. Many activities had preventive goals (for example, physio training programmes). Nurses also ensured patients understood new prescriptions and visited patients who were admitted to hospital to provide further information to staff caring for them. Duration 24 months. Concurrent medication/care: Usual care</p> <p>(n=174) Intervention 2: Standard care. Usual health and social care provided by primary care centres, in and outpatient hospital care and social care as usual. Duration 24 months. Concurrent medication/care: Usual care</p>
Funding	Academic or government funding
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: CGA versus STANDARD CARE	
Protocol outcome 1: Health-related quality of life at Define	

Study	Ekdahl 2015
	<p>- Actual outcome: HRQoL - full EQ-5D-3 L at 24 months; Group 1: mean 0.6 (SD 0.3); n=144, Group 2: mean 0.62 (SD 0.3); n=103; EQ-5D-3L 0-1 Top=High is good outcome; Risk of bias: High; Indirectness of outcome: No indirectness</p> <p>Protocol outcome 2: Mortality at Define</p> <p>- Actual outcome: Mortality at 24 months; Group 1: 39/208, Group 2: 47/174; Risk of bias: High; Indirectness of outcome: No indirectness</p> <p>- Actual outcome: Mortality at 24 months; HR 0.66 (95%CI 0.43 to 1.01) Reported; Risk of bias: High; Indirectness of outcome: No indirectness</p> <p>Protocol outcome 3: Length of hospital stay at Define</p> <p>- Actual outcome: Mean number of inpatient days per patient at 24 months; Group 1: mean 11.1 Mean number of inpatient days per patient per 24 months (SD 15.9); n=208, Group 2: mean 15.2 Mean number of inpatient days per patient per 24 months (SD 20.2); n=174; Risk of bias: High; Indirectness of outcome: No indirectness</p> <p>Protocol outcome 4: Unscheduled care at Define</p> <p>- Actual outcome: Mean number of hospitalisations per patient at 24 months; Group 1: mean 2.1 hospitalisations per patient per 24 months (SD 2.6); n=146, Group 2: mean 2.4 hospitalisations per patient per 24 months (SD 2.5); n=106; Risk of bias: High; Indirectness of outcome: No indirectness</p> <p>Protocol outcome 5: Admission to care facility at Define</p> <p>- Actual outcome: Nursing home admittance at 24 months; Group 1: 26/208, Group 2: 33/174; Risk of bias: High; Indirectness of outcome: No indirectness</p> <p>- Actual outcome: Nursing home admittance at 24 months; HR 0.61 (95%CI 0.41 to 1.03) Reported; Risk of bias: High; Indirectness of outcome: No indirectness</p>
Protocol outcomes not reported by the study	Functional outcomes (mobility, activities of daily living) at Define; Patient & carer satisfaction at Define; Continuity of care at Define; Patient/carers treatment burden at Define; to be deleted at Define

Table 181: Epstein 1990

Study	Epstein 1990 ⁴⁰⁴
Intensity subgroup	High
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=390)
Countries and setting	Conducted in USA; Setting: Rhode Island Group Health Association (health maintenance association), Providence, Rhode Island
Line of therapy	Unclear

Study	Epstein 1990 ⁴⁰⁴
Duration of study	Follow up (post intervention): 1 year
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Older adults (aged 70 or older); mean number of conditions : intervention 2.5±1.6, control 2.3±1.7
Stratum	Community CGA
Subgroup analysis within study	Not applicable
Inclusion criteria	All patients at a health maintenance organisation aged 70 years or older were rated by their primary physicians in terms of their current health (very poor; poor; fair; good; very good) and their likelihood of deterioration (very likely; probably; possibly; unlikely). Two groups of patients were invited to participate: aged over 74 years; aged 70-74 years rated as having fair or worse health or as experiencing very likely or probable deterioration
Exclusion criteria	None stated
Recruitment/selection of patients	All eligible patients were recruited
Age, gender and ethnicity	Age - Mean (SD): CGA 76.7 (4.9); control 76.9 (4.6). Gender (M:F): 49:51. Ethnicity: White 94%
Further population details	1. Age: >65 years (Aged 70 years or older). 2. Deprivation: Not stated. 3. Ethnicity: White >80% (White 94%). 4. Number of conditions: Unclear (Mean number of conditions 2.4 (SD 1.7)). 5. Type of condition: Physical with MH (Psychological disorder 13%).
Extra comments	Stroke 6%; TIA 3%; dementia 4%; Parkinson's 1%; Arthritis 35%; congestive heart failure 8%; MI 10%; angina pectoris 16%; peripheral vascular disease 11%; valvular heart disease 3%; hypertension 50%; renal failure 1%; COPD 13%; cancer 13%; diabetes 13%; psychological disorder 13%
Indirectness of population	Serious indirectness: older adult
Interventions	(n=185) Intervention 1: CGA - CGA (team). 2 hour examination by geriatrician, geriatric nurse practitioner and a geriatric social worker. They reviewed the patient's medical record and performed a comprehensive physical examination that focused on drugs, nutrition, new diagnoses and the function impact of illness. The nurse administered a standard protocol for clinical assessment, including an instrument that measured cognitive function patterned after Katz activities of daily function scale and the OARS instrumental ADL scale. The social worker reviewed social support, social activities, coping style, psychological function, and economic and environmental issues. The team generally met for approximately 15 minutes after seeing the patient to generate a care plan and consult as a group with the patient and family. In some cases, indicated by the findings of the assessment, follow-up (for example, laboratory tests, diagnostic test, consultations with specialists) were ordered immediately following telephone confirmation with the patient's physician. Geriatric assessment personnel also initiated 3 follow-up telephone contacts with the patient or family during the first 2 months after the examination. These were intended to facilitate adjustment of care plans as well as maximize the likelihood of their adoption. Duration 1 year. Concurrent medication/care: None stated Further details: 1. Post-CGA intervention: CGA + various (Generated a care plan (unclear if short or long term)); 3

Study	Epstein 1990⁴⁰⁴
	telephone follow-ups during 2 months post-CGA).
	(n=205) Intervention 2: Standard care. Standard care using traditional health maintenance organisation services. Duration 1 year. Concurrent medication/care: None stated
Funding	Academic or government funding (John A. Hartford Foundation; Massachusetts Fund for Cooperative Innovation; Henry J. Kaiser Family Foundation; National Institutes of Aging)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: CGA (TEAM) versus STANDARD CARE	
Protocol outcome 1: Mortality - Actual outcome: Mortality at 1 year; Group 1: 10/185, Group 2: 13/205; Risk of bias: Low; Indirectness of outcome: No indirectness	
Protocol outcome 2: Functional outcomes (mobility, activities of daily living) - Actual outcome: Sickness Impact Profile (4 physical function scales, 51 items) at 1 year; Group 1: mean 91 (SD 11); n=181, Group 2: mean 89 (SD 13); n=201; Risk of bias: High; Indirectness of outcome: No indirectness	
Protocol outcome 3: Patient & carer satisfaction - Actual outcome: Patient satisfaction (developed from literature, based primarily on scale of DiMatteo and Hays, 12 item) at 1 year; Group 1: mean 4.39 (SD 0.78); n=181, Group 2: mean 4.28 (SD 0.89); n=201; Risk of bias: High; Indirectness of outcome: No indirectness	
Protocol outcome 4: Unscheduled care - Actual outcome: Hospitalisation at 1 year; Group 1: 46/185, Group 2: 54/205; Risk of bias: Low; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Health-related quality of life; Continuity of care; Admission to care facility; Patient/carers treatment burden

Table 182: Frese 2012

Study	Frese 2012⁴⁵⁰
Intensity subgroup	Low
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=1620)
Countries and setting	Conducted in Germany; Setting: Community

Study	Frese 2012 ⁴⁵⁰
Line of therapy	Adjunctive to current care
Duration of study	Intervention + follow up: 6.2 years (mean follow-up)
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Aged 70 years and older
Stratum	Community CGA
Subgroup analysis within study	Not applicable
Inclusion criteria	Community-living persons aged 70 years and older
Exclusion criteria	Death, move and refusal before or at the appointment time for the intervention
Recruitment/selection of patients	All general practitioners in the area were contracted. Twenty volunteered to participate and were asked to keep records over 3 months for every patients older than 70 years
Age, gender and ethnicity	Age - Mean (range): Intervention: 79.65-84.04 years. Control: 79.74-87.94 years. Gender (M:F): 460/1137. Ethnicity: Not stated
Further population details	1. Age: Mean (range): Intervention: 79.65-84.04. Control: 79.74-87.94 2. Deprivation: Not stated Unclear 3. Ethnicity: Not stated 4. Number of conditions: Unclear 5. Type of condition: Not stated
Indirectness of population	Serious indirectness: older adult
Interventions	(n=630) Intervention 1: CGA - CGA (team). Preventative in-home CGA, using the STEP-tool (standardised assessment of elderly people in primary care in Europe; a combination of a structured questionnaire and a structured physical examination) and additional tests, followed by recommendations for the general practitioner. Duration 5-7 years (mean 6.2 years). Concurrent medication/care: Geriatric assessment (intervention group): visited at home and a geriatric assessment was performed. Home visits with CGA were performed using the STEP-assessment and each of the following additional tests: Barthel-Index, Lambeth-disability screening questionnaire, Tinetti-gait score, Hamilton depression Rating Scale, Hospital anxiety and depression scale, Mini Mental State Examination, Hierarchic Dementia Scale, clock drawing test and COOP-Charts. Four specially trained medical students performed all of these tests. The STEP-assessment consists of standardised questionnaires concerning functional (mobility and falls) and social status, life style, physical (history, medication and current problems) and mental (depression and dementia) status. The STEP-assessment tool also includes a short physical examination, taking pulse and blood pressure, and the inspection of homes towards safety hazards and help for daily living. An overview of all documented problems of each patient was given to the patient's GP, including the recommendation. The GPs were responsible for implementing them. GPs were asked to rate every patient's state of health regardless of which group the patients belonged to. All the patients have in principle equal access to the necessary health care resources. Further details: 1. Post-CGA intervention: CGA + short-term care plan

Study	Frese 2012⁴⁵⁰
	(n=990) Intervention 2: Standard care. Controls received usual general practitioner care. GPs were asked to rate every patient's state of health regardless of which group the patients belonged to. Controls received usual care including home visits by their GP when necessary. In the context of the German health care system, usual care means that the patient should consult their GP at first, but they can also directly consult specialists. All the patients have in principle equal access to the necessary health care resources. . Duration 5-7 years (mean 6.2 years). Concurrent medication/care: No other information
Indirectness of intervention	94 of 630 patients were lost to follow-up, of the 536 patients whose data was analysed only 336 had received a CGA. Of the 336 patients, 100 had 2 CGAs, 3 years apart.
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: CGA (TEAM) versus STANDARD CARE	
Protocol outcome 1: Mortality - Actual outcome: Mortality at 6.2 years; OR 0.78 (95%CI 0.67 to 0.91); Risk of bias: High; Indirectness of outcome: No indirectness	
Protocol outcome 2: Admission to care facility - Actual outcome: Admission to care facility at 6.2 years; OR 0.80 (95%CI 0.68 to 0.95); Risk of bias: High; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Health-related quality of life; Functional outcomes (mobility, activities of daily living); Patient & carer satisfaction; Length of hospital stay; Unscheduled care; Continuity of care; Patient/carers treatment burden

Table 183: Karppi 1995

Study (subsidiary papers)	Karppi 1995⁶⁷⁵ (Karppi 1995⁶⁷⁶)
Intensity subgroup	High
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=312)
Countries and setting	Conducted in Finland; Setting: Community, Central Finland
Line of therapy	Unclear
Duration of study	Follow up (post intervention): 1 year

Study (subsidiary papers)	Karppi 1995⁶⁷⁵ (Karppi 1995⁶⁷⁶)
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Older adult (aged 65 years or older); several conditions
Stratum	Community CGA
Subgroup analysis within study	Not applicable
Inclusion criteria	Community-dwelling supervised home care population of Central Finland; aged 64 years or older; multiple problems (for example, several diseases, underdiagnoses, polypharmacy, problems coping at home); anticipated benefit from geriatric intervention (for example, curable disease, rehabilitation potential, prevention of admission to care facility)
Exclusion criteria	Terminal phase of illness; only a single acute disease or injury; psychosis; care in the geriatric unit in the last year
Recruitment/selection of patients	GP and home nurses selected study patients from supervised home care population of Central Finland
Age, gender and ethnicity	Age - Mean (SD): 78.5 (4.3). Gender (M:F): 22:78. Ethnicity: Not reported
Further population details	1. Age: >65 years (Aged 65 years or older). 2. Deprivation: Not stated. 3. Ethnicity: Not stated. 4. Number of conditions: Unclear ('multiple'). 5. Type of condition: Not stated
Indirectness of population	Serious indirectness: older adult
Interventions	(n=104) Intervention 1: CGA - CGA (ward). Comprehensive multidisciplinary assessment in an inpatient geriatric rehabilitation unit. In the ward there were 1 geriatrician, 5 nurses, 7 auxiliary nurses, 3 assistants, 2 physiotherapists, 1 psychologist, 1 occupational therapist and 1 part-time social worker. 1 psychiatrist visited once a week. Specialists were consulted when needed. Given a rehabilitation plan to be followed at home. Duration Mean stay 16.5 days. Concurrent medication/care: Received inpatient care Further details: 1. Post-CGA intervention: (n=208) Intervention 2: Standard care. Usual supervised home care. Duration 12 months. Concurrent medication/care: None stated
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: CGA (WARD) versus STANDARD CARE	
Protocol outcome 1: Mortality - Actual outcome: Mortality at 12 months; Group 1: 14/104, Group 2: 25/208; Risk of bias: High; Indirectness of outcome: No indirectness	
Protocol outcome 2: Functional outcomes (mobility, activities of daily living) - Actual outcome: Katz ADLs at 3 months; Group 1: mean 5 (SD 1.1); n=93, Group 2: mean 4.9 (SD 1.6); n=208; Risk of bias: High; Indirectness of outcome: No	

Study (subsidiary papers)	Karppi 1995 ⁶⁷⁵ (Karppi 1995 ⁶⁷⁶)
indirectness	- Actual outcome: Lawton & Brody IADLs at 3 months; Group 1: mean 4 (SD 2.1); n=93, Group 2: mean 4 (SD 2.1); n=208; Risk of bias: High; Indirectness of outcome: No indirectness
Protocol outcome 3: Admission to care facility	- Actual outcome: Admission to care facility at 12 months; Group 1: 11/104, Group 2: 18/208; Risk of bias: High; Indirectness of outcome: No indirectness
Health-related quality of life; Patient & carer satisfaction; Length of hospital stay; Unscheduled care; Continuity of care; Patient/carers treatment burden	

Table 184: Lampela 2013

Study (subsidiary papers)	GEMS: Geriatric Multidisciplinary Strategy for the Good Care of the Elderly trial: Lampela 2013 ⁷³⁴ (Lampela 2010 ⁷³³ , Lihavainen 2012 ⁷⁶⁹ , Lihavainen 2012 ⁷⁷⁰)
Intensity subgroup	High
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	4 (n=1000)
Countries and setting	Conducted in Finland; Setting: Unclear
Line of therapy	Adjunctive to current care
Duration of study	Intervention + follow up: 3 years
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Aged ≥75 years. Arthritis: intervention 39%, control 37%; Cardiovascular disease: intervention 63%, control 65%; Asthma: intervention 8%, control: 10%; Diabetes: intervention: 14%. Control 19%; Depression: intervention: 8%, control 11%.
Stratum	Community CGA
Subgroup analysis within study	Not applicable
Inclusion criteria	Inhabitants aged ≥75 years of the City of Kuopio, Finland.
Exclusion criteria	Not reported
Recruitment/selection of patients	Contact information on the target population was gathered from the Finnish population register
Age, gender and ethnicity	Age - Mean (SD): 81.1 (5.0). Gender (M:F): 30:70. Ethnicity: Not stated
Further population details	1. Age: Mean (SD): 81.1 (5.0) 2. Deprivation: Not stated 3. Ethnicity: Not stated 4. Number of conditions: Not stated 5. Type of condition: Not stated

Study (subsidiary papers)	GEMS: Geriatric Multidisciplinary Strategy for the Good Care of the Elderly trial: Lampela 2013⁷³⁴ (Lampela 2010⁷³³, Lihavainen 2012⁷⁶⁹, Lihavainen 2012⁷⁷⁰)
Extra comments	Mainly home-dwelling population (96%) but part of the sample were living in care facility
Indirectness of population	Serious indirectness: older adult
Interventions	<p>(n=500) Intervention 1: CGA - CGA (team). A CGA, including evaluation of the adequacy of the medication, was performed annually in the intervention group. Duration 3 years. Concurrent medication/care: The health status of persons in both groups was monitored annually by a trained nurse during the years 2004-2007. This included blood pressure measurements. In addition to health status monitoring by a trained nurse, those in the intervention group underwent CGA. This included an overall health status assessment including medication assessment (where the adequacy of the medication, both in terms of the drugs and their doses, was reviewed annually and modified when necessary) by a physician (trainee in geriatrics). These modifications were monitored if needed. The health status assessment took place generally within 2 weeks after the patient's visit at the study nurse. In case of orthostatic hypotension (OH), the physician attempted to decrease OH by searching for possible medications and other conditions that may provoke OH. The CGA also included nutritional status assessment and mobility, balance and muscle strength assessment. Persons in the intervention group also had counselling and case manager services by a trained nurse</p> <p>Further details: 1. Post-CGA intervention: CGA + short-term care plan</p> <p>(n=500) Intervention 2: Standard care. Persons in the control group received no interventions. Duration 3 years. Concurrent medication/care: Standard health care services in public and private sector were available for them. The health status of persons in both groups was monitored annually by a trained nurse during the years 2004-2007. This included blood pressure measurements</p>
Funding	Academic or government funding (Social Insurance Institution of Finland and City of Kuopio)
<p>RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: CGA (TEAM) versus STANDARD CARE</p> <p>Protocol outcome 1: Mortality - Actual outcome: Mortality at By 3 year follow-up; Group 1: 81/500, Group 2: 72/500; Risk of bias: Very high; Indirectness of outcome: No indirectness</p>	
Protocol outcomes not reported by the study	Health-related quality of life; Functional outcomes (mobility, activities of daily living); Patient & carer satisfaction; Length of hospital stay; Unscheduled care; Continuity of care; Admission to care facility; Patient/carers treatment burden

Table 185: Li 2010

Study	Li 2010 ⁷⁶⁴
Intensity subgroup	Low
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=310)
Countries and setting	Conducted in Taiwan
Line of therapy	Adjunctive to current care
Duration of study	Intervention + follow up: 6 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Aged 65 years old and above
Stratum	Community CGA
Subgroup analysis within study	Not applicable
Inclusion criteria	Pre-frail and frail community-dwelling elderly.
Exclusion criteria	Conditions such as being bedridden, receiving home care by visiting nurses, less than 6 months' life expectancy (such as terminal cancer patients), and difficulty in verbal communication (such as severe cognitive or hearing impairments).
Recruitment/selection of patients	Two neighbourhoods with 1,843 registered older people age 65 years and over were chosen for this study
Age, gender and ethnicity	Age - Mean (SD): Intervention: 78.4 (8.2). Control: 79.3 (8.5). Gender (M:F): 162/148. Ethnicity: Not stated
Further population details	1. Age: Mean (SD): Intervention: 78.4 (8.2). Control: 79.3 (8.5) 2. Deprivation: Not stated 3. Ethnicity: Not stated 4. Number of conditions: Not stated 5. Type of condition: Not stated
Indirectness of population	Serious indirectness: older adult
Interventions	(n=152) Intervention 1: CGA - CGA (team). Comprehensive geriatric assessment and subsequent intervention in pre-frail and frail. Intervention group for CGA and appropriate intervention by medication adjustment, exercise instruction, nutrition support, physical rehabilitation, social worker consultation, and specialty referral.. Duration 6 months. Concurrent medication/care: Subjects in the intervention group were screened by CGA and an appropriate intervention program followed when indicated when based on assessment results. The intervention programs were conducted by medical professionals at the community hospital, as well as at appropriate community facilities. The research assistants were skilled nurses trained specially for this study. They used standardised questionnaires as assessment tools to collect information on geriatric syndromes, scores on the mini-mental state examination, and the short-form geriatric depression scale, and nutritional status using the mini nutritional assessment. Screening also included a visual acuity test, the timed up and go test, orthostatic hypotension screening, and the functional reach test. Two board-certified geriatricians independently reviewed the participants' assessment results along with their present and past medical histories, current medication, and recent laboratory data. The treatment provided included

Study	Li 2010⁷⁶⁴
	medication adjustment, exercise instruction, nutrition support, physical rehabilitation, social worker consultation, and specialty referrals. Further details: 1. Post-CGA intervention: CGA + short-term care plan (n=158) Intervention 2: Standard care. The control group received screening evaluation only. Duration 6 months. Concurrent medication/care: none stated
Funding	Academic or government funding (Grant from the National Science Council, Taiwan)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: CGA (TEAM) versus STANDARD CARE	
Protocol outcome 1: Mortality - Actual outcome: Mortality at 6 months; Group 1: 1/152, Group 2: 0/158; Risk of bias: Very high; Indirectness of outcome: No indirectness	
Protocol outcome 2: Functional outcomes (mobility, activities of daily living) - Actual outcome: Barthel Index at 6 months; Group 1: mean 95.6 (SD 14.7); n=129, Group 2: mean 91.6 (SD 20.7); n=140; Barthel Index 0-100 Top=High is good outcome; Risk of bias: Very high; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Health-related quality of life; Patient & carer satisfaction; Length of hospital stay; Unscheduled care; Continuity of care; Admission to care facility; Patient/carer treatment burden

Table 186: Melis 2008

Study (subsidiary papers)	Melis 2008
Intensity subgroup	High
Study type	RCT (Cluster randomised; Parallel)
Number of studies (number of participants)	1 (n=151)
Countries and setting	Conducted in Netherlands; Setting: Netherlands, community.
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 6 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis

Study (subsidiary papers)	Melis 2008
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Lived in own home or retirement home, 70 or older, 1 or more limitations in cognition, instrumental activities of daily living or mental well-being, health problem that recently presented to the physician, request for help due to cognitive disorders/symptoms of dementia/mood disorders/mobility disorders/malnutrition, patient & physician have goal to achieve, MMSE <27 or GARS-3 >24 or MOS-20 mental health <76.
Exclusion criteria	Request for help has an acute nature or purely medical diagnostic issue, MMSE <20 or proven moderate to severe dementia, patient already receiving form of intermediate care from social care/geriatrician, patient on waiting list for nursing home, life expectancy <6 months.
Recruitment/selection of patients	Recruited by primary care physicians when patients presented with problems of cognition, nutrition, behaviour, mood or mobility requiring nursing assessment, coordination of care, therapeutic monitoring or case management.
Age, gender and ethnicity	Age - Range of means: 82.8 (6.6) - 81.7 (5.9). Gender (M:F): 48:113. Ethnicity: Not reported
Further population details	1. Age: >65 years 2. Deprivation: Not applicable / Not stated / Unclear 3. Ethnicity: Not applicable / Not stated / Unclear 4. Number of conditions: Not applicable / Not stated / Unclear 5. Type of condition: Not applicable / Not stated / Unclear
Indirectness of population	Serious indirectness: Age >70, baseline characteristics suggest multimorbid
Interventions	<p>(n=88) Intervention 1: CGA. Geriatric specialist nurse visited the patient at home. Up to 6 visits for additional geriatric evaluation and management were planned within the next 3 months. Starting with a wide multidimensional assessment, the team developed an individualised, integrated treatment plan for each patient. The nurse conducted the main part of the intervention. The nurse and geriatrician made recommendations to the primary care physicians.. Duration 6 months. Concurrent medication/care: Primary care physicians continued usual care. Further details: 1. Post-CGA intervention: CGA + long-term care plan</p> <p>(n=67) Intervention 2: Standard care. Usual care as per primary care physician. Duration 6 months. Concurrent medication/care: Nil else Further details: 1. Post-CGA intervention:</p>
Funding	Academic or government funding

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DUTCH GERIATRIC INTERVENTION PROGRAM versus STANDARD CARE

Protocol outcome 1: Health-related quality of life at Define

- Actual outcome: MOS-20 mental health at 6 months; Risk of bias: High; Indirectness of outcome: No indirectness

Study (subsidiary papers)	Melis 2008
	<ul style="list-style-type: none"> - Actual outcome: MOS-20 physical performance at 3 months; MD 4.3 (95%CI -2.9 to 11.2); Risk of bias: High; Indirectness of outcome: No indirectness - Actual outcome: MOS-20 role functioning at 3 months; MD 4.7 (95%CI -9.8 to 19.3); Risk of bias: High; Indirectness of outcome: No indirectness
	<p>Protocol outcome 2: Mortality at Define</p> <ul style="list-style-type: none"> - Actual outcome: Mortality at 2 years; Group 1: 16/88, Group 2: 18/67; Risk of bias: High; Indirectness of outcome: No indirectness
	<p>Protocol outcome 3: Functional outcomes (mobility, activities of daily living) at Define</p> <ul style="list-style-type: none"> - Actual outcome: GARS-3 at 6 months; MD -1.6 (95%CI -3.9 to 0.7); Risk of bias: High; Indirectness of outcome: No indirectness
Protocol outcomes not reported by the study	Patient & carer satisfaction at Define; Length of hospital stay at Define; Unscheduled care at Define; Continuity of care at Define; Admission to care facility at Define; Patient/carer treatment burden at Define; to be deleted at Define

Table 187: Monteserin 2010

Study (subsidiary papers)	Monteserin 2010 ⁸⁷⁵
Intensity subgroup	Low
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=620)
Countries and setting	Conducted in Spain; Setting: Primary Care
Line of therapy	Adjunctive to current care
Duration of study	Follow up (post intervention): 18 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Inclusion criteria of age>75, scoring high risk of frailty by authors composite score
Stratum	Overall: Patients deemed at high risk of frailty by authors based on composite of multiple scoring systems
Subgroup analysis within study	Unclear: After CGA patients were deemed at risk of frailty or not, results extracted for risk of frailty group only
Inclusion criteria	>75 years old
Exclusion criteria	Concurrent inclusion in another study, diagnosis of terminal disease, institutionalisation, severe cognitive impairment, difficulties in accessing primary health care centre, inability/unwillingness to give consent

Study (subsidiary papers)	Monteserin 2010 ⁸⁷⁵
Recruitment/selection of patients	Random sample from people registered at primary health care centre in Barcelona
Age, gender and ethnicity	Age - Mean (SD): 81.2 years (4.6). Gender (M:F): 40:60. Ethnicity: Not stated
Further population details	Subgroup of patients at risk of frailty when at least 2 of the following conditions were met: age >85, 9 or more points on Gijon scale, 2 or more points on Pfeiffer test, 2 or more points in the Charlson comorbidity index, 1 or more points in the Yesavage Depression scale, 91 or more points in the Barthel index, 12 or more points in the Mini-Nutritional Assessment Short Form, polymedication (higher than the mean number of drugs taken by the study population), more than 1 fall in the last 6 months or suffering daily urinary incontinence in the last 6 months
Indirectness of population	Serious indirectness: Patients deemed at high risk of frailty by authors based on composite of multiple scoring systems, not necessarily multimorbid
Interventions	<p>Intervention (n=151) CGA - CGA by trained nurses including sociodemographic data, health status, sensory evaluation, falls, urinary incontinence, Charlson Index (co-morbidity), Barthel index (functional status), Lawton index (ADLs), 5-Y Depression scale, Pfeiffer's test (mental state), nutritional assessment, Gijon social scale. If patients were deemed at risk of frailty, they had an individual educational session by a geriatrician including an extended visit informing patient about lifestyle changes, making shared plans re: drug therapy, sensory impairment, falls, incontinence aids, dietary modifications etc.. Duration 18 months.</p> <p>Control (n=134) CGA + USUAL CARE - CGA by trained nurses including sociodemographic data, health status, sensory evaluation, falls, urinary incontinence, Charlson Index (co-morbidity), Barthel index (functional status), Lawton index (ADLs), 5-Y Depression scale, Pfeiffer's test (mental state), nutritional assessment, Gijon social scale + usual standard care from their GP, no care plan was formulated and care was not anticipated to change . Duration 18 months.</p> <p>Both groups received a CGA but only the intervention group received any care planning or intervention beyond usual care thereafter.</p>
Funding	Academic or government funding (Sociedad Espanola de Geriatria y Gerontologia)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: CGA + PATIENT SUPPORT versus CGA + USUAL CARE	
Protocol outcome 1: Mortality - Actual outcome: Mortality at 18 months; Group 1: 9/151, Group 2: 13/134; Risk of bias: Very high; Indirectness of outcome: No indirectness	
Protocol outcome 2: Admission to care facility - Actual outcome: Admission to nursing home at 18 months; Group 1: 2/151, Group 2: 3/134; Risk of bias: Very high; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by	Health-related quality of life; Functional outcomes (mobility, activities of daily living); Patient & carer satisfaction; Length of

Study (subsidiary papers)	Monteserin 2010 ⁸⁷⁵
the study	hospital stay; Unscheduled care; Continuity of care ; Patient/carer treatment burden;

Table 188: Senior 2014

Study	Promoting Independence Programmes (PIP) trial: Senior 2014 ¹¹⁰³
Intensity subgroup	Low
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=105)
Countries and setting	Conducted in New Zealand
Line of therapy	Adjunctive to current care
Duration of study	Intervention + follow up: 24 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: older adult (age 65 or over)
Stratum	Outpatient
Subgroup analysis within study	Not applicable
Inclusion criteria	Aged 65 years or older
Exclusion criteria	1) To maintain the person's safety they required immediate permanent residential care placement 2) inability to communicate in English.
Recruitment/selection of patients	The regional geriatric assessment team forwarded the contact details of eligible potential participants to the research team. Assessment service records were audited regularly to ensure all possible eligible participants were referred.
Age, gender and ethnicity	Age - Mean (SD): Intervention: 83.6 (6.9). Control: 81.9 (6.8). Gender (M:F): 46:54. Ethnicity: Not stated
Further population details	1. Age: Mean (SD): Intervention: 83.6 (6.9). Control: 81.9 (6.8) 2. Deprivation: Not stated 3. Ethnicity: Not 4. Number of conditions: Not stated 5. Type of condition: Not applicable / Not stated / Unclear
Indirectness of population	Serious indirectness: older adult
Interventions	(n=52) Intervention 1: CGA. The restorative care service was delivered in short-stay residential care facilities and at participants' residences with the aim of reducing the requirement for permanent residential care. It included a comprehensive geriatric assessment and care plan developed and delivered, initially by a multi-disciplinary team and subsequently by home care assistants.. Duration 24 months. Concurrent medication/care: New health service, 'the Promoting Independence Programmes (PIP)'. The PIP model provided case-managed restorative care delivered within both residential care and at home by a multi-disciplinary team. The PIP case manager's met with key hospital staff prior to the discharge to facilitate seamless transition from the hospital (medical ward or rehabilitation service) to

Study	Promoting Independence Programmes (PIP) trial: Senior 2014¹¹⁰³
	<p>short-term residential care. The case manager met with the older person, explained the service, and conducted a standardised comprehensive geriatric assessment. The older person set meaningful goals that, in conjunction with comprehensive geriatric assessment guided task assessment, directed care plan development. The team included a case manager, nurse, occupational therapist (OT) and physiotherapist, who contributed to development of care plans. The care plan delivered in short-term residential care aimed to restore function and return the older person to living in the community. A key component of the care plan was integration of physical activity by repetitive ADL exercises. Prior to discharge from residential care based rehabilitation, the PIP occupational therapist conducted a home visit to assess the home environment and arranged for any environmental modifications to be made. A family meeting was held at the residential care facility to facilitate discharge. After discharge from residential care, the PIP case manager arranged home support, and the PIP outpatient service delivered care. The older person was visited at home by the PIP rehabilitation assistant for individualised rehabilitation (3-4 times per week over 2 to 3 months), until sufficient progress occurred allowing a handover of the ADL rehabilitation to home support workers employed by another agency. Support workers were trained by PIP rehabilitation assistants in the correct delivery of the programme. The case manager was responsible for liaising with the home support service, health professionals; arranging community support, and holding weekly team meetings. The PIP therapy team completed 3-monthly assessments for care plan modification. If the older person's goal was attained, the older person was monitored only by phone and contacted monthly. If progress waned, they were referred to specialised care.</p> <p>Further details: 1. Post-CGA intervention: CGA + short-term care plan</p> <p>(n=53) Intervention 2: Standard care. The control group were assigned usual care that included community services or permanent placement in residential care. Older people were assessed and service coordinated by a centrally based needs co-ordinator. Duration 24 months. Concurrent medication/care: No other information</p> <p>Further details: 1. Post-CGA intervention: Not applicable / Not stated / Unclear</p>
Funding	Academic or government funding (Department of Health, New Zealand Government)
<p>RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: CGA (TEAM) versus STANDARD CARE</p> <p>Protocol outcome 1: Mortality</p> <ul style="list-style-type: none"> - Actual outcome: Mortality at 24 months; Group 1: 10/52, Group 2: 14/53; Risk of bias: High; Indirectness of outcome: No indirectness - Actual outcome: Mortality (GIV HR) at 24 months; HR 0.94 (95%CI 0.51 to 0.72); Risk of bias: High; Indirectness of outcome: No indirectness <p>Protocol outcome 2: Admission to care facility</p> <ul style="list-style-type: none"> - Actual outcome: Admission to care facility - residential care placements at 24 months; Group 1: 17/52, Group 2: 22/53; Risk of bias: High; Indirectness of outcome: No 	

Study	Promoting Independence Programmes (PIP) trial: Senior 2014 ¹¹⁰³
indirectness - Actual outcome: Admission to care facility (GIV HR) at 24 months; HR 0.63 (95%CI 0.35 to 1.15); Risk of bias: High; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Health-related quality of life ; Functional outcomes (mobility, activities of daily living) ; Patient & carer satisfaction ; Length of hospital stay ; Unscheduled care ; Continuity of care ; Patient/carers treatment burden ; to be deleted

H.6 Self-management

Table 189: Battersby 2013¹⁰³

Battersby 2013 ¹⁰³	Flinders Program trial
Study type	RCT (patient randomised; parallel)
Number of studies (number of participants)	2 (n=77)
Countries and setting	Conducted in Australia; setting: Adelaide metropolitan area, Australia
Line of therapy	Unclear
Duration of study	Follow up (post intervention): 18 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Cardiovascular: intervention 71.7%, comparison 80.6%. Musculoskeletal: intervention 60.9%, comparison 51.6%. Gastrointestinal: intervention 45.7%, comparison 38.7%. Respiratory: intervention 21.7%, comparison 25.8%. Diabetes: intervention 6.5%, comparison 12.9%. Skin conditions: intervention 8.7%, comparison 9.7%. Cancer: intervention 13%, comparison 0. CNS: intervention 4.3% comparison 9.7%. Ear, nose and throat: intervention 8.7%, comparison 3.2%. Genitourinary: intervention 6.5%, comparison 3.2%. Alcohol dependence: intervention 60.9%, comparison 41.9%. PTSD: intervention 97.8%, comparison 41.9%. Major depression: intervention: 76.1%, comparison 83.9%. Generalised anxiety disorder: intervention 13%, comparison 6.5%. Panic disorder: intervention 8.7%, comparison 6.5%.
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Vietnam veteran; having an Alcohol Use Disorders Identification Test (AUDIT) score ≥ 8 ; having a chronic condition;

Battersby 2013 ¹⁰³	Flinders Program trial
	being eligible for veteran medical benefits
Exclusion criteria	Having a debilitating physical or mental condition which would prevent participation in the study
Recruitment/selection of patients	9 month wait-list, opt-in design with Vietnam veterans being informed about the study through their healthcare professionals, Veterans and Veterans Family Counselling Service, Repatriation General Hospital Daw Park, Vietnam veteran ex-service organisations and the media. Interested veterans rang and completed a screening interview with research officer to determine eligibility.
Age, gender and ethnicity	Age - mean (SD): intervention 60.55 (3.4), control 60.18 (2.24). Gender (M:F): 1:0. Ethnicity: not stated
Further population details	1. Age: not applicable/not stated/unclear (intervention 60.55 [3.4], control 60.18 [2.24]). 2. Deprivation: not applicable/not stated/unclear. 3. Ethnicity: not applicable/not stated/unclear. 4. Number of conditions: not applicable/not stated/unclear. 5. Type of conditions: physical and mental conditions
Indirectness of population	No indirectness
Interventions	<p>(n=46) Intervention 1: Self-management programmes. Flinders Program. Aims to engage patient in care by providing structured clinical process for a health professional to use that will motivate the patient to change their behaviour and achieve long lasting medical and psychosocial goal. (1) Completion of Partners in Health (PIH) questionnaire, 14-item, assesses self-management, knowledge, shared decision making, symptom management, adherence to medical management, impact of the condition(s) and lifestyle behaviours, and a Cure and Response (C&R) interview, uses open ended questions to explore same items as PIH. This helps the patient and health professional to decide which of the 14 items require intervention, identify main problems and set medium term goal (6-12 months) and to document a care plan over the next 12 months. (2) Education and self-help materials given out that provide information on how to measure alcohol consumption and steps to reduce alcohol use. (3) SCDSMP - group sessions conducted weekly for 2.5 hours, lasts for 6 weeks, led by peers or health professionals – teaches skills in problems solving, decision making, resource utilisation, managing the patient-provider partnership, action planning, emotional management. Duration 12 months. Concurrent medication/care: none stated.</p> <p>(n=31) Intervention 2: Standard care. Usual care available from public and private medical and mental health services. Duration 12 months. Concurrent medication/care: none stated.</p>
Funding	Academic or government funding (American Department of Veteran's Affairs)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: SELF-MANAGEMENT PROGRAMMES versus STANDARD CARE

Protocol outcome 1: Health-related quality of life

Battersby 2013 ¹⁰³	Flinders Program trial
- Actual outcome: Assessment of Quality of Life (AQoL) at 18 months; MD 0.35 (SD 0.25); risk of bias: low; indirectness of outcome: no indirectness	
Protocol outcome 2: Patient self-efficacy	
- Actual outcome: Partners in Health (PIH) at 18 months; risk of bias: low; indirectness of outcome: no indirectness	
Protocol outcomes not reported by the study	Mortality; functional outcomes (mobility, activities of daily living); patient and carer satisfaction; unplanned hospital admissions; length of hospital stay; continuity metrics; patient/carer treatment burden

Table 190: Blakeman 2014¹⁴⁵

Blakeman 2014 ¹⁴⁵	Bringing Information and Guided Help Together (BRIGHT) trial
Study type	RCT (patient randomised; parallel)
Number of studies (number of participants)	1 (n=436)
Countries and setting	Conducted in United Kingdom; setting: primary care
Line of therapy	Adjunctive to current care
Duration of study	Intervention + follow up: 6 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: number of comorbid long-term conditions: 0 (n=5); 1-2 (n=131); 3-4 (n=192); 5-6 (n=79); 7+ (n=29)
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Eligible patients were registered with 24 general practices in Greater Manchester. Patients coded with an existing clinical diagnosis of stage 3 chronic kidney disease both stages 3a and 3b, with and without proteinuria, were eligible.
Exclusion criteria	Patients were excluded if they were unable to communicate in English, had reduced capacity to provide informed consent or were in receipt of palliative care. Only one person per household was eligible to take part to avoid potential contamination.
Recruitment/selection of patients	Patients were invited through the practice registers at GP practices
Age, gender and ethnicity	Age - mean (SD): 72.1 (9.1). Gender (M:F): 181/255. Ethnicity: White: 98.6%; Non-white: 1.4%.
Further population details	1. Age: older adults (mean age = 72 years). 2. Deprivation: not applicable/not stated/unclear. 3. Ethnicity: 98.6% of participants reported as white. 4. Number of conditions: not applicable/not stated/unclear. 5. Type of condition:

Blakeman 2014¹⁴⁵	Bringing Information and Guided Help Together (BRIGHT) trial
	overall
Indirectness of population	No indirectness
Interventions	<p>(n=215) Intervention 1: Collaborative care. Intervention providing information and telephone-guided access to community support. A key element of the programme was to improve links between different providers of support for health, including professionals, voluntary, and community resources in order to widen the options of self-management support. With a particular focus on the interface between primary care and resources in the community, the BRIGHT intervention aimed to explore the potential of network-focused self-management support in the context of chronic kidney disease (CKD). The intervention provided information about self-management, tailored access to local community resources and telephone-guidance. The BRIGHT intervention was designed to align with patients' routine disease review appointments conducted by participating general practices. Telephone support was available throughout the course of the trial. Both arms had usual access to primary care. Duration 6 months. Concurrent medication/care: the intervention entailed provision of a kidney information guidebook; a booklet and interactive website that tailored access to community resources; and telephone-guided help from a lay health worker. (1) The kidney disease guidebook: provided information based on the experiences of patients, their expressed information needs and medical evidence about treatment options. The guidebook was intended to encourage patients to consider changes they could make to maintain general vascular health in the context of having a diagnosis of early stage CKD. (2) Tailored access to community resources: the booklet and website were designed to address the range of health and social problems related to living with a long-term health problem. PLANS is a needs-led self-assessment tool for users to assess and prioritise their health and social needs, with links to relevant community resources and local support. As well as offering lifestyle options (weight management classes, exercise groups, etc.), PLANS had been designed to increase social contact and promote community support awareness and engagement to sustain independent living. (3) Two telephone calls from a lay health worker, one call at 1-week post-administration of the kidney information guidebook and the PLANS booklet, followed by another call 4-weeks later. For the first call, patients were guided through the PLANS booklet and website and discussed the PLANS results. PLANS and the telephone support were designed to focus on patients' needs, everyday living arrangements, and personal preferences. Patients were offered a set of results of local activities and services. For the second telephone call, patients were asked if they had tried any of the recommended activities.</p> <p>(n=221) Intervention 2: Standard care. Standard care. Duration 6 months. Concurrent medication/care: patients in the control arm were sent the kidney information guidebook and the PLANS booklet with links to the website at the end of the trial period. Both arms had usual access to primary care.</p>
Funding	Academic or government funding (NIHR CLAHRC (Collaboration for Leadership in Applied Health Research and Care) Greater Manchester)

Blakeman 2014 ¹⁴⁵	Bringing Information and Guided Help Together (BRIGHT) trial
<p>RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: COLLABORATIVE CARE versus STANDARD CARE</p> <p>Protocol outcome 1: Health-related quality of life</p> <ul style="list-style-type: none"> - Actual outcome: HRQL - EuroQoL EQ-5D at 6 months; MD 0.05 (95%CI 0.01 to 0.08); risk of bias: very high; indirectness of outcome: no indirectness - Actual outcome: HRQL - EuroQoL EQ-5D at 6 months; group 1: mean 0.71 (SD 0.28); n=179, risk of bias: very high; indirectness of outcome: no indirectness <p>Protocol outcome 2: Functional outcomes (mobility, activities of daily living)</p> <ul style="list-style-type: none"> - Actual outcome: Functional outcomes - Positive & active engagement in life at 6 months; risk of bias: very high; indirectness of outcome: no indirectness - Actual outcome: Functional outcomes - Positive & active engagement in life at 6 months; group 1: mean 66.4 (SD 19.7); n=180, risk of bias: very high; indirectness of outcome: no indirectness - Actual outcome: Functional outcomes - MOS social/role activities limitations at 6 months; risk of bias: very high; indirectness of outcome: no indirectness - Actual outcome: Functional outcomes - MOS social/role activities limitations at 6 months; group 1: mean 73.2 (SD 28.2); n=177, risk of bias: very high; indirectness of outcome: no indirectness 	
Protocol outcomes not reported by the study	Mortality; patient and carer satisfaction; length of hospital stay; unscheduled care; continuity of care; admission to care facility; patient/carers treatment burden

Table 191: Druss 2010³⁷⁷

Druss 2010 ³⁷⁷	Health and Recovery Peer (HARP) programme trial
Study type	RCT (patient randomised; parallel)
Number of studies (number of participants)	1 (n=80)
Countries and setting	Conducted in USA; setting was a Community Mental Health Centre (CMHC)
Line of therapy	Unclear
Duration of study	Follow up (post intervention): 6 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: schizophrenia: intervention 26.8%, comparison 30.8%. Bipolar: intervention 34.1%, comparison 30.8%. Major depression: intervention 22%, comparison 30.8%. PTSD: intervention 17.1%, comparison 5.1%. Hypertension: intervention 60.9%, comparison 64.1%. Arthritis: intervention 56.1%, comparison 41%. Asthma: intervention 24.4%, comparison 20.5%. Heart disease: intervention 24.4%, comparison 20.5%.
Stratum	Overall

Druss 2010 ³⁷⁷	Health and Recovery Peer (HARP) programme trial
Subgroup analysis within study	Not applicable
Inclusion criteria	Patients on the active patient roster at the CMHC, diagnosed with a severe mental illness, have one or more chronic medical condition, and have the capacity to provide informed consent
Exclusion criteria	None
Recruitment/selection of patients	Recruited through waiting rooms and flyers posted in outpatient clinics at 2 facilities
Age, gender and ethnicity	Age - mean (SD): intervention 47.8 (10.1), comparison 48.4 (10.1). Gender (M:F): 24:56. Ethnicity: African American: intervention 73.2%, comparison 92.3%. White: intervention 24.4%, comparison 7.7%. Other: intervention 2.4%, comparison 0.
Further population details	1. Age: overall. 2. Deprivation: Majority of participants described as “poor” (mean annual income = \$7,704; CI = \$2,520 - \$12,306). 3. Ethnicity: Black (>80%) (African American: intervention 73.2%, comparison 92.3%). 4. Number of conditions: not applicable/not stated/ unclear. 5. Type of conditions: comorbid physical and mental conditions.
Indirectness of population	No indirectness
Interventions	<p>(n=41) Intervention 1: Self-management programmes. HARP, an adaption of the Chronic Disease Self-Management Program (CDSMP). Attended up to 6 group sessions led by trained mental health peer specialists. Sessions covered the following: 1. Overview of self-management; 2. Exercise and physical activity; 3. Pain and fatigue management; 4. Healthy eating on a limited budget; 5. Medication management; 6. Finding and working with a regular doctor. Peer educator modelled appropriate behaviours and responses, and participation from each group member helped model behaviour and improve motivation for other members. Attendees taught to develop short term 'action plans' for choosing domains of health behaviour change. This involves identifying a problem that is of particular concern, listing ideas for solving the problem, developing a plan outlining specific short-term goals for improvement. Duration 6 weeks. Concurrent medication/care: none stated.</p> <p>(n=39) Intervention 2: Inactive control intervention. Usual care. Duration 6 weeks. Concurrent medication/care: none stated.</p>
Funding	Academic or government funding (NIMH)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: SELF-MANAGEMENT PROGRAMMES versus INACTIVE CONTROL INTERVENTION

Protocol outcome 1: Health-related quality of life

- Actual outcome: HRQOL at 6 months; risk of bias: low; indirectness of outcome: no indirectness

- Actual outcome: Mental Component Summary QOL at 6 months; risk of bias: low; indirectness of outcome: no indirectness

Druss 2010 ³⁷⁷	Health and Recovery Peer (HARP) programme trial
<p>Protocol outcome 2: Functional outcomes (mobility, activities of daily living) - Actual outcome: Minutes per week spent in moderate/vigorous exercise at 6 months; risk of bias: low; indirectness of outcome: no indirectness</p> <p>Protocol outcome 3: Patient self-efficacy - Actual outcome: Patient Activation Measure (PAM) at 6 months; risk of bias: low; indirectness of outcome: no indirectness</p>	
Protocol outcomes not reported by the study	Mortality; patient and carer satisfaction; unplanned hospital admissions; length of hospital stay; continuity metrics; patient/carer treatment burden

Table 192: Dunbar 2014³⁸⁰

Dunbar 2014 ³⁸⁰	
Study type	RCT (patient randomised; parallel)
Number of studies (number of participants)	1 (n=61)
Countries and setting	Conducted in USA
Line of therapy	Unclear
Duration of study	Follow up (post intervention): 3 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Diabetes type II 100%, CHF 100%, peripheral vascular disease 11.9%, renal disease 31.1%
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Admitting diagnosis of heart failure with left ventricular systolic dysfunction; concomitant diabetes type II treated with oral agents; aged 21-80 years; planned discharge from hospital to home setting; fluent in English; without cognitive impairment
Exclusion criteria	Haemodynamically significant angina pectoris; renal failure; HF secondary to untreated medical condition; planned cardiac surgery; impaired cognition because of neurologic comorbidity; psychiatric diagnosis; uncorrected visual or hearing problem, insulin therapy, depressive symptoms (PHQ-9 > 10), evaluation for transplant or ventricular assist devices

Dunbar 2014³⁸⁰	
Recruitment/selection of patients	During an inpatient HF exacerbation at 1 of 3 hospitals
Age, gender and ethnicity	Age - mean (SD): 59.7 (10.6). Gender (M:F): 67:33. Ethnicity: 60% black
Further population details	1. Age: not applicable/not stated/unclear. 2. Deprivation: not applicable/not stated/unclear. 3. Ethnicity: not applicable/not stated/unclear. 4. Number of conditions: 2 chronic conditions. 5. Type of conditions: only physical conditions.
Indirectness of population	No indirectness
Interventions	<p>(n=46) Intervention 1: Self-management programmes. Integrated heart failure and diabetes education and self-management support delivered by trained research nurses. Intervention was developed to address the themes of self-care dilemmas identified through prior focus groups. Intervention nurse uses flip chart and script for educational sessions with purpose of increasing knowledge and skills related to diet, medication taking, symptom monitoring, physical activity. Patients given an intervention resource notebook which presented all information in written form and additional materials to which they could refer to in the home setting. Two 30-40 minutes individual education/counselling sessions delivered before discharge from hospital provided at bedside. Provision of self-care brochures (one on heart failure, one on diabetes). Follow-up education and counselling for integrated self-care was provided with a 15 minute phone call 48-72 hours after discharge during which verification of the medication regimen, filling of prescriptions, and daily self-monitoring were emphasised. During clinic visit 2-4 weeks after discharge the research nurse assessed for difficulty in performing self-care behaviours of diet, physical activity, and symptoms and self-monitoring and provided reinforcing information and guidance. Duration 90 day follow-up. Concurrent medication/care: smoking cessation referrals made for those who reported smoking or tobacco use.</p> <p>(n=19) Intervention 2: Standard care. Usual care. Duration: 90 day follow-up. Concurrent medication/care: provision of self-care brochures (one on heart failure, one on diabetes).</p>
Funding	Academic or government funding (National Institute of Nursing Research grant, National Centre for Advancing Translational Sciences of the National Institutes of Health)
<p>RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: SELF-MANAGEMENT PROGRAMMES versus STANDARD CARE</p> <p>Protocol outcome 1: Health-related quality of life</p> <ul style="list-style-type: none"> - Actual outcome: Minnesota Living with Heart Failure (MLWHF) at 90 days; risk of bias: high; indirectness of outcome: no indirectness - Actual outcome: Audit of Diabetes Dependent Quality of Life (ADDQOL) at 90 days; risk of bias: high; indirectness of outcome: no indirectness <p>Protocol outcome 2: Patient self-efficacy</p>	

Dunbar 2014³⁸⁰	
<ul style="list-style-type: none"> - Actual outcome: Self-efficacy (Self-Care in Heart Failure Index (SCHFI) confidence scores) at 90 days; risk of bias: high; indirectness of outcome: no indirectness - Actual outcome: Self-efficacy (Perceived Diabetes Self-Management Scale (PDSMS)) at 90 days; risk of bias: high; indirectness of outcome: no indirectness 	
Protocol outcomes not reported by the study	Mortality; functional outcomes (mobility, activities of daily living); patient and carer satisfaction; unplanned hospital admissions; length of hospital stay; continuity metrics; patient/carers treatment burden

Table 193: Dunbar 2015³⁸¹

Study	Dunbar 2015 ³⁸¹
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=134)
Countries and setting	Conducted in USA
Line of therapy	Unclear
Duration of study	Intervention + follow up: 6 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: People with comorbid heart failure and diabetes
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Define
Exclusion criteria	Define
Recruitment/selection of patients	Enrolled during hospitalisation or within 3 months of discharge
Age, gender and ethnicity	Age - Mean (SD): 57.4 (10.6). Gender (M:F): Define. Ethnicity: African American 69.4%
Further population details	1. Age: Unclear (21-80 years). 2. Deprivation: Unclear (Education high school or less 37.3%). 3. Ethnicity: Ethnicity as defined by studies: (African American 69.4%). 4. Number of conditions: 2 chronic conditions (heart failure and type II diabetes). 5. Type of conditions: Only physical conditions
Indirectness of population	No indirectness
Interventions	(n=70) Intervention 1: Self-management programmes - Self-management programmes. 7 sessions: immediately after enrolment; 48-72 hours afterwards; 7 days; 14 days; 1, 2, and 4.5 months. A trained research nurse provided an overview of the content with the use of a semi structured script and coordinated set of PowerPoint illustrations viewed on a laptop computer. Corresponding written materials were developed at a 6th-grade reading level and

	<p>provided in the form of an “HF-DM tool kit” to be used at home. HF and DM knowledge questionnaires were used as part of the pre-teaching assessment, which allowed the nurse to tailor the information to the patient's need. Time was allowed for individual questions and goal setting in each category of self-care. Content included: Overview of HF and DM; brief description of how HF and DM interact and worsen the other condition; Expected self-care for HF and DM; potential conflicts in HF and DM self-care; Diet: principles for an integrated low sodium and carbohydrate diet; portion control, label reading for HF and DM, and sample menus; eating out with HF-DM; Medications: overview of HF and DM medication goals; individualized HF-DM medications, potential medication conflicts, over-the-counter medications, and medication-taking behaviour to promote adherence; Symptom monitoring: how to assess, interpret, and report edema, fatigue, shortness of breath, sleep difficulties, depressive symptoms, and mood; Self-monitoring: blood glucose and weight; how to interpret together; relationship to HF-DM symptoms; Physical activity: rationale, frequency, duration, safety (physical and effect on glucose levels), walking and alternate activities; Oral and foot care. Educational strategies included: Individual teaching and discussion with illustrated content; Coordinated written materials; Health literacy: 6th-grade reading level and multiple illustrations; Demonstration, return demonstration (e.g., label reading for portion, sodium, carbohydrates, symptom and self-monitoring interpretation); Questions and answers; Repetition of content, recheck of learning (follow-up home and clinic visits, telephone calls). Behavioural strategies included: Goal setting and evaluation; Symptom and self-monitoring; Problem solving; Seeking support; Motivational messages.. Duration 4.5 months. Concurrent medication/care: None</p> <p>(n=64) Intervention 2: Standard care. Usual care. Duration 4.5 months. Concurrent medication/care: Provided with informational brochures on “Taking Control of Your Heart Failure” (developed by the Heart Failure Society of America) and “Four Steps to Control Your Diabetes for Life” (developed by the National Diabetes Education Program).</p>
Funding	Academic or government funding (National Institutes of Health National Institute of Nursing Research grant; National Center for Advancing Translational Sciences of the National Institutes of Health; Atlanta Veterans Administration Medical Center)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: INTERGRATED HF-DM SELF-CARE GROUPS versus STANDARD CARE	
Protocol outcome 1: Health-related quality of life	
- Actual outcome: EQ-5D at 6 months; Group 1: mean 0.75 (SD 0.2); n=54, Group 2: mean 0.69 (SD 0.2); n=54. Risk of bias: ; Indirectness of outcome: No indirectness	
Protocol outcome 2: Functional outcomes (mobility, activities of daily living)	
- Actual outcome: Six minute walk test at 6 months; Group 1: mean 84.4 Feet (SD 297.6); n=33, Group 2: mean 39.2 Feet (SD 336.7); n=33; Risk of bias: High; Indirectness of outcome: No indirectness	
- Actual outcome: Community Healthy Activities Model Program for Seniors (CHAMPS) score >6 at 6 months; Group 1: 40/54, Group 2: 30/54; Risk of bias: High; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Mortality; Patient and carer satisfaction; Unplanned hospital admissions; Length of hospital stay; Continuity;

	Patient/carer treatment burden; Patient self-efficacy
--	---

Table 194: Eakin 2007³⁸²

Eakin 2007 ³⁸²	The Resources for Health Trial
Study type	RCT (patient randomised; parallel)
Number of studies (number of participants)	1 (n=200)
Countries and setting	Conducted in USA; setting: primary care
Line of therapy	Mixed line
Duration of study	Intervention time: 6 months
Method of assessment of guideline condition	Partially adequate method of assessment/diagnosis: participants with only one chronic condition: intervention, n= 8 (7.9%); control, n= 17 (17.2%)
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Diagnosis of one or more chronic condition, age 30 years and over, having a telephone, and not planning to move from the area during the study's time frame
Exclusion criteria	None specified
Recruitment/selection of patients	Names and contact information for all patients meeting age and chronic condition criteria were obtained from the clinic medical records database. Letters were sent from clinic providers to patients. Included in the letter was a stamped addressed postcard to be returned by those who did not want to be contacted. Patients for whom postcards had not been returned were followed up with a phone call. Recruitment calls were made by bilingual research assistants. The study was conducted at a community health centre that provides health care services to low-income and medically underserved individuals in an urban area. The clinic sample is largely Spanish-speaking and have generally spent fewer than 5 years living in the United States.
Age, gender and ethnicity	Age - mean (SD): 49.51 (13.01). Gender (M:F): 43/157. Ethnicity: Hispanic/Latino: intervention, n= 81; control, n=69.
Further population details	1. Age: not applicable/not stated/unclear. 2. Deprivation: not applicable/not stated/unclear. 3. Ethnicity: not applicable/not stated/unclear. 4. Number of conditions: not applicable/not stated/unclear. 5. Type of conditions: not applicable/not stated/unclear.
Extra comments	Adults with greater than one or more chronic condition for which a lifestyle intervention focused on physical activity and diet would be appropriate (that is, hypertension, chronic pain, hypercholesterolemia, depression, type 2 diabetes, osteoarthritis, obesity, chronic lung disease, heart disease, osteoporosis, hepatitis, history of cancer, previous stroke, multiple sclerosis).

Eakin 2007 ³⁸²	The Resources for Health Trial
Indirectness of population	Serious indirectness: Participants with only one chronic condition: intervention, n= 8 (7.9%); control, n= 17 (17.2%)
Interventions	<p>(n=99) Intervention 1: Standard care. Patients in the usual care condition were mailed a local area community resources guide and 3 newsletters on basic financial management (that is, careers and employment, budgeting skills, and establishing credit). Duration 6 months. Concurrent medication/care: no other information provided.</p> <p>(n=101) Intervention 2: Self-management programmes . Diet and physical activity intervention with self-management support delivered by a health educator; involving 2 face-to-face (60-90 minutes) meetings three months apart, 3 follow-up phone calls, and 3 newsletters. Duration 6 months. Concurrent medication/care: intervention was based on behavioural-ecological approach to chronic disease self-management that emphasises assessment, feedback, goal setting, and problem solving; as well as on social-ecological theory with a focus on identification of multi-level/community supports for health behaviour change. The intervention was culturally adapted and translated into Spanish for an urban, low-income, largely Latino patient population. The intervention was conducted by an experienced, bilingual, health educator, and involved face-to-face visits (60-90 minutes) 3 months apart, 3 follow-up calls, and 3 newsletters tailored to the behavioural goals of each participant. The face-to-face visits took place either at the clinic or in the participant's home. Due to low levels of literacy, the use of visual aids was emphasised. The intervention protocol followed the 5 As approach (Ask, Assess, Advise, Agree, Arrange). Participants received information on national physical activity and dietary recommendations. Participants then chose a self-management goal related to physical activity or healthy eating, and identified one or two types of social-environmental resources they could use to help them reach their goal. At the conclusion of the session, participants received a 1-page goal sheet summarising their personal action plan. At 2 and 6 weeks after the initial visit, the health educator made a brief follow-up call to reinforce progress toward goal attainment and to problem-solving barriers. During the second face-to-face visit, participants were encouraged to consider setting a goal for the second target behaviour. A third follow-up phone call, the last point of contact, occurred 2 weeks after to discuss maintenance of behaviour change. To reinforce behaviour change goals, 3 tailored newsletters were mailed to participants over the course of the 6-month intervention, to remind participants of their goals, address barriers and suggest examples of multilevel support resources.</p>
Funding	Other (funded by Robert Wood Johnson Foundation Grant for its national program on Improving Chronic Illness Care)
<p>RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: SELF-MANAGEMENT versus STANDARD CARE</p> <p>Protocol outcome 1: Functional outcomes (mobility, activities of daily living) - Actual outcome: Change minutes walking/week at 6 months; risk of bias: high; indirectness of outcome: no indirectness</p>	

Eakin 2007³⁸²	The Resources for Health Trial
Protocol outcomes not reported by the study	Health-related quality of life; mortality; patient and carer satisfaction; unplanned hospital admissions; length of hospital stay; continuity metrics; patient/carer treatment burden; patient self-efficacy

Table 195: Friedman 2014⁴⁵⁷

Friedman 2014⁴⁵⁷	Effects of a home visiting nurse intervention versus care as usual on individual activities of daily living: a secondary analysis of a randomised controlled trial: Friedman 2014⁴⁵⁷
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=766)
Countries and setting	Conducted in USA; Community, West Virginia, Ohio and New York State
Line of therapy	Adjunctive to current care
Duration of study	Follow up (post intervention): 22 months
Method of assessment of guideline condition	No information on morbidity but average age of patients 77.7
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Needing help with 2 or more ADLs or 3 or more instrumental ADLs, recent significant healthcare use, living in the community, enrolled in Medicare Part A & B
Exclusion criteria	None stated
Recruitment/selection of patients	Via primary care physicians
Age, gender and ethnicity	Age - Mean (SD): 77.7 (11.4). Gender (M:F): 239:527. Ethnicity: 96% white
Further population details	1. Age: >65 years (Mean age 77). 2. Deprivation: Low SES (85% have a household income of <\$30,000pa). 3. Ethnicity: White (>80%) (96% white). 4. Number of conditions: more than 3 chronic conditions (4.4 mean number of chronic conditions). 5. Type of conditions: Not applicable / Not stated / Unclear (Not stated but generally frail and with ADL difficulties).
Extra comments	Population is a secondary analysis of data from Medicare Primary Care Development Corporation (PCDC) Demonstration originally designed to compare nurse interventions with no nurse interventions on patient satisfaction, empowerment and disability status.
Indirectness of population	No indirectness
Interventions	(n=382) Intervention: Home visiting nurse visited patients for an hour in their home once a month for 24 months or until study withdrawal. HVNs empowered patients and educated them on using behaviour change models to facilitate

Friedman 2014 ⁴⁵⁷	Effects of a home visiting nurse intervention versus care as usual on individual activities of daily living: a secondary analysis of a randomised controlled trial: Friedman 2014 ⁴⁵⁷
	<p>chronic disease self-management. HVNs reviewed medication at each visit. HVNs used the PRECEDE-PROCEED health education planning model to organise disease prevention, health promotion, chronic disease self-management and health behaviour change. There was "often" telephone follow-up after the home visit. Hands-on nursing care (e.g. dressing changes) was minimal unless the patient was high risk. HVNs had prior special training in geriatrics and exercise education. Duration 24 months or until death/withdrawal. Concurrent medication/care: Usual care</p> <p>(n=384) Control group: Usual care of all types (hospital, nursing home, home care and ambulatory) as reimbursed by third parties or self-pay. These included home visits as usually provided by Medicare, other third party payers and self-pay. Duration 24 months. Concurrent medication/care: Usual care</p>
Funding	Academic or government funding (AHRQ)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: HVN versus STANDARD CARE	
<p>Protocol outcome 1: Mortality</p> <p>- Actual outcome: Mortality at 24 months; Group 1: 43/237, Group 2: 47/262; Risk of bias: Very high; Indirectness of outcome: No indirectness</p>	
<p>Protocol outcome 2: Functional outcomes (mobility, activities of daily living)</p> <p>- Actual outcome: Difficulty with bathing - some difficulty at 22 months; OR 0.58 (95%CI 0.37 to 0.9) (P value <0.05); Risk of bias: Very high; Indirectness of outcome: No indirectness</p> <p>- Actual outcome: Difficulty with bathing - great difficulty at 22 months; OR 0.40 (95%CI 0.2 to 0.81) (P value <0.01); Risk of bias: Very high; Indirectness of outcome: No indirectness</p> <p>- Actual outcome: Difficulty with dressing - some difficulty at 22 months; OR 0.75 (95%CI 0.48 to 1.17); Risk of bias: Very high; Indirectness of outcome: No indirectness</p> <p>- Actual outcome: Difficulty with dressing - great difficulty at 22 months; OR 0.39 (95%CI 0.18 to 0.82) (P value <0.01); Risk of bias: Very high; Indirectness of outcome: No indirectness</p> <p>- Actual outcome: Difficulty with eating - some difficulty at 22 months; OR 0.84 (95%CI 0.5 to 1.43); Risk of bias: Very high; Indirectness of outcome: No indirectness</p> <p>- Actual outcome: Difficulty with eating - great difficulty at 22 months; OR 0.36 (95%CI 0.1 to 1.26); Risk of bias: Very high; Indirectness of outcome: No indirectness</p> <p>- Actual outcome: Difficulty with toileting - some difficulty at 22 months; OR 0.7 (95%CI 0.44 to 1.12); Risk of bias: Very high; Indirectness of outcome: No indirectness</p> <p>- Actual outcome: Difficulty with toileting - great difficulty at 22 months; OR 0.76 (95%CI 0.27 to 2.09); Risk of bias: Very high; Indirectness of outcome: No indirectness</p> <p>- Actual outcome: Difficulty with transferring - some difficulty at 22 months; OR 1.14 (95%CI 0.72 to 1.79); Risk of bias: Very high; Indirectness of outcome: No indirectness</p> <p>- Actual outcome: Difficulty with transferring - great difficulty at 22 months; OR 0.82 (95%CI 0.35 to 1.9); Risk of bias: Very high; Indirectness of outcome: No indirectness</p>	

Friedman 2014 ⁴⁵⁷	Effects of a home visiting nurse intervention versus care as usual on individual activities of daily living: a secondary analysis of a randomised controlled trial: Friedman 2014 ⁴⁵⁷
- Actual outcome: Difficulty with walking - some difficulty at 22 months; OR 0.9 (95%CI 0.53 to 1.54); Risk of bias: Very high; Indirectness of outcome: No indirectness - Actual outcome: Difficulty with walking - great difficulty at 22 months; OR 0.76 (95%CI 0.34 to 1.69); Risk of bias: Very high; Indirectness of outcome: No indirectness "	
Protocol outcomes not reported by the study	Health-related quality of life ; Patient and carer satisfaction ; Unplanned hospital admissions ; Length of hospital stay ; Continuity metrics ; Patient/carers treatment burden ; Patient self-efficacy

Table 196: Garvey 2015⁴⁷⁴

Study	Garvey 2015 ⁴⁷⁴
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=50)
Countries and setting	Conducted in Irish Republic
Line of therapy	Unclear
Duration of study	Intervention + follow up: 6 weeks + 2 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: People with 2 or more chronic conditions
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Aged over 18 years; two or more chronic conditions; minimum 4 repeat prescriptions
Exclusion criteria	None stated
Recruitment/selection of patients	Family practitioners and other primary care clinicians in the area were emailed with information and study inclusion criteria and encourage to refer any eligible patients over a three month period (December 2013 - February 2013)
Age, gender and ethnicity	Age - Median (range): intervention 65 (50-83); control 67.5 (42-84). Gender (M:F): 34.6:65.4. Ethnicity: Not reported
Further population details	1. Age: Unclear (Aged over 18 years). 2. Deprivation: Unclear (completed secondary education: intervention 26.9%; control 29.2%). 3. Ethnicity: Not stated. 4. Number of conditions: Unclear (median number of conditions (range): intervention 4 (2-9); control 5 (2-9)). 5. Type of conditions: Physical and mental conditions
Indirectness of population	No indirectness
Interventions	(n=26) Intervention 1: Self-management programmes - Self-management programmes. Occupational therapy led self-management support programme for people with multimorbidity (OPTIMAL) delivered in primary care. OPTIMAL is led and facilitated by occupational therapy but incorporates elements of peer support available through the group

Study	Garvey 2015 ⁴⁷⁴
	<p>format. OPTIMAL has the following 4 elements: weekly group meetings for a 6 week period; occupational therapy focus; peer support; goal setting and prioritization based on patient preferences. Occupational therapy interventions to support patient self-management used in the groups include: self-management; fatigue and energy management; managing stress and anxiety and maintaining mental health and well-being; keeping physically active; healthy eating; managing medications; effective communication strategies; goal setting. One of the weekly sessions incorporated education on physical activity delivered by a physiotherapist and another incorporated medicines management, delivered by a pharmacist. . Duration 6 weeks. Concurrent medication/care: None stated</p> <p>(n=24) Intervention 2: Standard care. People allocated to control were placed on a waiting list and were invited to attend an OPTIMAL course following trial complement in their local occupational therapy department. Duration 6 weeks. Concurrent medication/care: None stated</p>
Funding	Academic or government funding (Health Research Board of Ireland funded Primary Care Research Centre)
<p>RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: SELF-MANGEMENT PROGRAMMES versus STANDARD CARE</p> <p>Protocol outcome 1: Health-related quality of life - Actual outcome: EQ-VAS at 2 weeks; Group 1: mean 65.73 (SD 20.18); n=22, Group 2: mean 50.5 (SD 16.3); n=22; Risk of bias: High; Indirectness of outcome: No indirectness</p> <p>Protocol outcome 2: Functional outcomes (mobility, activities of daily living) - Actual outcome: Canadian Occupational Performance Measure (COPM): satisfaction at 2 weeks; Group 1: mean 5.57 (SD 1.99); n=22, Risk of bias: High; Indirectness of outcome: No indirectness - Actual outcome: Nottingham Extended Activities of Daily Living (NEADL) at 2 weeks; Group 1: mean 47.18 (SD 11.87); n=22, Risk of bias: High; Indirectness of outcome: No indirectness - Actual outcome: Canadian Occupational Performance Measure (COPM): performance at 2 weeks; Group 1: mean 5.77 (SD 1.83); n=22, Risk of bias: High; Indirectness of outcome: No indirectness</p> <p>Protocol outcome 3: Unplanned hospital admissions - Actual outcome: Hospital admissions at 2 weeks; Group 1: mean 0.21 (SD 0.42); n=22, Group 2: mean 0.15 (SD 0.37); n=22; Risk of bias: High; Indirectness of outcome: No indirectness</p> <p>Protocol outcome 4: Patient self-efficacy - Actual outcome: Stanford Chronic Disease Self-Efficacy 6-item Scale at 2 weeks; Group 1: mean 6.79 (SD 1.51); n=22, Risk of bias: High; Indirectness of outcome: No indirectness</p>	

Study	Garvey 2015⁴⁷⁴
Protocol outcomes not reported by the study	Mortality; Patient and carer satisfaction; Length of hospital stay; Continuity metrics; Patient/carers treatment burden

Table 197: Gitlin 2006⁴⁹¹ (Gitlin 2009⁴⁸⁹, Gitlin 2006⁴⁹⁰)

Gitlin 2006⁴⁹¹ (Gitlin 2009⁴⁸⁹, Gitlin 2006⁴⁹⁰)	ABLE programme trial
Study type	RCT (patient randomised; parallel)
Number of studies (number of participants)	1 (n=319)
Countries and setting	Conducted in USA
Line of therapy	Mixed line
Duration of study	Intervention + follow up: Intervention: 12 months. Follow-up: 48 months.
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: mean number of health conditions: interventions, 7.1/control, 6.7. 84% arthritis, 71% hypertension, 43% cataracts or macular degeneration, 39% cardiovascular problems, 23% diabetes mellitus.
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	All participants were aged 70 or older, cognitively intact (Mini Mental State Examination [MMSE] score 423 on a scale ranging from 0 to 30) and English speaking, were not receiving home care, and reported the need for help or difficulties with two IADLs (instrumental activities of daily living) or one or more ADLs (activities of daily living).
Exclusion criteria	None specified
Recruitment/selection of patients	Participants were recruited from an area agency on ageing, media announcements, and posters at senior housing and community settings
Age, gender and ethnicity	Age - mean (SD): 79 (5.925). Gender (M:F): 58/261. Ethnicity: intervention: white 53.1%, African American 45.0%, other 1.9%. Control: white 52.2%, African American 45.9%, other 1.9%.
Further population details	1. Age: not applicable/not stated/unclear. 2. Deprivation: not applicable/not stated/unclear. 3. Ethnicity: not applicable/not stated/unclear. 4. Number of conditions: not applicable/not stated/unclear. 5. Type of conditions: not applicable/not stated/unclear.
Indirectness of population	No indirectness
Interventions	(n=159) Intervention 1: Standard care. Participants assigned to the no-treatment control group did not receive any intervention contact. At the conclusion of the 12-month follow-up interview, control participants were provided with educational materials on home safety and safe performance techniques. Duration 12 months. Concurrent

Gitlin 2006⁴⁹¹ (Gitlin 2009⁴⁸⁹, Gitlin 2006⁴⁹⁰)	ABLE programme trial
	<p>medication/care: no more information provided.</p> <p>(n=160) Intervention 2: Self-management programmes. Multicomponent home intervention (the ABLE programme) delivered by occupational therapist (5 contacts, 4x face-to-face for 90 minutes and 1x 20 minute telephone contact) and physical therapist (90 minutes), aimed at reducing functional difficulties; over 6 months, followed by 6 month follow-up and 3 telephone contacts and final home visit. Due to considerable variability in home environments and functional difficulties, specific control-orientated strategies were individualised to the needs of participants, although the intervention was standardised in that each participant received 4 treatment components (education and problem-solving; home modification; energy conserving techniques; and balance, muscle strengthening, and fall-recovery techniques) for specific targeted functional areas. Duration 12 months. Concurrent medication/care: intervention goal was to compensate for declining abilities by training in the use of control-enhancing strategies including cognitive (problem-solving, reframing), behavioural (pace self, sit instead of stand to perform tasks), and environmental (grab bars) modifications. Occupational therapists (OTs) initially met with participants and conducted a semi-structured clinical interview to identify and prioritise problem areas. For each targeted area, an OT observed the participant's performance for safety, efficiency, and difficulty and presence of environmental barriers. In subsequent sessions, the OT engaged the participant in problem solving to identify behavioural and environmental contributors to performance difficulties. Specific strategies were derived and equipment options provided. In the fourth session, the physical therapist (PT) provided balance and muscle strengthening and fall-recovery techniques. In the fifth session (telephone), the OT reinforced strategy use; and in the sixth session, the OT reviewed problem solving, refined strategy use, and provided education and resources to address future needs for environmental adjustments. Before the sixth contact, home modifications (grab bars, rails, raised toilet seats) were installed. Over the following 6 months, OTs conducted 3 telephone calls to reinforce the use of intervention-derived strategies and generalise these strategies to new problem areas. A final home visit was conducted to obtain closure. Interventionists were licensed therapists with 1 or more years of home care experience, having received 35 hours of training. Treatment intervention was monitored and maintained in supervision meetings held every other week in which cases were systematically presented. Interventionists also submitted taped treatment sessions for review.</p>
Funding	Academic or government funding (National Institute on Aging grant)
<p>RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: SELF-MANAGEMENT versus STANDARD CARE</p> <p>Protocol outcome 1: Mortality - Actual outcome: Mortality at 4 years from study entry; HR 0.76 (95%CI 0.48 to 1.2) calculated – from logrank P-value; risk of bias: low; indirectness of outcome: no indirectness</p>	

Gitlin 2006 ⁴⁹¹ (Gitlin 2009 ⁴⁸⁹ , Gitlin 2006 ⁴⁹⁰)	ABLE programme trial
<p>- Actual outcome: Mortality at 2 years from study entry; HR 0.4 (95%CI 0.18 to 0.86) calculated – from logrank P-value; risk of bias: low; indirectness of outcome: no indirectness</p> <p>- Actual outcome: Mortality at 3 years from study entry; HR 0.74 (95%CI 0.44 to 1.24) calculated – from logrank P-value; risk of bias: low; indirectness of outcome: no indirectness</p>	
<p>Protocol outcome 2: Functional outcomes (mobility, activities of daily living)</p> <p>- Actual outcome: ADL (mean difficulty across 6 items: dressing above waist, dressing below waist, grooming, bathing/showering, toileting, feeding) at 6 months; risk of bias: high; indirectness of outcome: no indirectness</p> <p>- Actual outcome: Mobility (mean difficulty across 6 items: getting in/out of car, walking indoors, walking one block, climbing one flight of stairs, moving in/out chair, moving in/out of bed) at 6 months; risk of bias: high; indirectness of outcome: no indirectness</p> <p>- Actual outcome: IADL (mean difficulty across 6 items: light housework, shopping, preparing meals, managing money, telephone use, taking medications) at 6 months; risk of bias: high; indirectness of outcome: no indirectness</p>	
<p>Protocol outcome 3: Patient self-efficacy</p> <p>- Actual outcome: Functional self-efficacy (mean confidence in managing difficulties across 17 items: ADLs, IADLs and mobility) at 6 months; risk of bias: high; indirectness of outcome: no indirectness</p>	
Protocol outcomes not reported by the study	Health-related quality of life; patient and carer satisfaction; unplanned hospital admissions; length of hospital stay; continuity metrics; patient/carers treatment burden

Table 198: Goldberg 2013⁴⁹⁷

Goldberg 2013 ⁴⁹⁷	Living Well trial
Study type	RCT (patient randomised; parallel)
Number of studies (number of participants)	1 (n=63)
Countries and setting	Conducted in USA; setting: 1 outpatient clinic, 3 psychiatric rehabilitation day programmes in Baltimore area
Line of therapy	Unclear
Duration of study	Intervention time: 13 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: serious mental illness and at least 1 chronic general medical condition (mean 2.6, SD 1.5)
Stratum	Overall
Subgroup analysis within study	Not applicable

Goldberg 2013 ⁴⁹⁷	Living Well trial
Inclusion criteria	Diagnosis of a schizophrenia spectrum disorder or bipolar disorder with psychotic features; diagnosis of at least one chronic general medical condition (for example diabetes, asthma, COPD, CV disease, arthritis); community residence; capacity to provide consent
Exclusion criteria	None stated
Age, gender and ethnicity	Age - mean (SD): 49.5 (9.1). Gender (M:F): 10:11. Ethnicity: Caucasian n=18, Black n=42, Mixed race n=3.
Further population details	1. Age: not applicable/not stated/unclear. 2. Deprivation: not applicable/not stated/unclear. 3. Ethnicity: not applicable/not stated/unclear. 4. Number of conditions: not applicable/not stated/unclear. 5. Type of conditions: physical and mental conditions.
Indirectness of population	No indirectness
Interventions	<p>(n=32) Intervention 1: Self-management programmes. Living Well, modified version of Chronic Disease Self-Management Programme. 13 sessions, of 60-75 minutes each, delivered by 2 mental health peers or mental health provider and a peer co-leader. Sessions 1-3 focus on basic strategies of self-management including action planning, peer feedback and support, modelling and problem solving. Remaining sessions focus on training in specific disease management techniques and the application of these skills to the topics of nutrition, exercise, sleep, medication management, addictive behaviours, and coordination of medical services. Between sessions peer facilitators telephoned group participants to review progress on their weekly action plan. Materials including a tool to track action plans and self-management goals. Complete a personal health workbook. Module focusing on communicating with medical providers. Curriculum addresses interconnections between physical and emotional wellbeing, how serious mental illness can affect general medical status and vice versa. 2 monthly booster sessions held in 2 months after intervention. Duration 13 weeks. Concurrent medication/care: none stated.</p> <p>(n=31) Intervention 2: Standard care. Usual care. Duration 13 weeks. Concurrent medication/care: none stated.</p>
Funding	Academic or government funding (NIMH)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: SELF-MANAGEMENT PROGRAMMES versus STANDARD CARE

Protocol outcome 1: Functional outcomes (mobility, activities of daily living)

- Actual outcome: SF-12 general health functioning at 2 months; risk of bias: high; indirectness of outcome: no indirectness

- Actual outcome: Instrument to Measure Self-Management – physical activity at 2 months; risk of bias: high; indirectness of outcome: no indirectness

Protocol outcome 2: Unplanned hospital admissions

Goldberg 2013⁴⁹⁷	Living Well trial
<p>- Actual outcome: Use of emergency department for medical services at 2 months; risk of bias: high; indirectness of outcome: no indirectness</p> <p>Protocol outcome 3: Patient self-efficacy</p> <p>- Actual outcome: Self-Management Self-Efficacy Scale at 2 months; risk of bias: high; indirectness of outcome: no indirectness</p> <p>- Actual outcome: Patient Activation Scale - activation level at 2 months; risk of bias: high; indirectness of outcome: no indirectness</p>	
Protocol outcomes not reported by the study	Health-related quality of life; mortality; patient and carer satisfaction; length of hospital stay; continuity metrics; patient/carer treatment burden

Table 199: Hochhalter 2010⁵⁹²

Hochhalter 2010⁵⁹²	
Study type	RCT (patient randomised; parallel)
Number of studies (number of participants)	1 (n=79)
Countries and setting	Conducted in USA; setting: primary care
Line of therapy	Adjunctive to current care
Duration of study	Intervention + follow up: intervention ran during 3 months following baseline data, follow-up at 6 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: treated for at least two of seven qualifying chronic illnesses (arthritis, lung disease, heart disease, diabetes, hypertension, depression, osteoporosis)
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	65 years of age or older and had been treated for at least two of seven chronic illnesses, including: arthritis, lung disease, heart disease, diabetes, hypertension, depression, and osteoporosis defined by International Classification of Diseases (ICD-9) codes. Participants had received treatment for the qualifying illnesses in the 12 months prior to baseline, communicated in English for healthcare interactions, had access to a telephone, and expected to receive most of their care within the healthcare system for at least 8 months following baseline.
Exclusion criteria	Potential participants diagnosed with dementia, receiving hospice care, unable to travel to the clinic for a workshop or living outside of the recruitment area were excluded
Recruitment/selection of patients	Primary care patients in a large Internal Medicine clinic were identified through a two-step screening process. First, electronic billing data was scanned to identify persons likely to meet inclusion criteria. Second, a subset of those identified were randomly selected for additional screening by medical chart review to confirm eligibility, identify a

Hochhalter 2010⁵⁹²	
	primary care physician, and extract contact information. Primary care physicians co-signed invitation letters and excluded patients they felt should not be contacted.
Age, gender and ethnicity	Age - mean (SD): 74.5 (6.69). Gender (M:F): 27/52. Ethnicity: Non-Hispanic/Latino: 98%. White: 92.4%.
Further population details	1. Age: >65 years (aged > 65 years). 2. Deprivation: medium SES (majority of participants had an annual household income of \$50000 or more). 3. Ethnicity: White (>80%) (92.4% white). 4. Number of conditions: 3 chronic conditions (Range of 3.3 - 3.8 chronic conditions across groups). 5. Type of conditions: not applicable/not stated/unclear (overall: mixed physical and mental health conditions [the majority of included conditions were physical, with depression the only included mental health condition]).
Indirectness of population	No indirectness
Interventions	<p>(n=26) Intervention 1: Standard care. Usual care. Duration 6 months. Concurrent medication/care: not reported.</p> <p>(n=26) Intervention 2: Self-management programmes. Patient engagement intervention ('making the most of your healthcare'), comprising one 2-hour workshop and two follow-up telephone calls (one before and one after) a subsequent routine/naturally occurring medical appointment, delivered by 'coaches' and individualised to patients' pre- and post-healthcare appointment needs. The intervention group discussed patient engagement concepts from publicly distributed content. The intervention offered tools and taught skills to (a) prepare for healthcare appointments, (b) communicate effectively and gather information and support during healthcare appointments, and (c) follow through on plans of care. Following the workshop, coaches monitored participants' upcoming healthcare appointment using electronic records available in the integrated healthcare system in which the intervention was implemented. Coaches and participants took part in a brief (approximately 15 minutes) coaching phone call within a week before a scheduled appointment and another call within a week after that appointment. Participants received print copies of 'A guide for older people: Talking with your doctor, bound for your good health' and a list of local community resources. Duration 6 months. Concurrent medication/care: not reported.</p> <p>(n=27) Intervention 3: Inactive control intervention. Control intervention consisting of the same type and number of contacts as the self-management intervention, except with a focus on general safety for older adults. This included arranging the home environment to avoid falls risks and fire risks, identity theft and caregiver stress. Duration 6 months. Concurrent medication/care: not reported.</p>
Funding	Other (supported by a grant from the Scott & White Healthcare Research Foundation and conducted in collaboration with physicians, nurses, and other personnel at the Scott & White Centre for Diagnostic Medicine)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: SELF-MANAGEMENT versus STANDARD CARE

Hochhalter 2010 ⁵⁹²	
<p>Protocol outcome 1: Health-related quality of life - Actual outcome: HRQOF (unhealthy days) at 6 months; other: -0.45 (95%CI -1.43 to 0.53) (p value 0.360); risk of bias: low; indirectness of outcome: no indirectness</p> <p>Protocol outcome 2: Patient self-efficacy - Actual outcome: Self-efficacy for managing chronic disease at 6 months; group 1: mean 7.4 (SD 1.8); n=20, risk of bias: low; indirectness of outcome: no indirectness</p> <p>RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: SELF-MANAGEMENT versus CONTROL INTERVENTION</p> <p>Protocol outcome 1: Health-related quality of life - Actual outcome: HRQOF (unhealthy days) at 6 months; other: 0.39 (95%CI -0.63 to 1.42) (p value 0.444); risk of bias: high; indirectness of outcome: no indirectness</p> <p>Protocol outcome 2: Patient self-efficacy - Actual outcome: Self-efficacy for managing chronic disease at 6 months; group 1: mean 7.4 (SD 1.8); n=20, group 2: mean 8 (SD 1.2); n=23; risk of bias: high; indirectness of outcome: no indirectness</p>	
Protocol outcomes not reported by the study	Mortality; functional outcomes (mobility, activities of daily living); patient and carer satisfaction; unplanned hospital admissions; length of hospital stay; continuity metrics; patient/carers treatment burden

Table 200: Lorig 1999⁷⁸⁰

Lorig 1999 ⁷⁸⁰	Chronic disease self-management program
Study type	RCT (patient randomised; parallel)
Number of studies (number of participants)	1 (n=1140 [566 in multimorbid subgroup])
Countries and setting	Conducted in USA; setting: the programme was held in multiple community sites; including in churches, senior and community centres, public libraries, and health care facilities. Programs were also planned at varied times; including both during the day, as well as at evenings and weekends.
Line of therapy	Adjunctive to current care
Duration of study	Intervention + follow up: 6-months
Method of assessment of guideline condition	Unclear method of assessment/diagnosis: no clear definition of which conditions included in multimorbid subgroup. All participants in the study were required to have a physician confirmed diagnosis of 1 or more of the following conditions: chronic lung disease (asthma, chronic bronchitis, or emphysema), heart disease (coronary artery disease or congestive heart failure), stroke (completed cerebrovascular accident with neurologic handicap and normal

Lorig 1999 ⁷⁸⁰	Chronic disease self-management program
	mentation), and/or chronic arthritis. The study also reports that participants may also have had other conditions. Unclear from the study whether the multimorbid subgroup is those participants with 2 or more of the target conditions, or whether it included participants with one of the target conditions and another unspecified condition, which may or may not be chronic.
Stratum	Overall
Subgroup analysis within study	Not stratified but pre-specified
Inclusion criteria	All participants in the study were required to have a physician-confirmed diagnosis of 1 or more of the following conditions: chronic lung disease (asthma, chronic bronchitis, or emphysema), heart disease (coronary artery disease or congestive heart failure), stroke (completed cerebrovascular accident with neurologic handicap and normal mentation), and/or chronic arthritis.
Exclusion criteria	Patients with compromised mentation, patients who received chemotherapy or radiation as part of treatment for cancer within the last year, and any patients < 40 years of age.
Recruitment/selection of patients	Participants were recruited using public service announcements in the media, referrals from flyers left in physicians' offices and community clinics, posters at senior citizen centres, announcements in health maintenance organization (HMO) patient newsletters and referrals from county government employers.
Age, gender and ethnicity	Age – range: 40-90 years. Mean age = 65 years. Gender (M:F): not reported for multimorbid subgroup. For overall sample 337/615. Ethnicity: not reported for multimorbid subgroup. For overall sample % white = 89 - 91% across control and intervention group.
Further population details	1. Age: not applicable/not stated/unclear (overall [aged 40-90 years]). 2. Deprivation: not applicable/not stated/unclear (no overall SES data provided. Mean education = 15 years). 3. Ethnicity: White (>80%) (90% white). 4. Number of conditions: not applicable/not stated/unclear (unclear). 5. Type of conditions: not applicable/not stated/unclear (not stated. Possibly physical conditions only [no specific reference to mental health conditions]).
Indirectness of population	No indirectness
Interventions	(n=664) Intervention 1: Self-management programmes. Weekly 2.5 hour group sessions led by a pair of trained, volunteer lay leaders in a variety of settings. Topics covered by the Chronic Disease Self-Management Program (CDSMP) include: exercise; use of cognitive symptom management techniques; nutrition; fatigue and sleep management; use of community resources; use of medications; dealing with the emotions of fear, anger, and depression; communication with others including health professionals; problem-solving; and decision-making. The content of the course is based on Bandura's Self-efficacy theory, including strategies suggested by Bandura to enhance self-efficacy. These include weekly action planning and feedback, modelling of behaviours and problem-solving by participants for each other, reinterpretation of symptoms by giving many possible causes for each symptom as well as several different management techniques, group problem solving, and individual decision-making. The

Lorig 1999⁷⁸⁰	Chronic disease self-management program
	<p>leaders act more as facilitators than as lecturers. For example, they do not prescribe specific behaviour changes, but rather they assist participants in making management choices and achieving success in reaching self-selected goals. Duration 7 weeks. Concurrent medication/care: treatment as usual.</p> <p>(n=476) Intervention 2: Standard care. Waiting list control. Duration 6-months. Concurrent medication/care: treatment as usual.</p>
Funding	Academic or government funding (grant received from the University of California Tobacco Related Disease Research Program)
<p>RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: CHRONIC DISEASE SELF-MANAGEMENT PROGRAM (CDSMP) versus STANDARD CARE</p> <p>Protocol outcome 1: Health-related quality of life</p> <ul style="list-style-type: none"> - Actual outcome: Self-reported health status (National health interview survey) at 6-months; group 1: mean -0.08 (SD 0.68); n=311, risk of bias: high; indirectness of outcome: no indirectness - Actual outcome: Disability (modified from the Health Assessment Questionnaire disability scale) at 6-months; group 1: mean -0.01 (SD 0.3); n=311, risk of bias: high; indirectness of outcome: no indirectness - Actual outcome: Psychological wellbeing scale (MHI-5, as taken from the SF-36) at 6-months; group 1: mean 0.07 (SD 0.67); n=311, group 2: mean 0.03 (SD 0.69); n=225; 0-5 top=high is good outcome; risk of bias: high; indirectness of outcome: no indirectness - Actual outcome: Social/role activities limitations at 6-months; group 1: mean 0.01 (SD 0.86); n=311, risk of bias: high; indirectness of outcome: no indirectness <p>Protocol outcome 2: Functional outcomes (mobility, activities of daily living)</p> <ul style="list-style-type: none"> - Actual outcome: Energy/fatigue (as used in the Medical Outcomes study) at 6-months; group 1: mean 0.08 (SD 0.73); n=311, risk of bias: high; indirectness of outcome: no indirectness <p>Protocol outcome 3: Patient/carer treatment burden</p> <ul style="list-style-type: none"> - Actual outcome: Health distress at 6-months; group 1: mean -0.23 (SD 0.97); n=311, risk of bias: high; indirectness of outcome: no indirectness 	
Protocol outcomes not reported by the study	Mortality; patient and carer satisfaction; unplanned hospital admissions; length of hospital stay; continuity metrics; patient/carer treatment burden

Table 201: Marek 2013⁸¹⁰

Marek 2013⁸¹⁰	
Study type	RCT (patient randomised; parallel)
Number of studies (number of participants)	1 (n=414)
Countries and setting	Conducted in USA
Line of therapy	Unclear
Duration of study	Intervention time: 12 months
Method of assessment of guideline condition	Unclear method of assessment/diagnosis: aged 60 or older
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Aged 60 or older; Medicare primary payer; impaired ability to manage medications as indicated by score of 1 or higher on the Outcome and Assessment Information Set (OASIS) and/or impaired cognitive functioning but able to follow directions with prompting as indicated by a score of 1 or 2 on OASIS item M0560; working telephone line and electricity.
Exclusion criteria	Terminal diagnosis or hospice care that would make attrition likely; use of other device for medications (for example pager or prompt)
Recruitment/selection of patients	Patients provided verbal permission to a home care nurse for the research staff to contact them
Age, gender and ethnicity	Age - other: aged 60 or older. Gender (M:F): paper states majority of participants were female. Ethnicity: not stated.
Further population details	1. Age: >65 years (aged 60 or older). 2. Deprivation: not applicable/not stated/unclear. 3. Ethnicity: White (>80%) (MD.2: 81.6% White. Planner: 83.2% White. Comparison: 90.4% White). 4. Number of conditions: not applicable/not stated/unclear. 5. Type of conditions: not applicable/not stated/unclear.
Indirectness of population	Serious indirectness: no multimorbidity reported. Aged 60 or older; impaired ability to manage medications as indicated by score of 1 or higher on the Outcome and Assessment Information Set.
Interventions	(n=125) Intervention 1: Standard care. No intervention beyond pharmacy screen. Notified all prescribing providers that their patient was a participant in the study, was in the control group and would not receive any additional intervention from the research project. Duration 12 months. Concurrent medication/care: each participant received a pharmacy screen on admission, which involved a review of all medications identified by the participant with corresponding medical diagnoses. They used a program to identify drug interactions and Beers criteria for inappropriate medication use. Each participant's prescribing provider(s) received the pharmacy screen, with

Marek 2013⁸¹⁰	
	<p>suggestions.</p> <p>(n=137) Intervention 2: Self-management programmes. A team of nurse care coordinators (advanced practice nurses and registered nurses) worked closely with participants to identify their goals in care and provide education and tools for the participants to manage their chronic conditions. Nurse care coordination enhanced participant ability to communicate with multiple physicians, pharmacies, social service agencies and other individuals or organisations involved in their healthcare. Care coordinators created care plans specific to the clinical conditions of each participant. The care plans included monitoring of specific signs and symptoms related to medical diagnoses, medications and other individualised problem areas. The care coordinator communicated with the participant ordering physician, pharmacist, and visited the participant at least every 2 weeks to fill their med planner and perform activities identified in their care plan. The care coordinator made additional visits if a participant had a change in medication type, dose, or frequency before the biweekly scheduled visit or when clinical condition required additional visits. If a participant was hospitalised, the care coordinator visited during and after hospitalisation and participated in discharge planning. The med planner is a box with separate compartments for individual medication times over the course of a week. Care coordinators filled two med planners to cover a 2-week period, and recorded the number of medications remaining in the med planner before refilling. Duration 1 year. Concurrent medication/care: each participant received a pharmacy screen on admission, which involved a review of all medications identified by the participant with corresponding medical diagnoses. They used a program to identify drug interactions and Beers criteria for inappropriate medication use. Each participant's prescribing provider(s) received the pharmacy screen, with suggestions.</p>
Funding	Academic or government funding (National Institute of Nursing Research)
<p>RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: CARE COORDINATION + MEDS PLANNER versus STANDARD CARE</p> <p>Protocol outcome 1: Health-related quality of life</p> <ul style="list-style-type: none"> - Actual outcome: SF-36 (physical) at 12-months; risk of bias: high; indirectness of outcome: no indirectness - Actual outcome: SF-36 (mental) at 12-months; risk of bias: high; indirectness of outcome: no indirectness <p>Protocol outcome 2: Functional outcomes (mobility, activities of daily living)</p> <ul style="list-style-type: none"> - Actual outcome: Physical performance test at 12-months; risk of bias: high; indirectness of outcome: no indirectness 	
Protocol outcomes not reported by the study	Mortality; patient and carer satisfaction; unplanned hospital admissions; length of hospital stay; continuity metrics; patient/carers treatment burden; patient self-efficacy

Table 202: Park 2014⁹⁴⁴

Park 2014 ⁹⁴⁴	
Study type	RCT (patient randomised; parallel)
Number of studies (number of participants)	1 (n=50)
Countries and setting	Conducted in South Korea; setting: nursing home
Line of therapy	Adjunctive to current care
Duration of study	Intervention time: 8 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: diagnosis of 2 or more chronic diseases within 1 year of study
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Greater than or equal to 65 years and a diagnosis of two or more chronic conditions within one year prior to the study
Exclusion criteria	Inability to understand and participate in the program process
Recruitment/selection of patients	All older people residing in the nursing home were identified
Age, gender and ethnicity	Age – range: 62-88 years. Gender (M:F): >70% female. Ethnicity: Korean (south).
Further population details	1. Age: >65 years (62 years and above [mean age = 77.6 years]). 2. Deprivation: not applicable/not stated/unclear (not reported). 3. Ethnicity: Asian (>80%) (Korean). 4. Number of conditions: not applicable/not stated/unclear (not reported). 5. Type of conditions: not applicable/not stated/unclear (not reported). Possibly only physical health conditions, as no reference to mental health).
Extra comments	People from one nursing home in South Korea. Intervention: 72.7% stroke, 4.6% Parkinson's disease, 22.7% dementia. Control (conventional/waiting list): 71.4% stroke, 23.8% Parkinson's disease, 4.8% dementia.
Indirectness of population	No indirectness
Interventions	(n=25) Intervention 1: Self-management programmes. Intervention group received twice weekly group-level activities and an individual approach to self-management during 8 weeks. The health coaching self-management program (HCSMP) was designed for older nursing home residents to explore their health status and apply self-management strategies to achieve their individual goals based on their needs. It was systematised as three major categories: individual-level, group-level and facility-level approach. Major components of the programme included group health education and group exercise in the group-level approach and individual counselling for goal setting in the individual-level approach. The categories consisted of: individual health assessment; goal setting and counselling; group discussion; enhancing cognition activities; exercise sessions; and an activity to encourage the facility's cooperation. The structured group health education was offered to the nursing home residents once a week for 8 weeks, each session lasted approximately 1 hour; and delivered by pairs of research team members, who were geriatric nurse

Park 2014⁹⁴⁴	<p>specialists and trained to provide health coaching strategies. Each session started with a short introduction to the topic and focused on the group discussion to share personal experiences associated with the topic for that session, followed by physical activities to enhance their cognition and body movements. The separate 1 hour exercise sessions were provided once a week for 8 weeks, and consisted of stretching, hands and feet exercise, and joint movement training. Prior to every group activity, individual counselling for goal setting by trained research team members was done to encourage the initiation and maintenance of self-management behaviours, and to help goal setting (approximately 20-30 minutes). The principal investigator conducted the training sessions for the research team, and had several meetings with the director and chief manager to support participants' individual endeavour to achieve their health goals. Duration 8 weeks. Concurrent medication/care: not stated.</p> <p>(n=25) Intervention 2: Inactive control intervention. Participants in the conventional group were asked to maintain their regular lifestyle including dietary and exercise habits for 8 weeks until they were re-examined. The conventional group received conventional care. Duration 8 weeks. Concurrent medication/care: none stated.</p>
Funding	Academic or government funding (Research Institute of Nursing Science of Seoul National University and Basic Science Research Program)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: SELF-MANAGEMENT versus WAITING LIST

Protocol outcome 1: Health-related quality of life
 - Actual outcome: Self-rated health (chronic disease self-management program questionnaire) at 8 weeks; group 1: mean 2.8 (SD 0.6); n=22, risk of bias: very high; indirectness of outcome: no indirectness
 - Actual outcome: Health assessment questionnaire at 8 weeks; MD Intervention = -0.5; control = -0.5; risk of bias: very high; indirectness of outcome: no indirectness

Protocol outcome 2: Functional outcomes (mobility, activities of daily living)
 - Actual outcome: Social role/activities limitations (chronic disease self-management program questionnaire) at 8 weeks; risk of bias: very high; indirectness of outcome: no indirectness

Protocol outcome 3: Patient/carer treatment burden
 - Actual outcome: Health distress (chronic disease self-management program questionnaire) at 8 weeks; MD Intervention = 0.2; control = -0.8; risk of bias: very high; indirectness of outcome: no indirectness

Protocol outcome 4: Patient self-efficacy
 - Actual outcome: Chronic disease self-efficacy at 8 weeks; group 1: mean 30.6 (SD 11.5); n=22, risk of bias: very high; indirectness of outcome: no indirectness

Park 2014⁹⁴⁴	
Protocol outcomes not reported by the study	Mortality; patient and carer satisfaction; unplanned hospital admissions; length of hospital stay; continuity metrics

H.7 Format of encounters

Table 203: Hopp 2006

Study	Hopp 2006 ⁶⁰¹
Study type	RCT (patient randomised; parallel)
Number of studies (number of participants)	1 (n=37)
Countries and setting	Conducted in USA; setting: home
Line of therapy	Unclear
Duration of study	Intervention + follow up: 6 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: 68% had 3 or more comorbid conditions
Stratum	Outpatient
Subgroup analysis within study	Not applicable
Inclusion criteria	Receiving home care services at the Richard L Roudebush VAMC in Indianapolis; 1 or more hospitalisations, 2 or more emergency department visits, or 10 or more outpatient visits in last 12 months; care plan specifying 2 or more home visits per month and expected need for future visits for at least 1 month
Exclusion criteria	Not having telephone; being judged incapable of operating the telemedicine system if sufficient caregiver support was lacking; having survival expectation of less than 6 months
Recruitment/selection of patients	Research assistant contacted eligible patients by telephone to explain the study and arrange a meeting
Age, gender and ethnicity	Age - mean (SD): intervention 69.8 years (11.6), comparison 69.5 years (12.7). Gender (M:F): 1:0. Ethnicity: Hispanic: intervention 11%, comparison 16%. African American: intervention 33%, comparison 37%. Caucasian: 56%, comparison 47%.
Further population details	1. Age: overall. 2. Deprivation: not stated. 3. Ethnicity: 51% Caucasian; 35% African American; 19% Hispanic. 4. Number of conditions: 3-4 conditions (intervention 3±1.8, comparison 3.8±1.7, 68% had 3 or more comorbid conditions). 5. Type of comorbid conditions: physical multimorbidity (diabetes; hyperlipidaemia; hypertension; CAD; atrial fibrillation; CHF; stroke; COPD).

Study	Hopp 2006 ⁶⁰¹
Indirectness of population	No indirectness
Interventions	<p>(n=18) Intervention 1: Other. Telemonitoring. Used Aviva 1010 video monitor - home unit with voice, video and camera technology. Some patients given units with peripheral attachments such as blood pressure monitors, stethoscope and glucose monitors. During video sessions patients and clinical staff were able to see and communicate with each other using the unit. Video sessions included the following components: discussion of the patient's overall health status; review of medications; discussions of any health concerns by the patient; and nurse reminders concerning the appropriate self-care behaviours (diet, exercise, monitoring of symptoms for example blood pressure and weight). The frequency of video encounters was determined by the home care nurse, in consultation with the patient's primary care provider and a review of the patient's medical record. Duration 6 months. Concurrent medication/care: none stated.</p> <p>(n=19) Intervention 2: Usual care. Nursing services at home and periodic telephone contact with the clinical staff concerning their home care services. Duration 6 months. Concurrent medication/care: none stated.</p>
Funding	Academic or government funding (VA Health Services Research and Development grant)
<p>RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: OTHER versus USUAL CARE</p> <p>Protocol outcome 1: Quality of life - Actual outcome: SF-36V physical at 6 months; group 1: mean 1.56 (SD 11.6); group 2 mean 0.64 (SD 10.6); risk of bias: very high; indirectness of outcome: no indirectness - Actual outcome: SF-36V mental at 6 months; group 1: mean 4.05 (SD 10.16); group 2 mean -4.11 (SD 18.29); risk of bias: very high; indirectness of outcome: no indirectness</p> <p>Protocol outcome 2: Mortality - Actual outcome: mortality at 6 months; group 1: 2/18, group 2: 2/19; risk of bias: low; indirectness of outcome: no indirectness</p> <p>Protocol outcome 3: Patient/carer satisfaction - Actual outcome: General Home Care Satisfaction Scale (change score) at 6 months; group 1: mean -1 (SD 3.14); group 2 mean -1.56 (SD 5.42); risk of bias: very high; indirectness of outcome: no indirectness</p> <p>Protocol outcome 4: Length of hospital stay - Actual outcome for Inpatient: mean hospital days at 6 months; group 1: mean 2.83 days (SD 4.12); n=18, group 2: mean 7.11 days (SD 12.86); n=19; risk of bias: low; Indirectness of outcome: no indirectness</p>	

Study	Hopp 2006 ⁶⁰¹
<p>Protocol outcome 5: Unscheduled care</p> <ul style="list-style-type: none"> - Actual outcome: mean hospital admissions at 6 months; group 1: mean 0.67 (SD 1.03); n=18, group 2: mean 1.26 (SD 2); n=19; risk of bias: low; indirectness of outcome: no indirectness - Actual outcome: mean emergency department visits at 6 months; group 1: mean 1 (SD 1.33); n=18, group 2: mean 2.11 (SD 2.89); n=19; risk of bias: low; indirectness of outcome: no indirectness 	
Protocol outcomes not reported by the study	Functional outcomes; continuity of care; patient/carer treatment burden; admission to care facility

Table 204: Integrated Telehealth Education and Activation of Mood (I-TEAM) study trial: Gellis 2014

Study	Integrated Telehealth Education and Activation of Mood (I-TEAM) study trial: Gellis 2014 ⁴⁷⁵
Study type	RCT (patient randomised; parallel)
Number of studies (number of participants)	1 (n=102)
Countries and setting	Conducted in USA
Line of therapy	Unclear
Duration of study	Intervention + follow up: 3+9 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: depression, and HF or COPD
Stratum	Outpatient
Subgroup analysis within study	Not applicable
Inclusion criteria	Aged 65 or older; ≥1 days in hospital in past 12 months, in emergency department in past 2 months or required ≥3 home visits per week; primary diagnosis of HF or COPD; score ≥3 on PHQ
Exclusion criteria	MMSE score <24; dementia; inability to use telemonitoring device because of physical disability; behavioural problems (for example agitation, delirium, paranoia) that would interfere with use of device
Recruitment/selection of patients	Recruited from a single large hospital-affiliated home care agency, using hospital's computerised medical records databases
Age, gender and ethnicity	Age - mean (SD): intervention 78.3 years (6.9), comparison 80.1 years (7.8). Gender (M:F): 35:65. Ethnicity: not stated
Further population details	1. Age: older adult (65+ years) (aged 65 or older). 2. Deprivation: not stated. 3. Ethnicity: not stated. 4. Number of conditions: 2 conditions. 5. Type of comorbid conditions: physical and mental health multimorbidity.
Indirectness of population	No indirectness

Study	Integrated Telehealth Education and Activation of Mood (I-TEAM) study trial: Gellis 2014 ⁴⁷⁵
Interventions	<p>(n=57) Intervention 1: Other. Telemonitoring. Daily monitoring of weight, blood pressure, pulse, oxygen saturation and temperature were conducted at a scheduled time. Data were assessed to ascertain which were of higher priority to intervene to allow immediate determination of nurse treatment tasks. Nurse contacted participants with abnormal readings for follow-up evaluation. Duration 3 months. Concurrent medication/care: problem-solving treatment for depression 35 minute sessions, over 8 weeks; tailored counselling including medication use, psychoeducation, problem solving strategy and behavioural activation.</p> <p>(n=58) Intervention 2: Usual care. Usual care - 1 hour long face-to-face home visits at least once a week. Duration 3 months. Concurrent medication/care: psychoeducation (including instruction on disease process and counselling about the importance of daily monitoring of body weight, smoking cessation, diet and medication adherence).</p>
Funding	Academic or government funding (New York State Department of Health)
<p>RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: OTHER versus USUAL CARE</p> <p>Protocol outcome 1: Quality of life - Actual outcome: SF-12 mental at 6 months; group 1: mean 52.1 (SD 24.3); n=46, group 2: mean 40.3 (SD 27.4); n=48; risk of bias: high; indirectness of outcome: no indirectness</p> <p>Protocol outcome 2: Patient/carer satisfaction - Actual outcome: patient satisfaction at 3 months; group 1: mean 4.4 (SD 1.4); n=46, group 2: mean 4.5 (SD 1.3); n=48, risk of bias: very high; indirectness of outcome: no indirectness</p> <p>Protocol outcome 3: Length of hospital stay - Actual outcome for inpatient: mean hospital days at 12 months; group 1: mean 7.5 days (SD 4.3); n=46, group 2: mean 10.5 days (SD 6.5); n=48; risk of bias: low; indirectness of outcome: no indirectness - Actual outcome: mean episodes of care at 12 months; group 1: mean 1.3 days (SD 1); n=46, group 2: mean 1.8 days (SD 1.5); n=48; risk of bias: low; indirectness of outcome: no indirectness</p> <p>Protocol outcome 4: Unscheduled care - Actual outcome: mean emergency department visits at 12 months; group 1: mean 0.6 (SD 1.6); n=46, group 2: mean 1.4 (SD 1.2); n=48; risk of bias: low; indirectness of outcome: no indirectness</p>	
Protocol outcomes not reported by the study	Mortality; functional outcomes; continuity of care; patient/carer treatment burden; admission to care facility

Table 205: Noel 2004

Study	Noel 2004 ⁹¹¹
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=104)
Countries and setting	Conducted in USA; Setting: Community
Line of therapy	Unclear
Duration of study	Intervention time: 6-12 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: 79% MM: 21% CHF+COPD; 34% CHF+DM; 13% COPD+DM; 11% CHF+COPD+DM
Stratum	Outpatient
Subgroup analysis within study	Not applicable
Inclusion criteria	Documented high use of healthcare resources and barrier to accessing healthcare services due to geographic, economic, physical, linguistic and/or cultural factors
Exclusion criteria	None stated
Recruitment/selection of patients	Not reported
Age, gender and ethnicity	Age - Mean (SD): 71. Gender (M:F): 97:3. Ethnicity: Not reported
Further population details	1. Age: Adult (18-65 years) (Mean age 71). 2. Deprivation: Not applicable / Not stated / Unclear (not stated). 3. Ethnicity: Not applicable / Not stated / Unclear (not stated). 4. Number of conditions: Not applicable / Not stated / Unclear (2 conditions 68%, 3 conditions 11%). 5. Type of comorbid conditions: Physical multimorbidity (CHF, COPD, DM).
Indirectness of population	Serious indirectness: 79% MM
Interventions	(n=47) Intervention 1: Other. Home telehealth. Vital sign data and answers to quizzes related to disease-specific education modules were acquired via the home-based telehealth units collect data for temperature, blood pressure, pulse, blood glucose, 3-lead electrocardiogram, stethoscope for heart and lung sounds, pulse oximetry, and weight. Pain level (0–9) is self-reported using a simple questionnaire. Data are transmitted over POTS (plain old telephone system) lines to VA Connecticut’s Web-based Intranet system and directly into the facility’s electronic database (VISTA). A patient-specific intake form was completed before deployment of the healthcare unit. The intake form addresses demographics and needs assessment for peripheral devices and safe range settings. Out-of range patient data trigger VA alerts via the Web to nurse case managers. The device supports on-screen hospital-to-home

Study	Noel 2004⁹¹¹
	<p>messaging, scheduling, and advice from providers to patients. Incoming data were automatically written into the VA's electronic patient record to templated progress notes or the vital sign record. A digital camera (Nikon Coolpix 880) was used to monitor wound care with images transmitted to the Web server. Disease-specific patient education modules included pass/fail tests to demonstrate learning achieved. Patients completed on-screen assessment surveys for pain, wellbeing, and patient satisfaction. . Duration 6-12 months. Concurrent medication/care: Nurse case management for at least 6 months prior to study</p> <p>(n=57) Intervention 2: Usual care. Usual care. Duration 6-12 months. Concurrent medication/care: Nurse case management for at least 6 months prior to study</p>
Funding	Academic or government funding (VA Health Service and Development)
<p>RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: OTHER versus USUAL CARE</p> <p>Protocol outcome 1: Quality of life</p> <ul style="list-style-type: none"> - Actual outcome for functional level (OARS Multidimensional Functional assessment) at 6 months; Group 1: mean 37.91 (SD 9.22); n=47, Group 2: mean 40.19 (SD 5.81); n=57; Risk of bias: Very high; Indirectness of outcome: No indirectness - Actual outcome for cognitive status (OARS Multidimensional Functional assessment)at 6 months; Group 1: mean 19.7 (SD 1.06); n=47, Group 2: mean 19.68 (SD 0.69); n=57; Risk of bias: Very high; Indirectness of outcome: No indirectness - Actual outcome for patient satisfaction (OARS Multidimensional Functional assessment)at 6 months; Group 1: mean 106.38 (SD 20.99); n=47, Group 2: mean 97.14 (SD 18.22); n=57; Risk of bias: Very high; Indirectness of outcome: No indirectness - Actual outcome for self-rated health status (OARS Multidimensional Functional assessment)at 6 months; Group 1: mean 82.47 (SD 12.89); n=47, Group 2: mean 85.14 (SD 16.28); n=57; Risk of bias: Very high; Indirectness of outcome: No indirectness <p>Protocol outcomes not reported by the study</p>	
	Mortality; Functional outcomes; Patient/carer satisfaction; Length of hospital stay; Unscheduled care; Continuity of care; Patient/carer treatment burden; Admission to care facility

Table 206: Tele-ERA study trial: Takahashi 2012A

Study (subsidiary papers)	Tele-ERA study trial: Takahashi 2012A^{953,1165,1166,1220}
Study type	RCT (patient randomised; parallel)
Number of studies (number of participants)	1 (n=205)
Countries and setting	Conducted in USA; setting: at home
Line of therapy	Unclear

Study (subsidiary papers)	Tele-ERA study trial: Takahashi 2012A ^{953,1165,1166,1220}
Duration of study	Follow up (post intervention): 12 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: older adult (aged 65 or older)
Stratum	Outpatient
Subgroup analysis within study	Not applicable
Inclusion criteria	Aged 60 years or older; in 1 of 4 sites within Mayo Clinic's program of employee and community health; Elder A Risk Assessment score >15, patients in top 10% of ERA scores were identified as eligible for recruitment
Exclusion criteria	Patients who lived in a nursing home; had diagnosis of dementia; score of 29 or lower on the Kokmen Short Test of Mental Status; patients who felt they could not use the home telemonitoring system
Age, gender and ethnicity	Age - mean (SD): 80.3±8.2. Gender (M:F): 46:54. Ethnicity: not stated
Further population details	1. Age: older adult (65+ years) (aged 60 or older, mean 80.3 years ±8.2). 2. Deprivation: not stated. 3. Ethnicity: not stated. 4. Number of conditions: not stated. 5. Type of comorbid conditions: physical multimorbidity.
Indirectness of population	Serious indirectness: older adult (aged 65 or older)
Interventions	<p>(n=102) Intervention 1: Other. Telemonitoring. Used Intel Health Guide in patient's home. Patients performed daily 5-10 minute monitoring sessions for symptoms and biometric information. Device worked asynchronously and data were downloaded to website, which was then reviewed by healthcare team daily. One research nurse oversaw ~100 subjects and communicated with subject via phone or videoconference if alerts arose. Nurse provided assessment of symptoms and communicated with primary provider for treatment options if needed. Duration 1 year. Concurrent medication/care: none stated.</p> <p>(n=103) Intervention 2: Usual care. Access to primary and speciality office visits; routinely received post-hospital outpatient visits within a timely fashion and a nurse generated phone call within 1 business day of hospital dismissal. Duration 1 year. Concurrent medication/care: none stated.</p>
Funding	Study funded by industry (Mayo Foundation Institutional Funds for clinical support; Intel Health Guides and support provided by Care Innovations (GE/Intel))

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: OTHER versus USUAL CARE

Protocol outcome 1: Quality of life

- Actual outcome: SF-12 physical at 1 year; group 1:mean 32.8 (SD 10.6); n=77 , group 2: mean 34.2 (SD 10.2); n=89; risk of bias: high; indirectness of outcome: no indirectness

- Actual outcome: SF-12 mental at 1 year; group 1:mean 56 (SD 8.9); n=77 , group 2: mean 58.1 (SD 7.6) ; n=89; risk of bias: high; indirectness of outcome: no

Study (subsidiary papers)	Tele-ERA study trial: Takahashi 2012A ^{953,1165,1166,1220}
indirectness	
Protocol outcome 2: Mortality - Actual outcome: mortality at 1 year; group 1: 15/102, group 2: 4/103; risk of bias: high; indirectness of outcome: no indirectness	
Protocol outcome 3: Functional outcomes - Actual outcome: Barthel ADL index at 1 year; group 1: mean 90.5 (SD 16.5); n=77, group 2: mean 93.1 (SD 13.4); n=89; risk of bias: high; indirectness of outcome: no indirectness	
Protocol outcome 4: Length of hospital stay - Actual outcome: mean hospital days at 1 year; group 1: mean 4.1 days (SD 8.1); n=102, group 2: mean 6.1 days (SD 20.1); n=103; risk of bias: high; indirectness of outcome: no indirectness	
Protocol outcome 5: Unscheduled care - Actual outcome: hospital admissions at 1 year; group 1: 53/102, group 2: 45/103; risk of bias: low; indirectness of outcome: no indirectness - Actual outcome: ER visits at 1 year; group 1: 36/102, group 2: 29/103; risk of bias: low; indirectness of outcome: no indirectness - Actual outcome: mean number of ER visits at 1 year; group 1: mean 0.71 (SD 1.3); n=102, group 2: mean 0.45 (SD 0.83); n=103; risk of bias: high; indirectness of outcome: no indirectness - Actual outcome: mean number of hospital admissions at 1 year; group 1: mean 1.1 (SD 1.7); n=102, group 2: mean 0.83 (SD 1.2); n=103; risk of bias: high; indirectness of outcome: no indirectness	
Protocol outcome 6: Admission to care facility - Actual outcome: mean hospice visits at 1 year; group 1: mean 13.8 (SD 24.4); n=94, group 2: mean 14.5 (SD 17.4); n=100; risk of bias: high; indirectness of outcome: no indirectness - Actual outcome: mean hospice days at 1 year; group 1: mean 57.9 days (SD 99.2); n=94, group 2: mean 119.3 days (SD 123.8); n=100; risk of bias: high; indirectness of outcome: no indirectness - Actual outcome: time to hospice entry at 1 year; HR 1.28 (95%CI 0.94 to 1.74) calculated – from Kaplan Meier curve; risk of bias: very high; indirectness of outcome: no indirectness	
Protocol outcomes not reported by the study	Patient/carer satisfaction; continuity of care; patient/carer treatment burden

Appendix I: Health economic evidence tables

I.1 Principles/Barriers of care

I.1.1 Principles of care

No health economic evidence was identified for this review.

I.1.2 Barriers of care

No health economic evidence was identified for this review.

I.2 Identification

I.2.1 Unplanned hospital admissions

No health economic evidence was identified for this review.

I.2.2 Health-related quality of life

No health economic evidence was identified for this review.

I.2.3 Admission to care facility

No health economic evidence was identified for this review.

I.2.4 Life expectancy risk tools

No health economic evidence was identified for this review.

I.2.5 Polypharmacy: unplanned hospital admissions

No health economic evidence was identified for this review.

I.2.6 Polypharmacy: health-related quality of life

No health economic evidence was identified for this review.

I.2.7 Polypharmacy: admission to care facilities

No health economic evidence was identified for this review.

I.2.8 Polypharmacy: mortality

No health economic evidence was identified for this review.

I.3 Frailty

No health economic evidence was identified for this review.

I.4 Delivering an approach to care that takes account of multimorbidity

I.4.1 Treatment burden

No health economic evidence was identified for this review.

I.4.2 Ranking

No health economic evidence was identified for this review.

I.4.3 Stopping antihypertensive treatment

No health economic evidence was identified for this review.

I.4.4 Stopping drugs for osteoporosis

No health economic evidence was identified for this review.

I.4.5 Stopping statins

No health economic evidence was identified for this review.

I.5 Interventions

I.5.1 Models of care

No health economic evidence was included in this review.

I.5.2 Holistic Assessment

Table 207: MACNEILVROOMEN2012⁷⁹⁹

MacNeil Vroomen JL, Boorsma M, Bosmans JE, Frijters DH, Nijpels G, van Hout HP. Is it time for a change? A cost-effectiveness analysis comparing a Multidisciplinary Integrated Care model for residential homes to usual care. PloS One. Netherlands 2012; 7(5):e37444. (Guideline Ref ID MACNEILVROOMEN2012)				
Study details	Population & interventions	Costs	Health outcomes	Cost effectiveness
<p>Economic analysis: CUA (health outcome: QALYs)</p> <p>Study design: Within-trial analysis (RCT, associated clinical paper Boorsma 2011)¹⁶⁰</p> <p>Approach to analysis:</p>	<p>Population: Residential care facility residents, with physical or cognitive disabilities.</p> <p>Cohort settings: Mean age: 86 in the intervention arm; 85 in the</p>	<p>Total costs (mean per patient):</p> <p>Intervention 1: £1,246 Intervention 2: £1,551 Incremental (2–1): £305 (95% CI: -£10; £622; p=NR)</p> <p>Cost breakdown</p>	<p>QALYs (mean per patient):</p> <p>Intervention 1:0.32 Intervention 2:0.31 Incremental (2–1): 0.00 (95% CI: -0.01;0.01) p=NR</p>	<p>ICER (Intervention 2 versus Intervention 1): Intervention 1 dominates intervention 2 95% CI: N/A Probability Intervention 2 cost-effective (£20K): ~5% (from graph)</p> <p>Analysis of uncertainty: Bootstrapping undertaken to estimate</p>

<p>Analysis of individual level health outcomes (SF-12) and resource use collected at baseline and 6 months follow-up. SF-12 converted to SF-6D utility values to estimate QALYs. Unit costs applied. Missing values for cost and effect data imputed. People who did not provide baseline data or died were excluded from analyses.</p> <p>Perspective: Netherlands healthcare payer perspective</p> <p>Follow-up 6 month follow up</p> <p>Treatment effect duration^(a): n/a</p> <p>Discounting: n/a</p>	<p>control arm Male: 24% in intervention group and 26% in control group</p> <p>Intervention 1: Usual Care: family physician responsible for medical care and offered it on request.</p> <p>Intervention 2: Multidisciplinary Integrated Care : geriatric assessment of functional health every 3 months (using InterRAI software) and individualised care plan</p>	<p>Intervention cost (mean per patient): Intervention 1: £17 Intervention 2: £169 Incremental (2–1): £152 (95% CI: NR; p=NR)</p> <p>Currency & cost year: 2007 Euros (presented here as 2007 UK pounds^(b))</p> <p>Cost components incorporated: Informal care, primary and secondary care, medication use and costs associated with the interventions. For intervention 1 intervention costs included costs of multidisciplinary meetings. For intervention 2 intervention costs included: organisation costs, training of staff, interRAI costs and meeting costs.</p>		<p>uncertainty surrounding ICER.</p> <p>Three further sensitivity analyses were undertaken:-Including only the complete cases in the analysis.</p> <p>-Including only the licensing and subscription costs associated with InterRAI.</p> <p>- Including people who provided no baseline data or died, with missing cost and effect data imputed (intention-to treat).</p> <p>None of these analyses resulted in a change in the conclusion regarding cost-effectiveness.</p>
--	--	---	--	--

Data sources

Health outcomes: Within-trial analysis (RCT, associated clinical paper Boorsma 2011)¹⁶⁰. Health outcomes included patient reported SF-12 collected at baseline and 6 months follow-up, other outcomes included functional outcomes other quality of life indicators (see clinical review, Boorsma 2011). QALYs were calculated by converting SF-12 into SF-6D utility values. **Quality-of-life weights:** SF-12 converted to SF-6D values, UK tariff. **Cost sources:** Resource use collected by patient or proxy interview and medical records at baseline and at 6 months. Dutch unit costs applied including medications unit costs from the Royal Dutch Society for Pharmacy.

Comments

Source of funding: ZONMW provided a grant to undertake this study. ZONMW is the Netherlands Organisation for Health Research and Development. **Limitations:** Dutch resource use data (2006-7) and unit costs (2007) may not reflect current NHS context. Residential care facility residents aged >65 years, may not represent all people with multimorbidity. Time horizon may not be sufficient to capture all benefits and costs if benefits persist beyond 6 months. QALYs calculated from SF-12/SF-

6D rather than EQ-5D. Within-trial analysis and so does not reflect full body of available evidence for this comparison; Boorsma 2011 is 1 of 28 studies included in the clinical review for comprehensive geriatric assessments. **Other:** n/a

Overall applicability^(c): Partially applicable **Overall quality**^(d): Potentially serious limitations

Abbreviations: 95% CI: 95% confidence interval; CUA: cost–utility analysis; EQ-5D: Euroqol 5 dimensions (scale: 0.0 [death] to 1.0 [full health], negative values mean worse than death); ICER: incremental cost-effectiveness ratio; n/a: not applicable; NR: not reported; pa: probabilistic analysis; QALYs: quality-adjusted life years; SF-6D: Short form 6 dimensions (scale: 0.0 [death] to 1.0 [full health], negative values mean worse than death); SF-12: short-form 12, 0-100.

- (a) For studies where the time horizon is longer than the treatment duration, an assumption needs to be made about the continuation of the study effect. For example, does a difference in utility between groups during treatment continue beyond the end of treatment and if so for how long.
- (b) Converted using 2007 purchasing power parities⁹²⁹
- (c) Directly applicable / Partially applicable / Not applicable
- (d) Minor limitations / Potentially serious limitations / Very serious limitations

Table 208: BRETTSCHEIDER 2015¹⁹⁰

Brettschneider,Christian; Luck,Tobias; Fleischer,Steffen; Roling,Gudrun; Beutner,Katrin; Lupp,Melanie; Behrens,Johann; Riedel-Heller,Steffi G.; Konig,Hans Helmut. Cost-utility analysis of a preventive home visit program for older adults in Germany. *BMC health services research*: 15: 141, 2015. Netherlands 2012; 7(5):e37444. (Guideline Ref ID BRETTSCHEIDER2015)

Study details	Population & interventions	Costs	Health outcomes	Cost effectiveness
<p>Economic analysis: CUA (health outcome: QALYs)</p> <p>Study design: Within-trial analysis (RCT, same associated clinical paper)</p> <p>Approach to analysis: EQ5D data used to estimate QALYs at 18 months using linear interpolation between measurement points.</p> <p>Total costs for each individual estimated dividing the total costs measured at follow up over 18 months and multiplying this by the number of days between the measurement points.</p> <p>Differences in mean costs and QALYs adjusted for study region, age, gender, baseline HRQoL, cost at baseline, by</p>	<p>Population: Community dwelling adults 80 years or older.</p> <p>Cohort settings: Mean age: 85 Male/female ratio: 31:69 N = 304 (1 patient was excluded from the analysis ex post)</p> <p>Intervention 1: Usual Care: every service offered by statutory health insurance system and utilised at patient's own initiative. Duration 4 weeks.</p> <p>Intervention 2:</p>	<p>Total costs (mean per patient):</p> <p>Intervention 1: adjusted cost NR (unadjusted was £7,144)</p> <p>Intervention 2: adjusted cost NR (unadjusted was £6,835)</p> <p>Incremental (2–1): £648 (95% CI: NR; p=NR)</p> <p>Currency & cost year: 2008 Euros (presented here as 2008 UK pounds^(b))</p> <p>Cost components</p>	<p>QALYs (mean per patient):</p> <p>Intervention 1: adjusted QALYs NR (unadjusted was 0.8270)</p> <p>Intervention 2: adjusted QALYs NR (unadjusted was 0.8256)</p> <p>Incremental (2–1): 0.0061 (95% CI: NR;p=0.88)</p>	<p>ICER (Intervention 2 versus Intervention 1): £106,229 per QALY gained 95% CI: NR Probability Intervention 2 cost-effective (£20K): NR for health care perspective only.</p> <p>Analysis of uncertainty: Probability of Intervention 2 cost effective at a threshold of 50,000 euros per QALY using a societal perspective was 15%. When only patients with complete data were used Intervention 2 was more costly</p>

<p>means of OLS regression.</p> <p>Perspective: German health care perspective (societal perspective was used but the difference between intervention and control for all cost categories was reported and only medical categories were used in this analysis)</p> <p>Follow-up 18 months</p> <p>Treatment effect duration^(a): n/a</p> <p>Discounting: no discounting used for costs or QALYs</p>	<p>Holistic assessment: on first visit performed by trained personnel (nursing scientist, psychologist or sociologist), followed by a case conference with nursing scientist, psychologist, gerontopsychiatrist, nutritionist and social worker, which provided individualised recommendations. Second visit performed by same personnel who performed first visit. A third visit evaluated adherence to recommendations and identified obstacles and facilitators, recommendations were reviewed and further support offered. Duration was 4 weeks.</p>	<p>incorporated:</p> <p>Intervention costs (assessment, case conference, home visit), inpatient services, outpatient services (including GP), medication, medical devices, ambulatory care.</p> <p>Cost of nursing home care, informal care, modification of buildings, transportation not included in this analysis.</p>		<p>and less effective than intervention 1.</p>
Data sources				
<p>Health outcomes: Within-trial analysis. Health outcomes included patient reported EQ5D collected at baseline and 18 months. Quality-of-life weights: EQ5D, UK tariff.</p> <p>Cost sources: Resource use assessed retrospectively over different time periods using questionnaires. German unit costs applied using market prices.</p>				
Comments				
<p>Source of funding: NR. Limitations: German resource use data (2007-08) and unit costs (2008) may not reflect current NHS context. Community dwelling adults aged >80 years may not represent all people with multimorbidity. Time horizon may not be sufficient to capture all benefits and costs if benefits persist beyond 18 months. Within-trial analysis and so does not reflect full body of available evidence for this comparison. Other: Intervention 2 saves £1,510 when a broader perspective is adopted and costs include also nursing home care, informal care, modification of buildings, transportation.</p>				
<p>Overall applicability^(c): Partially applicable Overall quality^(d): Potentially serious limitations</p>				
<p><i>Abbreviations: 95% CI: 95% confidence interval; CUA: cost–utility analysis; EQ-5D: Euroqol 5 dimensions (scale: 0.0 [death] to 1.0 [full health], negative values mean worse than death); ICER: incremental cost-effectiveness ratio; n/a: not applicable; NR: not reported; pa: probabilistic analysis; QALYs: quality-adjusted life years; HRQoL: health-related quality of life.</i></p>				
<p><i>(a) For studies where the time horizon is longer than the treatment duration, an assumption needs to be made about the continuation of the study effect. For example, does a difference in utility between groups during treatment continue beyond the end of treatment and if so for how long.</i></p>				
<p><i>(b) Converted using 2008 purchasing power parities⁹²⁹</i></p>				
<p><i>(c) Directly applicable / Partially applicable / Not applicable</i></p>				
<p><i>(d) Minor limitations / Potentially serious limitations / Very serious limitations</i></p>				

Table 209: EKDAHL 2015³⁹¹

Ekdahl AW, Wirehn AB, Alwin J, Jaarsma T, Unosson M, Husberg M, Eckerblad J, Milberg A, Krevers B, and Carlsson P; Costs and Effects of an Ambulatory Geriatric Unit (the AGE-FIT Study): A Randomized Controlled Trial. <i>Journal of the American Medical Directors Association</i> : 16: 497-503; 2015. (Guideline Ref ID EKDAHL2015)				
Study details	Population & interventions	Costs	Health outcomes	Cost effectiveness
<p>Economic analysis: CCA (health outcome: HRQoL and mortality, not combined)</p> <p>Study design: Within-trial analysis (RCT, same associated clinical paper)</p> <p>Approach to analysis: EQ5D data and mortality not combined.</p> <p>Perspective: Swedish health care (societal perspective reported in the study but only health care costs were used in this analysis)</p> <p>Follow-up 24 months</p> <p>Treatment effect duration^(a): n/a</p> <p>Discounting: NR</p>	<p>Population: Community dwelling adults aged 75 years or older who had received inpatient care 3 or more times in the past 12 months and had 3 or more concomitant medical diagnoses.</p> <p>Cohort settings: Mean age: 82.5 Male/female ratio: 52:48 N = 844</p> <p>Intervention 1: Usual Care</p> <p>Intervention 2: Outpatients high-intensity CGA in addition to usual care</p>	<p>Total costs (mean per patient): Intervention 1: £15,575 Intervention 2: £17,356 Incremental (2-1): £1,781 (95% CI: NR; p=NR)</p> <p>Currency & cost year: 2014 GBP</p> <p>Cost components incorporated: Intervention costs, other ambulatory care in hospital, primary health care, inpatient care. Cost of home help services and institutional living not included here.</p>	<p>Mortality rate Intervention 1: 27/100 Intervention 2: 18.8/100 (95% CI: NR; p=0.057)</p> <p>EQ5D at 12 months Intervention 1: 0.64 Intervention 2: 0.62 (95% CI: NR; p=0.6)</p> <p>EQ5D at 24 months Intervention 1: 0.62 Intervention 2: 0.60 (95% CI: NR; p=0.6)</p>	<p>ICER (Intervention 2 versus Intervention 1): NR</p> <p>Analysis of uncertainty: Using alternative methods for missing data replacement did not lead to any change in the conclusion on the EQ5D data.</p>
Data sources				
Health outcomes: Within-trial analysis. Cost sources: Resource use collected from the care data warehouse of the county council.				
Comments				
Source of funding: public grant. Limitations: Swedish resource use data may not reflect current NHS context; conversion rate used to GBP not reported. Within-trial analysis and so does not reflect full body of available evidence for this comparison. No QALYs reported. Other: Intervention 2 increases costs by £2,881 when a broader perspective is used.				
Overall applicability ^(c) : Partially applicable Overall quality ^(d) : Potentially serious limitations				

Abbreviations: 95% CI: 95% confidence interval; CCA: cost-consequences analysis; EQ-5D: Euroqol 5 dimensions (scale: 0.0 [death] to 1.0 [full health], negative values mean worse than death); ICER: incremental cost-effectiveness ratio; n/a: not applicable; NR: not reported; QALYs: quality-adjusted life years.

- (a) For studies where the time horizon is longer than the treatment duration, an assumption needs to be made about the continuation of the study effect. For example, does a difference in utility between groups during treatment continue beyond the end of treatment and if so for how long.
- (b) Directly applicable / Partially applicable / Not applicable
- (c) Minor limitations / Potentially serious limitations / Very serious limitations

Table 210: TANAJEWSKI 2015¹¹⁶⁹

Tanajewski L, Franklin M, Gkountouras G, Berdunov V, Edmans J, Conroy S, Bradshaw LE, Gladman JRF, and Elliott RA; Cost-Effectiveness of a Specialist Geriatric Medical Intervention for Frail Older People Discharged from Acute Medical Units: Economic Evaluation in a Two-Centre Randomised Controlled Trial (AMIGOS). PloS one: 10: e0121340; 2015.(Guideline Ref ID TANAJEWSKI2015)				
Study details	Population & interventions	Costs	Health outcomes	Cost effectiveness
<p>Economic analysis: CUA (health outcome: QALYs)</p> <p>Study design: Within-trial analysis (RCT, associated clinical paper Edmans 2013³⁸⁵)</p> <p>Approach to analysis: EQ5D data and cost collected for each individual. Missing data imputed using multiple imputation by chained equations. Adjusted costs and QALYs estimated using ordinary least squares (OLS) method controlling for age, sex, hospital location and baseline utility.</p> <p>Perspective: UK NHS and social care</p> <p>Follow-up: 90 days</p> <p>Treatment effect duration^(a): n/a</p>	<p>Population: Patients discharged from an acute medical unit within 72 hours of attending hospital, aged 70 or over, and identified as being at heightened risk of future health problems (defined by a score of at least 2/6 on the Identification of Seniors At Risk tool).</p> <p>Cohort settings: Mean age: 83 Male/female ratio: 159/274 N =433</p> <p>Intervention 1: Usual care</p> <p>Intervention 2: Inpatient CGA: usual care plus interface geriatrician.</p>	<p>Total costs (mean per patient): Intervention 1: £4,110 Intervention 2: £4,412 Incremental (2–1): £302 (95% CI: £193 - £410; p=NR)</p> <p>Currency & cost year: 2012 GBP</p> <p>Cost components incorporated: Intervention cost (geriatrician time), primary care services, ambulance services, hospital care, social care (assessments and care plans including home, day, residential and telephone care, housing and meals-on-wheels). The cost of delivering the intervention was £208</p>	<p>QALYs (mean per patient): Intervention 1: 0.107 Intervention 2: 0.106 Incremental (2–1): -0.001 (95% CI: -0.009 – 0.007;p=NR)</p>	<p>ICER (Intervention 2 versus Intervention 1): Intervention 1 dominates intervention 2 95% CI: N/A Probability Intervention 2 cost-effective (£20K): 0%</p> <p>Analysis of uncertainty: Using only the complete (adjusted) case data, the incremental cost and QALYs of Intervention 2 vs 1 are respectively £235 and 0.002, with a resulting ICER of £116,326 per QALY gained. The probability of Intervention 2 being cost effective at £20k threshold is 1%</p>

Discounting: NA
Data sources
Health outcomes: Within-trial analysis. Cost sources: Resource use collected from the trial; unit costs from UK national sources applied.
Comments
Source of funding: National Institute for Health Research (NIHR). Limitations: patients may not represent all people with multimorbidity. Time horizon may not be sufficient to capture all benefits and costs if benefits persist beyond 90 days. Within-trial analysis and so does not reflect full body of available evidence for this comparison. Unclear if social care costs include only the assessment and care plan formulation or also other modifications.
Overall applicability^(c): Partially applicable Overall quality^(d): Potentially serious limitations

Abbreviations: 95% CI: 95% confidence interval; CUA: cost–utility analysis; ICER: incremental cost-effectiveness ratio; n/a: not applicable; NR: not reported; QALYs: quality-adjusted life years.

(a) For studies where the time horizon is longer than the treatment duration, an assumption needs to be made about the continuation of the study effect. For example, does a difference in utility between groups during treatment continue beyond the end of treatment and if so for how long.

(b) Directly applicable / Partially applicable / Not applicable

(c) Minor limitations / Potentially serious limitations / Very serious limitations

I.6 Self-management

No health economic evidence was identified for this review.

I.7 Format of encounters

No health economic evidence was identified for this review.

Appendix J: GRADE tables

J.1 Principles/Barriers of care

J.1.1 Principles of care

None.

J.1.2 Barriers of care

None.

J.2 Identification

J.2.1 Unplanned hospital admissions

None.

J.2.2 Health-related quality of life

None.

J.2.3 Admission to care facility

None.

J.2.4 Life expectancy risk tools

None.

J.2.5 Polypharmacy: unplanned hospital admissions

J.2.5.1 Community-dwelling

Table 211: Risk of hospitalisation at various thresholds of polypharmacy

Quality assessment							Adjusted effects	Quality
Number of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other, including publication bias where possible	Pooled effect with 95% CIs [if meta-analysed] OR Effect and CI in single study	
Polypharmacy (≥5 drugs) vs. no polypharmacy (<5 drugs) for predicting hospitalisation (unadjusted HR) [older adults, community-dwelling]								
1	Cohort	LOW ^a	No serious inconsistency	Serious indirectness ^b	Serious imprecision ^c	None	Unadjusted HR [95% CI]: 1.00 [0.78 – 1.28]	LOW

(a) Risk of bias was assessed using QUIPS

(b) Downgraded once as the majority of the evidence included an indirect population

(c) Downgraded once as the 95% CI crosses the null line

J.2.5.2 Living in care facility

Table 212: Risk of hospitalisation at various thresholds of polypharmacy

Quality assessment							Adjusted effects	Quality
Number of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other, including publication bias where possible	Pooled effect with 95% CIs [if meta-analysed] OR Effect and CI in single study	
Polypharmacy (5-9 drugs) vs. no polypharmacy (<5 drugs) for predicting ambulatory care sensitive hospitalisation (subhazard RR) [older adults, living in care facility]								
1	Cohort	LOW ^a	No serious inconsistency	Serious indirectness ^b	Serious imprecision ^c	None	Subhazard RR [95% CI]: 1.10 (0.96 – 1.25)	VERY LOW
Polypharmacy (5-9 drugs) vs. no polypharmacy (<5 drugs) for predicting nursing home sensitive hospitalisation (subhazard RR) [older adults, living in care facility]								

1	Cohort	LOW ^a	No serious inconsistency	Very serious indirectness ^b	No serious imprecision	None	Subhazard RR [95% CI]: 1.19 (1.07 – 1.33)	LOW
Polypharmacy (5-9 drugs) vs. no polypharmacy (<5 drugs) for predicting 'unavoidable' hospitalisation (subhazard RR) [older adults, living in care facility]								
1	Cohort	LOW ^a	No serious inconsistency	Very serious indirectness ^b	No serious imprecision	None	Subhazard RR [95% CI]: 1.21 (1.09 – 1.33)	LOW
Polypharmacy (10-14 drugs) vs. no polypharmacy (<5 drugs) for predicting ambulatory care sensitive hospitalisation (subhazard RR) [older adults, living in care facility]								
1	Cohort	LOW ^a	No serious inconsistency	Very serious indirectness ^b	No serious imprecision	None	Subhazard RR [95% CI]: 1.24 (1.09 – 1.42)	LOW
Polypharmacy (10-14 drugs) vs. no polypharmacy (<5 drugs) for nursing home sensitive hospitalisation (subhazard RR) [older adults, living in care facility]								
1	Cohort	LOW ^a	No serious inconsistency	Very serious indirectness ^b	No serious imprecision	None	Subhazard RR [95% CI]: 1.33 (1.19 – 1.49)	LOW
Polypharmacy (10-14 drugs) vs. no polypharmacy (<5 drugs) for 'unavoidable' hospitalisation (subhazard RR) [older adults, living in care facility]								
1	Cohort	LOW ^a	No serious inconsistency	Very serious indirectness ^b	No serious imprecision	None	Subhazard RR [95% CI]: 1.39 (1.25 – 1.54)	LOW
Polypharmacy (≥15 drugs) vs. no polypharmacy (<5 drugs) for predicting ambulatory care sensitive hospitalisation (subhazard RR) [older adults, living in care facility]								
1	Cohort	LOW ^a	No serious inconsistency	Very serious indirectness ^b	No serious imprecision	None	Subhazard RR [95% CI]: 1.41 (1.22 – 1.63)	LOW
Polypharmacy (≥15 drugs) vs. no polypharmacy (<5 drugs) for predicting nursing home sensitive hospitalisation (subhazard RR) [older adults, living in care facility]								
1	Cohort	LOW ^a	No serious inconsistency	Very serious indirectness ^b	No serious imprecision	None	Subhazard RR [95% CI]: 1.42 (1.26 – 1.61)	LOW
Polypharmacy (≥15 drugs) vs. no polypharmacy (<5 drugs) for predicting 'unavoidable' hospitalisation (subhazard RR) [older adults, living in care facility]								
1	Cohort	LOW ^a	No serious inconsistency	Very serious indirectness ^b	No serious imprecision	None	Subhazard RR [95% CI]: 1.38 (1.23 – 1.54)	LOW

(a) Risk of bias was assessed using QUIPS

(b) Downgraded twice as the majority of the evidence included an indirect population and the outcome included unplanned admissions within 1 year of baseline

(c) Downgraded once as the 95% CI crosses the null line

J.2.6 Polypharmacy: health-related quality of life

None.

J.2.7 Polypharmacy: admission to care facilities

Table 213: Risk of mortality at various thresholds of polypharmacy

Quality assessment							Adjusted effects		Quality
Number of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other, including publication bias where possible	Pooled effect with 95% CIs [if meta-analysed] OR	Effect and CI in single study	
Polypharmacy (≥ 13 drugs) for predicting admission to care facility (unadjusted RR) [older adults, community dwelling]									
1	Cohort studies	LOW ^a	No serious inconsistency	Serious indirectness ^b	No serious imprecision	None	Unadjusted RR [95% CI]: 3.31 [3.16 – 3.46]		MODERATE

(a) Risk of bias was assessed using QUIPS

(b) The majority of the evidence included an indirect population

J.2.8 Polypharmacy: mortality

J.2.8.1 Prognostic accuracy data

Table 214: Prognostic accuracy of polypharmacy for predicting mortality

Quality assessment							Prognostic accuracy data				Quality
Number of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations, including publication bias where possible	Sensitivity	Specificity	AUC	R ²	
Polypharmacy (≥ 5 drugs) vs. no polypharmacy (< 5 drugs) for predicting mortality											
1	Cohort studies	HIGH ^a	No serious inconsistency	Serious indirectness ^b	Not estimable	None	0.51	0.65	0.61	-	LOW

(a) Risk of bias was assessed using the PROBAST checklist

Polypharmacy (≥ 6 drugs) vs. no medication (0 drugs) for predicting mortality (unadjusted HR)Polypharmacy (6-9 drugs) vs. no polypharmacy (<5 drugs) for predicting mortality (unadjusted HR)Polypharmacy (≥ 10 drugs) vs. no polypharmacy (<5 drugs) for predicting mortality (unadjusted HR)*(b) Downgraded once as the majority of the evidence included an indirect population***J.2.8.2 Unadjusted data****Table 215: Risk of mortality at various thresholds of polypharmacy**

Quality assessment							Adjusted effects	Quality
Number of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations, including publication bias where possible	Pooled effect with 95% CIs [if meta-analysed] OR Effect and CI in single study	
Polypharmacy (≥ 5 drugs) vs. no polypharmacy (<5 drugs) for predicting mortality (unadjusted HR)								
2	Cohort	LOW ^a	No serious inconsistency	Serious indirectness ^b	No serious imprecision	None	Unadjusted HR [95% CI]: 1.87 [1.77 - 1.98]	MODERATE
1	Cohort	LOW ^a	No serious inconsistency	Serious indirectness ^b	No serious imprecision	None	Unadjusted HR [95% CI]: 2.78 [2.36 - 3.27]	MODERATE
1	Cohort	LOW ^a	No serious inconsistency	Serious indirectness ^b	No serious imprecision	None	Unadjusted HR [95% CI]: 1.50 [1.14 - 1.98]	MODERATE
1	Cohort	LOW ^a	No serious inconsistency	Serious indirectness ^b	No serious imprecision	None	Unadjusted HR [95% CI]: 2.87 [2.20 - 3.74]	MODERATE

*(a) Risk of bias was assessed using QUIPS**(b) The majority of the evidence included an indirect population***Table 216: Risk of mortality with increasing polypharmacy (polypharmacy as a continuous predictor)**

Quality assessment	Adjusted effects	Quality
--------------------	------------------	---------

Number of drugs for predicting mortality (unadjusted OR)								
Number of drugs for predicting mortality (unadjusted OR)								
Quality assessment							Adjusted effects	Quality
Number of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations, including publication bias where possible	Pooled effect with 95% CIs [if meta-analysed] OR Effect and CI in single study	
Number of drugs for predicting mortality (unadjusted HR)								
2	Cohort	LOW ^a	No serious inconsistency	Serious indirectness ^b	No serious imprecision	None	Unadjusted HR [95% CI]: 1.16 [1.14 – 1.18]	MODERATE
2	Cohort	LOW ^a	No serious inconsistency	Serious indirectness ^b	No serious imprecision	None	Unadjusted OR [95% CI]: 1.16 [1.13 – 1.20]	MODERATE
1	Cohort	LOW ^a	No serious inconsistency	Serious indirectness ^b	Not estimable	None	Unadjusted OR: 1.26 [not reported] ^c	MODERATE

(a) Risk of bias was assessed using QUIPS

(b) Downgraded once as the majority of the evidence included an indirect population

(c) OR calculated by $\text{Exp}(\beta \text{ coefficient})$

Table 217: Risk of mortality with increasing polypharmacy (polypharmacy as a continuous predictor as assessed using number of drug classes)

Quality assessment							Adjusted effects	Quality
Number of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations, including publication bias where possible	Pooled effect with 95% CIs [if meta-analysed] OR Effect and CI in single study	
Number of drug classes for predicting mortality (unadjusted HR)								
1	Cohort	VERY HIGH ^a	No serious inconsistency	Serious indirectness ^b	No serious imprecision	None	Unadjusted HR [95% CI]: 1.19 [1.15 – 1.22]	VERY LOW

(a) Risk of bias was assessed using QUIPS; downgraded twice as the majority of evidence was at high risk of bias

(b) Downgraded once as the majority of the evidence included an indirect population

Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Stopping	Continuing antihypertensive treatment	Relative (95% CI)	Absolute		
-------------------	--------	--------------	---------------	--------------	-------------	----------------------	----------	---------------------------------------	-------------------	----------	--	--

J.3 Frailty

None.

J.4 Delivering an approach to care that takes account of multimorbidity

J.4.1 Treatment burden

None.

J.4.2 Ranking

None.

J.4.3 Stopping antihypertensive treatment

Table 218: Clinical evidence profile: stopping versus continuing antihypertensive treatment

Quality assessment							Number of patients	Effect	Quality	Importance		
Cardiovascular mortality (follow-up 52-72 weeks)												
2	Randomised trials	Serious ¹	Very serious ²	No serious indirectness	Very serious ³	None	1/91 (1.1%)	1/57 (1.8%)	OR 0.65 (0.04 to 11.68) ⁴	6 fewer per 1000 (from 17 fewer to 155 more)	VERY LOW	CRITICAL
Fatal myocardial infarction (follow-up 72 weeks)												
1	Randomised trials	Serious ¹	No serious inconsistency	No serious indirectness	Very serious ³	None	1/60 (1.7%)	0/26 (0%)	OR 4.19 (0.06 to 299.15) ⁴	17 more per 1000 (from 47 fewer to 81 more)	VERY LOW	CRITICAL

Non-fatal myocardial infarction (follow-up 1 years)												
1	Randomised trials	Serious ^a	No serious inconsistency	No serious indirectness	Very serious ^c	None	1/31 (3.2%)	0/31 (0%)	OR 7.39 (0.15 to 372.38) ^d	32 more per 1000 (from 53 fewer to 117 more)	VERY LOW	CRITICAL
Transient ischaemic attack (follow-up 1 year)												
1	Randomised trials	Serious ^a	No serious inconsistency	No serious indirectness	Very serious ^c	None	0/31 (0%)	1/31 (3.2%)	OR 0.14 (0 to 6.82) ^d	28 fewer per 1000 (from 32 fewer to 153 more)	VERY LOW	CRITICAL
Non-fatal congestive heart failure (follow-up 72 weeks)												
1	Randomised trials	Serious ^a	No serious inconsistency	No serious indirectness	Very serious ^c	None	5/60 (8.3%)	0/26 (0%)	OR 4.5 (0.64 to 31.79) ^d	83 more per 1000 (from 5 fewer to 171 more)	VERY LOW	CRITICAL
Atrial fibrillation (follow-up 72 weeks)												
1	Randomised trials	Serious ^a	No serious inconsistency	No serious indirectness	Very serious ^c	None	1/60 (1.7%)	0/26 (0%)	OR 4.19 (0.06 to 299.15) ^d	17 more per 1000 (from 47 fewer to 81 more)	VERY LOW	CRITICAL
Right bundle block (follow-up 72 weeks)												
1	Randomised trials	Serious ^a	No serious inconsistency	No serious indirectness	Very serious ^c	None	1/60 (1.7%)	0/26 (0%)	OR 4.19 (0.06 to 299.15) ^d	17 more per 1000 (from 47 fewer to 81 more)	VERY LOW	IMPORTANT
Return to hypertension (follow-up 1-2 years; assessed with: number of patients who revert to hypertension)												
2	Randomised trials	Serious ^a	no serious inconsistency	no serious indirectness	no serious imprecision	none	60/89 (67.4%)	4/56 (7.1%)	RR 7.66 (2.97 to 19.71)	476 more per 1000 (from 141 more to 1000 more)	MODERATE	IMPORTANT
Maintaining blood pressure												
1	Randomised trials	Serious ^a	no serious inconsistency	no serious indirectness	Serious ^c	none	57/129 (44.2%)	147/204 (72.1%)	RR 0.61 (0.5 to 0.76)	281 fewer per 1000 (from 173 fewer to 360 fewer)	LOW	IMPORTANT

All-cause mortality (critical) – no data
Stroke (critical) – no data
Quality of life (critical) – no data
Hospitalisation (critical) – no data
Admission to care facility (critical) – no data
Falls (important) – no data

- (a) Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias*
- (b) Downgraded by 1 or 2 increments because the point estimates varied widely across studies*
- (c) Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs*
- (d) Peto OR*

No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Stopping	Continuing bisphosphonates	Relative (95% CI)	Absolute		
---------------	--------	--------------	---------------	--------------	-------------	----------------------	----------	----------------------------	-------------------	----------	--	--

J.4.4 Stopping drugs for osteoporosis

Table 219: Clinical evidence profile: stopping versus continuing bisphosphonate treatment

Quality assessment							No of patients	Effect	Quality	Importance		
Clinical fracture (follow-up 3 years; any clinical fracture)												
2	randomised trials	Serious ^a	no serious inconsistency	no serious indirectness	very serious ^b	none	-	-	HR 0.95 (0.67 to 1.35)	- ^c	⊕○○○ VERY LOW	CRITICAL
Clinical vertebral fracture (follow-up 3 years)												
1	randomised trials	Serious ^a	no serious inconsistency	no serious indirectness	very serious ^b	none	-	-	HR 0.55 (0.16 to 1.89)	- ^c	⊕○○○ VERY LOW	CRITICAL
Clinical vertebral fracture (follow-up 5 years)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	Serious ^b	none	-	-	RR 2.22 (1.18 to 4.17)	- ^c	⊕⊕⊕○ MODERATE	CRITICAL
Clinical non-vertebral fracture (follow-up 3 years)												
1	randomised trials	Serious ^a	no serious inconsistency	no serious indirectness	very serious ^b	none	-	-	HR 1.01 (0.67 to 1.52)	- ^c	⊕○○○ VERY LOW	CRITICAL
Clinical non-vertebral fracture (follow-up 2-5 years)												
3	randomised trials	no serious risk of bias	Serious ^d	no serious indirectness	Serious ^b	none	-	-	RR 0.98 (0.76 to 1.27)	- ^c	⊕⊕○○ LOW	CRITICAL
Morphometric vertebral fracture (follow-up 3-5 years)												
3	randomised	Serious ^a	no serious	no serious	Serious ^b	none	-	-	OR 1.36	- ^c	⊕⊕○○	CRITICAL

	trials		inconsistency	indirectness					(0.97 to 1.91)		LOW	
Hospitalisation (follow-up 3 years)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	125/437 (28.6%)	183/662 (27.6%)	RR 1.03 (0.85 to 1.25)	8 more per 1000 (from 41 fewer to 69 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Atypical femur fracture (follow-up 3 years)												
1	randomised trials	Serious ^a	no serious inconsistency	no serious indirectness	no serious imprecision	none	0/486 (0%)	0/469 (0%)	See comment ^e	- ^e	⊕⊕⊕○ MODERATE	IMPORTANT
Discontinuation of study due to side effects (follow-up 2-3 years)												
4	randomised trials	no serious risk of bias	Serious ^d	no serious indirectness	very serious ^b	none	67/1186 (5.6%)	94/1401 (6.7%)	RR 0.96 (0.71 to 1.29)	3 fewer per 1000 (from 19 fewer to 19 more)	⊕○○○ VERY LOW	IMPORTANT
Health related quality of life												
0	-	-	-	-	-	-	-	-	-	-	-	-
Functional outcome												
0	-	-	-	-	-	-	-	-	-	-	-	-
Falls												
0	-	-	-	-	-	-	-	-	-	-	-	-
Pain												
0	-	-	-	-	-	-	-	-	-	-	-	-
Admission to care facility												
0	-	-	-	-	-	-	-	-	-	-	-	-
GI bleed												

No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Stop statins	Continue statins	Relative (95% CI)	Absolute
0	-	-	-	-	-	-	-	-	-	-
Osteonecrosis jaw										
0	-	-	-	-	-	-	-	-	-	-

(a) Downgraded once if the majority of evidence was at high risk of bias and twice if the majority of the evidence was at very high risk of bias

(b) Downgraded once if the CI crossed one MID and twice if the CI crossed two MIDs

(c) Not calculated as (adjusted) raw data was not reported

(d) Downgraded once if I² >50% and/or there was serious variation in point estimates, and twice if I² >75% and/or there was very serious variation in point estimates

(e) Not calculated as zero events in both groups

J.4.5 Stopping statins

Table 220: Clinical evidence profile – stopping statins versus continuing

Quality assessment			No of patients				Effect	Quality	Importance			
Quality of life - Total (follow-up 20 weeks; measured with: MacGill (0-10) area under the curve at 20 weeks; range of scores: 0-10; Better indicated by higher values)												
1	randomised trials	Serious ^a	no serious inconsistency	no serious indirectness	serious imprecision	none	189	192	-	MD 0.26 higher (0.02 to 0.5 higher)	⊕⊕⊕ LOW	CRITICAL
All-cause mortality (time to event) (follow-up median 18 weeks)												
1	randomised trials	Serious ^a	no serious inconsistency	no serious indirectness	very serious ^b	none	88/189 (46.6%)	98/192 (51%)	HR 0.95 (0.7 to 1.28)	18 fewer per 1000 (from 117 fewer to 89 more)	⊕⊕⊕ VERY LOW	CRITICAL
Cardiovascular-related events (follow-up median 18 weeks)												
1	randomised trials	Serious ^a	no serious inconsistency	no serious indirectness	very serious ^b	none	13/182 (7.1%)	11/189 (5.8%)	RR 1.23 (0.56 to 2.67)	13 more per 1000 (from 26 fewer to 97 more)	⊕⊕⊕ VERY LOW	CRITICAL
Hospitalisation – no data												
Cardiovascular mortality – no data												

Stroke – no data
Admission to care home – no data
Myalgia – no data

(a) Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

(b) Downgraded by one increment if the confidence interval crossed one MID or by two increments if the confidence interval crossed both MIDs

No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Alkema 2007	Control	Relative (95% CI)	Absolute		
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Beck 1997	Control	Relative (95% CI)	Absolute		

J.5 Interventions

J.5.1 Models of care

J.5.1.1 Models of care

Table 221: Clinical evidence profile: interventions versus usual care – Alkema 2007

Quality assessment							No. of patients	Effect	Quality	Importance		
Mortality (died during total study) (follow-up mean 24 months)												
1	randomised trials	very serious ^a	no serious inconsistency	Serious ^b	none	none	51/377 (13.5%)	90/404 (22.3%)	RR 0.61 (0.44 to 0.83)	87 fewer per 1000 (from 38 fewer to 125 fewer)	⊕○○○ VERY LOW	CRITICAL

(a) Downgraded by 1 increment if the majority of the evidence was at a high risk of bias, and downgraded by 2 increments if the majority of the evidence was at a very high risk of bias

(b) Downgraded by 1 or 2 increments because the majority of the evidence included an indirect population (downgrade by 1 increment) or a very indirect population (downgrade by 2 increments)

Table 222: Clinical evidence profile: interventions versus usual care – Beck 1997

Quality assessment							No of patients	Effect	Quality	Importance		
Mortality (follow-up 12 months)												
1	randomised trials	no serious risk of bias	no serious inconsistency	Serious ^a	Serious ^b	none	5/160 (3.1%)	9/161 (5.6%)	RR 0.56 (0.19 to 1.63)	25 fewer per 1000 (from 45 fewer to 35 more)	⊕⊕○○ LOW	CRITICAL
Unscheduled care (urgent care visits per patient) (follow-up 12 months; Better indicated by lower values)												

No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Berglund 2015	Control	Relative (95% CI)	Absolute		
1	randomised trials	Serious ^c	no serious inconsistency	Serious ^a	no serious imprecision ^b	none	160	161	-	MD 0.06 lower (0.23 lower to 0.11 higher)	⊕⊕⊕⊕ LOW	CRITICAL
Unscheduled care (emergency care visits per patient) (follow-up 12 months; Better indicated by lower values)												
1	randomised trials	Serious ^c	no serious inconsistency	Serious ^a	no serious imprecision ^b	none	160	161	-	MD 0.26 lower (0.54 lower to 0.02 higher)	⊕⊕⊕⊕ LOW	CRITICAL
Unscheduled care (proportion of patients hospitalised) (follow-up 12 months; Better indicated by lower values)												
1	randomised trials	Serious ^c	no serious inconsistency	Serious ^a	no serious imprecision ^b	none	160	161	-	MD 0.07 lower (0.14 lower to 0 higher)	⊕⊕⊕⊕ LOW	CRITICAL

(a) The majority of the evidence included an indirect population (downgrade by 1 increment) or a very indirect population (downgrade by 2 increments)

(b) Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs

(c) Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

Table 223: Clinical evidence profile: interventions versus usual care – Berglund 2015

Quality assessment							No of patients	Effect			Quality	Importance
Mortality (follow-up 12 months)												
1	randomised trials	Serious ^a	no serious inconsistency	Serious ^b	Serious ^c	none	14/83 (16.9%)	9/76 (11.8%)	RR 1.42 (0.65 to 3.1)	50 more per 1000 (from 41 fewer to 249 more)	⊕⊕⊕⊕ VERY LOW	CRITICAL

(a) Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

(b) The majority of the evidence included an indirect population (downgrade by 1 increment) or a very indirect population (downgrade by 2 increments)

(c) Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs

Table 224: Clinical evidence profile: interventions versus usual care – Bouman 2008

Quality assessment							No of patients	Effect			Quality	Importance
--------------------	--	--	--	--	--	--	----------------	--------	--	--	---------	------------

No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Bouman 2008	Control	Relative (95% CI)	Absolute		
1	randomised trials	serious ^a	no serious inconsistency	serious ^b	no serious imprecision	none	-	-	OR 0.14 (0.04 to 0.45)	~3	⊕⊕⊕ LOW	CRITICAL
Mortality (follow-up 18 months)												
1	randomised trials	Serious ^a	no serious inconsistency	serious ^b	serious ^c	none	29/160 (18.1%)	23/170 (13.5%)	RR 1.34 (0.81 to 2.22)	46 more per 1000 (from 26 fewer to 165 more)	⊕⊕⊕ VERY LOW	CRITICAL
Length of hospital stay (days per patient) (follow-up 18 months; Better indicated by higher values)												
1	randomised trials	Serious ^a	no serious inconsistency	serious ^b	no serious imprecision ^c	none	160	170	-	MD 0.40 lower (4.3 lower to 3.5 higher)	⊕⊕⊕ LOW	CRITICAL
Unscheduled care (hospital admissions) (follow-up 18 months)												
1	randomised trials	serious ^a	no serious inconsistency	Serious ^b	serious ^c	none	80/160 (50%)	71/170 (41.8%)	RR 1.20 (0.95 to 1.52)	84 more per 1000 (from 21 fewer to 217 more)	⊕⊕⊕ VERY LOW	CRITICAL
Unscheduled care (nursing home admissions) (follow-up 18 months)												
1	randomised trials	serious ^a	no serious inconsistency	serious ^b	serious ^c	none	10/160 (6.3%)	11/170 (6.5%)	RR 0.97 (0.42 to 2.21)	2 fewer per 1000 (from 38 fewer to 78 more)	⊕⊕⊕ VERY LOW	CRITICAL

(a) Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

(b) The majority of the evidence included an indirect population (downgrade by 1 increment) or a very indirect population (downgrade by 2 increments)

(c) Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs

Table 225: Clinical evidence profile: interventions versus usual care – Courtney 2009

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Courtney 2009	Control	Relative (95% CI)	Absolute		
Unscheduled care (emergency hospital readmission) (follow-up mean 6 months)												

1	randomised trials	very serious ^a	no serious inconsistency	serious ^b	no serious imprecision	none	15/58 (25.9%)	43/64 (67.2%)	RR 0.38 (0.24 to 0.61)	417 fewer per 1000 (from 262 fewer to 511 fewer)	⊕000 VERY LOW	CRITICAL
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	EII 2010	Control	Relative (95% CI)	Absolute		
Unscheduled care (emergency GP visits) (follow-up mean 6 months)												

- (a) Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
 (b) Downgraded by 1 or 2 increments because: the majority of the evidence included an indirect population (downgraded by 1 increment) or by a very indirect population (downgraded by 2 increments)
 (c) Multivariate analysis with no adjusted raw data

Table 226: Clinical evidence profile: interventions versus usual care – Eklund 2013

Quality assessment							No. of patients	Effect	Quality	Importance		
Mortality (follow-up 12 months)												
1	randomised trials	very serious ^a	no serious inconsistency	serious ^b	serious ^c	none	30/85 (35.3%)	18/76 (23.7%)	RR 1.49 (0.91 to 2.45)	116 more per 1000 (from 21 fewer to 343 more)	⊕000 VERY LOW	CRITICAL
Functional outcomes (any improvement in ADL) (follow-up 12 months)												
1	randomised trials	very serious ^a	no serious inconsistency	serious ^b	serious ^c	none	33/85 (38.8%)	18/76 (23.7%)	RR 1.64 (1.01 to 2.66)	152 more per 1000 (from 2 more to 393 more)	⊕000 VERY LOW	CRITICAL
Functional outcomes (any worsening in ADL) (follow-up 12 months)												
1	randomised trials	very serious ¹	no serious inconsistency	serious ^b	serious ^c	none	32/85 (37.6%)	36/76 (47.4%)	RR 0.79 (0.55 to 1.14)	99 fewer per 1000 (from 213 fewer to 66 more)	⊕000 VERY LOW	CRITICAL

- (a) Downgraded by 1 increment if the majority of the evidence was at a high risk of bias, and downgraded by 2 increments if the majority of the evidence was at a very high risk of bias
 (b) Downgraded by 1 or 2 increments because: the majority of the evidence included an indirect population (downgraded by 1 increment) or a very indirect population (downgraded by 2 increments)
 (c) Downgraded by 1 increment if the confidence interval crossed one 1 MID or by 2 increments if the confidence interval crossed both MIDs

Table 227: Clinical evidence profile: interventions versus usual care – EII 2010

Quality assessment							No. of	Effect	Quality	Importance
--------------------	--	--	--	--	--	--	--------	--------	---------	------------

No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	EII 2010	Control	Relative (95% CI)	Absolute		
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Hogg 2009	Control	Relative (95% CI)	Absolute		
								patients				e
HRQoL (SF12 mental) (follow-up mean 18 months; measured with: HRQoL: SF12 mental component; Better indicated by higher values)												
1	randomised trials	very serious ^a	no serious inconsistency	no serious indirectness	serious ^b	none	194	193	-	MD 1.61 higher (0.77 lower to 3.99 higher)	⊕○○○ VERY LOW	CRITICAL
HRQoL (SF12 physical) (follow-up mean 18 months; measured with: HRQoL: SF12 physical component; Better indicated by higher values)												
1	randomised trials	very serious ^a	no serious inconsistency	no serious indirectness	serious ^b	none	194	193	-	MD 1.28 lower (3.53 lower to 0.97 higher)	⊕○○○ VERY LOW	CRITICAL
Functional outcome (scale of functional impairment) (follow-up mean 18 months; measured with: Sheehan Disability Scale of functional impairment; range of scores: 1-10; Better indicated by lower values)												
1	randomised trials	very serious ^a	no serious inconsistency	no serious indirectness	no serious imprecision	none	194	193	-	MD 0.1 higher (0.5 lower to 0.7 higher)	⊕⊕○○ LOW	CRITICAL

(a) Downgraded by 1 increment if the majority of the evidence was at a high risk of bias, and downgraded by 2 increments if the majority of the evidence was at a very high risk of bias

(b) Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs

Table 228: Clinical evidence profile: interventions versus usual care – Hogg 2009

Quality assessment							No. of patients	Effect	Quality	Importance		
Health-related quality of life (SF36 physical) (follow-up mean 15 months; measured with: HRQuality of life: SF36 physical component; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	serious ^a	no serious inconsistency	serious ^b	serious ^c	none	109	114	-	MD 1.6 higher (0.85 lower to 4.05 higher)	⊕○○○ VERY LOW	CRITICAL
Health-related quality of life (SF36 mental) (follow-up mean 15 months; measured with: HRQuality of life: SF36 mental component; range of scores: 0-100; Better indicated by higher values)												

No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Naylor 2004	Control	Relative (95% CI)	Absolute		
1	randomised trials	serious ^a	no serious inconsistency	serious ^b	serious ^c	none	109	114	-	MD 1.1 lower (3.75 lower to 1.55 higher)	⊕○○○ VERY LOW	CRITICAL
Health-related quality of life (total no days unhealthy in last 30 days) (follow-up mean 15 months; Better indicated by lower values)												
1	randomised trials	serious ^a	no serious inconsistency	serious ^b	very serious ^c	none	112	116	-	MD 1.4 lower (4.54 lower to 1.74 higher)	⊕○○○ VERY LOW	CRITICAL
Mortality (follow-up mean 15 months)												
1	randomised trials	serious ^a	no serious inconsistency	serious ^b	serious ^c	none	3/120 (2.5%)	0/121 (0%)	RR 7.06 (0.37 to 135.18)	-	⊕○○○ VERY LOW	CRITICAL
Unscheduled care (average no of ED visits) (follow-up mean 15 months; Better indicated by lower values)												
1	randomised trials	serious ^a	no serious inconsistency	serious ^b	no serious imprecision	none	120	121	-	MD 0.1 lower (0.37 lower to 0.17 higher)	⊕⊕○○ LOW	CRITICAL
Unscheduled care (average no of hospital admission) (follow-up mean 15 months; Better indicated by lower values)												
1	randomised trials	serious ^a	no serious inconsistency	serious ^{a,b}	no serious imprecision	none	120	121	-	MD 0.06 lower (0.31 lower to 0.19 higher)	⊕⊕○○ LOW	CRITICAL
Patient/Carer treatment burden (caregiver burden) (follow-up mean 15 months; Better indicated by lower values)												
1	randomised trials	serious ^a	no serious inconsistency	serious ^b	no serious imprecision	none	61	68	-	MD 5 lower (8.59 to 1.41 lower)	⊕⊕○○ LOW	IMPORTANT

(a) Downgraded by 1 increment if the majority of the evidence was at a high risk of bias, and downgraded by 2 increments if the majority of the evidence was at a very high risk of bias

(b) Downgraded by 1 or 2 increments because: the majority of the evidence included an indirect population

(c) Downgraded by 1 increment if the confidence interval crossed on MID or by 2 increments if the confidence interval crossed both MIDs

Table 229: Clinical evidence profile: interventions versus usual care – Metzeltin 2013

Quality assessment	No. of patients	Effect	Quality	Importance
Functional outcome (GARS - ADL subscale, 11-44, higher is worse outcome) (follow-up 2 years; range of scores: 11-44; Better indicated by lower values)				

No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Naylor 2004	Control	Relative (95% CI)	Absolute		
1	randomised trials	very serious ^a	no serious inconsistency	serious ^b	no serious imprecision	none	193	153	-	MD 0.77 higher (0.05 lower to 1.59 higher)	⊕000 VERY LOW	CRITICAL
Functional outcome (GARS - IADL subscale, 7-28, higher is worse outcome) (follow-up 2 years; range of scores: 7-28; Better indicated by lower values)												
1	randomised trials	very serious ^a	no serious inconsistency	serious ^b	no serious imprecision	none	193	153	-	MD 0.40 higher (0.54 lower to 1.34 higher)	⊕000 VERY LOW	CRITICAL

(a) Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

(b) Downgraded by 1 or 2 increments because the majority of the evidence included an indirect population (downgraded by 1 increment) or by a very indirect population (downgraded by 2 increments)

Table 230: Clinical evidence profile: interventions versus usual care – Naylor 2004

Quality assessment							No. of patients	Effect			Quality	Importance
Quality of life (Minnesota Living with Heart Failure Questionnaire) (follow-up mean 12 months; measured with: Minnesota Living with Heart Failure Questionnaire; range of scores: 0-105; Better indicated by lower values)												
1	randomised trials	serious ^a	no serious inconsistency	serious ^b	serious ^c	none	75	74	-	MD 0.2 higher (0.36 lower to 0.76 higher)	⊕000 VERY LOW	CRITICAL
Mortality (follow-up mean 12 weeks)												
1	randomised trials	serious ^a	no serious inconsistency	serious ^b	serious ^c	none	11/118 (9.3%)	13/121 (10.7%)	RR 0.87 (0.41 to 1.86)	14 fewer per 1000 (from 63 fewer to 92 more)	⊕000 VERY LOW	CRITICAL
Functional Status (Functional status score) (follow-up mean 12 months; measured with: The Enforced Social Dependency Scale; range of scores: 12-72; Better indicated by lower values)												
1	randomised trials	serious ^a	no serious inconsistency	serious ^a	serious ^c	none	76	71	-	MD 0.2 higher (0.3 lower to 0.7 higher)	⊕000 VERY LOW	CRITICAL

No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Sandberg 2015	Control	Relative (95% CI)	Absolute
---------------	--------	--------------	---------------	--------------	-------------	----------------------	---------------	---------	-------------------	----------

Patient & Carer Satisfaction (Patient satisfaction) at 6 weeks (follow-up 12 weeks; range of scores: 44-100; Better indicated by higher values)

1	randomised trials	serious ^a	no serious inconsistency	serious ^b	no serious imprecision	none	92	91	-	MD 5.3 higher (2.28 to 8.32 higher)	⊕⊕⊕⊕ LOW	CRITICAL
---	-------------------	----------------------	--------------------------	----------------------	------------------------	------	----	----	---	-------------------------------------	-------------	----------

(a) Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

(b) Downgraded by 1 or 2 increments because the majority of the evidence included an indirect population (downgraded by 1 increment) or by a very indirect population (downgraded by 2 increments)

(c) Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDS

Table 231: Clinical evidence profile: interventions versus usual care – Sandberg 2015

Quality assessment		No of patients			Effect	Quality	Importance					
Mortality (follow-up 12 months)												
1	randomised trials	serious ^a	no serious inconsistency	serious ^b	serious ^c	none	10/80 (12.5%) 3/73 (4.1%) RR 3.04 (0.87 to 10.62)	84 more per 1000 (from 5 fewer to 395 more)	⊕⊕⊕⊕ VERY LOW	CRITICAL		
Length of hospital stay (days per patient) (follow-up 12 months; Better indicated by lower values)												
1	randomised trials	serious ^a	no serious inconsistency	serious ^b	no serious imprecision	none	80	73	-	MD 0.55 higher (3.77 lower to 4.87 higher)	⊕⊕⊕⊕ LOW	CRITICAL
Unscheduled care (hospital admissions per patient) (follow-up 12 months; Better indicated by lower values)												
1	randomised trials	very serious ^a	no serious inconsistency	serious ^b	no serious imprecision	none	80	73	-	MD 0.01 higher (0.25 lower to 0.27 higher)	⊕⊕⊕⊕ VERY LOW	CRITICAL

(a) Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

(b) Downgraded by 1 or 2 increments because the majority of the evidence included an indirect population (downgraded by 1 increment) or by a very indirect population (downgraded by 2 increments)

(c) Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDS

Table 232: Clinical evidence profile: interventions versus usual care – Slaets 1997

Quality assessment	No. of patients	Effect	Quality	Importance
--------------------	-----------------	--------	---------	------------

No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Slaets 1997	Control	Relative (95% CI)	Absolute		
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Sommers 2000	Control	Relative (95% CI)	Absolute		
Mortality at unclear time point												
1	randomised trials	serious ^a	no serious inconsistency	serious ^a	serious ^b	none	18/140 (12.9%)	5/97 (5.2%)	RR 2.49 (0.96 to 6.49)	77 more per 1000 (from 2 fewer to 283 more)	⊕000 VERY LOW	CRITICAL
Unscheduled care (hospital readmission)												
1	randomised trials	serious ^a	no serious inconsistency	serious ^a	serious ^b	none	24/138 (17.4%)	29/97 (29.9%)	RR 0.58 (0.36 to 0.93)	126 fewer per 1000 (from 21 fewer to 191 fewer)	⊕000 VERY LOW	IMPORTANT

(a) Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

(b) Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDS

Table 233: Clinical evidence profile: interventions versus usual care – Sommers 2000

Quality assessment							No. of patients	Effect	Quality	Importance		
Mortality (follow-up mean 24 months)												
1	randomised trials	very serious ^a	no serious inconsistency	no serious indirectness	serious ^c	none	24/280 (8.6%)	26/263 (9.9%)	OR 0.63 (0.41 to 0.97)	-	⊕000 VERY LOW	CRITICAL
Unscheduled care (hospital admissions per year) (follow-up mean 24 months)												
1	randomised trials	very serious ^a	no serious inconsistency	no serious indirectness	serious ^c	none	94/383 (24.5%)	118/351 (33.6%)	RR 0.72 (0.51 to 1.02)	94 fewer per 1000 (from 165 fewer to 7 more)	⊕000 VERY LOW	CRITICAL

(a) Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

(b) Downgraded by 1 or 2 increments because: the majority of the evidence included an indirect population

(c) Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDS

Quality of life - group meetings vs control - deterioration in self-rated health by SF-36 (follow-up 24 months)
Quality of life - single visit vs control - deterioration in satisfaction with physical health (follow-up 24 months)
Quality of life - group meetings vs control - deterioration in satisfaction with physical health (follow-up 24 months)
Quality of life - single visit vs control - deterioration in satisfaction with psychological health (follow-up 24 months)
Quality of life - group vs control - deterioration in satisfaction with psychological health (follow-up 24 months)

J.5.1.2 Models of care including a self-management component

Table 234: Clinical evidence profile: interventions versus usual care – Behm 2014

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Behm 2014	Control	Relative (95% CI)	Absolute		
Quality of life - single visit vs control - deterioration in self-rated health by SF-36 (follow-up 24 months)												
1	randomised trials	Serious ^a	no serious inconsistency	serious ^b	serious ^c	none	42/174 (24.1%)	33%	OR 0.64 (0.38 to 1.07)	90 fewer per 1000 (from 172 fewer to 15 more)	⊕○○○ VERY LOW	CRITICAL
1	randomised trials	serious ^a	no serious inconsistency	serious ^b	very serious ^c	none	55/171 (32.2%)	33%	OR 0.95 (0.57 to 1.57)	11 fewer per 1000 (from 111 fewer to 106 more)	⊕○○○ VERY LOW	CRITICAL
1	randomised trials	serious ^a	no serious inconsistency	serious ^b	serious ^c	none	17/174 (9.8%)	21%	OR 0.43 (0.22 to 0.84)	107 fewer per 1000 (from 27 fewer to 155 fewer)	⊕○○○ VERY LOW	CRITICAL
1	randomised trials	serious ^c	no serious inconsistency	serious ^b	no serious imprecision	none	12/171 (7%)	21%	OR 0.28 (0.14 to 0.59)	141 fewer per 1000 (from 74 fewer to 174 fewer)	⊕⊕○○ LOW	CRITICAL
1	randomised trials	serious ^c	no serious inconsistency	serious ^b	no serious imprecision	none	19/174 (10.9%)	29%	OR 0.30 (0.16 to 0.56)	181 fewer per 1000 (from 104 fewer to 229 fewer)	⊕⊕○○ LOW	CRITICAL
1	randomised trials	serious ^c	no serious inconsistency	serious ^b	no serious imprecision	none	24/171 (14%)	29%	OR 0.40 (0.22 to 0.72)	150 fewer per 1000 (from 63 fewer to 208 fewer)	⊕⊕○○ LOW	CRITICAL

(a) Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

(b) Downgraded by 1 or 2 increments because: the majority of the evidence included an indirect population

(c) Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDS

No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Boult 2008 (Boyd 2010, Boult 2011)	Control	Relative (95% CI)	Absolute		
----------------	--------	--------------	---------------	--------------	-------------	----------------------	------------------------------------	---------	-------------------	----------	--	--

Table 235: Clinical evidence profile: interventions versus usual care – Boult 2008

Quality assessment							No. of patients	Effect		Quality	Importance	
Health-related quality of life (SF-36 physical) at 32 months (follow-up mean 6 months; measured with: SF36; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	very serious ^a	no serious inconsistency	serious ^b	serious ^c	none	408	359	-	MD 1.31 lower (3.02 lower to 0.4 higher)	⊕000 VERY LOW	CRITICAL
Health-related quality of life (SF-36 mental) at 32 months (follow-up mean 6 months; measured with: SF36; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	very serious ^a	no serious inconsistency	serious ^b	serious ^c	none	408	359	-	MD 1.05 higher (1.06 lower to 3.16 higher)	⊕000 VERY LOW	CRITICAL
Mortality at 32 months (follow-up mean 6 months)												
1	randomised trials	very serious ^a	no serious inconsistency	serious ^b	serious ^c	none	28/485 (5.8%)	24/419 (5.7%)	RR 0.88 (0.59 to 1.31)	7 fewer per 1000 (from 23 fewer to 18 more)	⊕000 VERY LOW	CRITICAL
Patient satisfaction (PACIC) at 32 months (follow-up mean 6 months; Better indicated by lower values)												
1	randomised trials	very serious ^a	no serious inconsistency	serious ^b	serious ^c	none	408	359	-	MD 0.27 higher (0.08 to 0.46 higher)	⊕000 VERY LOW	CRITICAL
Patient satisfaction ('very satisfied' with regular healthcare) at 32 months (follow-up mean 6 months; Better indicated by higher values)												
1	randomised trials	very serious ^a	no serious inconsistency	serious ^b	serious ^c	none	408	359	OR 1.50 (0.77 to 2.90)	- ^d	⊕000 VERY LOW	CRITICAL
Unscheduled care (emergency department visits) at 6-8 months (follow-up mean 6 months; Better indicated by lower values)												
1	randomised trials	very serious ^a	no serious inconsistency	serious ^b	no serious imprecision	none	408	359	OR 1.04 (0.81 to 1.34)	- ^d	⊕000 VERY LOW	CRITICAL
Continuity of care (integration subscale) at 32 months (follow-up mean 6 months; Better indicated by lower values)												

No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Chow 2014	Control	Relative (95% CI)	Absolute		
1	randomised trials	very serious ^a	no serious inconsistency	serious ^b	very serious ^c	none	408	359	-	MD 2.79 higher (0.97 lower to 6.55 higher)	⊕○○○ VERY LOW	IMPORTANT
Continuity of care (communication subscale) at 32 months (follow-up mean 6 weeks; Better indicated by lower values)												
1	randomised trials	very serious ^a	no serious inconsistency	serious ^b	very serious ^c	none	408	359	-	MD 2.97 higher (0.68 lower to 6.62 higher)	⊕○○○ VERY LOW	IMPORTANT
Continuity of care (same day access to GP) at 32 months (follow-up mean 6 months; Better indicated by higher values)												
1	randomised trials	very serious ^a	no serious inconsistency	serious ^b	very serious ^c	none	408	359	OR 1.20 (0.65 to 2.22)	- ^d	⊕○○○ VERY LOW	IMPORTANT

(a) Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

(b) Downgraded by 1 or 2 increments because: the majority of the evidence included an indirect population

(c) Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs

(d) Multivariate analysis with no adjusted raw data

Table 236: Clinical evidence profile: interventions versus usual care – Chow 2015

Quality assessment							No of patients	Effect		Quality	Importance	
Health related quality of life - phone vs control - mental (follow-up 12 weeks; measured with: SF-36 mental; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	serious ^a	no serious inconsistency	no serious indirectness	serious ^b	none	96	98	-	MD 1.2 higher (1.5 lower to 3.9 higher)	⊕⊕○○ LOW	CRITICAL
Health related quality of life - phone vs control - physical (follow-up 12 weeks; measured with: SF-36 physical; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	serious ^a	no serious inconsistency	no serious indirectness	serious ^b	none	96	98	-	MD 3.3 higher (1.2 to 5.4 higher)	⊕⊕○○ LOW	CRITICAL
Health related quality of life - visit vs phone - mental (follow-up 12 weeks; measured with: SF-36 mental; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	serious ^a	no serious inconsistency	no serious indirectness	serious ^b	none	87	96	-	MD 0.7 higher (1.89 lower to 3.29 higher)	⊕⊕○○ LOW	CRITICAL
Health related quality of life - visit vs phone - physical (follow-up 12 weeks; measured with: SF-36 physical; range of scores: 0-100; Better indicated by higher values)												

No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Coburn 2012	Control	Relative (95% CI)	Absolute		
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Gitlin 2006 (Gitlin 2009, Gitlin 2006A)	Control	Relative (95% CI)	Absolute		
1	randomised trials	serious ^a	no serious inconsistency	no serious indirectness	no serious imprecision ^b	none	87	96	-	MD 0.2 lower (2.37 lower to 1.97 higher)	⊕⊕⊕⊕ MODERATE	CRITICAL
Health related quality of life - visit vs control - mental (follow-up 12 weeks; measured with: SF-36 mental; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	serious ^a	no serious inconsistency	no serious indirectness	serious ^b	none	87	98	-	MD 1.9 higher (0.18 lower to 3.98 higher)	⊕⊕⊕⊕ LOW	CRITICAL
Health related quality of life - visit vs control - physical (follow-up 12 weeks; measured with: SF-36 physical; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	serious ^a	no serious inconsistency	no serious indirectness	serious ^b	none	87	98	-	MD 3.1 higher (0.98 to 5.22 higher)	⊕⊕⊕⊕ LOW	CRITICAL

(a) Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

(b) Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs

Table 237: Clinical evidence profile: interventions versus usual care – Coburn 2012

Quality assessment							No. of patients	Effect	Quality	Importance		
Mortality (follow-up mean 4.2 years)												
1	randomised trials	very serious ^a	no serious inconsistency	serious ^b	no serious imprecision	none	- ^d	- ^d	HR 0.73 (0.55 to 0.97)	- ^d	⊕⊕⊕⊕ VERY LOW	CRITICAL

(a) Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

(b) Downgraded by 1 or 2 increments because: the majority of the evidence included an indirect population

(c) Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs

(d) Multivariate analysis with no adjusted raw data

Table 238: Clinical evidence profile: interventions versus usual care – Gitlin 2006

Quality assessment				No. of patients	Effect	Quality	Importance
--------------------	--	--	--	-----------------	--------	---------	------------

No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Katon 2010 (Von Kroff 2012)	Control	Relative (95% CI)	Absolute		
Survival - 2 years (follow-up mean 24 months)												
1	randomised trials	no serious risk of bias	no serious inconsistency	serious ^a	no serious imprecision	none	- ^c	- ^c	HR 0.39 (0.18 to 0.86)	- ^c	⊕⊕⊕⊕ MODERATE	CRITICAL
Survival - 3 years (follow-up mean 36 months)												
1	randomised trials	no serious risk of bias	no serious inconsistency	serious ^a	serious ^b	none	- ^c	- ^c	HR 0.74 (0.45 to 1.23)	- ^c	⊕⊕⊕⊕ LOW	CRITICAL
Survival - 4 years (follow-up mean 48 months)												
1	randomised trials	no serious risk of bias	no serious inconsistency	serious ^a	serious ^b	none	- ^c	- ^c	HR 0.76 (0.49 to 1.2)	- ^c	⊕⊕⊕⊕ LOW	CRITICAL
Function - ADL (all adjusted MD) (follow-up mean 6 months; range of scores: 1-5; Better indicated by lower values)												
1	randomised trials	serious ^d	no serious inconsistency	serious ^a	no serious imprecision	none	154	146	-	MD 0.1 lower (0.22 lower to 0.02 higher)	⊕⊕⊕⊕ LOW	CRITICAL
Function - IADL (follow-up mean 6 months; range of scores: 1-5; Better indicated by higher values)												
1	randomised trials	serious ^d	no serious inconsistency	serious ^a	no serious imprecision	none	154	146	-	MD 0.12 lower (0.27 lower to 0.03 higher)	⊕⊕⊕⊕ LOW	CRITICAL
Function - Mobility (follow-up mean 6 months; range of scores: 1-5; Better indicated by lower values)												
1	randomised trials	serious ^d	no serious inconsistency	serious ^a	no serious imprecision	none	154	146	-	MD 0.14 lower (0.29 lower to 0.01 higher)	⊕⊕⊕⊕ LOW	CRITICAL

(a) Downgraded by 1 or 2 increments because: the majority of the evidence included an indirect population

(b) Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs

(c) Multivariate analysis with no adjusted raw data

(d) Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

Table 239: Clinical evidence profile: interventions versus usual care – Katon 2010

Quality assessment	No. of patients	Effect	Quality	Importance

Health-related quality of life (Global quality of life rating) (follow-up mean 12 months; measured with: health related quality of life; range of scores: 0-10; Better indicated by higher values)												
1	randomised trials	very serious ^a	no serious inconsistency	no serious indirectness	no serious imprecision	none	92	92	-	MD 0.8 higher (3.11 lower to 4.71 higher)	⊕⊕⊕ LOW	CRITICAL
Mortality at 12 months (follow-up mean 12 months)												
1	randomised trials	very serious ^a	no serious inconsistency	no serious indirectness	serious ^b	none	1/106 (0.94%)	2/108 (1.9%)	RR 0.51 (0.05 to 5.53)	9 fewer per 1000 (from 18 fewer to 84 more)	⊕⊕⊕ VERY LOW	CRITICAL
Functional outcome (Sheehan social role disability scale) (follow-up mean 12 months; measured with: Sheehan social role disability scale; range of scores: 0-10; Better indicated by lower values)												
1	randomised trials	very serious ^a	no serious inconsistency	no serious indirectness	serious ^b	none	92	92	-	MD 0.7 lower (1.55 lower to 0.15 higher)	⊕⊕⊕ VERY LOW	CRITICAL
Functional outcome (WHODAS-2 activities of daily living) (follow-up mean 12 months; measured with: WHODAS-2 activities of daily living; range of scores: 0-4; Better indicated by lower values)												
1	randomised trials	very serious ^a	no serious inconsistency	no serious indirectness	no serious imprecision	none	92	92	-	MD 0 higher (3.07 lower to 3.07 higher)	⊕⊕⊕ LOW	CRITICAL
Patient & Carer Satisfaction(as assessed by the number of patients satisfied with care for diabetes, heart disease or both) (follow-up mean 12 months)												
1	randomised trials	very serious ^a	no serious inconsistency	no serious indirectness	serious ^b	none	79/92 (85.9%)	62/88 (70.5%)	RR 1.22 (1.04 to 1.43)	155 more per 1000 (from 28 more to 303 more)	⊕⊕⊕ VERY LOW	CRITICAL
Unscheduled care (proportion hospitalised, at least one hospitalisation) (follow-up mean 12 months)												
1	randomised trials	very serious ^a	no serious inconsistency	no serious indirectness	very serious ^b	none	27/106 (25.5%)	23/108 (21.3%)	RR 1.20 (0.73 to 1.95)	43 more per 1000 (from 58 fewer to 202 more)	⊕⊕⊕ VERY LOW	CRITICAL

(a) Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

(b) Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs

Table 240: Clinical evidence profile: interventions versus usual care – Legrain 2011

Quality assessment	No. of patients	Effect	Quality	Importanc
--------------------	-----------------	--------	---------	-----------

No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Legrain 2011	Control	Relative (95% CI)	Absolute		
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Holistic assessment versus usual care	Control	Relative (95% CI)	Absolute		
												e
Mortality (follow-up mean 6 weeks)												
1	randomised trials	serious ^a	no serious inconsistency	serious ^c	serious ^b	none	56/317 (17.7%)	65/348 (18.7%)	RR 0.86 (0.62 to 1.19)	26 fewer per 1000 (from 71 fewer to 35 more)	⊕○○○ VERY LOW	CRITICAL
Unscheduled care (attended emergency department) (follow-up mean 6 months)												
1	randomised trials	serious ^a	no serious inconsistency	serious ^c	very serious ^b	none	19/317 (6%)	22/348 (6.3%)	RR 0.95 (0.52 to 1.72)	3 fewer per 1000 (from 30 fewer to 46 more)	⊕○○○ VERY LOW	CRITICAL
Unscheduled care (readmission to acute geriatric unit) (follow-up mean 6 months)												
1	randomised trials	serious ^a	no serious inconsistency	serious ^c	serious ^b	none	103/317 (32.5%)	133/348 (38.2%)	RR 0.85 (0.69 to 1.05)	57 fewer per 1000 (from 118 fewer to 19 more)	⊕○○○ VERY LOW	CRITICAL

(a) Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

(b) Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs

(c) Downgraded by 1 or 2 increments because: the majority of the evidence included an indirect population

J.5.2 Holistic assessment

J.5.2.1 Holistic assessment inpatient - Ward

Table 241: Clinical evidence profile: Holistic assessment (ward) versus usual care

Quality assessment	No of patients	Effect	Quality	Importance
--------------------	----------------	--------	---------	------------

Health-related quality of life (SF36) - Physical functioning (follow-up mean 12 months; measured with: 36-item Short-Form General Health ; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	no serious risk of bias	no inconsistency	serious ^b	serious ^c	none	696	692	-	MD 2.3 higher (1.4 to 3.2 higher)	⊕⊕⊕⊕ LOW	CRITICAL
Health-related quality of life (SF36) - Physical limitations (follow-up mean 12 months; measured with: 36-item Short-Form General Health ; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	no serious risk of bias	no inconsistency	serious ^b	serious ^c	none	696	692	-	MD 1.2 lower (4.02 lower to 1.62 higher)	⊕⊕⊕⊕ LOW	CRITICAL
Health-related quality of life (SF36) - Emotional limitations (follow-up mean 12 months; measured with: 36-item Short-Form General Health ; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	no serious risk of bias	no inconsistency	serious ^b	no serious imprecision	none	696	692	-	MD 1.9 higher (0.99 to 2.81 higher)	⊕⊕⊕⊕ MODERATE	CRITICAL
Health-related quality of life (SF36) - Bodily pain (follow-up mean 12 months; measured with: 36-item Short-Form General Health ; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	no serious risk of bias	no inconsistency	serious ^b	no serious imprecision	none	696	692	-	MD 1 lower (2.04 lower to 0.04 higher)	⊕⊕⊕⊕ MODERATE	CRITICAL
Health-related quality of life (SF36) - Energy (follow-up mean 12 months; measured with: 36-item Short-Form General Health ; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	no serious risk of bias	no inconsistency	serious ^b	no serious imprecision	none	696	692	-	MD 4.4 higher (4.04 to 4.76 higher)	⊕⊕⊕⊕ MODERATE	CRITICAL
Health-related quality of life (SF36) - Mental health (follow-up mean 12 months; measured with: 36-item Short-Form General Health ; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	no serious risk of bias	no inconsistency	serious ^b	no serious imprecision ^c	none	696	692	-	MD 5.5 higher (5.06 to 5.94 higher)	⊕⊕⊕⊕ MODERATE	CRITICAL
Health-related quality of life (SF36) - Social activity (follow-up mean 12 months; measured with: 36-item Short-Form General Health ; range of scores: 0-100; Better indicated by higher values)												

1	randomised trials	no serious risk of bias	no inconsistency	serious ^b	serious ^c	none	696	692	-	MD 1.9 higher (0.33 to 3.47 higher)	⊕⊕⊕⊕ LOW	CRITICAL
Health-related quality of life (SF36) - General health (follow-up mean 12 months; measured with: 36-item Short-Form General Health ; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	no serious risk of bias	no inconsistency	serious ^b	no serious imprecision ^c	none	696	692	-	MD 3.8 higher (3.13 to 4.47 higher)	⊕⊕⊕⊕ MODERATE	CRITICAL
Mortality (end of follow up) (follow-up 1-24 months)												
17	randomised trials	serious ^d	no serious inconsistency	serious ^b	serious ^c	none	701/3269 (21.4%)	716/3440 (20.8%)	RR 0.99 (0.9 to 1.08)	2 fewer per 1000 (from 21 fewer to 17 more)	⊕⊕⊕⊕ VERY LOW	CRITICAL
Functional outcomes (activities of daily living) (follow-up 6-12 months; Better indicated by lower values)												
4	randomised trials	very serious ^d	no serious inconsistency	serious ^b	serious ^c	none	535	432	-	SMD 0.11 higher (0.03 lower to 0.24 higher)	⊕⊕⊕⊕ VERY LOW	CRITICAL
Functional outcomes (improving ADLs)(follow-up at discharge)												
1	randomised trials	no serious risk of bias	no serious inconsistency	serious ^b	serious ^c	none	111/326 (34%)	78/324 (24.1%)	RR 1.41 (1.11 to 1.81)	99 more per 1000 (from 26 more to 195 more)	⊕⊕⊕⊕ LOW	CRITICAL
Functional outcomes (worsening ADLs)(follow-up at discharge)												
1	randomised trials	no serious risk of bias	no serious inconsistency	serious ^b	serious ^c	none	52/326 (16%)	68/324 (21%)	RR 0.76 (0.55 to 1.05)	50 fewer per 1000 (from 94 fewer to 10 more)	⊕⊕⊕⊕ LOW	CRITICAL
Functional outcomes (independent in at least 2 ADL)(follow-up 24 months)												
1	randomised trials	serious ^d	no serious inconsistency	serious ^b	serious ^c	none	28/63 (44.4%)	20/60 (33.3%)	RR 1.33 (0.85 to 2.10)	110 more per 1000 (from 50 fewer to 367 more)	⊕⊕⊕⊕ VERY LOW	CRITICAL
Functional outcomes (dependent in ADL, Barthel <12)(follow-up 12 months)												
1	randomised trials	no serious risk of bias	no serious inconsistency	serious ^b	very serious ^c	none	18/72 (25%)	14/61 (23%)	RR 1.09 (0.59 to 2.00)	21 more per 1000 (from 94 fewer to 230 more)	⊕⊕⊕⊕ VERY	CRITICAL

												LOW	
Functional outcomes (dependent in ADL, Barthel <12)(follow-up 12 months)													
1	randomised trials	no serious risk of bias	no serious inconsistency	serious ^b	very serious ^c	none	32/72 (44.4%)	26/59 (44.1%)	RR 1.01 (0.69 to 1.48)	21 more per 1000 (from 94 fewer to 230 more)	⊕○○○ VERY LOW	CRITICAL	
Patient & carer satisfaction (family/resident satisfaction) (follow-up mean 6 months)													
1	randomised trials	serious ^d	no serious inconsistency	serious ^b	serious ^c	none	19/20 (95%)	14/24 (58.3%)	RR 1.63 (1.14 to 2.32)	367 more per 1000 (from 82 more to 770 more)	⊕○○○ VERY LOW	CRITICAL	
Patient & carer satisfaction (caregiver satisfaction) (follow-up mean 12 months; range of scores: 0-100; Better indicated by higher values)													
1	randomised trials	serious ^d	no serious inconsistency	serious ^b	serious ^c	none	160	173	-	MD 3 higher (0.96 to 5.04 higher)	⊕○○○ VERY LOW	CRITICAL	
Patient & carer satisfaction (patient) (follow-up mean 12 months; range of scores: 0-100; Better indicated by higher values)													
1	randomised trials	serious ^d	no serious inconsistency	serious ^b	no serious imprecision	none	480	478	-	MD 3 higher (0.91 to 5.09 higher)	⊕⊕○○ LOW	CRITICAL	
Length of stay (follow-up 3-12 months; Better indicated by lower values)													
9	randomised trials	very serious ^d	Very serious ^a	serious ^b	very serious ^c	none	2015	1938	-	MD 1.41 higher (1.14 lower to 3.95 higher)	⊕○○○ VERY LOW	CRITICAL	
Unscheduled care (emergency department presentations) (follow-up mean 6 months)													
1	randomised trials	serious ^d	no serious inconsistency	serious ^b	serious ^c	none	19/57 (33.3%)	28/59 (47.5%)	RR 0.7 (0.45 to 1.11)	142 fewer per 1000 (from 261 fewer to 52 more)	⊕○○○ VERY LOW	CRITICAL	
Unscheduled care (hospital readmissions) (follow-up 1-24 months)													
8	randomised trials	serious ^d	no serious inconsistency	serious ^b	no serious imprecision	none	-	-	OR 1.01 (0.87 to 1.17)	- ^e	⊕⊕○○ LOW	CRITICAL	
Admission to care facility (follow-up 1-24 months)													

No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Holistic assessment versus usual care TEAM	Control	Relative (95% CI)	Absolute		
14	randomised trials	no serious risk of bias	no serious inconsistency	serious ^b	no serious imprecision	none	-	-	OR 0.73 (0.64 to 0.83)	- ^e	⊕⊕⊕○ MODERATE	CRITICAL
Carer treatment burden (poor self-rated physical health) (follow-up 3 months)												
1	randomised trials	serious ⁴	no serious inconsistency	serious ^b	serious ^c	none	-	-	OR 0.51 (0.29 to 0.90)	- ^e	⊕○○○ VERY LOW	IMPORTANT
Carer treatment burden (poor self-rated emotional health) (follow-up 3 months)												
1	randomised trials	serious ⁴	no serious inconsistency	serious ^b	serious ^c	none	-	-	OR 0.77 (0.49 to 1.21)	- ^e	⊕○○○ VERY LOW	IMPORTANT

(a) Downgraded by 1/2 increments because: Heterogeneity, I²=50%

(b) Downgraded by 1/2 increments because the majority of the evidence included an indirect population (downgraded by 1 increment) or by a very indirect population (downgraded by 2 increments)

(c) Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDS

(d) Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

(e) Could not be calculated as adjusted raw data was not provided

J.5.2.2 Holistic assessment inpatient - Team

Table 242: Clinical evidence profile: Holistic assessment (team) versus usual care

Quality assessment							No of patients	Effect		Quality	Importance	
Health-related quality of life (EQ-5D) (follow-up mean 90 days; measured with: EQ-ED; range of scores: 0-1; Better indicated by higher values)												
1	randomised trials	serious ^a	no serious inconsistency	serious ^b	no serious imprecision	none	146	139	-	MD 0 higher (0.07 lower to 0.07 higher)	⊕⊕○○ LOW	CRITICAL
Mortality (end of follow up) (follow-up mean 1-12 months)												
9	randomised trials	serious ^a	no serious inconsistency	serious ^b	no serious imprecision	none	499/2387 (20.9%)	415/2031 (20.4%)	RR 0.99 (0.88 to 1.11)	0 fewer per 1000 (from 16 fewer to 18 more)	⊕○○○ VERY LOW	CRITICAL

Mortality (time to mortality, HR) (follow-up mean 90 days)												
1	randomised trials	serious ^a	no serious inconsistency	serious ^b	serious ^c	none	-	-	HR 1.22 (0.57 to 2.61)	- ^d	⊕○○○ VERY LOW	CRITICAL
Functional outcomes (activities of daily living) (follow-up mean 12 months; Better indicated by lower values)												
2	randomised trials	serious ^a	no serious inconsistency	serious ^b	no serious imprecision	none	167	162	-	MD 0.25 lower (0.76 lower to 0.26 higher)	⊕⊕○○ LOW	CRITICAL
Functional outcomes (Barthel) (follow-up mean 90 days)												
1	randomised trials	serious ^a	no serious inconsistency	serious ^b	very serious ^c	none	-	-	OR 1.25 (0.72 to 2.17)	- ^d	⊕○○○ VERY LOW	CRITICAL
Functional outcomes (Katz ADL improved) (follow-up mean 12 months)												
1	randomised trials	no serious risk of bias	no serious inconsistency	serious ^b	very serious ^c	none	18/97 (18.6%)	21/97 (21.6%)	RR 0.86 (0.49 to 1.51)	30 fewer per 1000 (from 110 fewer to 110 more)	⊕○○○ VERY LOW	CRITICAL
Functional outcomes (Five-item OARS IADL improved) (follow-up mean 12 months)												
1	randomised trials	no serious risk of bias	no serious inconsistency	serious ^b	serious ^c	none	18/97 (18.6%)	9/97 (9.3%)	RR 2 (0.95 to 4.23)	93 more per 1000 (from 5 fewer to 300 more)	⊕⊕○○ LOW	CRITICAL
Length of stay (follow-up mean 12 months; Better indicated by lower values)												
5	randomised trials	very serious ^a	no serious inconsistency	serious ^b	very serious ^c	none	363	368	-	MD 0.79 lower (2.34 lower to 0.75 higher)	⊕○○○ VERY LOW	CRITICAL
Unscheduled care (hospital readmission) (follow-up 1-12 months)												
2	randomised trials	serious ^a	no serious inconsistency	serious ^b	serious ^c	none	-	-	OR 1.16 (0.87 to 1.56)	- ^d	⊕○○○ VERY LOW	CRITICAL
Admission to care facility (follow-up 1-12 months)												

No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Community holistic assessment	usual care	Relative (95% CI)	Absolute		
7	randomised trials	serious ^a	no serious inconsistency	serious ^b	serious ^c	none	-	-	OR 0.87 (0.64 to 1.19)	- ^d	⊕○○○ VERY LOW	CRITICAL
Patient and carer treatment burden (follow-up mean 12 months)												
1	randomised trials	no serious risk of bias	no serious inconsistency	serious ^b	serious ^c	none	19/60 (31.7%)	34/60 (56.7%)	RR 0.56 (0.36 to 0.86)	249 fewer per 1000 (from 79 fewer to 363 fewer)	⊕⊕○○ LOW	IMPORTANT

(a) Downgraded by 1 increment if the majority of the evidence was at a high risk of bias and downgraded by 2 increments if the majority of the evidence was at a very high risk of bias

(b) Downgraded by 1/2 increments because the majority of the evidence included an indirect population (downgraded by 1 increment) or by a very indirect population (downgraded by 2 increments)

(c) Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs

(d) Could not be calculated as adjusted raw data was not provided

J.5.2.3 Community holistic assessment - low intensity

Table 243: Clinical evidence profile: Community holistic assessment versus usual care

Quality assessment							No of patients	Effect	Quality	Importance		
Health-related Quality of Life (SF-12) (follow-up mean 6 months; measured with: Better indicated by higher values, scale from 0 to 100; Better indicated by lower values)												
1	randomised trials	serious ^a	no serious inconsistency	serious ^b	no serious imprecision	none	147	87	-	MD 0.25 lower (1.9 lower to 1.4 higher)	⊕⊕○○ LOW	CRITICAL
Mortality - 0-12 months follow-up (follow-up 6 months)												
2	randomised trials	serious ^a	serious ³	serious ^b	serious ^d	none	29/353 (8.2%)	25/297 (8.4%)	OR 1.1 (0.88 to 1.37)	8 more per 1000 (from 9 fewer to 28 more)	⊕○○○ VERY LOW	CRITICAL

Mortality - >12-24 months follow-up (follow-up 18-24 months)												
2	randomised trials	serious ^a	no serious inconsistency	serious ^b	serious ^d	none	19/203 (9.4%)	27/187 (14.4%)	OR 0.65 (0.35 to 1.23)	46 fewer per 1000 (from 89 fewer to 28 more)	⊕○○○ VERY LOW	CRITICAL
Mortality - 74 month follow-up (follow-up 74 months)												
1	randomised trials	serious ^a	no serious inconsistency	serious ^b	no serious imprecision	none	- ^e	- ^e	OR 0.78 (0.67 to 0.91)	- ^e	⊕⊕○○ LOW	CRITICAL
Mortality - time to event (follow-up 24-74 months; assessed with: Hazard Ratio)												
2	randomised trials	serious ^a	no serious inconsistency	serious ^b	no serious imprecision	none	- ^e	- ^e	HR 0.79 (0.69 to 0.9)	- ^e	⊕⊕○○ LOW	CRITICAL
Barthel Index (follow-up 6 months; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	very serious ^a	no serious inconsistency	serious indirectness ^c	very serious ^d	none	129	140	-	MD 4 higher (0.27 lower to 8.27 higher)	⊕○○○ VERY LOW	CRITICAL
Admission to care facility - 18-24 month follow-up (follow-up 18-24 months)												
2	randomised trials	serious ^a	no serious inconsistency	serious ^b	serious ^d	none	19/203 (9.4%)	27/187 (14.4%)	OR 0.67 (0.32 to 1.38)	43 fewer per 1000 (from 93 fewer to 45 more)	⊕○○○ VERY LOW	CRITICAL
Admission to care facility - 74 month follow-up (follow-up 74 months)												
1	randomised trials	serious ^a	no serious inconsistency	serious ^b	no serious imprecision	none	- ^e	- ^e	OR 0.8 (0.68 to 0.95)	- ^e	⊕⊕○○ LOW	CRITICAL
Time to admission to care facility (follow-up mean 24-74 months)												

No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Community holistic assessment	usual care	Relative (95% CI)	Absolute		
2	randomised trials	serious ^a	no serious inconsistency	serious ^b	no serious imprecision	none	- ^e	- ^e	HR 0.80 (0.69 to 0.92)	- ^e	⊕⊕⊕ LOW	CRITICAL
Unscheduled care (hospitalisation) (follow-up 6 months)												
1	randomised trials	serious ^a	no serious inconsistency	serious ^b	very serious ^d	none	22/142 (15.5%)	12/85 (14.1%)	OR 1.32 (0.94 to 1.85)	37 more per 1000 (from 7 fewer to 92 more)	⊕⊕⊕ VERY LOW	CRITICAL

(a) Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

(b) Downgraded by 1 or 2 increments because the point estimate varies widely across studies

(c) The majority of the evidence included an indirect population (downgrade by 1 increment) or a very indirect population (downgrade by 2 increments)

(d) Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs

(e) Could not be calculated as adjusted raw data was not provided

J.5.2.4 Community holistic assessment - high intensity

Table 244: Clinical evidence profile: Community holistic assessment versus usual care

Quality assessment							No of patients	Effect	Quality	Importance		
EQ-5D (follow-up 18-24 months; Better indicated by higher values)												
2	randomised trials	serious ^a	no serious inconsistency	serious ^b	no serious imprecision	none	277	248	-	MD 0 higher (0.06 lower to 0.05 higher)	⊕⊕⊕ LOW	CRITICAL
MOS-20 (mental) (follow-up 6 months; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	serious ^a	no serious inconsistency	serious ^b	serious ^c	none	88	67	-	MD 9.1 higher (2.4 to 15.6 higher)	⊕⊕⊕ VERY LOW	CRITICAL

MOS-20 (physical) (follow-up 3 months; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	serious ^a	no serious inconsistency	serious ^b	serious ^c	none	88	67	-	MD 4.3 higher (2.9 lower to 11.2 higher)	⊕○○○ VERY LOW	CRITICAL
HRQoL - MOS-20 (role functioning) (follow-up 3 months; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	serious ^a	no serious inconsistency	serious ^b	very serious ^c	none	88	67	-	MD 4.7 higher (9.8 lower to 19.3 higher)	⊕○○○ VERY LOW	CRITICAL
SF-36 (physical component) (follow-up 2 years; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	serious ^c	no serious imprecision	none	474	477	-	MD 0.5 higher (0.62 lower to 1.62 higher)	⊕⊕⊕○ MODERATE	CRITICAL
SF-36 (mental component) (follow-up 2 years; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	serious ^c	no serious imprecision	none	474	477	-	MD 2.4 higher (1.06 to 3.74 higher)	⊕⊕⊕○ MODERATE	CRITICAL
SF-36 scales - Physical functioning (follow-up 2 years; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	serious ^c	serious ^d	none	474	477	-	MD 1.5 higher (1.4 lower to 4.4 higher)	⊕⊕○○ LOW	IMPORTANT
SF-36 scales - Role-physical (follow-up 2 years; range of scores: 0-100; Better indicated by higher values)												

1	randomised trials	no serious risk of bias	no serious inconsistency	serious ^c	serious ^d	none	474	477	-	MD 4.6 higher (0.35 lower to 9.55 higher)	⊕⊕⊕⊕ LOW	CRITICAL
SF-36 scales - Bodily pain (follow-up 2 years; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	serious ^c	serious ^d	none	474	477	-	MD 0.7 lower (3.91 lower to 2.51 higher)	⊕⊕⊕⊕ LOW	CRITICAL
SF-36 scales - General health (follow-up 2 years; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	serious ^c	serious ^d	none	474	477	-	MD 2.5 higher (0.06 to 4.94 higher)	⊕⊕⊕⊕ LOW	CRITICAL
SF-36 scales - Vitality (follow-up 2 years; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	serious ^c	no serious imprecision	none	474	477	-	MD 5.2 higher (2.55 to 7.85 higher)	⊕⊕⊕⊕ MODERATE	CRITICAL
SF-36 scales - Social functioning (follow-up 2 years; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	serious ^c	serious ^d	none	474	477	-	MD 5.3 higher (1.43 to 9.17 higher)	⊕⊕⊕⊕ LOW	CRITICAL
SF-36 scales - Role-emotional (follow-up 2 years; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	serious ^c	serious ^d	none	474	477	-	MD 2.1 higher (3.42)	⊕⊕⊕⊕ LOW	CRITICAL

										lower to 7.62 higher)		
SF-36 scales - Mental health (follow-up 2 years; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	serious ^c	serious ^d	none	474	477	-	MD 3.9 higher (1.57 to 6.23 higher)	⊕⊕⊕ LOW	CRITICAL
Mortality (follow-up 0-12 months)												
2	randomised trials	no serious risk of bias	serious ^c	serious ^a	serious ^b	none	24/289 (8.3%)	38/413 (9.2%)	OR 0.99 (0.58 to 1.7)	1 fewer per 1000 (from 36 fewer to 55 more)	⊕⊕⊕ VERY LOW	CRITICAL
Mortality (follow-up >12-24 months)												
3	randomised trials	serious ^a	no serious inconsistency	serious ^b	no serious imprecision	none	100/429 (23.3%)	91/386 (23.6%)	OR 0.56 (0.39 to 0.8)	88 fewer per 1000 (from 38 fewer to 128 fewer)	⊕⊕⊕ LOW	CRITICAL
Mortality (follow-up >24-36 months)												
1	randomised trials	very serious ^d	no serious inconsistency	serious ^b	serious ^b	none	81/500 (16.2%)	72/500 (14.4%)	OR 1.15 (0.81 to 1.62)	18 more per 1000 (from 24 fewer to 70 more)	⊕⊕⊕ VERY LOW	CRITICAL
Mortality - time to event (follow-up 24 months)												
1	randomised trials	serious ^a	no serious inconsistency	no serious indirectness	serious ^c	none	81/500 (16.2%)	47/174 (27%)	HR 0.66 (0.43 to 1.01)	82 fewer per 1000 (from 143 fewer to 2 more)	⊕⊕⊕ LOW	CRITICAL

GARS ADL (follow-up 6 months; range of scores: 18-54; Better indicated by lower values)												
1	randomised trials	serious ^a	no serious inconsistency	serious ^b	no serious imprecision	none	88	67	-	MD 1.6 lower (3.9 lower to 0.7 higher)	⊕⊕⊕⊕ LOW	CRITICAL
Katz ADL (follow-up 0.4-2 years; range of scores: 0-6; Better indicated by higher values)												
2	randomised trials	serious ^a	no serious inconsistency	serious ^c	serious ^d	none	567	685	-	MD 0.06 lower (0.3 lower to 0.19 higher)	⊕⊕⊕⊕ VERY LOW	CRITICAL
Lawton & Brody IADL (follow-up 0.4-2 years; range of scores: 0-8; Better indicated by higher values)												
2	randomised trials	serious ^a	no serious inconsistency	serious ^c	serious ^d	none	567	685	-	MD 0.12 lower (0.45 lower to 0.22 higher)	⊕⊕⊕⊕ VERY LOW	CRITICAL
Sickness Impact Profile (follow-up 1 years; range of scores: 0-100; Better indicated by lower values)												
1	randomised trials	serious ^a	no serious inconsistency	serious indirectness ^c	very serious ^d	none	181	201	-	MD 2 higher (0.41 lower to 4.41 higher)	⊕⊕⊕⊕ VERY LOW	CRITICAL
Patient satisfaction (follow-up 12 months; measured with: unvalidated scale; range of scores: 0-5; Better indicated by lower values)												
1	randomised trials	serious ^a	no serious inconsistency	serious indirectness ^c	very serious ^d	none	181	201	-	MD 0.11 higher (0.06 lower to 0.28 higher)	⊕⊕⊕⊕ VERY LOW	CRITICAL

Length of hospital stay (follow-up 24 months; Better indicated by lower values)												
1	randomised trials	serious ^a	no serious inconsistency	no serious indirectness ^b	no serious imprecision ^c	none	208	174	-	MD 4.10 lower (7.80 to 0.40 lower)	⊕⊕⊕○ MODERATE	CRITICAL
Hospitalisations per patient (follow-up 24 months; Better indicated by lower values)												
1	randomised trials	serious ^a	no serious inconsistency	no serious indirectness ^b	no serious imprecision ^c	none	146	106	-	MD 0.30 lower (0.81 lower to 0.21 higher)	⊕⊕⊕○ MODERATE	CRITICAL
Hospitalisation (follow-up 1 year)												
1	randomised trials	no serious risk of bias	no serious inconsistency	serious ^a	serious ^b	none	46/185 (24.9%)	54/205 (26.3%)	RR 0.94 (0.67 to 1.33)	16 fewer per 1000 (from 87 fewer to 87 more)	⊕⊕○○ LOW	CRITICAL
Admission to care facility (follow-up 12-24 months)												
2	randomised trials	serious ^a	serious ^d	no serious indirectness	serious ^c	none	37/312 (11.9%)	51/382 (13.4%)	OR 0.78 (0.49 to 1.22)	26 fewer per 1000 (from 63 fewer to 25 more)	⊕○○○ VERY LOW	CRITICAL
Admission to care facility - time to event (follow-up 12-24 months)												
3	randomised trials	serious ^a	no serious inconsistency	serious ^b	serious ^c	none	-	-	HR 0.71 (0.48 to 1.05)	^e	⊕○○○ VERY LOW	CRITICAL

- (a) Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
 (b) Downgraded by 1 or 2 increments because the point estimate varies widely across studies
 (c) The majority of the evidence included an indirect population (downgrade by 1 increment) or a very indirect population (downgrade by 2 increments)
 (d) Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs
 (e) Could not be calculated as adjusted raw data was not provided

Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Self-management (conditions)	Usual care	Relative (95% CI)	Absolute		
-------------------	--------	--------------	---------------	--------------	-------------	----------------------	------------------------------	------------	-------------------	----------	--	--

J.6 Self-management

J.6.1.1 Self-management interventions aimed at improving individuals' management of their health conditions

Table 245: Clinical evidence profile: Self-management programmes versus usual care (participants with comorbid physical health conditions)

Quality assessment							Number of patients	Effect	Quality	Importance		
Health related quality of life (follow-up mean 6 months; measured with: EQ-5D; range of scores: 0-1; Better indicated by higher values)												
3	randomised trials	very serious ^a	serious ^c	no serious indirectness	no serious imprecision ^b	none	292	297	-	SMD 0.05 higher (0.02 to 0.09 higher)	⊕000 VERY LOW	CRITICAL
Self-rated health (follow-up 6 months; measured with: CDSMP questionnaire & National health interview survey; range of scores: 1-5; better indicated by lower values)												
1	Randomised trials	Serious ^b	No serious inconsistency	No serious indirectness	No serious imprecision	None	311	225	-	MD 0.12 lower (0.24 lower to 0 higher)	MODERATE	CRITICAL
Disability (follow-up mean 6 months; measured with: Modification of the Health Assessment Questionnaire - disability scale; range of scores: 0-3; better indicated by lower values)												
1	Randomised trials	Serious ^b	No serious inconsistency	No serious indirectness	No serious imprecision	None	311	225	-	MD 0.03 lower (0.09 lower to 0.03 higher)	MODERATE	CRITICAL
Psychological wellbeing (follow-up mean 6 months; measured with: MHI-5, as taken from the SF-36; range of scores: 0-5; better indicated by higher values)												
1	Randomised	Serious ^b	No serious	No serious	No serious	None	311	225	-	MD 0.04	MODERATE	CRITICAL

	trials		inconsistency	indirectness	imprecision					higher (0.08 lower to 0.16 higher)	E	
Positive & active engagement in life (follow-up mean 6 months; range of scores: 0-100; Better indicated by higher values)												
1	Randomised trials	very serious ^a	no serious inconsistency	no serious indirectness	no serious imprecision	none	180	194	-	MD 0 higher (3.2 lower to 3.2 higher)	LOW	CRITICAL
Role activities limitations (follow-up mean 6 months; range of scores: 0-4; better indicated by lower values)												
1	Randomised trials	Serious ^b	No serious inconsistency	No serious indirectness	No serious imprecision	None	311	225	-	MD 0.07 lower (0.22 lower to 0.08 higher)	MODERATE	CRITICAL
Social/role activities (follow-up mean 6 months; range of scores: 0-100; Better indicated by higher values)												
1	Randomised trials	very serious ^a	no serious inconsistency	no serious indirectness	no serious imprecision	none	177	194	-	MD 1.85 higher (3.68 lower to 7.38 higher)	LOW	CRITICAL
Mortality (follow-up 22 months)												
1	randomised trials	very serious ^a	no serious inconsistency	serious indirectness	very serious ^b	none	43/237 (18.1%)	47/262 (17.9%)	RR 1.01 (0.7 to 1.47)	2 more per 1000 (from 54 fewer to 84 more)	VERY LOW	CRITICAL
Some difficulty with ADL - Bathing (follow-up 22 months; assessed with: Patient interview)												
1	randomised trials	very serious ^a	no serious inconsistency	serious indirectness	serious ^b	none	92	140	OR 0.58 (0.37 to 0.91)	- ^d	VERY LOW	CRITICAL
Some difficulty with ADL - Dressing (follow-up 22 months; assessed with: Patient interview)												
1	randomised trials	very serious ^a	no serious inconsistency	serious indirectness	serious ^b	none	92	140	OR 0.75 (0.48 to 1.17)	- ^d	VERY LOW	CRITICAL
Some difficulty with ADL - Eating (follow-up 22 months; assessed with: Patient interview)												

1	randomised trials	very serious ^a	no serious inconsistency	serious indirectness	very serious ^b	none	92	140	OR 0.84 (0.5 to 1.41)	- ^d	VERY LOW	CRITICAL
Some difficulty with ADL - Toileting (follow-up 22 months; assessed with: Patient interview)												
1	randomised trials	very serious ^a	no serious inconsistency	serious indirectness	serious ^b	none	92	140	OR 0.7 (0.44 to 1.11)	- ^d	VERY LOW	CRITICAL
Some difficulty with ADL - Transferring (follow-up 22 months; assessed with: Patient interview)												
1	randomised trials	very serious ^a	no serious inconsistency	serious indirectness	very serious ^b	none	92	140	OR 1.14 (0.72 to 1.81)	- ^d	VERY LOW	CRITICAL
Some difficulty with ADL - Walking (follow-up 22 months; assessed with: Patient interview)												
1	randomised trials	very serious ^a	no serious inconsistency	serious indirectness	very serious ^b	none	92	140	OR 0.9 (0.53 to 1.53)	- ^d	VERY LOW	CRITICAL
Great difficulty with ADL - Bathing (follow-up 22 months; assessed with: Patient interview)												
1	randomised trials	very serious ^a	no serious inconsistency	serious indirectness	serious ^b	none	92	140	OR 0.4 (0.2 to 0.8)	- ^d	VERY LOW	CRITICAL
Great difficulty with ADL - Dressing (follow-up 22 months; assessed with: Patient interview)												
1	randomised trials	very serious ^a	no serious inconsistency	serious indirectness	serious ^b	none	92	140	OR 0.39 (0.18 to 0.85)	- ^d	VERY LOW	CRITICAL
Great difficulty with ADL - Eating (follow-up 22 months; assessed with: Patient interview)												
1	randomised trials	very serious ^a	no serious inconsistency	serious indirectness	very serious ^b	none	92	140	OR 0.36 (0.1 to 1.3)	- ^d	VERY LOW	CRITICAL
Great difficulty with ADL - Toileting (follow-up 22 months; assessed with: Patient interview)												
1	randomised trials	very serious ^a	no serious inconsistency	serious indirectness	very serious ^b	none	92	140	OR 0.76 (0.26 to 2.22)	- ^d	VERY LOW	CRITICAL

Great difficulty with ADL - Transferring (follow-up 22 months; assessed with: Patient interview)													
1	randomised trials	very serious ^a	no serious inconsistency	serious indirectness	very serious ^b	none	92	140	OR 0.82 (0.35 to 1.92)	- ^d	VERY LOW	CRITICAL	
Great difficulty with ADL - Walking (follow-up 22 months; assessed with: Patient interview)													
1	randomised trials	very serious ^a	no serious inconsistency	serious indirectness	very serious ^b	none	92	140	OR 0.76 (0.34 to 1.7)	- ^d	VERY LOW	CRITICAL	
Health distress (follow-up 2 months; range of scores: 0-20; better indicated by lower values)													
1	Randomised trials	Very serious ^c	No serious inconsistency	No serious indirectness	No serious imprecision	None	311	225	-	MD 0.16 lower (0.34 lower to 0.02 higher)	LOW	IMPORTANT	
Nottingham Extended Activities of Daily Living (NEADL) (follow-up 2 weeks; Better indicated by higher values)													
1	randomised trials	serious ^a	no serious inconsistency	no serious indirectness	very serious ^b	none	22	22	-	MD 6.45 higher (0.23 lower to 13.13 higher)	⊕○○○ VERY LOW	CRITICAL	
Hospital admissions (follow-up 2 weeks; Better indicated by lower values)													
1	randomised trials	serious ^a	no serious inconsistency	no serious indirectness	serious ^b	none	22	22	-	MD 0.06 higher (0.17 lower to 0.29 higher)	⊕⊕○○ LOW	CRITICAL	
Stanford Chronic Disease Self-Efficacy 6-item Scale (follow-up 2 weeks; range of scores: 0-10; Better indicated by higher values)													
1	randomised trials	serious ^a	no serious inconsistency	no serious indirectness	very serious ^b	none	22	22	-	MD 1.47 higher (0.45 to 2.49 higher)	⊕○○○ VERY LOW	IMPORTANT	
6 minute walk test (follow-up 6 months; Better indicated by higher values)													
1	randomised trials	serious ^a	no serious inconsistency	no serious indirectness	serious ^b	none	33	33	-	MD 45.2 higher	⊕⊕○○ LOW	IMPORTANT	

										(108.12 lower to 198.52 higher)		
Community Healthy Activities Model Program for Seniors (CHAMPS) score >6 (follow-up 6 months)												
1	randomised trials	serious ^a	no serious inconsistency	no serious indirectness	serious ^b	none	40/54 (74.1%)	30/54 (55.6%)	RR 1.33 (1 to 1.77)	183 more per 1000 (from 0 more to 428 more)	⊕⊕○○ LOW	IMPORTANT
Canadian Occupational Performance Measure (COPM): satisfaction (follow-up 2 weeks; range of scores: 0-10; Better indicated by higher values)												
1	randomised trials	serious ^a	no serious inconsistency	no serious indirectness	very serious ^b	none	22	22	-	MD 2.15 higher (1.01 to 3.29 higher)	⊕○○○ VERY LOW	CRITICAL
Canadian Occupational Performance Measure (COPM): performance (follow-up 2 weeks; range of scores: 0-10; Better indicated by higher values)												
1	randomised trials	serious ^a	no serious inconsistency	no serious indirectness	very serious ^b	none	22	22	-	MD 1.67 higher (0.72 to 2.62 higher)	⊕○○○ VERY LOW	
Patient and carer satisfaction												
Length of hospital stay												
Continuity metrics												
Patient/carer treatment burden												

(a) Downgraded by 1 increment as the CI crossed 1 MID

(b) Downgraded by 1 increment as the majority of the evidence was at high risk of bias

(c) Downgraded by 2 increments as the majority of the evidence was at very high risk of bias

(d) Adjusted odds ratios were provided in study but no information on event rates was provided

Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Self-management (conditions)	Control	Relative (95% CI)	Absolute		
-------------------	--------	--------------	---------------	--------------	-------------	----------------------	------------------------------	---------	-------------------	----------	--	--

Table 246: Clinical evidence profile: Self-management programmes versus usual care (participants with comorbid physical and mental health conditions)

Quality assessment							Number of patients	Effect	Quality	Importance		
Health-related quality of life - physical component (follow-up 2-6 months; measured with: HRQOL/SF-36; range of scores: 0-100; better indicated by higher values)												
2	Randomised trials	Serious ^a	No serious inconsistency	No serious indirectness	Serious ^b	None	69	68	-	MD 2.95 higher (1.26 lower to 7.17 higher)	LOW	CRITICAL
Health-related quality of life - mental component (follow-up 2-6 months; measured with: HRQOL/SF-36; range of scores: 0-100; better indicated by lower values)												
2	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	No serious imprecision	None	69	68	-	MD 1.11 higher (2.58 lower to 4.8 higher)	HIGH	CRITICAL
Health-related quality of life (follow-up mean 18 months; measured with: Assessment of Quality of Life (AQoL)³; range of scores: 0-45; better indicated by higher values)												
1	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	No serious imprecision	None	29	28	-	MD 0.35 higher (0.14 lower to 0.84 higher)	HIGH	CRITICAL
Physical activity (follow-up mean 2 months; range of scores: 0-5; better indicated by higher values)												
1	Randomised trials	Serious ^d	No serious inconsistency	Serious ^d	Serious ^b	None	28	29	-	MD 1 higher (0.32 to 1.68 higher)	VERY LOW	CRITICAL
Walking (measured with: change in minutes per week; better indicated by higher values)												
1	Randomised trials	Serious ^a	No serious inconsistency	No serious indirectness	No serious imprecision	None	84	78	-	MD 27 higher (20.34 to 33.66 higher)	MODERATE	CRITICAL
Moderate/vigorous activity (follow-up mean 6 months; measured with: minutes per week; better indicated by lower values)												

Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Self-management (conditions)	Usual care	Relative (95% CI)	Absolute		
1	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Serious ^b	None	84	78	-	MD 39 higher (42.17 lower to 120.17 higher)	MODERATE	CRITICAL
Use of emergency department (follow-up mean 2 months)												
1	Randomised trials	Serious ^a	No serious inconsistency	No serious indirectness	Very serious ^e	None	3/28 (10.7%)	27.6%	RR 0.39 (0.11 to 1.32)	168 fewer per 1000 (from 246 fewer to 88 more)	VERY LOW	CRITICAL
Self-efficacy (follow-up mean 2 months; measured with: Self-management self-efficacy scale; range of scores: 0-10; better indicated by higher values)												
1	Randomised trials	Serious ^a	No serious inconsistency	No serious indirectness	Serious ^b	None	28	29	-	MD 0.3 higher (0.79 lower to 1.39 higher)	LOW	IMPORTANT
Patient activation (follow-up 2-6 months; measured with: Patient activation scale/measure; range of scores: 0-100; better indicated by higher values)												
2	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Serious ^b	None	69	68	-	MD 6.71 higher (2.92 to 10.5 higher)	MODERATE	IMPORTANT

(a) Downgraded by 1 increment as the majority of the evidence was at high risk of bias

(b) Downgraded by 1 increment as the CI crossed 1 MID

(c) Range of the scale is not reported in the paper and the entry here is based on uses of the scale in other studies

(d) Downgraded by 1 increment as study sample included some participants who did not have multimorbidity

(e) Downgraded by 2 increments as the CI crossed 2 MIDs

Table 247: Clinical evidence profile: Self-management programmes versus usual care (participants with comorbid physical health conditions, including participants diagnosed with dementia)

Quality assessment						Number of patients	Effect	Quality	Importance		
Self-rated health (follow-up 8 weeks; measured with: CDSMP questionnaire & National health interview survey; range of scores: 1-5; better indicated by lower values)											
1	Randomised trials	Very serious ^b	No serious inconsistency	No serious indirectness	Serious ^a	22	21	-	MD 0.5 lower (1 lower to 0 higher)	VERY LOW	CRITICAL
Self-efficacy (follow-up 8 weeks; measured with: Chronic disease self-efficacy scale; range of scores: 6-60; better indicated by higher values)											

Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Self-management (treatment)	Usual care	Relative (95% CI)	Absolute		
1	Randomised trials	Very serious ^b	No serious inconsistency	No serious indirectness	Serious ^a	None	22	21	-	MD 2.3 higher (5.28 lower to 9.88 higher)	VERY LOW	IMPORTANT

(a) Downgraded by 1 increment as the CI crossed 1 MID

(b) Downgraded by 2 increments as the majority of the evidence was at very high risk of bias

J.6.1.2 Self-management interventions aimed at improving individuals' management of their treatment

Table 248: Clinical evidence profile: Self-management programmes versus usual care (participants with comorbid physical and mental health conditions)

Quality assessment							Number of patients	Effect	Quality	Importance		
Self-efficacy (follow-up mean 6 months; measured with: Self-efficacy for managing chronic disease; range of scores: 1-10; better indicated by higher values)												
1	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Serious ^a	None	20	21	-	MD 0.2 higher (0.84 lower to 1.24 higher)	MODERATE	IMPORTANT

(a) Downgraded by 1 increment as the CI crossed 1 MID

Table 249: Clinical evidence profile: Self-management programmes versus control intervention (participants with comorbid physical and mental health conditions)

Quality assessment							Number of patients	Effect	Quality	Importance
Self-efficacy (follow-up mean 6 months; measured with: Self-efficacy for managing chronic disease; range of scores: 1-10; better indicated by higher values)										

1	Randomised trials	Serious ^a	No serious inconsistency	No serious indirectness	Serious ^b	None	20	23	-	MD 0.6 lower (1.53 lower to 0.33 higher)	LOW	IMPORTANT
---	-------------------	----------------------	--------------------------	-------------------------	----------------------	------	----	----	---	--	-----	-----------

(a) Downgraded by 1 increment as the majority of the evidence was at high risk of bias

(b) Downgraded by 1 increment as the CI crossed 1 MID

Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Telemedicine	Usual care	Relative (95% CI)	Absolute		
-------------------	--------	--------------	---------------	--------------	-------------	----------------------	--------------	------------	-------------------	----------	--	--

J.7 Format of encounters

Table 250: Clinical evidence profile: Telemonitoring versus usual care

Quality assessment							Number of patients	Effect	Quality	Importance		
Mortality (follow-up 6 months)												
1	Randomised trials	No serious risk of bias	No serious inconsistency	serious indirectness ^b	Very serious ^c	None	2/18 (11.1%)	10.5%	OR 1.06 (0.13 to 8.47)	6 more per 1000 (from 90 fewer to 393 more)	VERY LOW	CRITICAL
Quality of life (physical component) (follow-up 6 months; measured with: SF-36V; range of scores: 0-100; better indicated by higher values)												
1	Randomised trials	Very serious ^a	No serious inconsistency	serious indirectness ^b	Very serious ^c	None	18	19	-	MD 0.92 higher (6.25 lower to 8.09 higher)	VERY LOW	CRITICAL
Quality of life (mental component) (follow-up 6 months; measured with: SF-36V; range of scores: 0-100; better indicated by higher values)												
1	Randomised trials	Very serious ^a	No serious inconsistency	serious indirectness ^b	Very serious ^c	None	18	19	-	MD 8.16 higher (1.31 lower to 17.63 higher)	VERY LOW	CRITICAL
Mean ER visits (follow-up 6 months; better indicated by lower values)												
1	Randomised trials	No serious risk of bias	No serious inconsistency	serious indirectness ^b	No serious imprecision	None	18	19	-	MD 1.11 lower (2.55 lower to 0.33 higher)	MODERATE	CRITICAL
Mean hospital admissions (follow-up 6 months; better indicated by lower values)												
1	Randomised	No serious	No serious	serious	Serious	None	18	19	-	MD 0.59 lower (1.61 lower to	LOW	CRITICAL

No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Telemedicine with alerts	Usual care	Relative (95% CI)	Absolute		
	trials	risk of bias	inconsistency	indirectness ^b	imprecision ^c					0.43 higher)		
Mean hospital days (follow-up 6 months; better indicated by lower values)												
1	Randomised trials	No serious risk of bias	No serious inconsistency	serious indirectness ^b	No serious imprecision	None	18	19	-	MD 4.28 lower (10.37 lower to 1.81 higher)	MODERATE	CRITICAL
Patient satisfaction (follow-up 6 months; measured with: General Home Care Satisfaction Scale; change score; range of scores not reported; better indicated by higher values)												
1	Randomised trials	Very serious ^a	No serious inconsistency	serious indirectness ^b	Serious ^c	None	18	19	-	MD 0.56 higher (2.28 lower to 3.4 higher)	VERY LOW	CRITICAL
Functional outcomes (critical) – no data												

(a) Downgraded by 1 increment as the majority of evidence was at high risk of bias

(b) The majority of the evidence included an indirect population (downgrade by 1 increment) or a very indirect population (downgrade by 2 increments)

(c) Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Table 251: Clinical evidence profile: Telemonitoring with alerts versus usual care

Quality assessment							No of patients	Effect		Quality	Importance	
Mortality (follow-up 1 years)												
1	randomised trials	serious ^a	no serious inconsistency	serious ^b	serious ^c	none	15/102 (14.7%)	4/103 (3.9%)	RR 3.79 (1.3 to 11.02)	108 more per 1000 (from 12 more to 389 more)	⊕○○○ VERY LOW	CRITICAL
Quality of life (physical health) (follow-up 1 years; measured with: SF-12; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	serious ^a	no serious inconsistency	serious ^b	serious ^c	none	77	103	-	MD 1.4 lower (4.48 lower to 1.68 higher)	⊕○○○ VERY LOW	CRITICAL
Quality of life (mental health) (follow-up 1 years; measured with: SF-12; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	serious ^a	no serious inconsistency	serious ^b	no serious imprecision	none	77	89	-	MD 2.1 lower (4.64 lower to 0.44 higher)	⊕⊕○○ LOW	CRITICAL
Activities of daily living (follow-up 1 years; measured with: Barthel ADL Index; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	serious ^a	no serious inconsistency	serious ^b	no serious imprecision	none	77	89	-	MD 2.6 lower (7.22 lower to 2.02 higher)	⊕⊕○○ LOW	CRITICAL
ER visits (follow-up 1 years)												
1	randomised trials	no serious risk of bias	no serious inconsistency	serious ^b	serious ^c	none	36/102 (35.3%)	29/103 (28.2%)	RR 1.25 (0.84 to 1.88)	70 more per 1000 (from 45 fewer to 248)	⊕⊕○○ LOW	CRITICAL

											more)		
Mean ER visits (follow-up 1 years; Better indicated by lower values)													
1	randomised trials	serious ¹	no serious inconsistency	serious ^b	no serious imprecision	none	102	103	-	MD 0.26 higher (0.04 lower to 0.56 higher)	⊕⊕○○ LOW	CRITICAL	
Hospital admissions (follow-up 1 years)													
1	randomised trials	no serious risk of bias	no serious inconsistency	serious ^b	serious ^c	none	53/102 (52%)	45/103 (43.7%)	RR 1.19 (0.89 to 1.59)	83 more per 1000 (from 48 fewer to 258 more)	⊕⊕○○ LOW	CRITICAL	
Mean hospital admissions (follow-up 1 years; Better indicated by lower values)													
1	randomised trials	serious ^a	no serious inconsistency	serious ^b	no serious imprecision	none	102	103	-	MD 0.27 higher (0.13 lower to 0.67 higher)	⊕⊕○○ LOW	CRITICAL	
Length of hospital stay (follow-up 1 years; Better indicated by lower values)													
1	randomised trials	serious ^a	no serious inconsistency	serious ^b	no serious imprecision	none	102	103	-	MD 2 lower (6.19 lower to 2.19 higher)	⊕⊕○○ LOW	CRITICAL	
Mean hospice visits (follow-up 1 years; Better indicated by lower values)													
1	randomised trials	serious ^c	no serious inconsistency	serious ^b	no serious imprecision	none	94	100	-	MD 0.7 lower (6.7 lower to 5.3 higher)	⊕⊕○○ LOW	IMPORTANT	
Length of hospice stay (follow-up 1 years; Better indicated by lower values)													
1	randomised trials	serious ^a	no serious inconsistency	serious ^b	no serious imprecision	none	94	100	-	MD 61.4 lower (92.88 to 29.92 lower)	⊕⊕○○ LOW	IMPORTANT	
Time to hospice entry (follow-up 1 years)													
1	randomised trials	very serious ^a	no serious inconsistency	serious ^b	serious ^c	none	9/9 (100%)	4/4 (100%)	HR 1.28 (0.94 to 1.74)	-	⊕○○○ VERY LOW	IMPORTANT	
Patient/carer satisfaction (critical) – no data													

(a) Downgraded by 1 increment as the majority of evidence was at high risk of bias

(b) The majority of the evidence included an indirect population (downgrade by 1 increment) or a very indirect population (downgrade by 2 increments)

(c) Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs

Table 252: Clinical evidence profile: Telemonitoring with alerts plus case management versus usual care plus case management

Quality assessment	No of patients	Effect	Quality	Importance
--------------------	----------------	--------	---------	------------

Mortality (critical) – no data												
Functional outcomes (critical) – no data												
Patient and carer satisfaction (critical) – no data												
Length of hospital stay (critical) – no data												
Unscheduled care (critical) – no data												
Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Telemonitoring (plus problem-solving and counselling)	Control	Relative (95% CI)	Absolute		
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Telemedicine plus case management	Usual care plus case management	Relative (95% CI)	Absolute		
QOL (functional level) (follow-up 6 months; Better indicated by higher values)												
1	randomised trials	very serious ^a	no serious inconsistency	serious ^b	no serious imprecision	none	47	57	-	SMD 0.3 lower (0.69 lower to 0.09 higher)	⊕000 VERY LOW	CRITICAL
QOL (cognitive status) (follow-up 6 months; Better indicated by higher values)												
1	randomised trials	very serious ^a	no serious inconsistency	serious ^b	very serious ^c	none	47	57	-	SMD 0.02 lower (0.36 lower to 0.41 higher)	⊕000 VERY LOW	CRITICAL
QOL (patient satisfaction) (follow-up 6 months; Better indicated by higher values)												
1	randomised trials	very serious ^a	no serious inconsistency	serious ^b	no serious imprecision	none	47	57	-	SMD 0.47 higher (0.08 to 0.86 higher)	⊕000 VERY LOW	CRITICAL
QOL (self-rated health) (follow-up 6 months; Better indicated by higher values)												
1	randomised trials	very serious ^a	no serious inconsistency	serious ^b	no serious imprecision	none	47	57	-	SMD 0.18 lower (0.57 lower to 0.21 higher)	⊕000 VERY LOW	CRITICAL

(a) Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

(b) The majority of the evidence included an indirect population (downgrade by 1 increment) or a very indirect population (downgrade by 2 increments)

(c) Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs

Table 253: Clinical evidence profile: Telemonitoring (plus self-management) versus usual care (plus psychoeducation)

Quality assessment	Number of patients	Effect	Quality	Importance
--------------------	--------------------	--------	---------	------------

Quality of life (mental component) (follow-up 6 months; measured with: SF-12; range of scores: 0-100; better indicated by higher values)												
1	Randomised trials	Serious ^a	No serious inconsistency	no serious indirectness	Serious ^b	None	46	48	-	MD 11.8 higher (1.34 to 22.26 higher)	LOW	CRITICAL
Mean ER visits (follow-up 12 months; better indicated by lower values)												
1	Randomised trials	No serious risk of bias	No serious inconsistency	no serious indirectness	Serious ^b	None	46	48	-	MD 0.8 lower (1.37 to 0.23 lower)	MODERATE	CRITICAL
Mean hospital days (follow-up 12 months; better indicated by lower values)												
1	Randomised trials	No serious risk of bias	No serious inconsistency	no serious indirectness	Serious ^b	None	46	48	-	MD 9.9 lower (11.8 to 8 lower)	MODERATE	CRITICAL
Mean episodes of care (follow-up 12 months; better indicated by lower values)												
1	Randomised trials	No serious risk of bias	No serious inconsistency	no serious indirectness	No serious imprecision	None	46	48	-	MD 0.5 lower (1.01 lower to 0.01 higher)	HIGH	CRITICAL
Patient satisfaction (follow-up 3 months; better indicated by higher values)												
1	Randomised trials	Very serious ^a	No serious inconsistency	no serious indirectness	No serious imprecision	None	46	48	-	MD 0.1 lower (0.65 lower to 0.45 higher)	LOW	CRITICAL
Mortality (critical) – no data												
Functional outcomes (critical) – no data												

(a) Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

(b) Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs

Appendix K: Forest plots

K.1 Principles/Barriers of care

K.1.1 Principles of care

None.

K.1.2 Barriers of care

None.

K.2 Identification

K.2.1 Unplanned hospital admissions

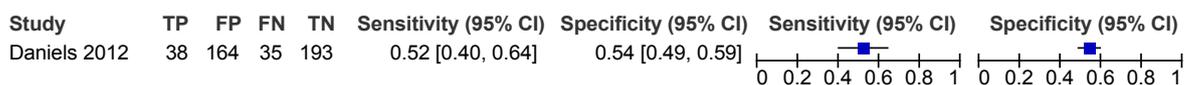
K.2.1.1 Dutch Tilburg Frailty Indicator

Figure 20: Dutch Tilburg Frailty Indicator (≥ 4)



K.2.1.2 Groningen Frailty Indicator

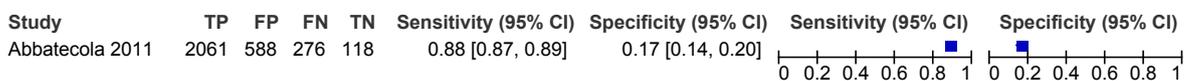
Figure 21: Groningen Frailty Indicator (≥ 5)



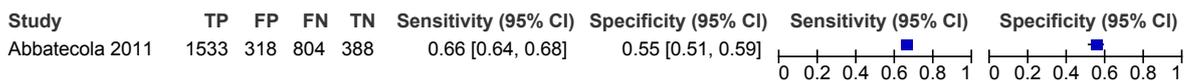
K.2.1.3 HOPE

Figure 22: HOPE

HOPE (≥ 4)



HOPE (≥ 8)



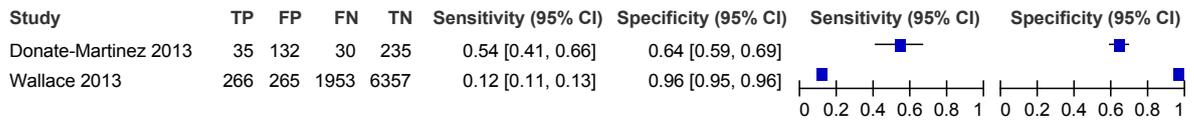
K.2.1.4 Sherbook Postal Questionnaire

Figure 23: Sherbook Postal Questionnaire (≥ 2)



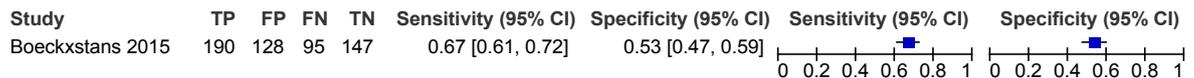
K.2.1.5 Pra

Figure 24: Pra (≥ 0.5)



K.2.1.6 Unweighted disease count

Figure 25: Unweighted disease count >3



K.2.2 Health-related quality of life

None.

K.2.3 Admission to care facility

None.

K.2.4 Life expectancy risk tools

K.2.4.1 Community-dwelling

Figure 26: CIRS (>3)

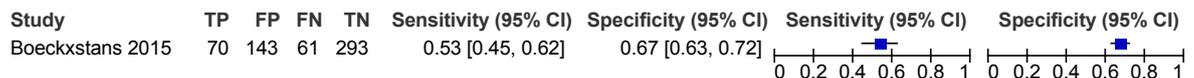


Figure 27: Dutch Tilburg Frailty Indicator (≥ 4)

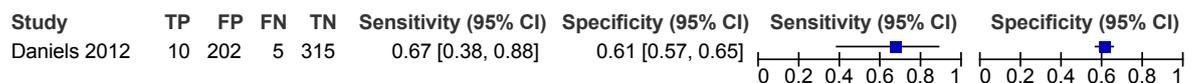


Figure 28: Groningen Frailty Indicator (≥ 5)



Figure 29: Pra (≥ 5)



Figure 30: Sherbook Postal Questionnaire (≥ 2)



Figure 31: VES-13

VES-13 (≥2)



VES-13 (≥3)



VES-13 (≥4)



VES-13 (≥5)



VES-13 (≥6)



VES-13 (≥7)



VES-13 (≥8)



VES-13 (≥9)



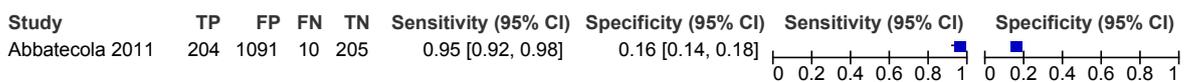
VES-13 (10)



K.3.1.1 Inpatient

Figure 32: HOPE^a

HOPE (≥4)



HOPE (≥8)

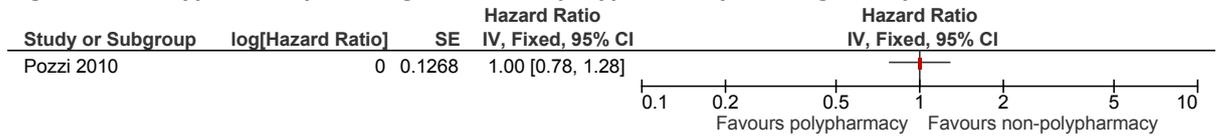


^aProximate sample size used

K.3.2 Polypharmacy: unplanned hospital admissions

K.3.2.1 Community-dwelling

Figure 33: Polypharmacy ≥5 drugs versus no polypharmacy <5 drugs (hospitalisation) (HR)



K.3.2.2 Living in care facility

Figure 34: Polypharmacy 5-9 drugs, 10-14 drugs, ≥15 drugs versus no polypharmacy <5 drugs (ambulatory care sensitive hospitalisation) (subhazard RR)

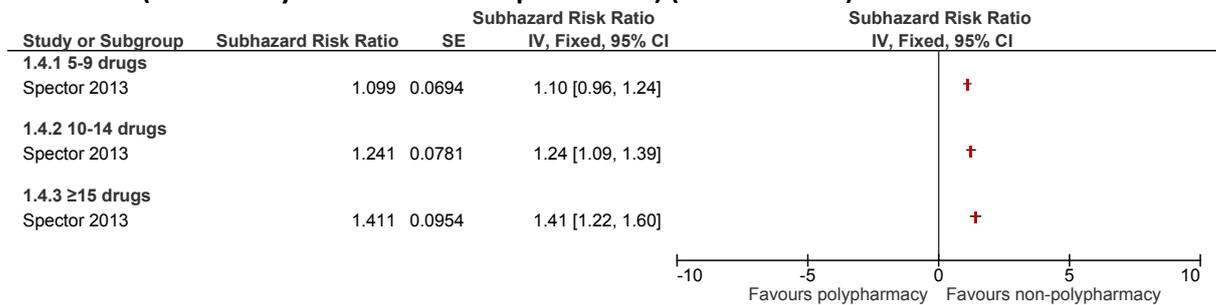


Figure 35: Polypharmacy 5-9 drugs, 10-14 drugs, ≥15 drugs versus no polypharmacy <5 drugs (nursing home sensitive hospitalisation) (subhazard RR)

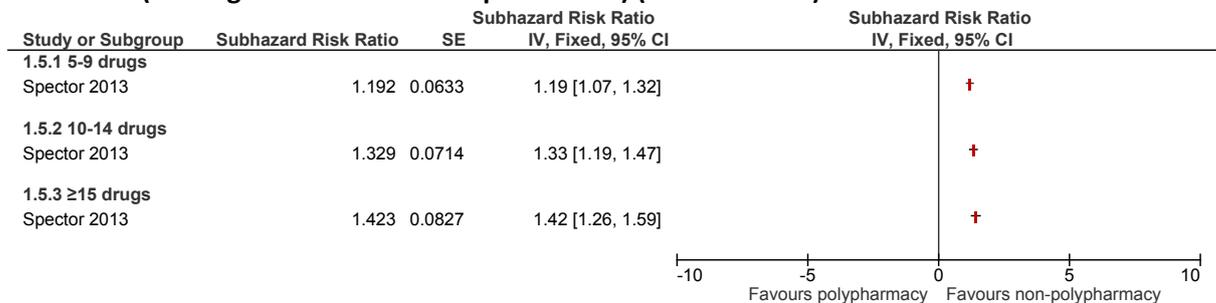
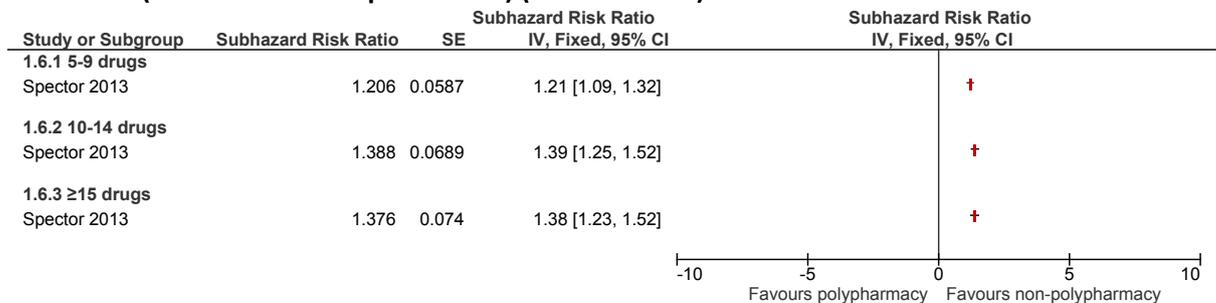


Figure 36: Polypharmacy 5-9 drugs, 10-14 drugs, ≥15 drugs versus no polypharmacy <5 drugs ('unavoidable' hospitalisation) (subhazard RR)

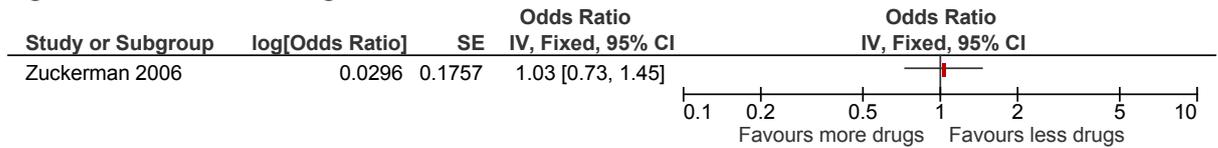


K.3.3 Polypharmacy: health-related quality of life

None.

K.3.4 Polypharmacy: admission to care facilities

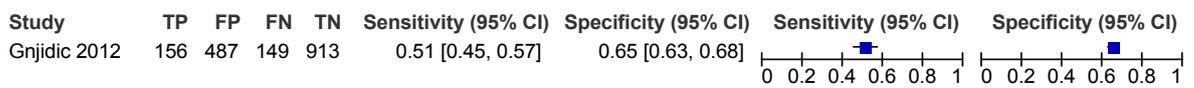
Figure 37: Number of drugs



K.3.5 Polypharmacy: mortality

K.3.5.1 Prognostic accuracy data

Figure 38: Polypharmacy (≥5 drugs) vs. no polypharmacy (<5 drugs)



K.3.5.2 Unadjusted data

Figure 39: Polypharmacy ≥5 drugs, ≥6 drugs, 6 – 9 drugs, ≥10 drugs (HR) vs. no polypharmacy (<5 drugs/0 drugs)

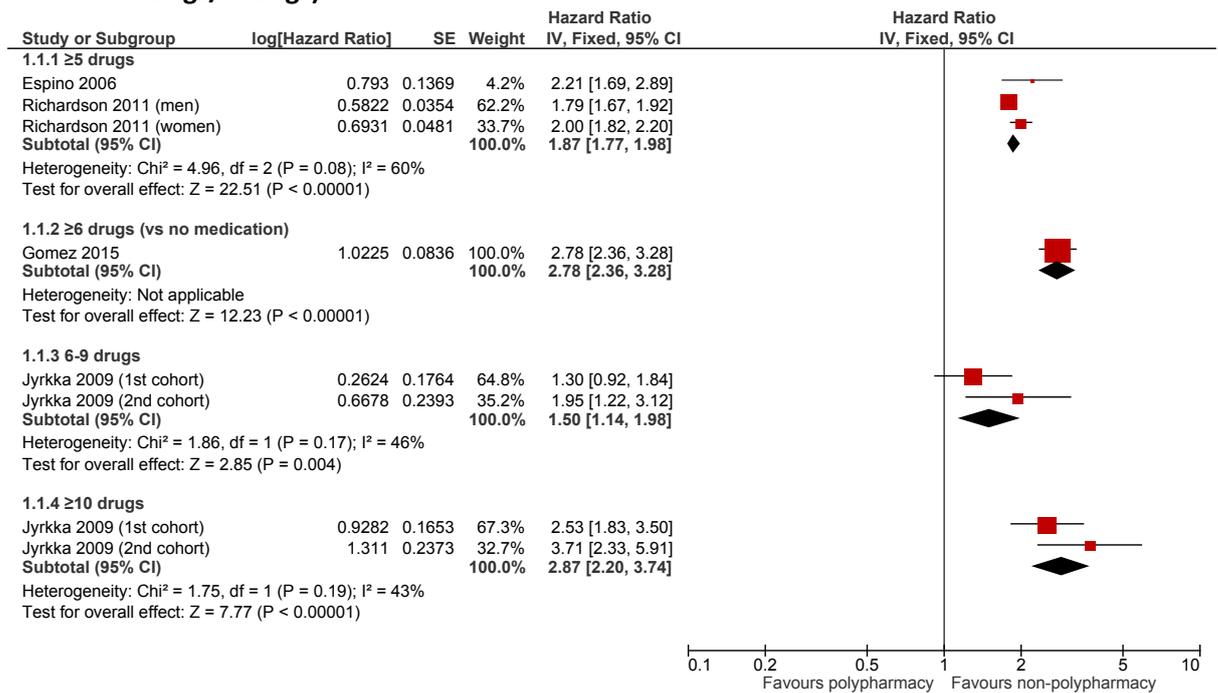


Figure 40: Number of drugs (HR)

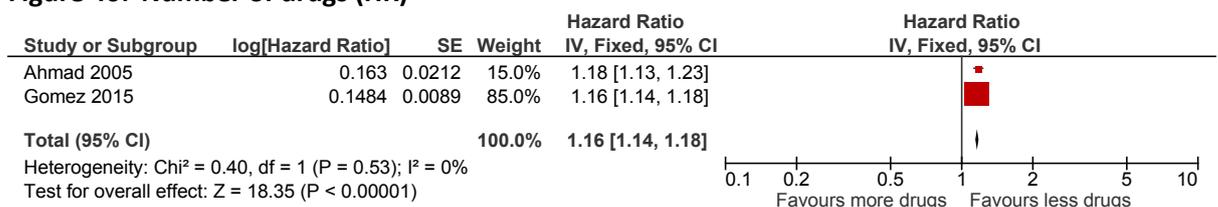


Figure 41: Number of drugs (OR)

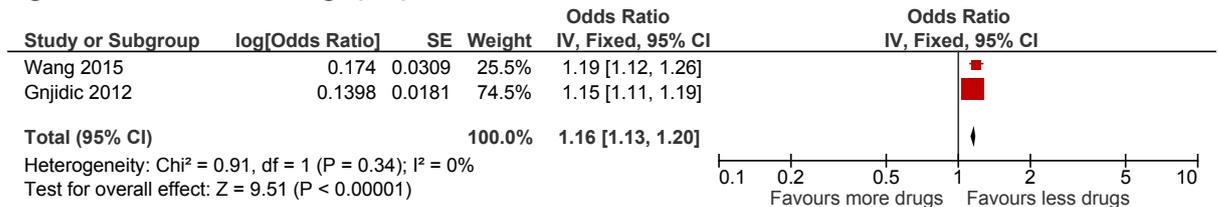


Figure 42: Number of drug classes (HR)



K.4 Frailty

K.4.1 Tests for identifying frailty (CGA as reference standard)

Figure 43: Sensitivity and specificity

aCGA

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Smets 2014	121	54	18	97	0.87 [0.80, 0.92]	0.64 [0.56, 0.72]		

GFI

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Smets 2014	103	41	36	110	0.74 [0.66, 0.81]	0.73 [0.65, 0.80]		

G8

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Smets 2014	104	47	35	104	0.75 [0.67, 0.82]	0.69 [0.61, 0.76]		

VES-13

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Smets 2014	114	32	25	119	0.82 [0.75, 0.88]	0.79 [0.71, 0.85]		

K.4.2 Tests for identifying frailty (Fried's phenotype as reference standard)

Figure 44: Sensitivity and Specificity (demographics and simple measures)

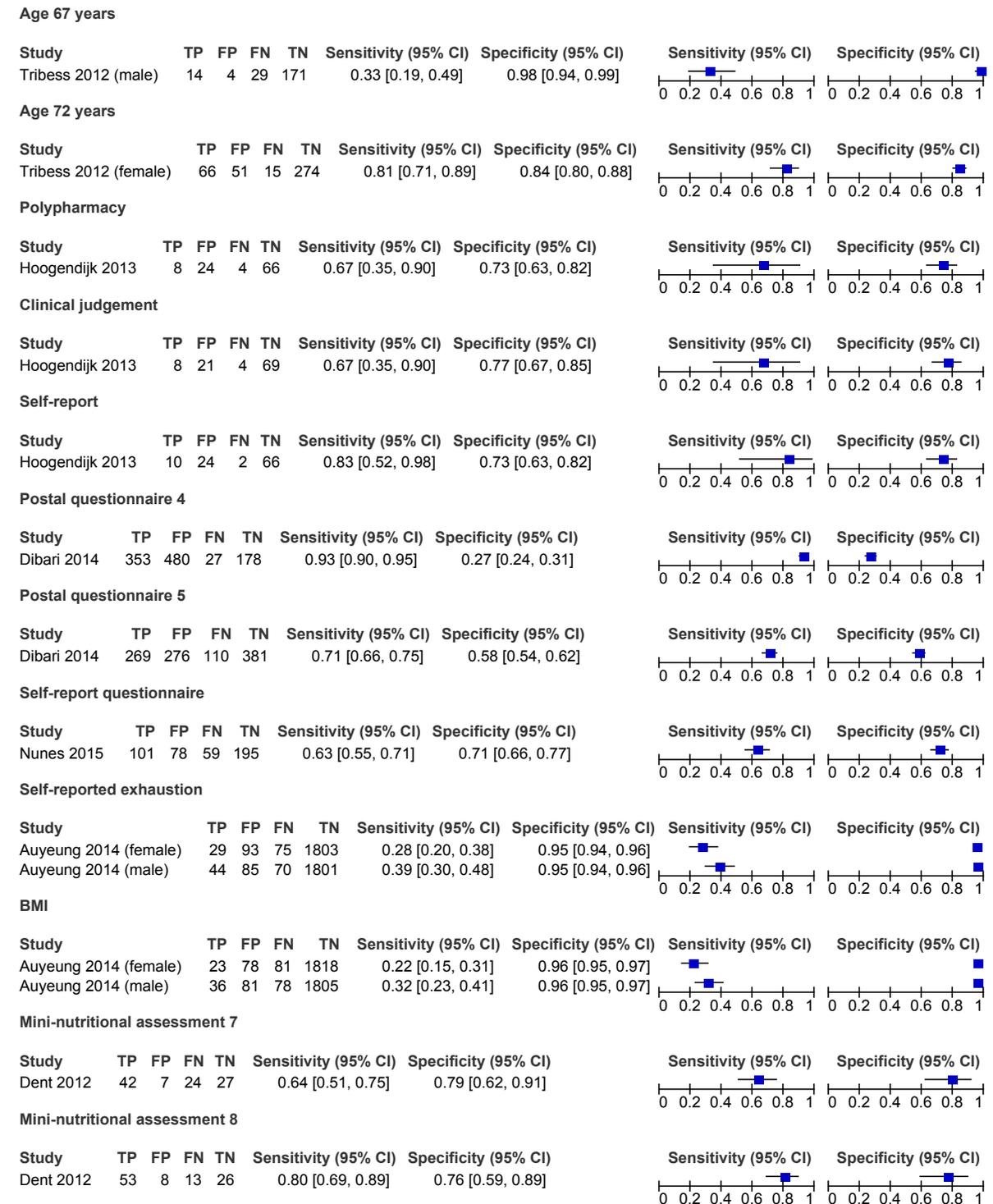
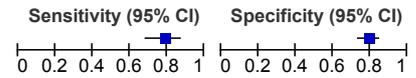


Figure 45: Sensitivity and Specificity (Brief assessments)

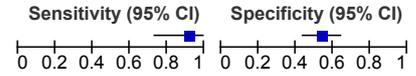
Chair stand

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Purser 2006	66	47	18	178	0.79 [0.68, 0.87]	0.79 [0.73, 0.84]



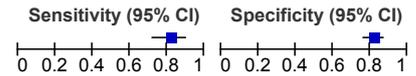
Chair stand (SPPB)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
DaCmara 2013	22	46	2	54	0.92 [0.73, 0.99]	0.54 [0.44, 0.64]



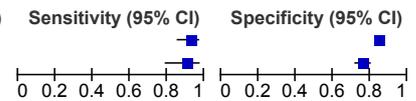
Gait speed 0.65 m/s

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Purser 2006	68	41	15	185	0.82 [0.72, 0.90]	0.82 [0.76, 0.87]



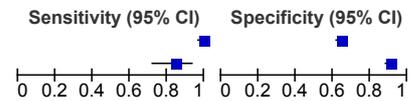
Gait speed 0.76 - 0.78 m/s

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Auyeung 2014 (female)	96	294	8	1602	0.92 [0.85, 0.97]	0.84 [0.83, 0.86]
Schoon 2014	47	112	5	354	0.90 [0.79, 0.97]	0.76 [0.72, 0.80]



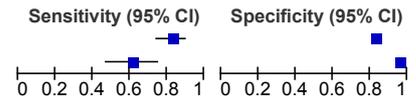
Gait speed 0.8 m/s

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Castell 2013	147	418	1	759	0.99 [0.96, 1.00]	0.64 [0.62, 0.67]
Schoon 2014	44	42	8	424	0.85 [0.72, 0.93]	0.91 [0.88, 0.93]



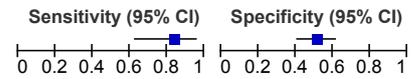
Gait speed 0.89-0.9 m/s

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Auyeung 2014 (male)	86	320	18	1576	0.83 [0.74, 0.89]	0.83 [0.81, 0.85]
Schoon 2014	32	19	20	448	0.62 [0.47, 0.75]	0.96 [0.94, 0.98]



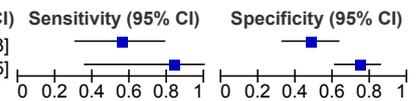
Gait speed (SPPB; all)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
DaCmara 2013	20	49	4	51	0.83 [0.63, 0.95]	0.51 [0.41, 0.61]



Gait speed (SPPB; subgroups)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
DaCmara 2013 (santa cruz)	10	24	8	22	0.56 [0.31, 0.78]	0.48 [0.33, 0.63]
DaCmara 2013 (st bruno)	5	14	1	41	0.83 [0.36, 1.00]	0.75 [0.61, 0.85]



Walking distance (6-min)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Boxer 2008	15	11	1	33	0.94 [0.70, 1.00]	0.75 [0.60, 0.87]

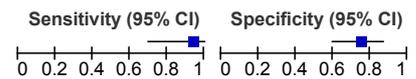
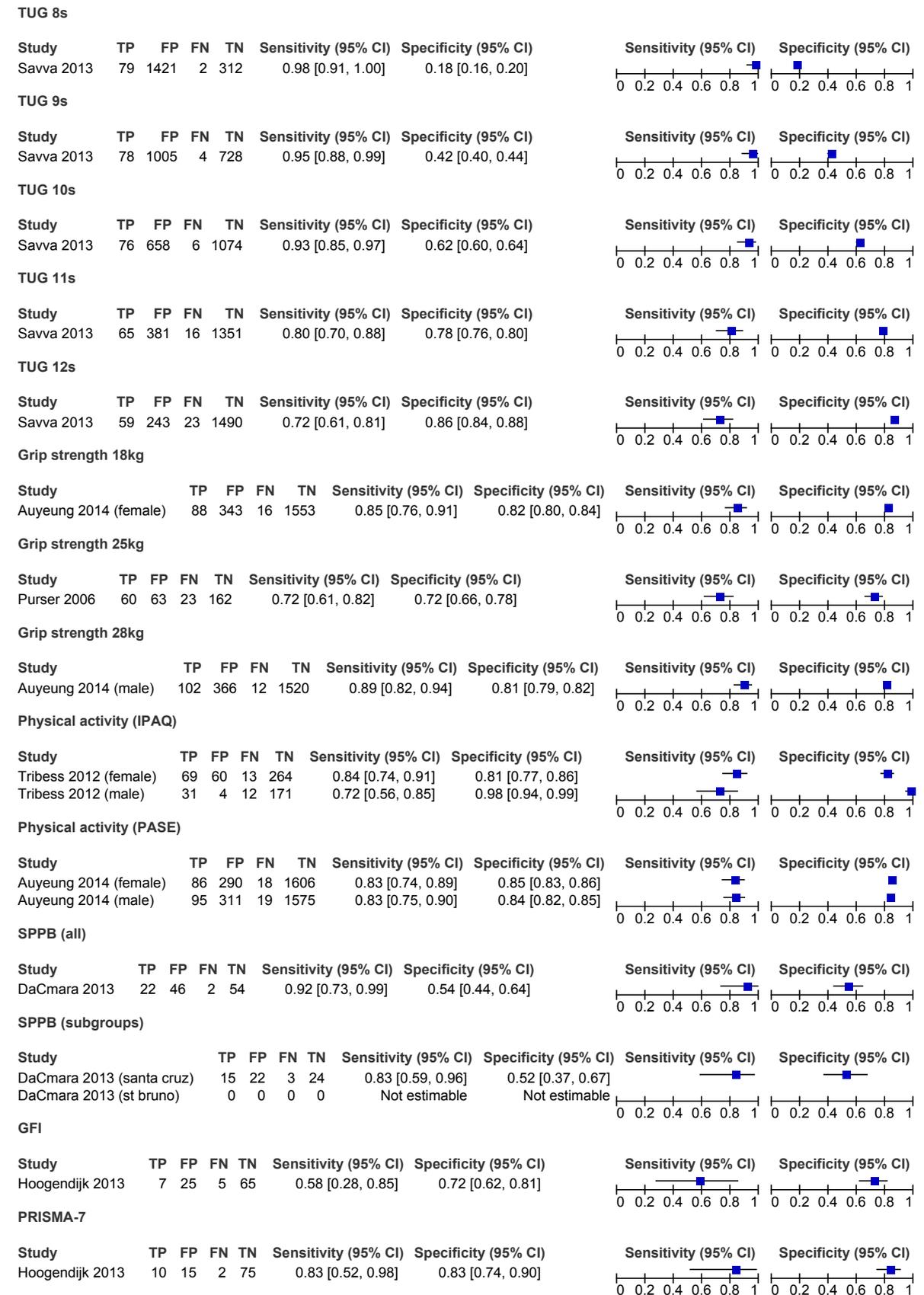


Figure 46: Sensitivity and Specificity (Brief assessments continued)



K.5 Delivering an approach to care that takes account of multimorbidity

K.5.1.1 Treatment burden

None.

K.5.2 Ranking

None.

K.5.3 Stopping antihypertensive treatment

Figure 47: CV mortality (1 – 1.5 years)

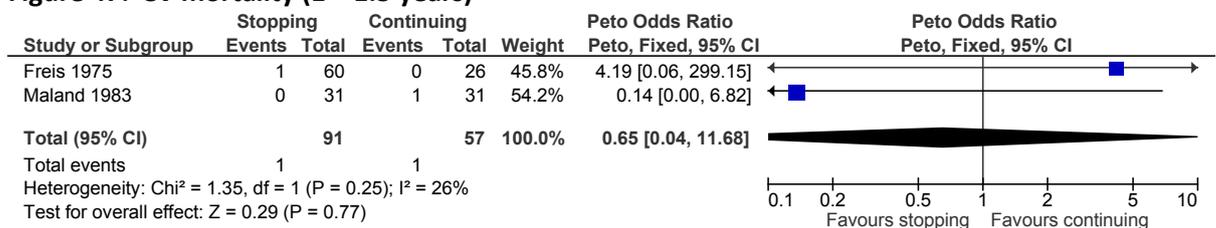


Figure 48: Fatal MI/myocardial infarction (1.5 years)

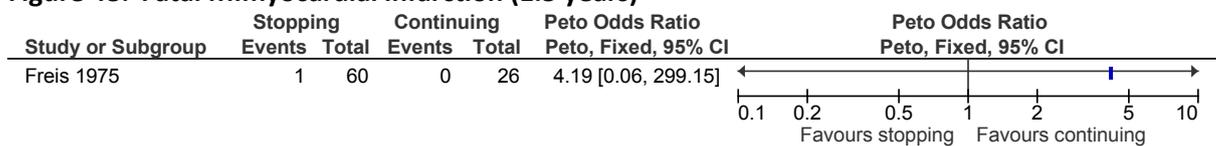


Figure 49: Non-fatal MI (1 year)



Figure 50: Transient Ischemic Attack (1 year)

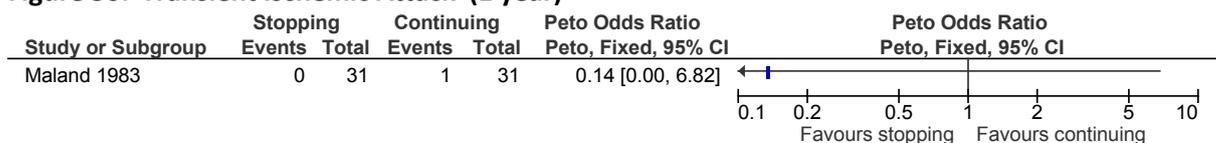


Figure 51: Non-fatal congestive heart failure (1.5 years)

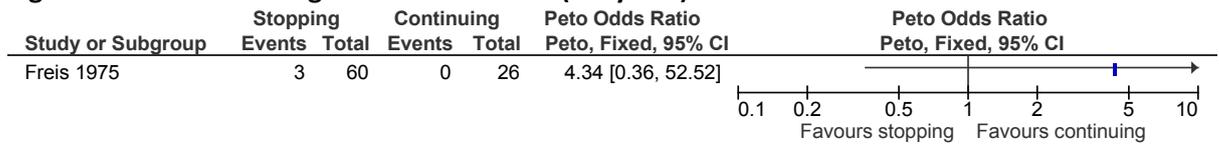


Figure 52: Atrial fibrillation (1.5 years)

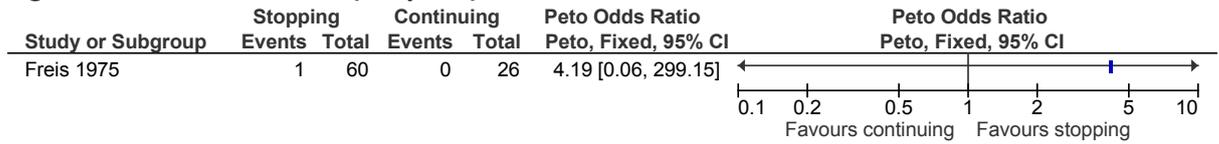


Figure 53: Right bundle block (1.5 years)



Figure 54: Return to hypertension (diastolic blood pressure ≥ 95 mm Hg) (12 -18 months)

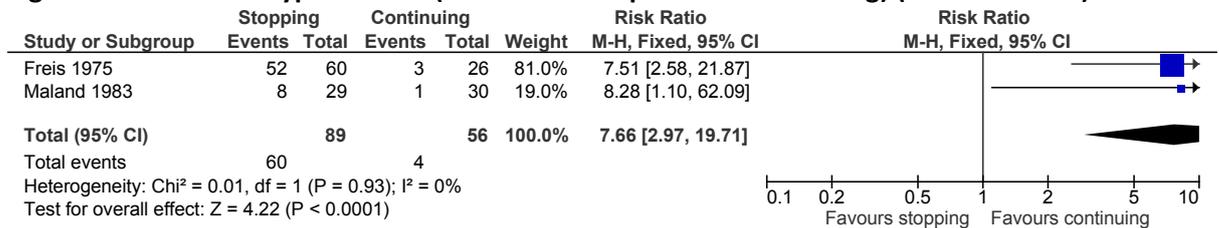
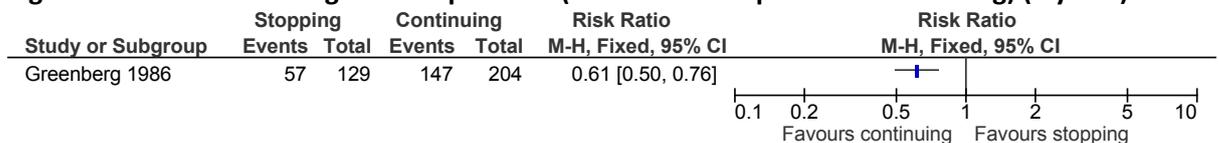


Figure 55: Maintained target blood pressure (diastolic blood pressure < 90 mm Hg) (2 years)



K.5.4 Stopping drugs for osteoporosis

K.5.4.1 Stopping versus continuing bisphosphonates after >1 year treatment

Figure 56: Clinical fracture (any) at 3 years

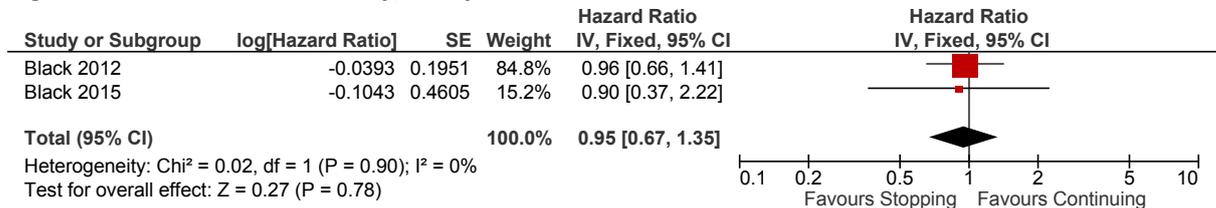


Figure 57: Clinical vertebral fracture at 3 years

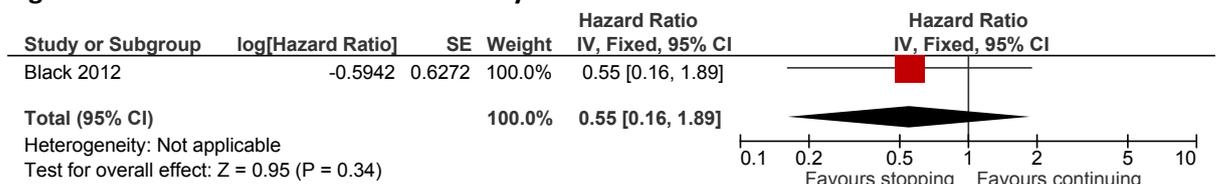


Figure 58: Clinical vertebral fracture at 5 years

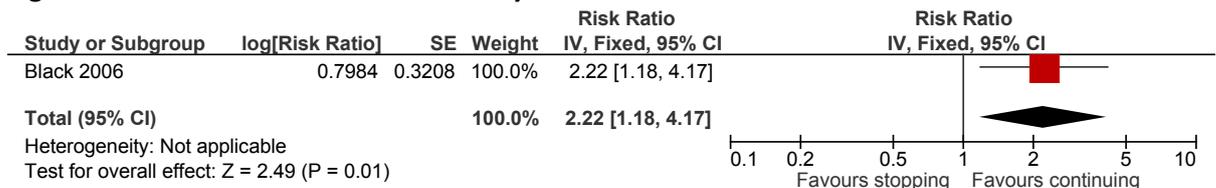


Figure 59: Clinical non-vertebral fracture at 3 years

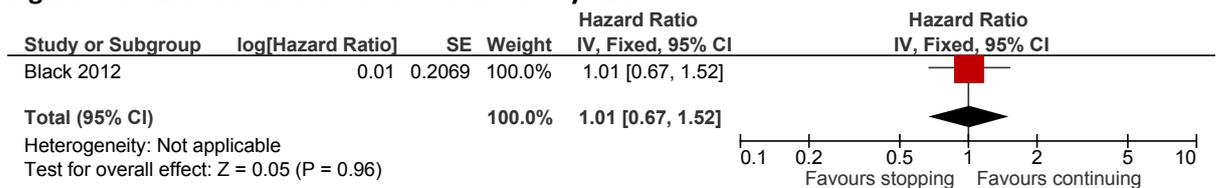


Figure 60: Clinical non-vertebral fracture at 2-5 years

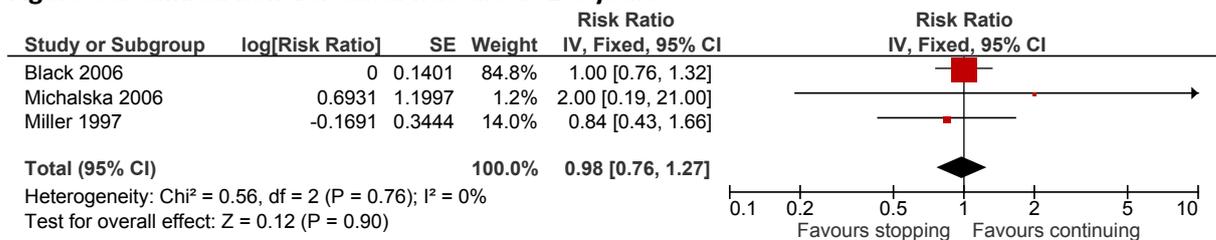


Figure 61: Morphometric vertebral fracture at 3-5 years

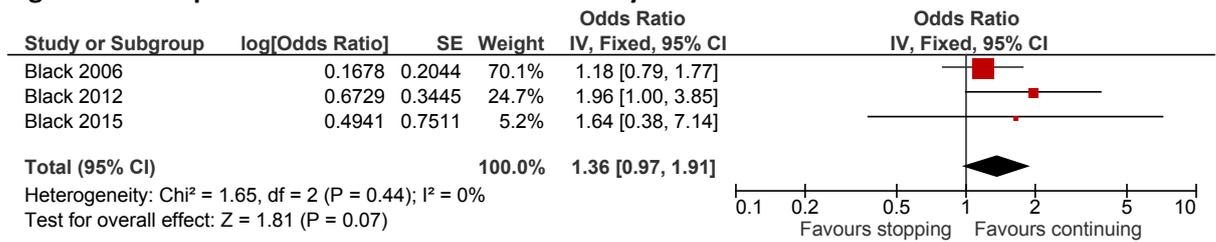


Figure 62: Hospitalisation at 3 years

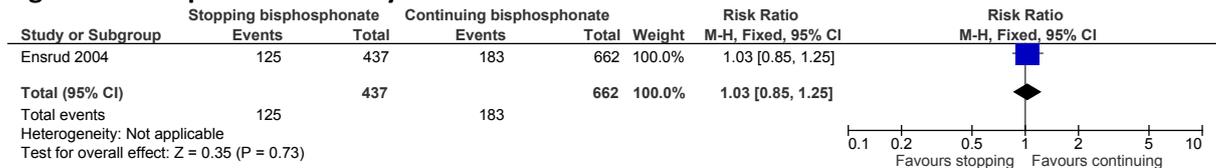


Figure 63: Clinical atypical femur fracture at 3 years

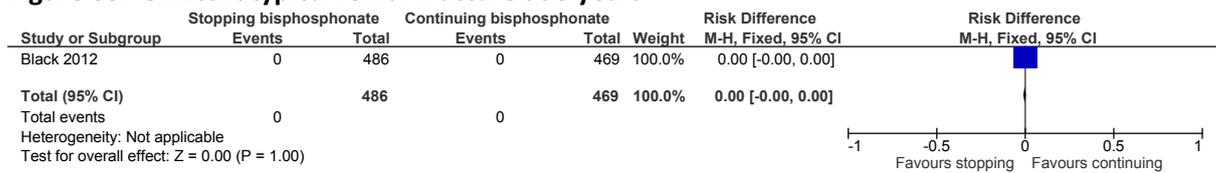
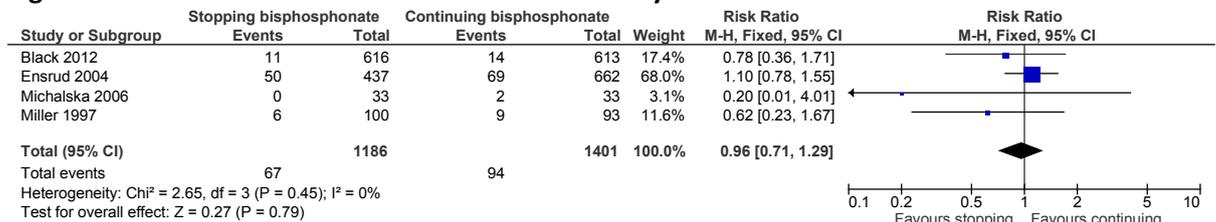


Figure 64: Discontinuation due to side effects at 2-3 years



K.5.5 Stopping statins

Figure 65: MacGill Quality of Life – Total (0-10), AUC between 0-20 weeks; higher score indicate better outcome

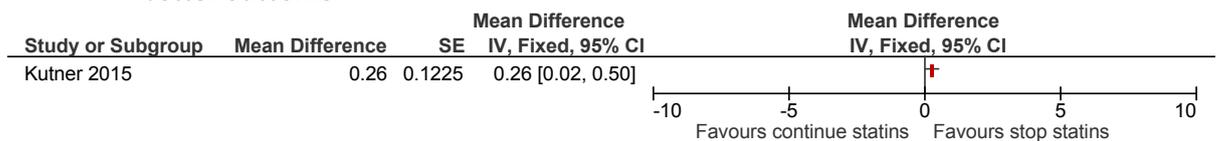


Figure 66: All-cause mortality (time to event, median follow-up 18 weeks)

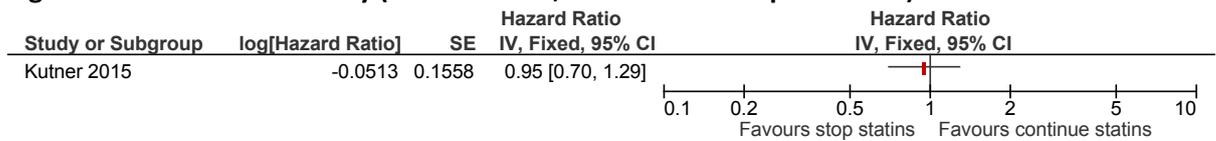
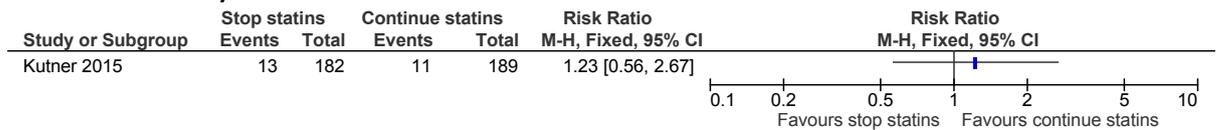


Figure 67: Cardiovascular-related events (new cardiovascular event or invasive cardiovascular procedure with hospital or emergency department admission, median follow-up 18 weeks)



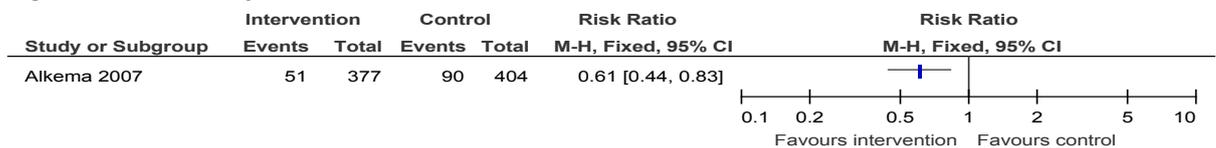
K.6 Interventions

K.6.1 Models of care

K.6.1.1 Models of care without self-management component

K.6.1.1.1 *Alkema 2007*

Figure 68: Mortality at 24 months



K.6.1.1.2 *Beck 1997*

Figure 69: Mortality at 12 months

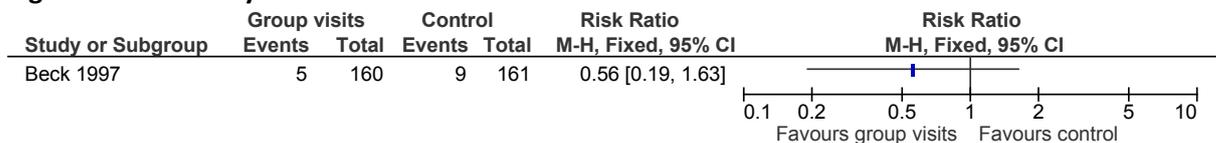


Figure 70: Urgent care visits per patient at 12 months

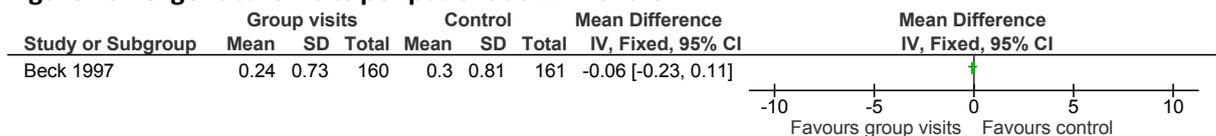


Figure 71: Emergency department visits per patient at 12 months

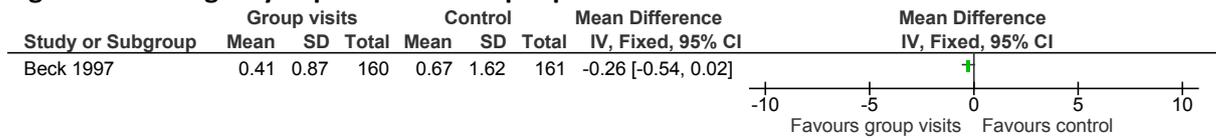
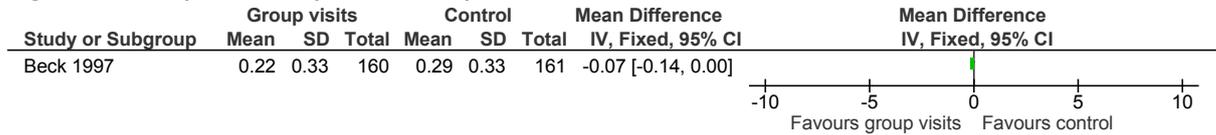
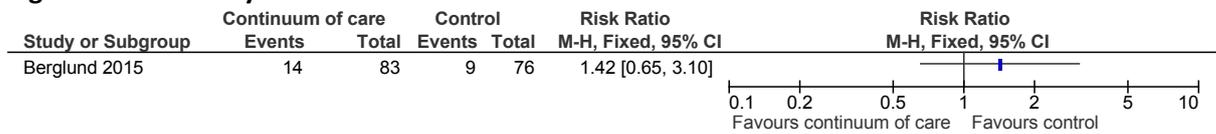


Figure 72: Proportion of patients hospitalised at 12 months



K.6.1.1.3 Berglund 2015

Figure 73: Mortality at 12 months



K.6.1.1.4 Bouman 2008

Figure 74: Mortality at 18 months

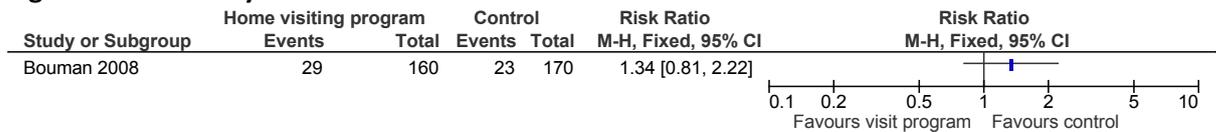


Figure 75: Bed days per patient at 18 months

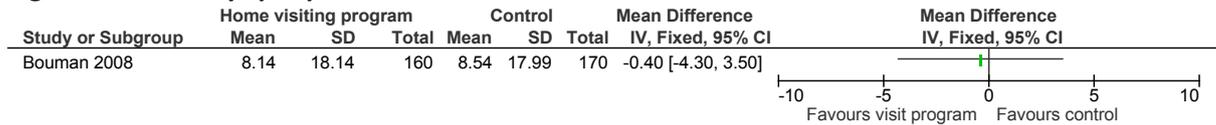


Figure 76: Hospital admissions at 18 months

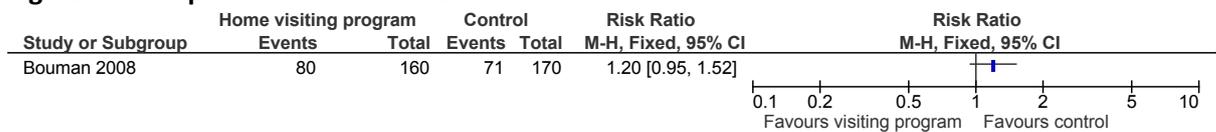
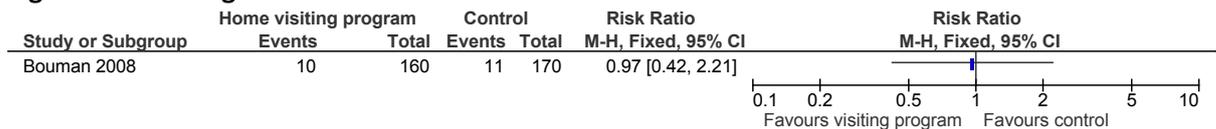


Figure 77: Nursing home admissions at 18 months



K.6.1.1.5 Courtney 2009

Figure 78: Unscheduled care (emergency hospital readmissions) at 6 months

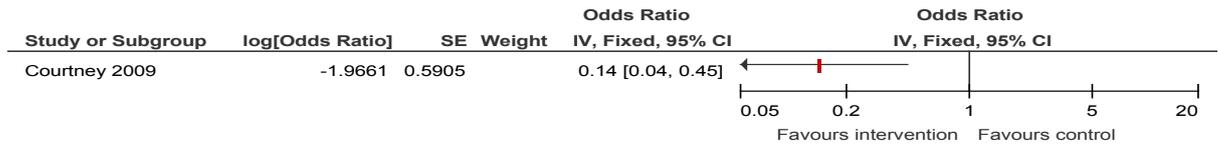
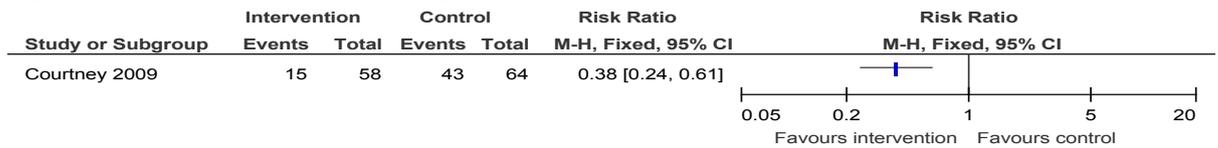


Figure 79: Unscheduled care (emergency GP visits) at 6 months



K.6.1.1.6 Eklund 2013

Figure 80: Mortality at 12 months

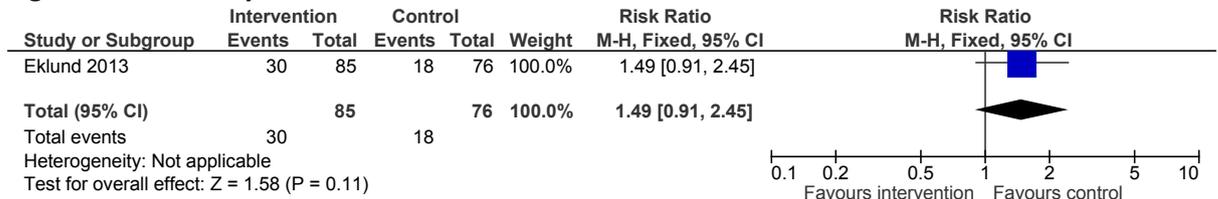


Figure 81: Functional outcomes (people improving ADL) at 12 months

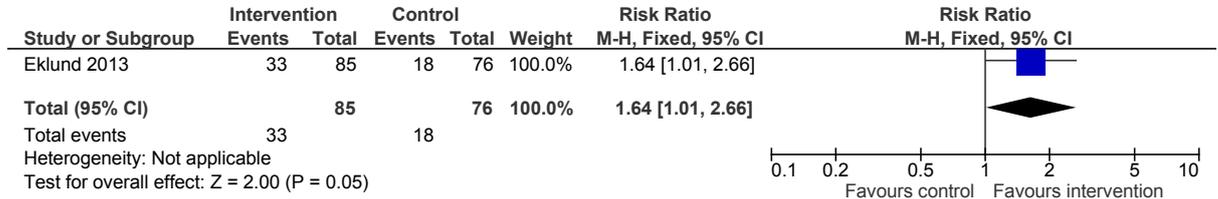
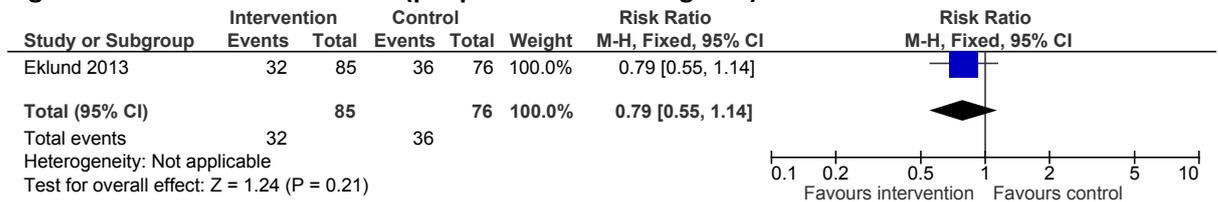


Figure 82: Functional outcomes (people with worsening ADL) at 12 months



K.6.1.1.7 EII 2010

Figure 83: Health-related quality of life(SF12, mental component, 0-100, higher is better) at 18 months

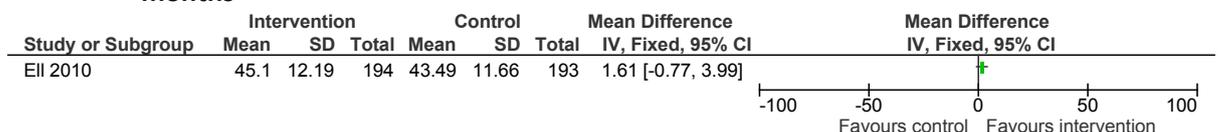


Figure 84: Health-related quality of life (SF12, physical component, 0-100, higher is better) at 18 months

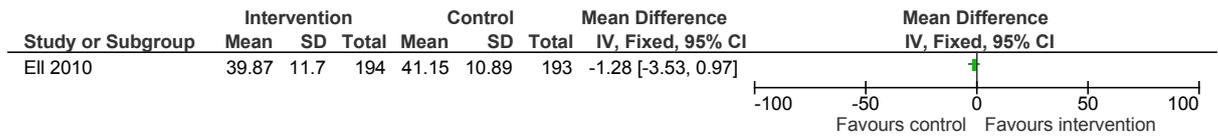
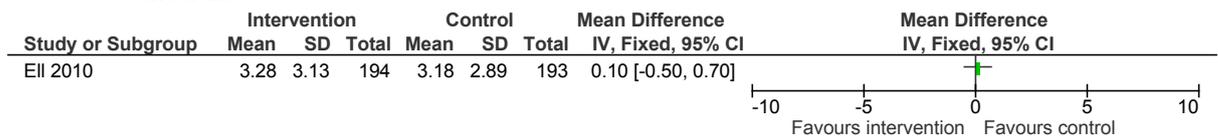


Figure 85: Functional outcomes (scale of functional impairment, 1-10, lower is better) at 18 months



K.6.1.1.8 Hogg 2009

Figure 86: Health-related quality of life (SF36, physical component, 0-100, higher is better) at 15 months

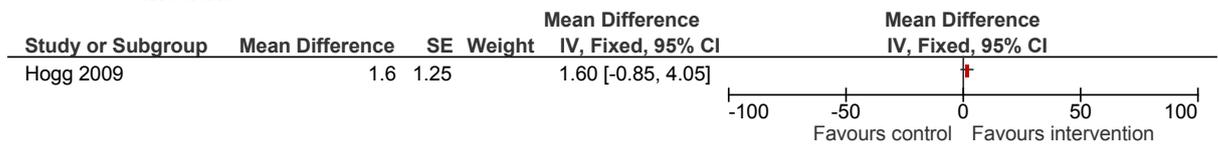


Figure 87: Health-related quality of life (SF36, mental component, 0-100, higher is better) at 15 months

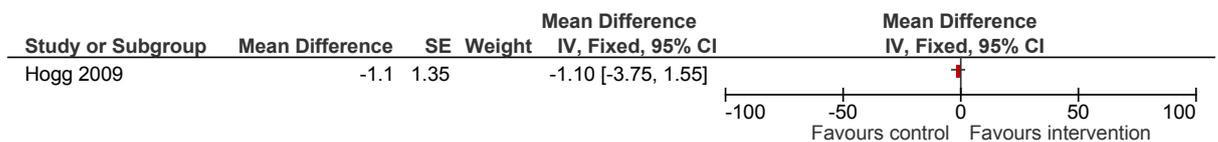


Figure 88: Health-related quality of life (SF36, mental component, 0-100, higher is better) at 15 months

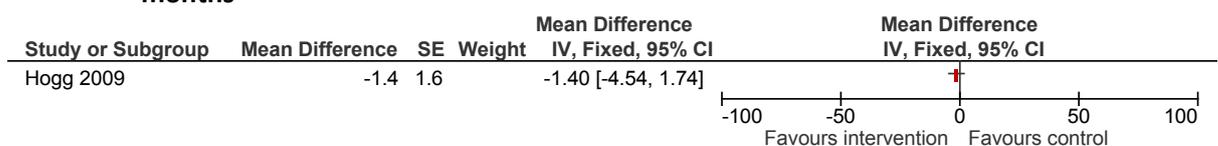


Figure 89: Mortality at 15 months

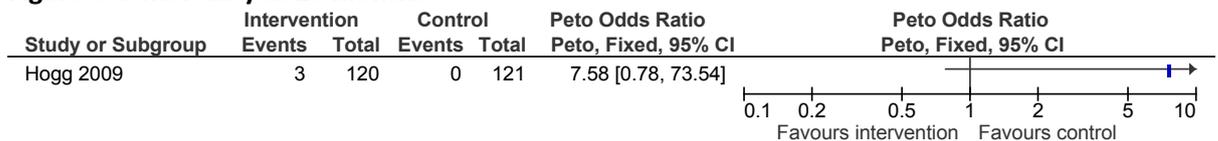


Figure 90: Unscheduled care (average number of ED visits) at 15 months

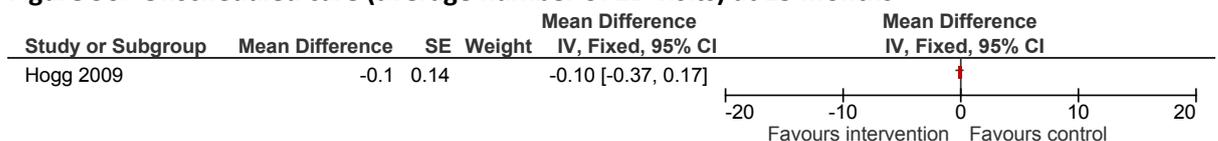


Figure 91: Unscheduled care (average number of hospital admissions) at 15 months

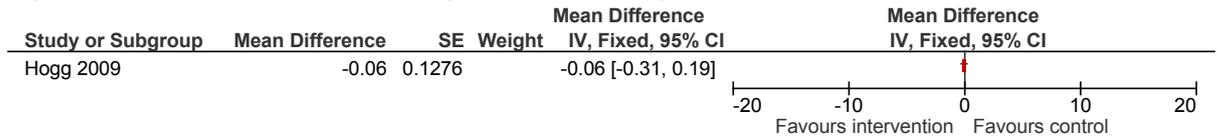
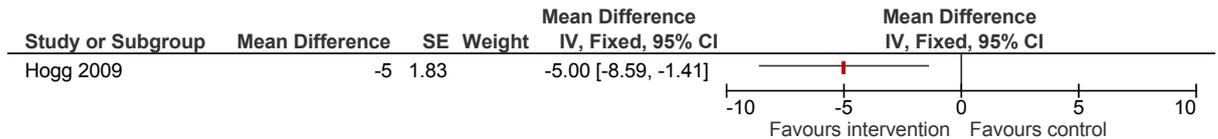


Figure 92: Patient/Carer treatment burden (caregiver burden, 0 to 88, higher is better) at 15 months



K.6.1.1.9 Metzelthin 2013

Figure 93: Functional outcomes (GARS – ADL subscale, 11-44, higher is worse outcome) at 24 months

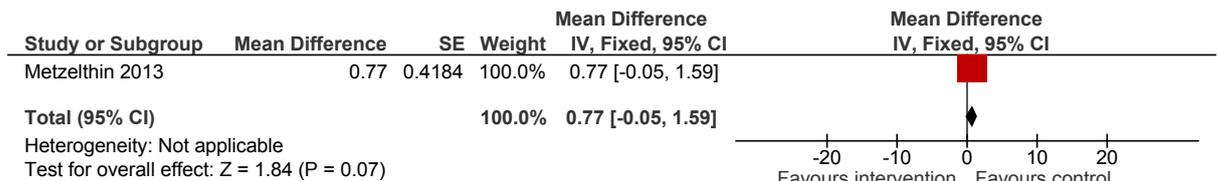
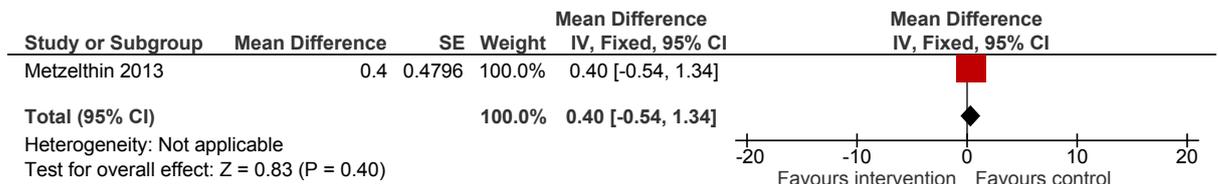


Figure 94: Functional outcomes (GARS – IADL subscale, 7-28, higher is worse outcome) at 24 months



K.6.1.1.10 Naylor 2004

Figure 95: Health-related quality of life (Minnesota Living with Heart Failure Questionnaire, 0-105, lower is better) at 12 months

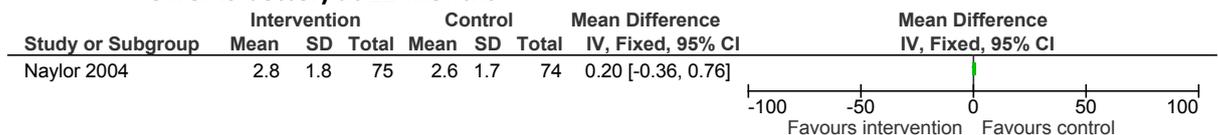


Figure 96: Mortality at 12 months

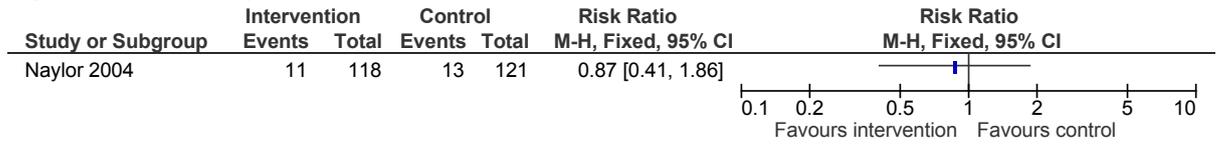


Figure 97: Functional outcomes (functional status score, 12-72, lower is better) at 12 months

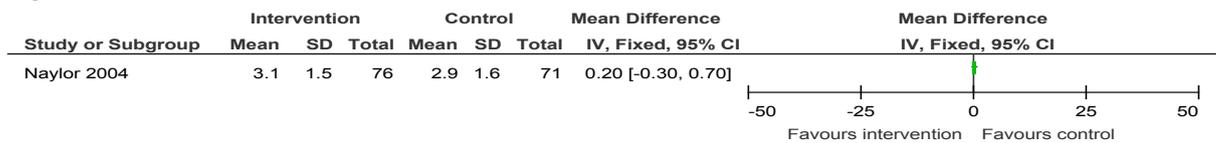
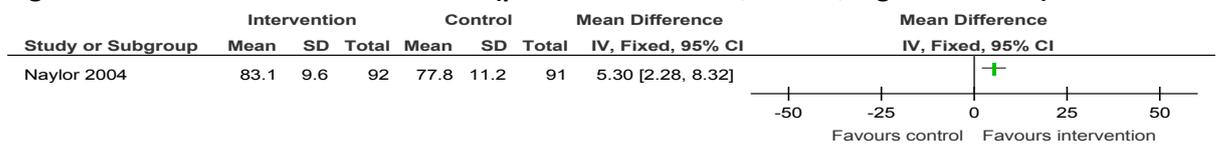


Figure 98: Patient & Carer Satisfaction (patient Satisfaction, 44-100, higher is better) at 6 weeks



K.6.1.1.11 Sandberg 2015

Figure 99: Mortality at 12 months

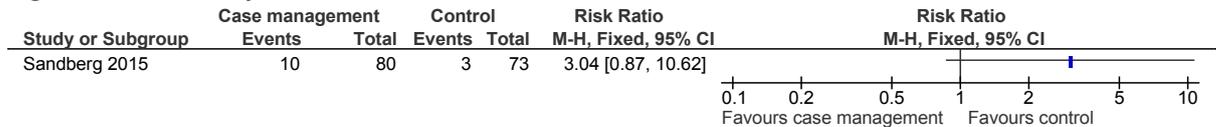


Figure 100: Length of stay at 12 months

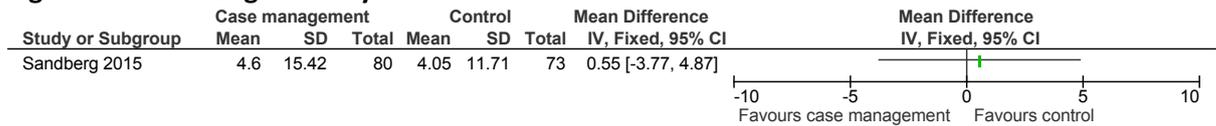
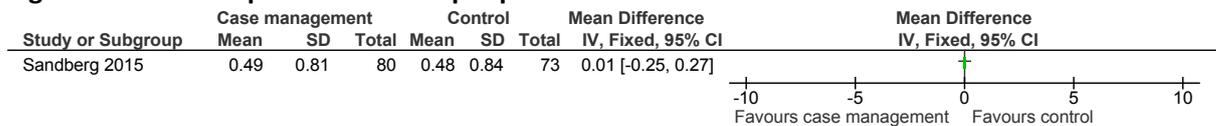


Figure 101: Hospital admissions per patient at 12 months



K.6.1.1.12 Slaets 1997

Figure 102: Mortality (unclear time point)

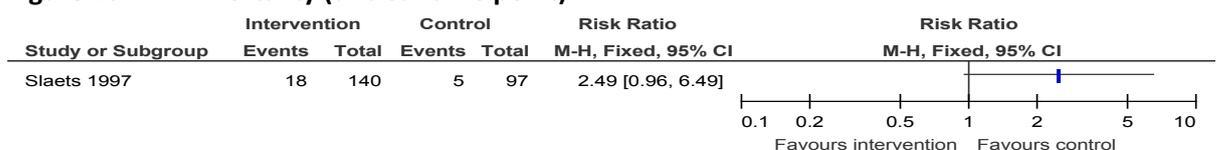
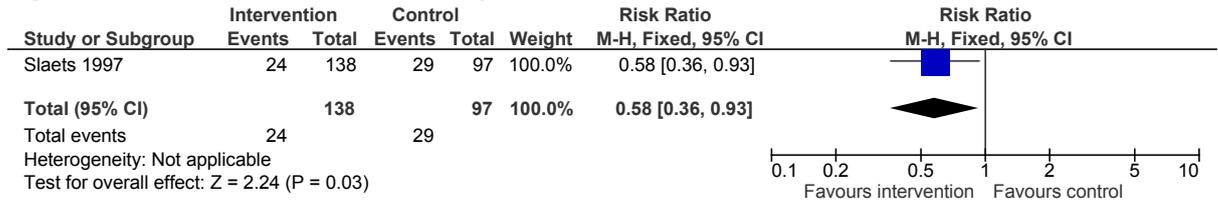


Figure 103: Unscheduled care (hospital readmission) at 6 months



K.6.1.1.13 Sommers 2000

Figure 39: Mortality at 24 months

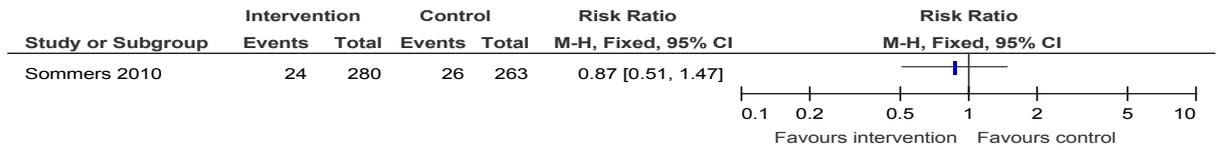
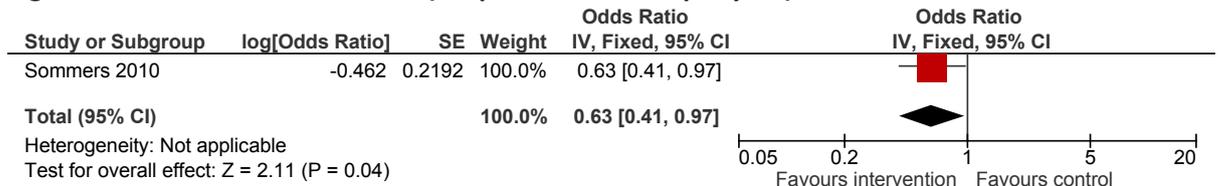


Figure 104: Unscheduled care (hospital admissions per year) at 24 months



K.6.1.2 Models of care with self-management component

K.6.1.2.1 Behm 2014

Figure 105: Health-related quality of life (participants with decline in self-rated health as per SF-36) at 24 months

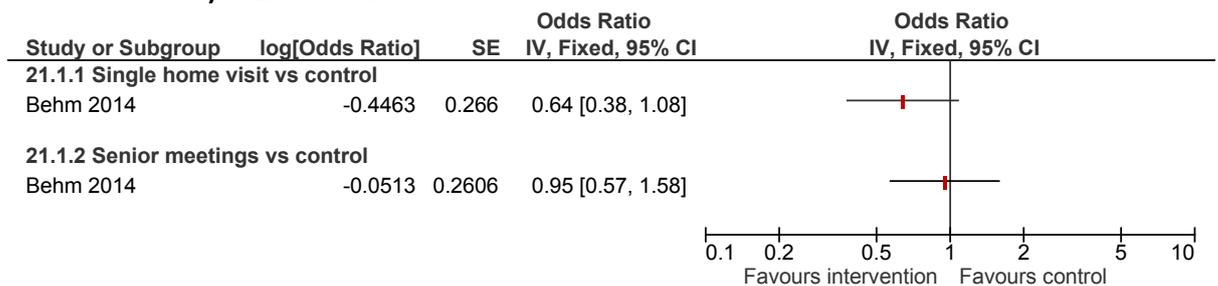


Figure 106: Health-related quality of life (participants with decline in satisfaction with physical health) at 24 months

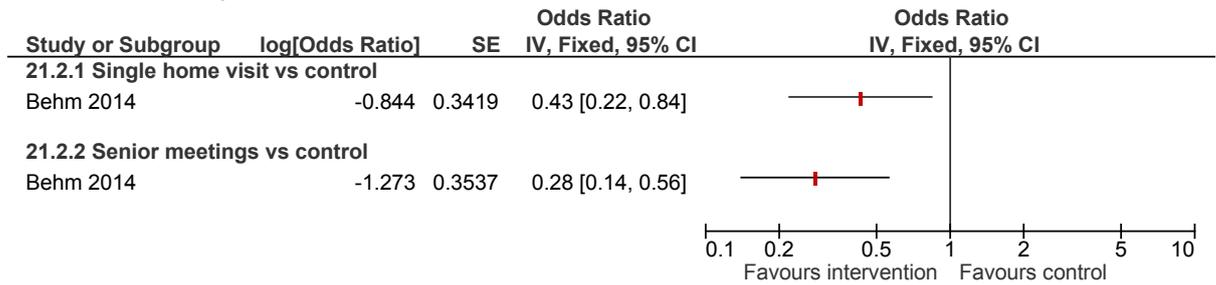
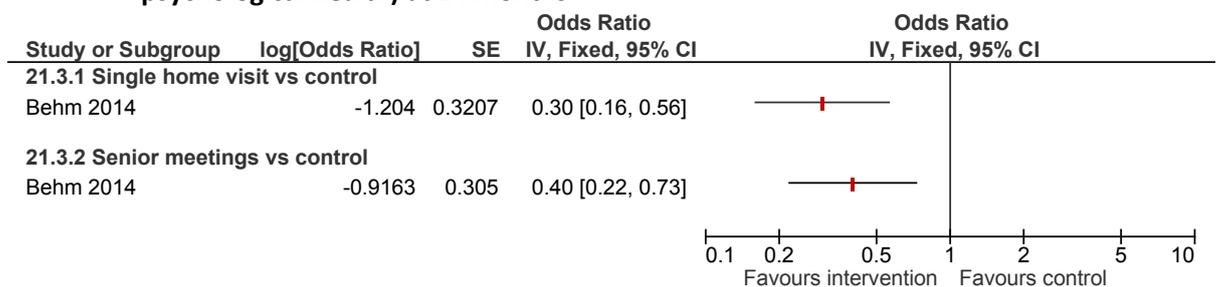


Figure 107: Health-related quality of life (participants with decline in satisfaction with psychological health) at 24 months



K.6.1.2.2 Boulton 2008

Figure 108: Health-related quality of life (SF-36, physical component, 0-100, higher is better) at 32 months

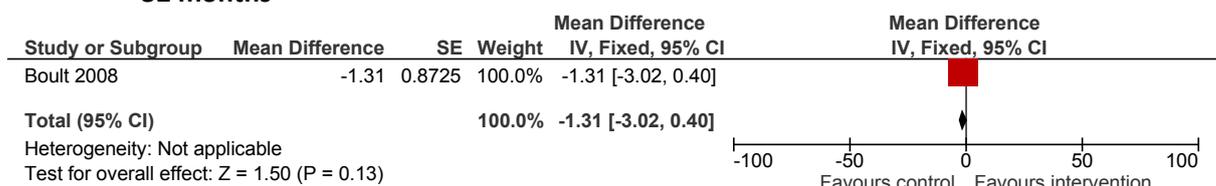


Figure 109: Health-related quality of life (SF-36, mental component, 0-100, higher is better) at 32 months

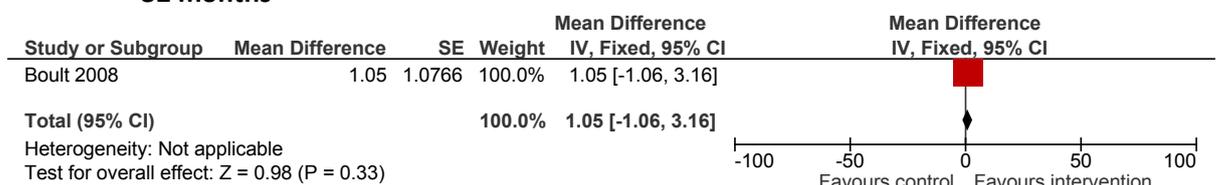


Figure 110: Mortality at 32 months

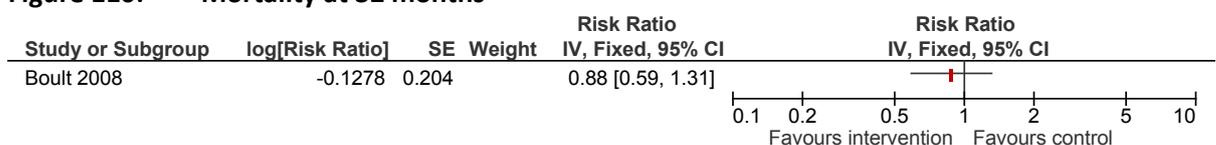


Figure 111: Patient and carer satisfaction (patient satisfaction, patient assessment of Chronic Illness Care (PACIC), scale not reported) at 32 months

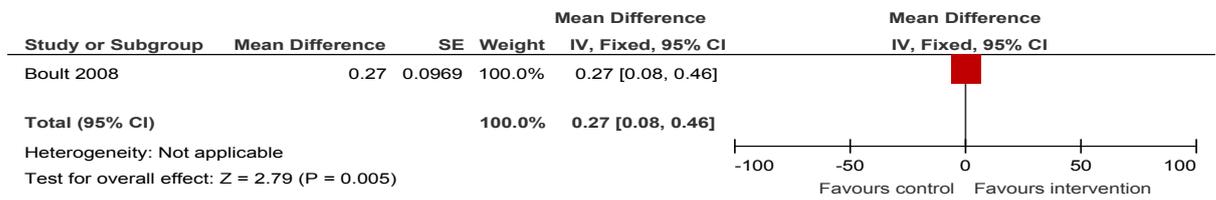


Figure 112: Patient satisfaction (patient satisfaction, 'very satisfied' with regular health care) at 32-months

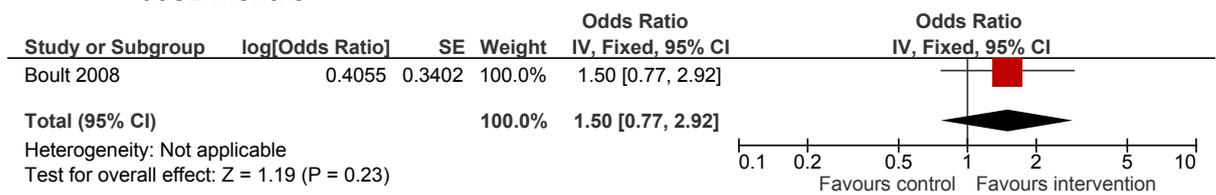


Figure 113: Unscheduled care (emergency department visits) at 6-8 months

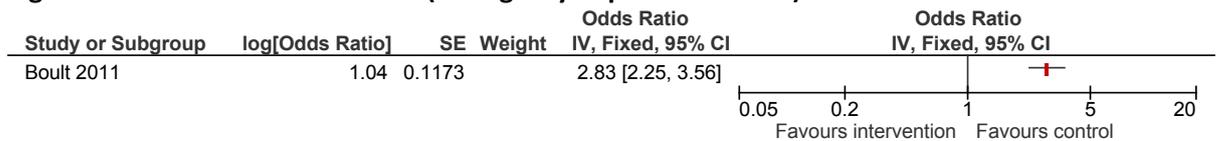


Figure 114: Continuity of care (Primary care assessment survey integration subscale, scale not reported) at 32 months

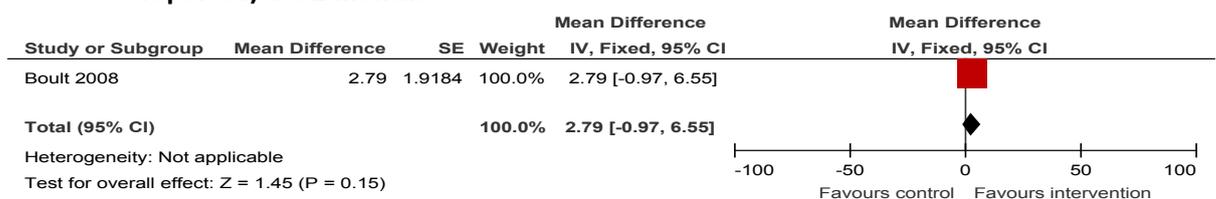


Figure 115: Continuity of care (Primary care assessment survey communication subscale, scale not reported) at 32 months

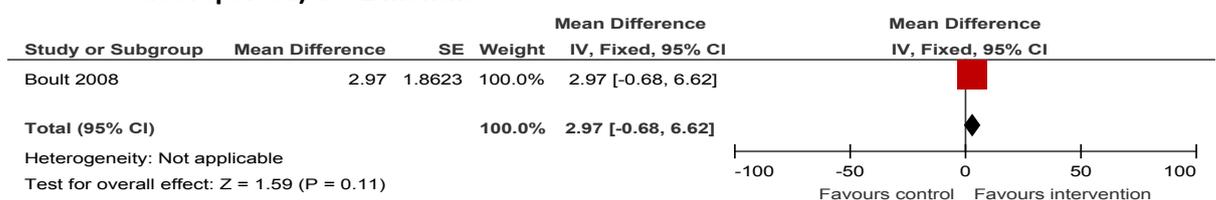
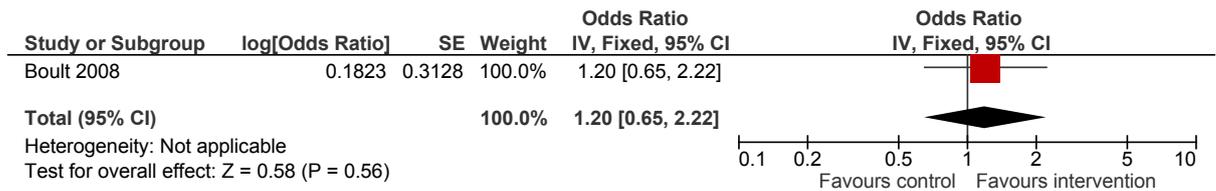


Figure 116: Continuity of care (Access to GP appointment on 'same day' when sick) at 32 months



K.6.1.2.3 Chow 2014

Figure 117: SF-36 mental component (0-100, higher is better), phone vs control at 12 weeks

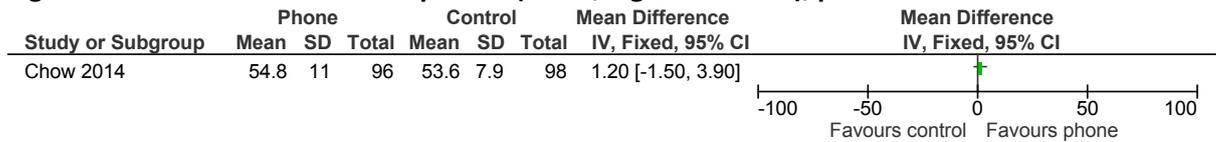


Figure 118: SF-36 physical component (0-100, higher is better), phone vs control at 12 weeks

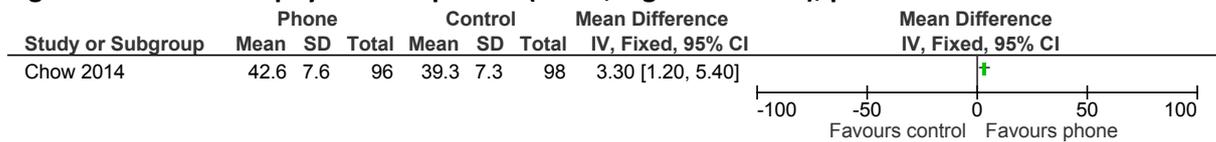


Figure 119: SF-36 mental component (0-100, higher is better), visit vs control at 12 weeks

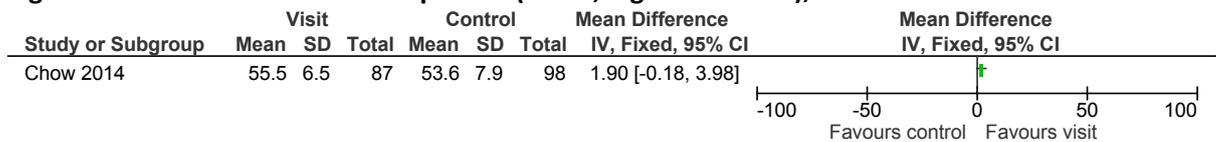


Figure 120: SF-36 physical component (0-100, higher is better), visit vs control at 12 weeks

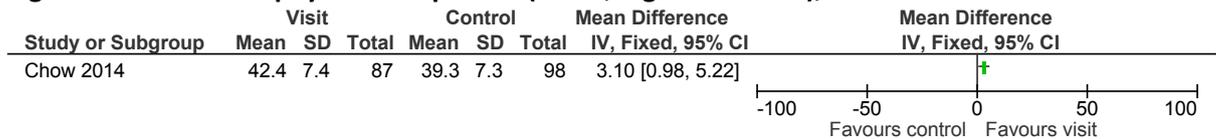


Figure 121: SF-36 mental component (0-100, higher is better), visit vs phone at 12 weeks

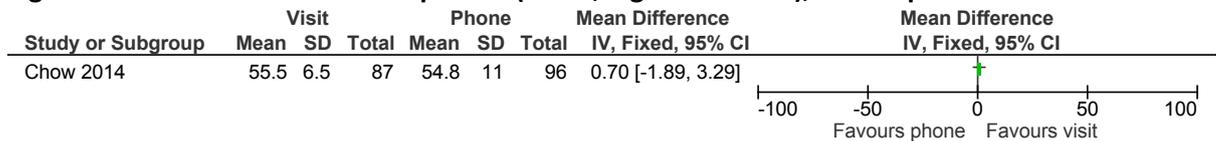
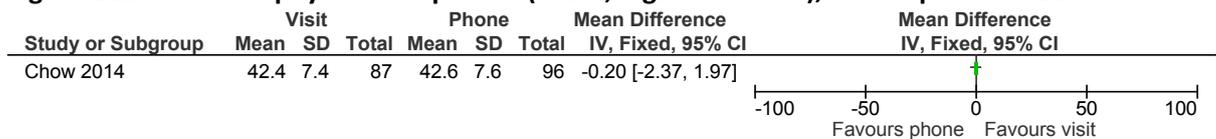


Figure 122: SF-36 physical component (0-100, higher is better), visit vs phone at 12 weeks



K.6.1.2.4 Coburn 2012

Figure 123: Mortality at 4.2 years



K.6.1.2.5 Gitlin 2006

Figure 124: Mortality (survival) at 2 years, 3 years, and 4 years

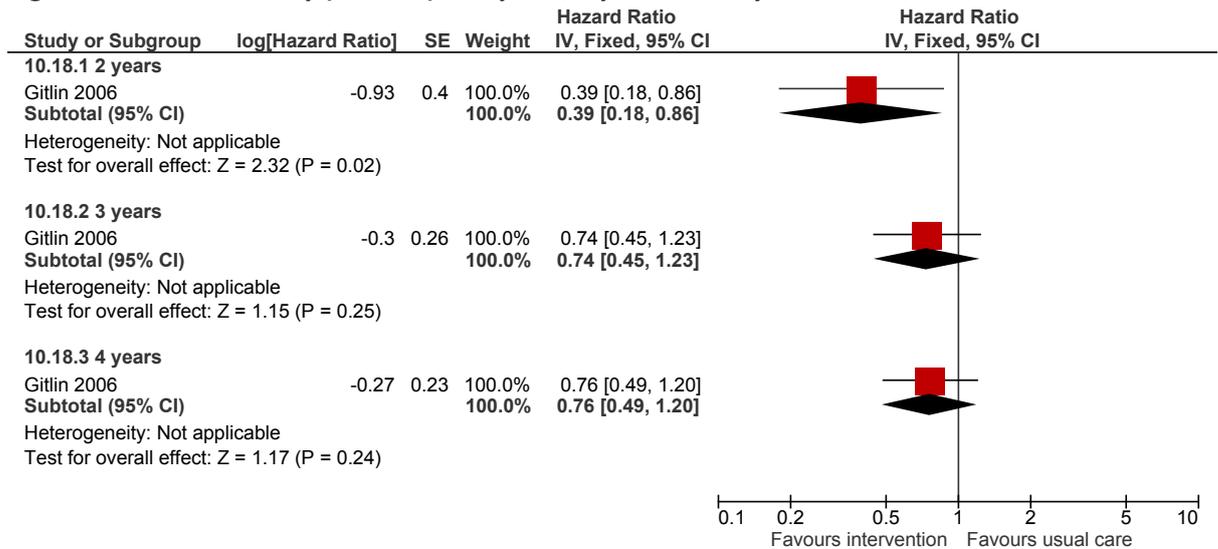
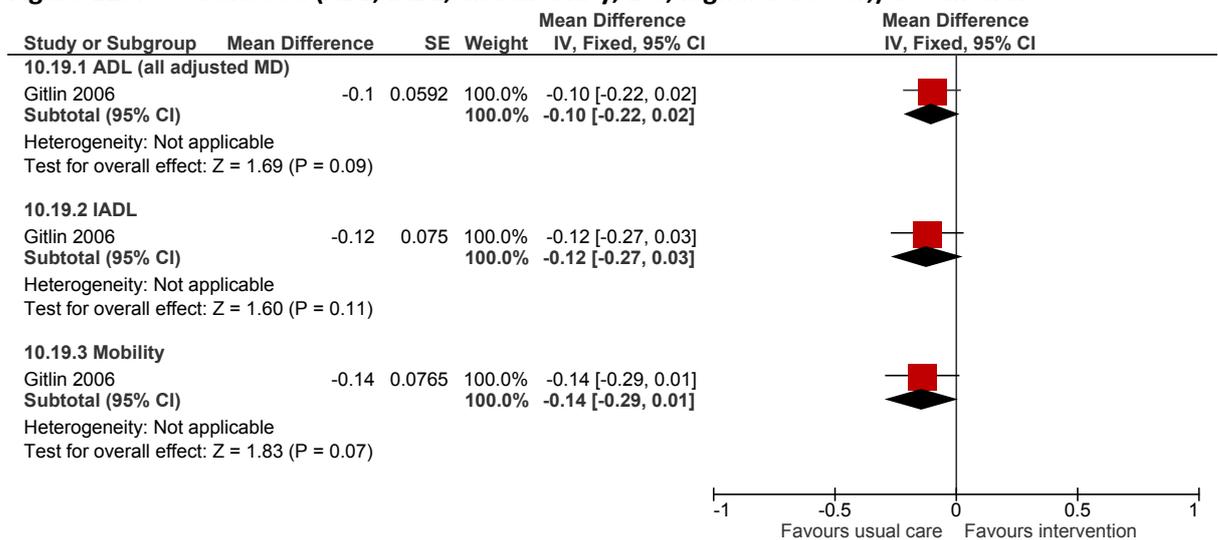


Figure 125: Function (ADL, IADL, and mobility, 1-5, higher is better,) at 6 months



K.6.1.2.6 Katon 2010

Figure 30: Health-related quality of life (Global quality of life rating, 0-10, higher is better) at 12 months

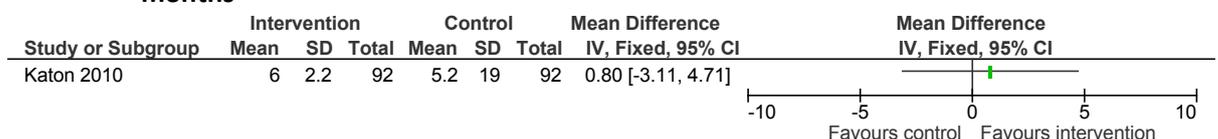


Figure 31: Mortality at 12 months

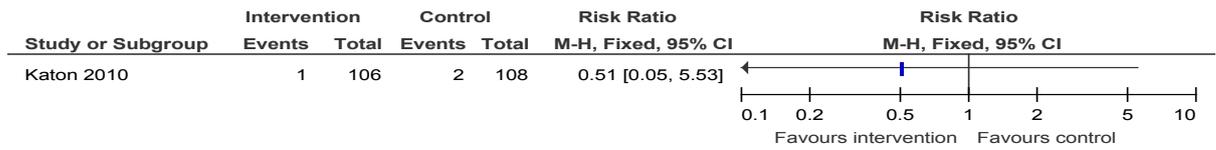


Figure 32: Functional outcomes (Sheehan social role disability scale, 0-10, lower is better) at 12 months

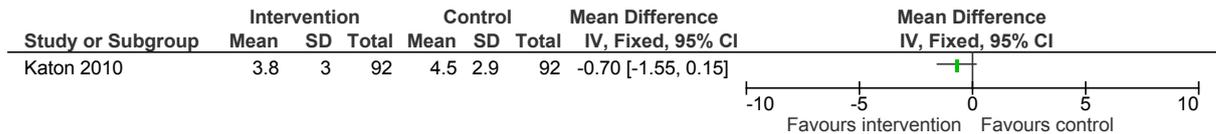


Figure 33: Functional outcomes (WHODAS-2 activities of daily living, 0-4, lower is better) at 12 months

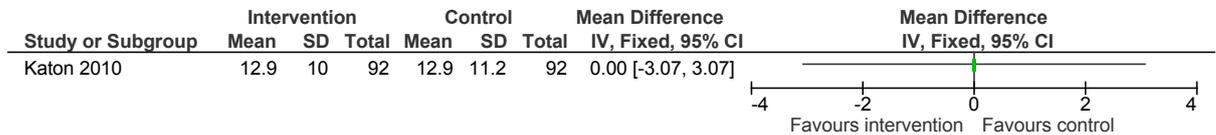


Figure 34: Patient & Carer satisfaction (as assessed by the number of patients satisfied with care for diabetes, heart disease or both) at 12 months

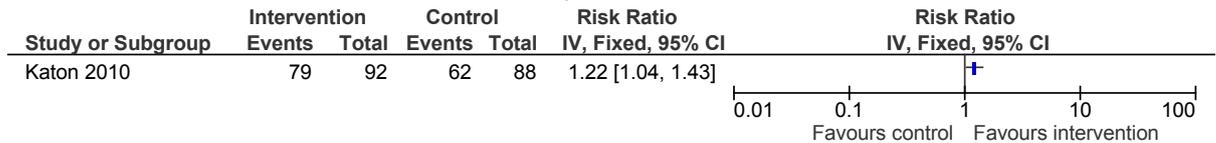
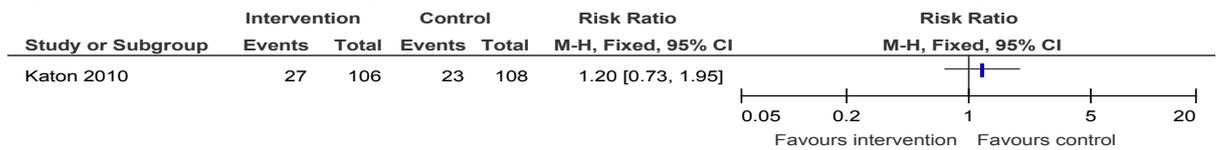


Figure 35: Unscheduled care (proportion hospitalised, at least 1 hospitalisation) at 12 months



K.6.1.2.7 Legrain 2011

Figure 36: Mortality at 6 months

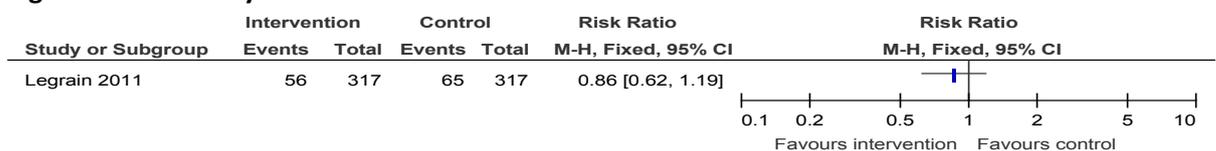


Figure 37: Unscheduled care (emergency department visit) at 6 months

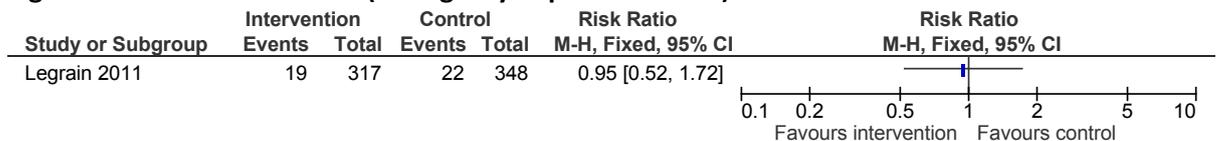
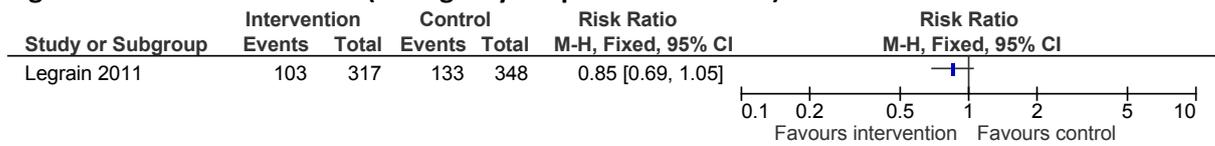


Figure 38: Unscheduled care (emergency hospital readmission) at 6 months



K.6.2 Holistic assessment

K.6.2.1 Holistic assessment inpatient - Ward

Figure 126: Health-related Quality of Life (SF-36, 0-100, higher is better), 12 months

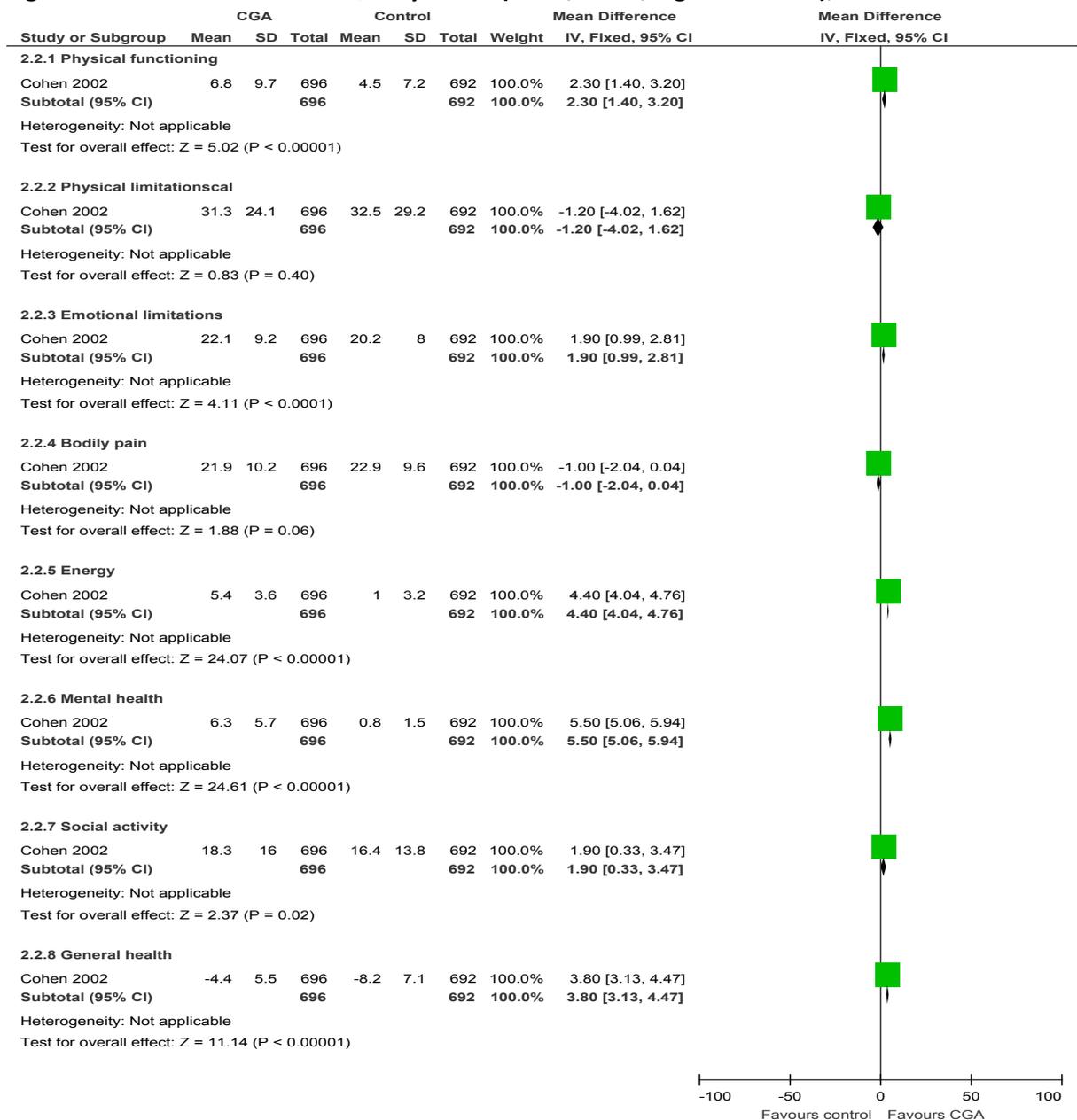


Figure 127: Mortality, end of follow-up , time point unclear

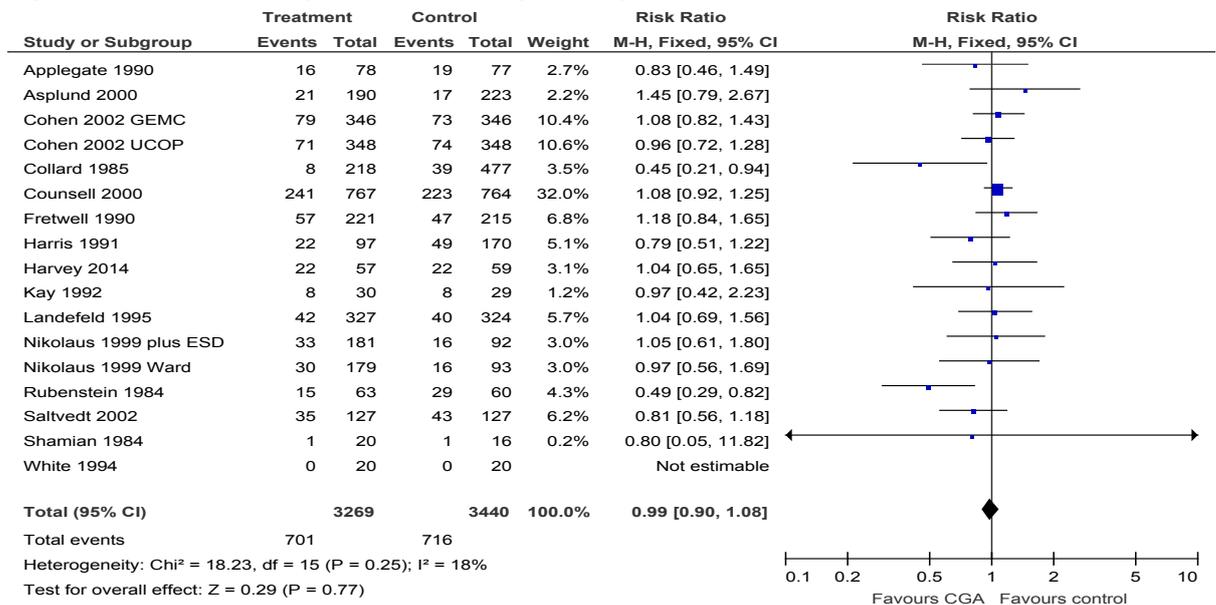


Figure 128: Functional outcomes: activities Of daily living, 6-12 months

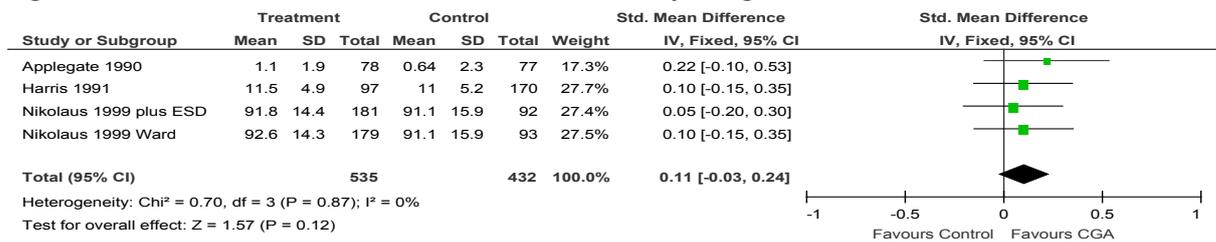


Figure 129: Functional outcomes (improving ADLs, at discharge)

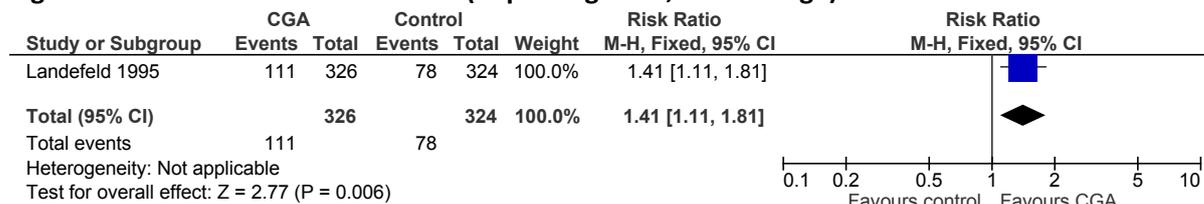


Figure 130: Functional outcomes (worsening ADLs, at discharge)

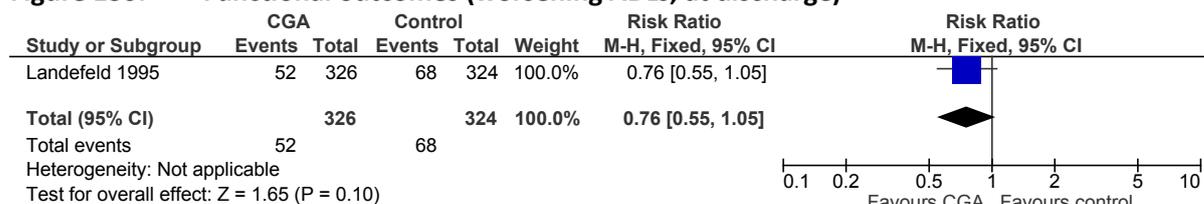


Figure 131: Functional outcomes (independent in at least 2 ADLs, 24 months)

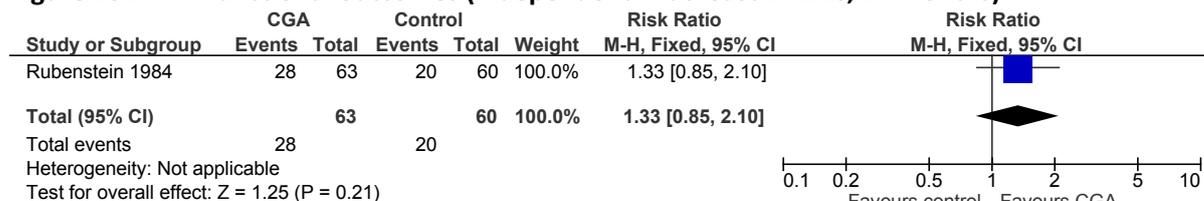


Figure 132: Functional outcomes (dependence in ADL, Barthel <12, 12 months)

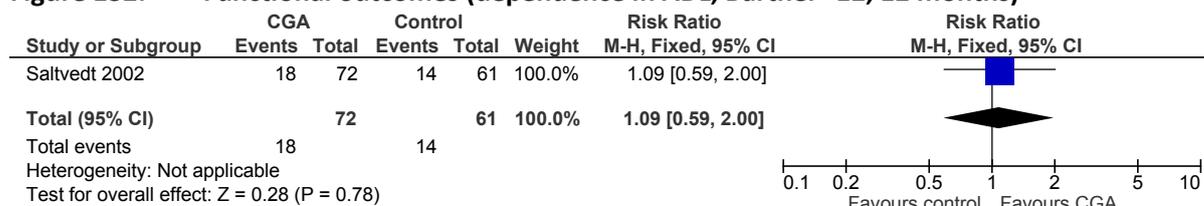


Figure 133: Functional outcomes (dependence in IADL, Lawton <4, 12 months)

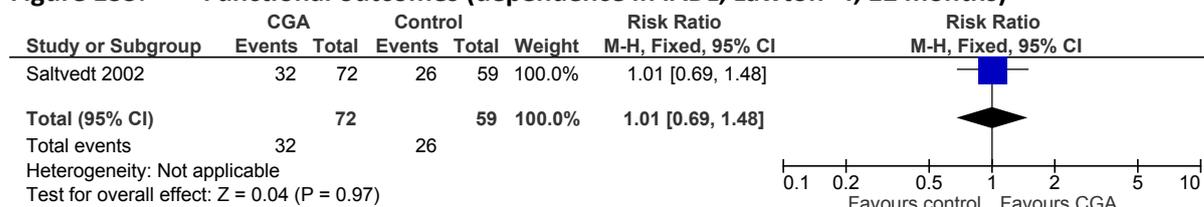


Figure 134: Patient & carer satisfaction: family/resident satisfaction, 6 months

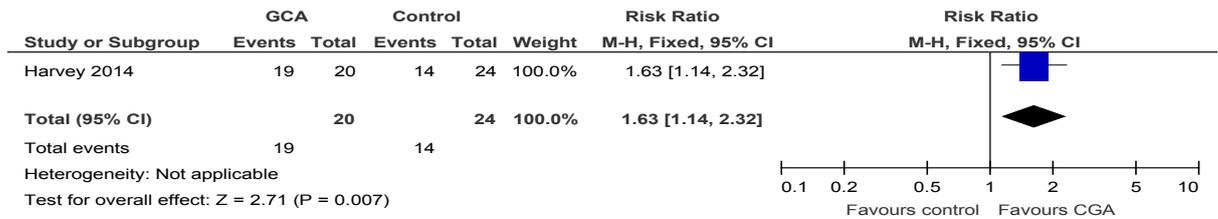


Figure 135: Patient & carer satisfaction: carer satisfaction, at discharge (unvalidated scoring system, 0-100, higher is better), 12 months

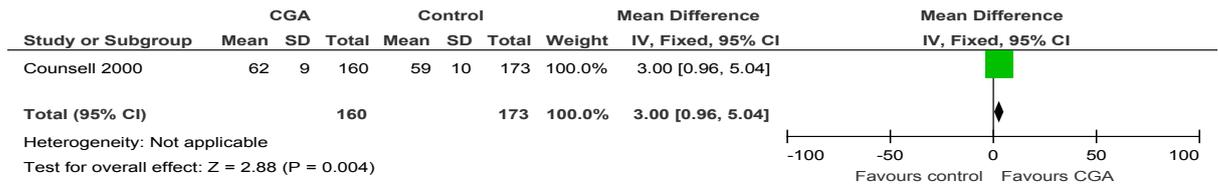


Figure 136: Patient & carer satisfaction: patient satisfaction, discharge (unvalidated scoring system, 0-100, higher is better outcome), 1 month

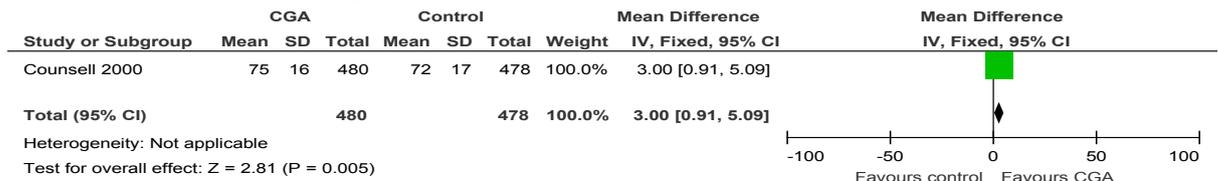


Figure 137: Length of stay, 3-12 months

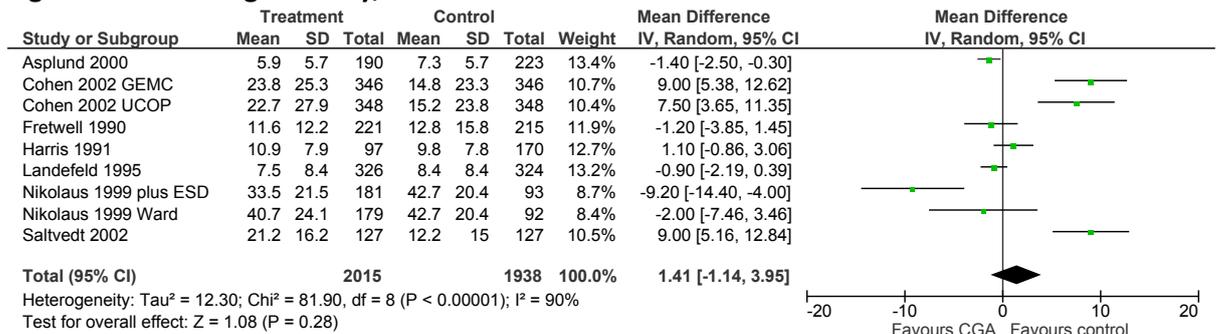


Figure 138: Unscheduled care : emergency department presentation, 6 months

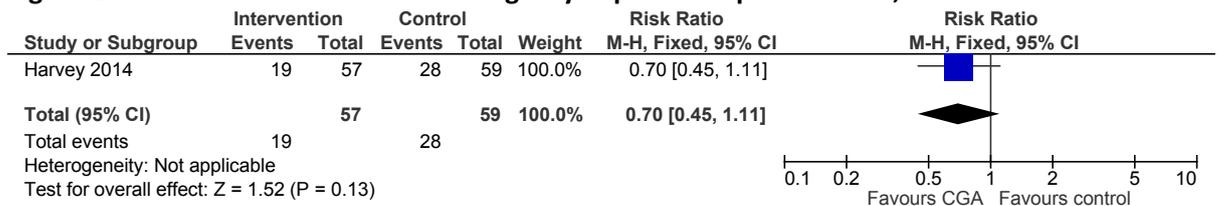


Figure 139: Unscheduled care : hospital readmissions

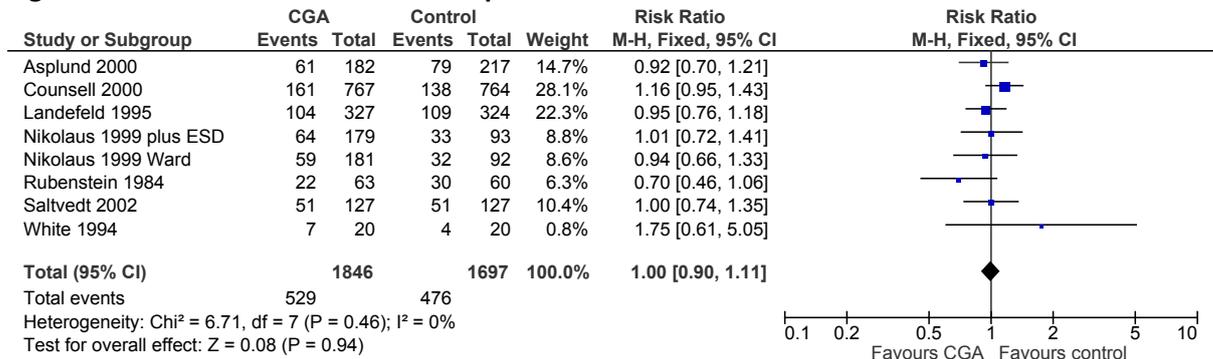


Figure 140: Admission to care facility, end of follow-up, 1-24 months

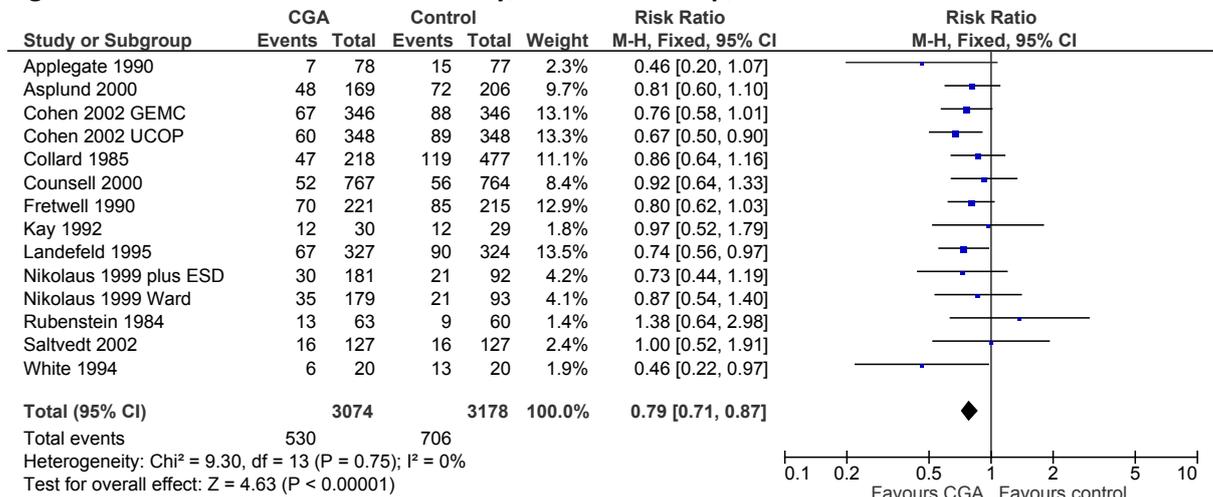


Figure 141: Carer treatment burden, self-reported physical health, 3 months

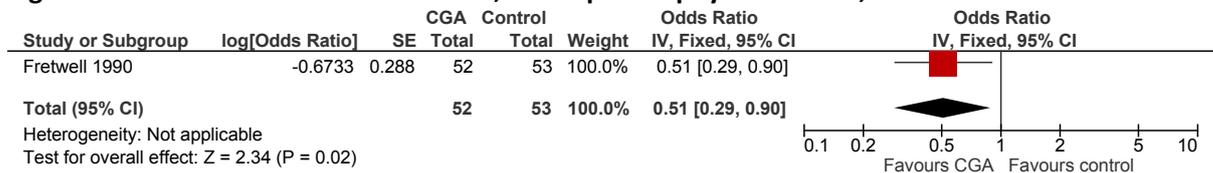
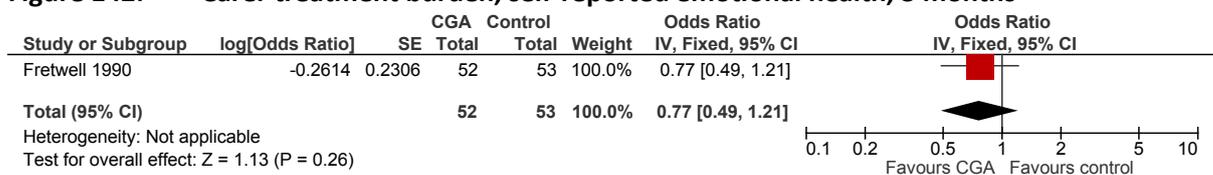


Figure 142: Carer treatment burden, self-reported emotional health, 3 months



K.6.2.2 Holistic assessment inpatient - Team

Figure 1430: Health-related Quality of Life (EQ-5D, 0-1, higher is better outcome), 90 day

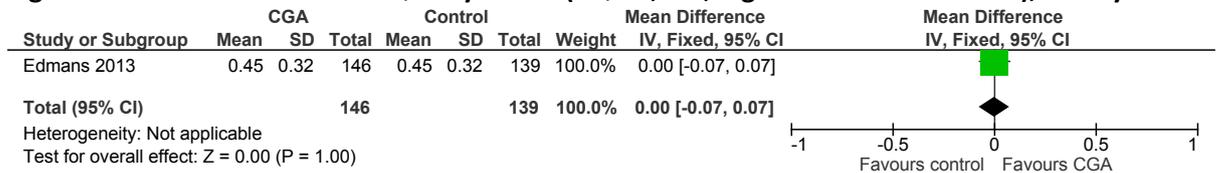


Figure 144: Mortality, end of follow-up, time point unclear

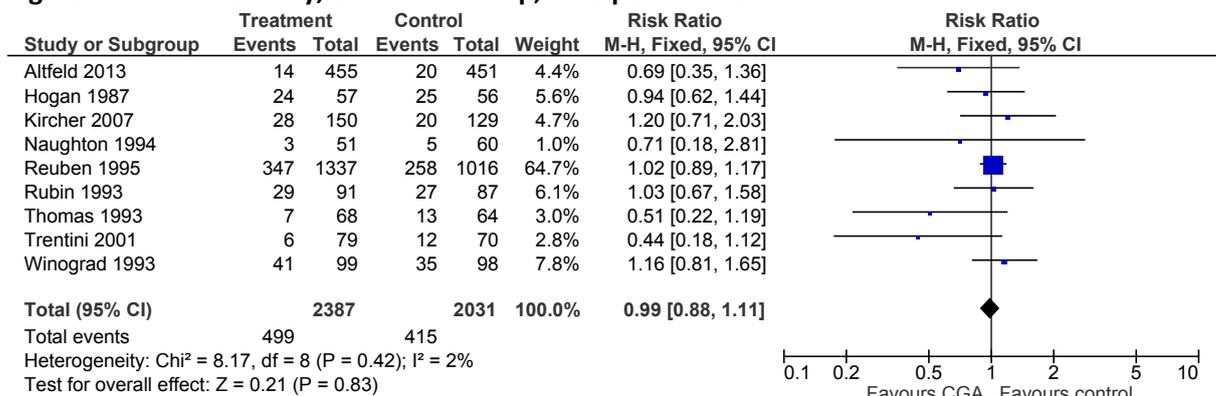


Figure 145: Mortality, time to mortality

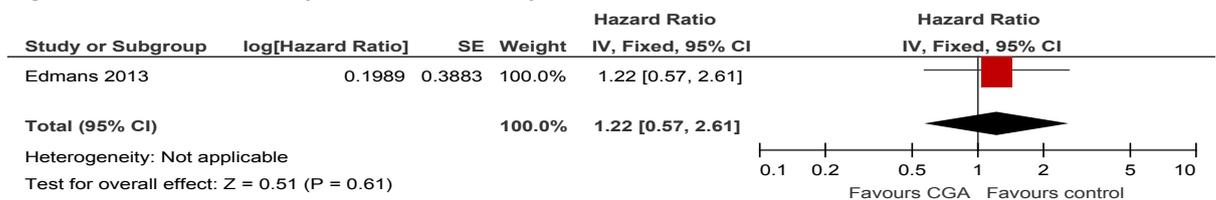


Figure 146: Functional outcomes (activities of daily living)

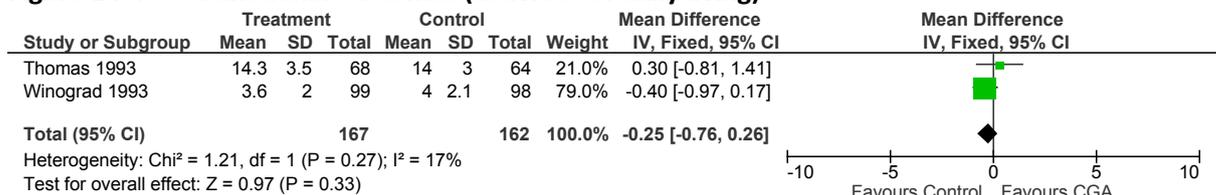


Figure 147: Functional outcomes (activities of daily living: Barthel ADL, Barthel ≥ 17), at 90 days

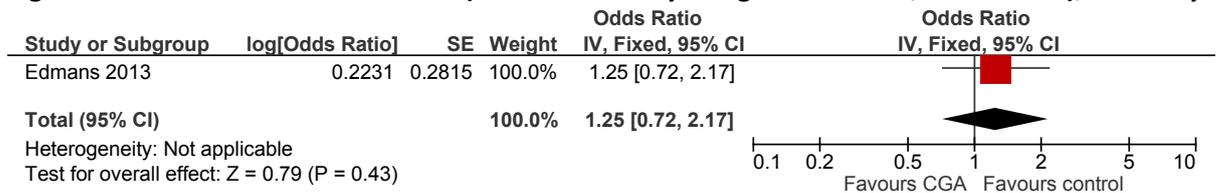


Figure 148: Functional outcomes (activities of daily living: Katz ADL – improved by any amount)



Figure 149: Functional outcomes (activities of daily living: five-items OARS IADL – improved by any amount)

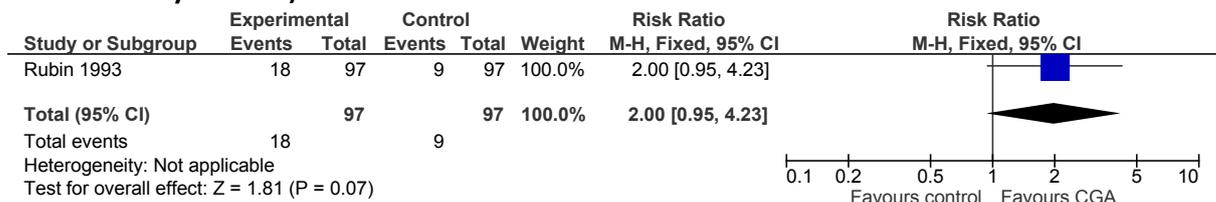


Figure 150: Length of hospital stay, at 12 months

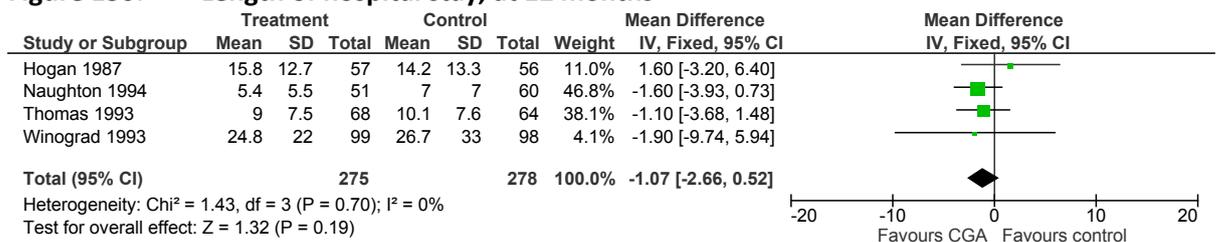


Figure 151: Unscheduled care (hospital readmissions)

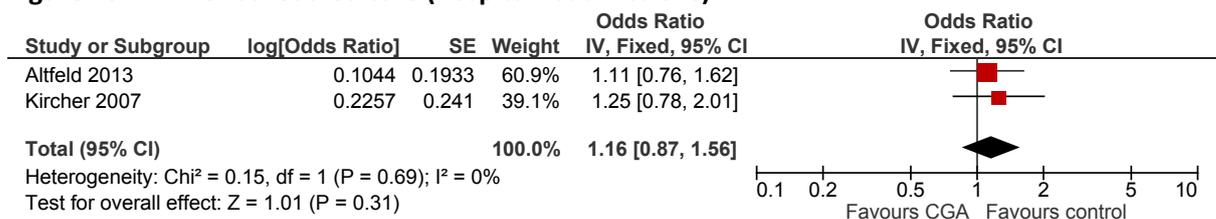


Figure 152: Admission to care facility, at end of follow-up

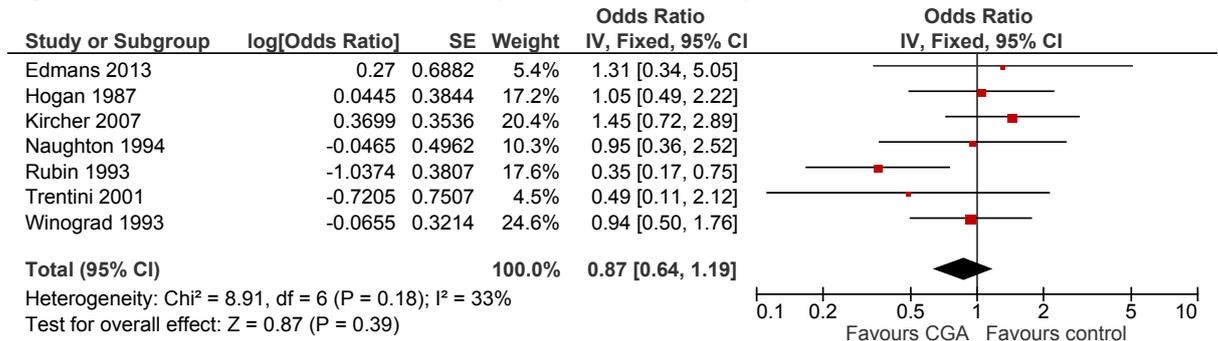
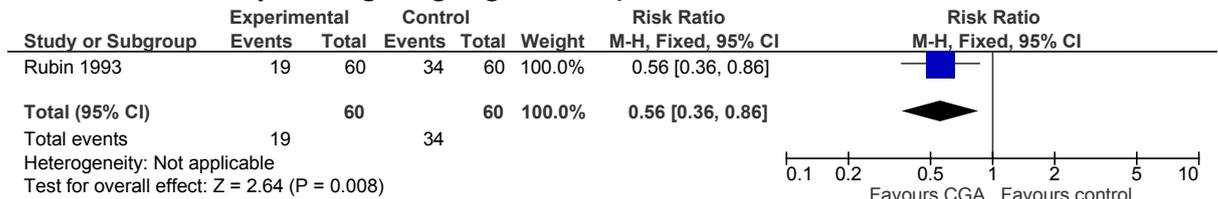


Figure 153: Patient /carer treatment burden (patient treatment burden, 'health troubles stand in the way of doing things a great deal')



K.7.2.3 Community holistic assessment – low intensity

Figure 154: Health-related quality of life: SF-12 (scale 0-100; higher is better), 6 months

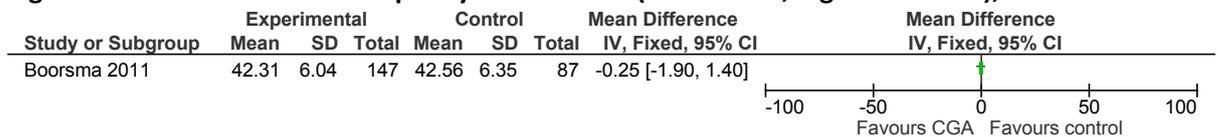


Figure 155: Mortality, 6-74 months follow-up

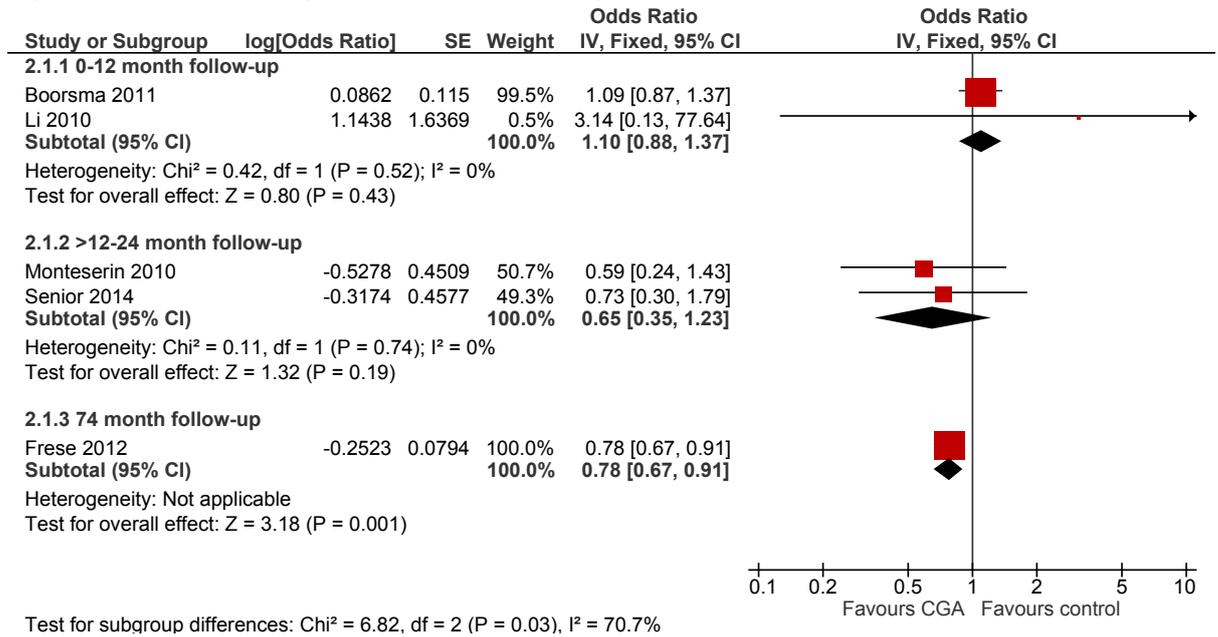


Figure 156: Mortality (time to event), 24-74 months

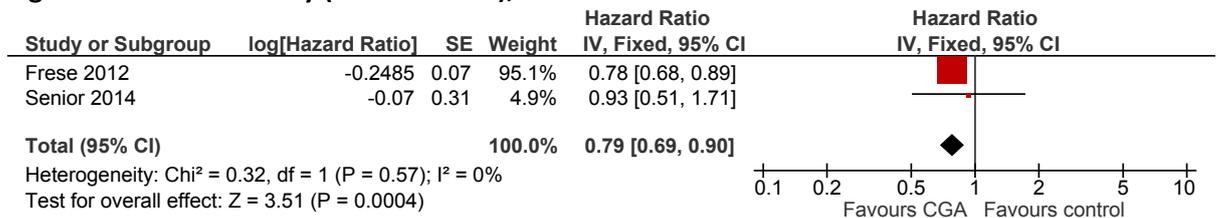


Figure 157: Functional outcomes: Activities of daily living: Barthel Index (scale 0-100; higher is better), 6 months

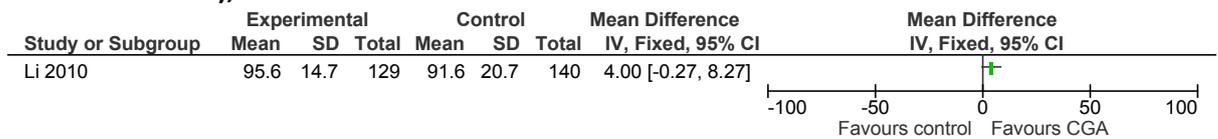


Figure 158: Unscheduled care (hospitalisation), 6 months

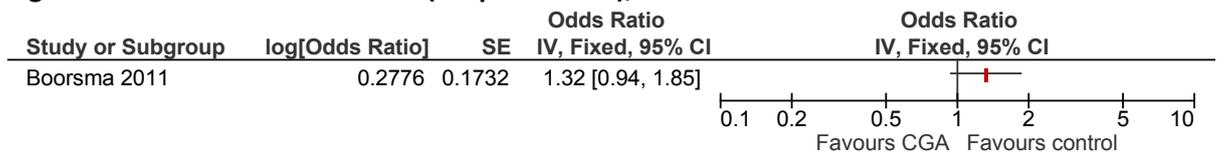


Figure 159: Admission to care facility, 1-7 years

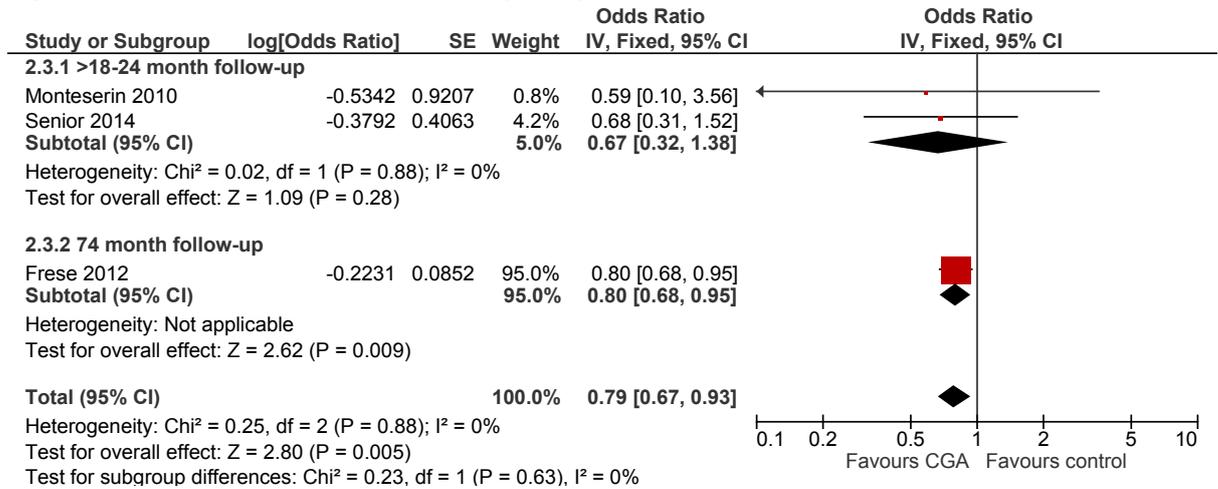
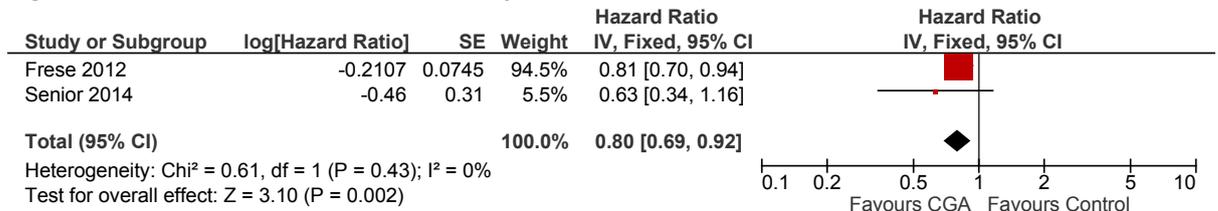


Figure 160: Admission to care facility (time to event), 24-74 months



K.6.2.4 Community holistic assessment – high intensity

Figure 161: Health-related quality of life: EQ-5D, (0-1, higher is better outcome), 18-24 months

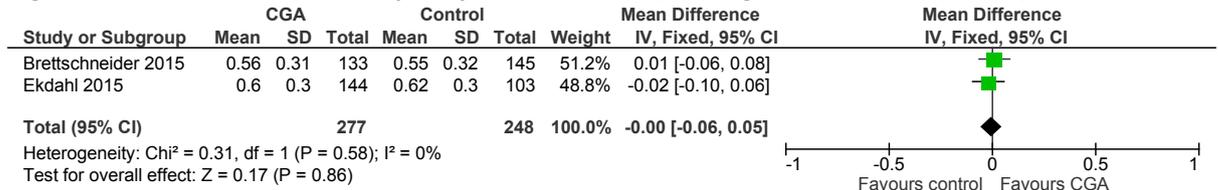


Figure 162: Health-related quality of life: MOS-20 (mental health, 0-100, higher is better outcome), 6 months

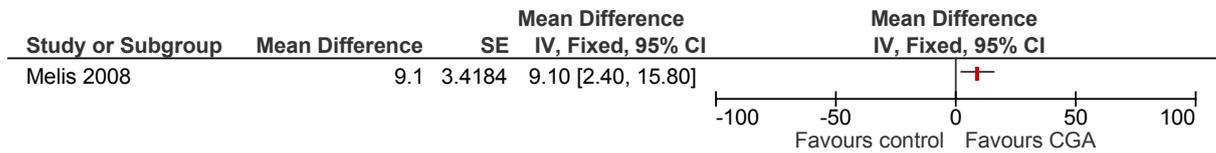


Figure 163: Health-related quality of life: MOS-20 (physical performance, 0-100, higher is better outcome), 3 months

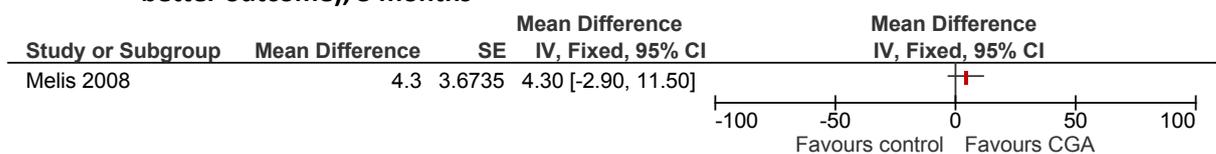


Figure 164: Health-related quality of life: MOS-20 (role functioning, 0-100, higher is better outcome), 3 months

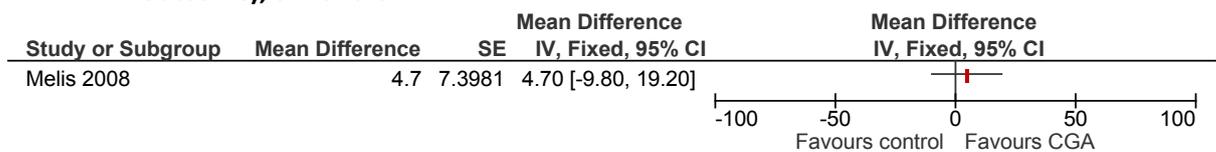


Figure 165: Health-related quality of life: SF-36 (physical component)(scale 0-100; higher is better), 2 years

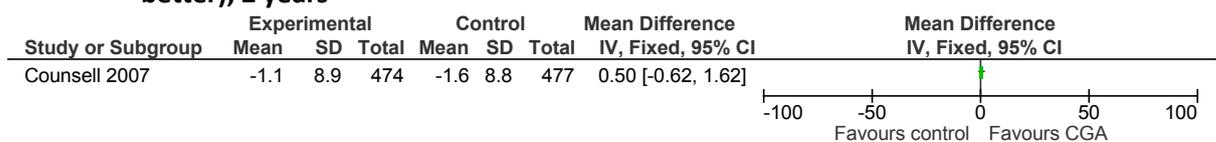


Figure 166: Health-related quality of life: SF-36 (mental component)(scale 0-100; higher is better), 2 years

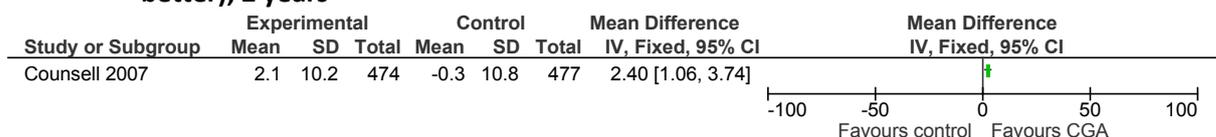


Figure 167: Health-related quality of life: SF-36 subscales (scale 0-100; higher is better), 2 years

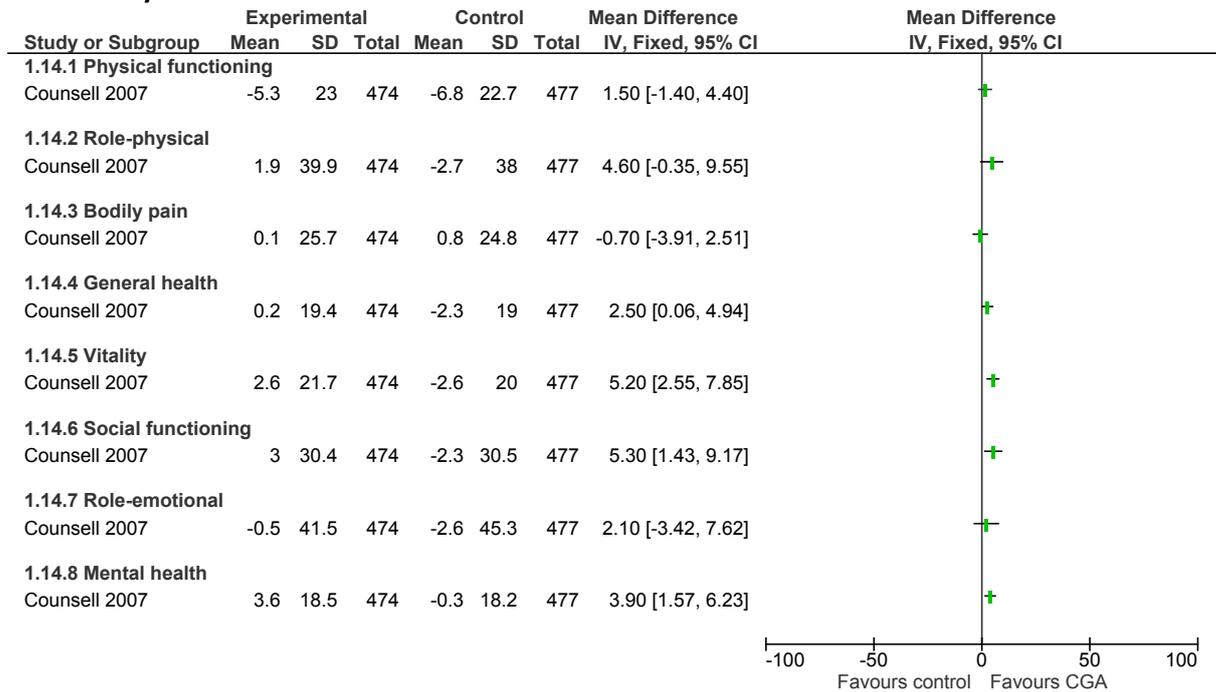


Figure 168: Mortality, 12-36 months

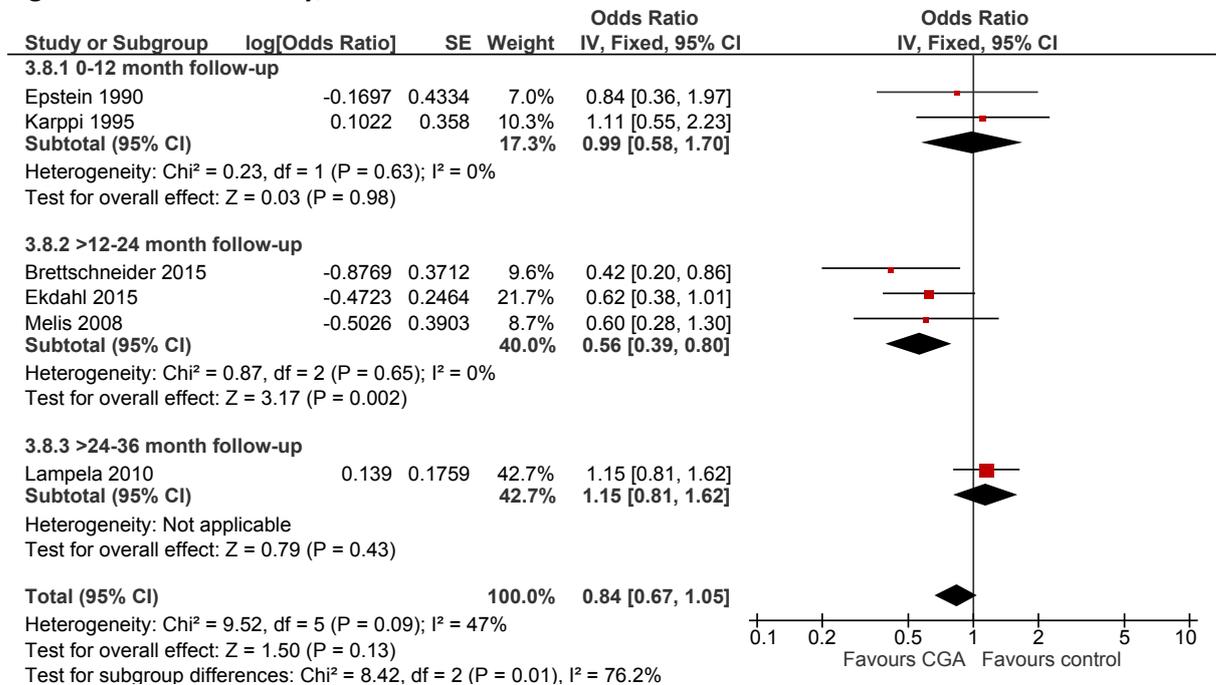


Figure 169: Mortality, time to event, 24 months

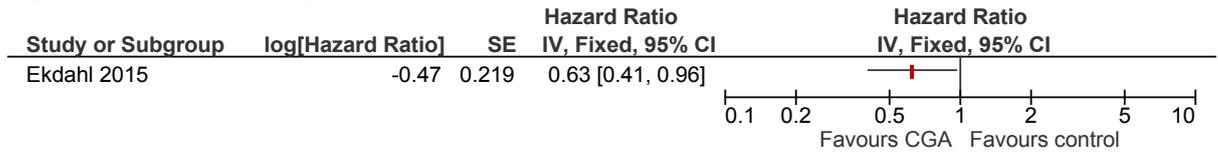


Figure 170: Functional outcomes: Activities of daily living: Katz basic ADL (scale 0-6; higher is better), 3 months – 2 years

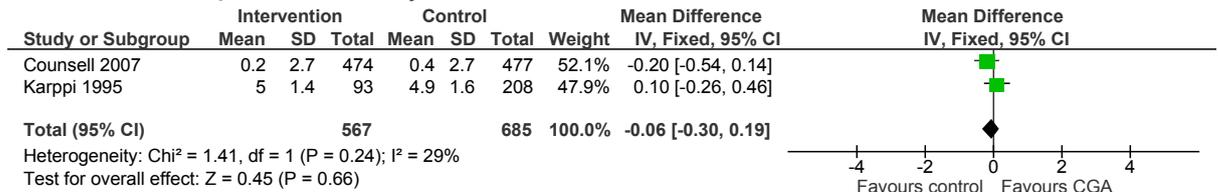


Figure 171: Functional outcomes: Activities of daily living: Lawton & Brody IADL (scale 0-8; higher is better), 3 months – 2 years

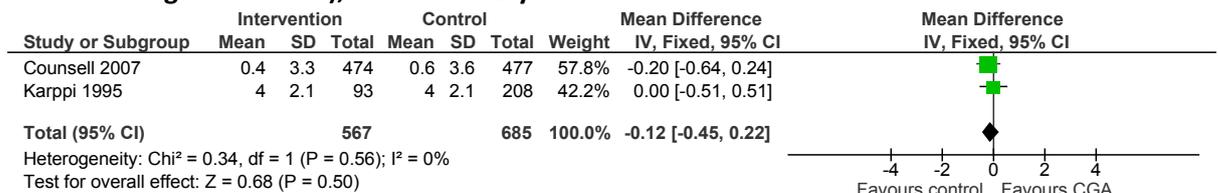


Figure 172: Functional outcomes: Sickness Impact Profile (scale 0-100; lower is better), 1 yearmonth

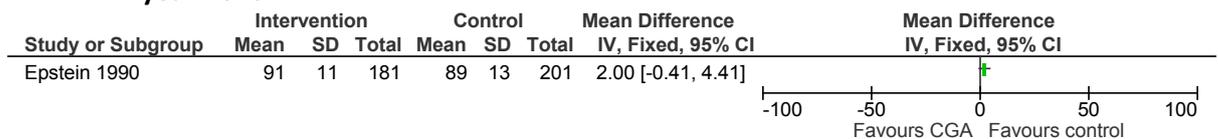


Figure 173: Functional outcomes: Sickness Impact Profile (scale 0-100; lower is better), 1 year6 months

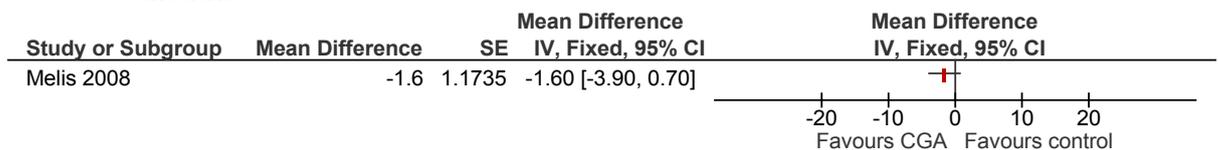


Figure 174: Patient & carer satisfaction (patient satisfaction (unvalidated; scale 0-5; higher is better), 12 months



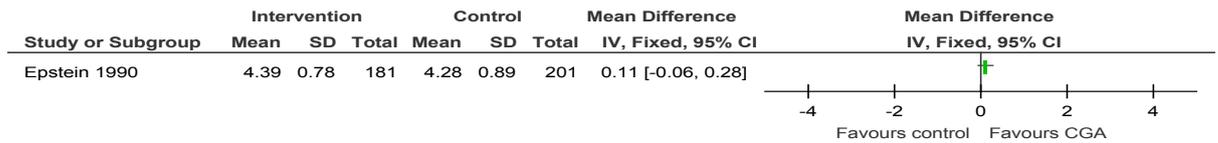


Figure 175: Length of hospital stay (days per patient), 24 months

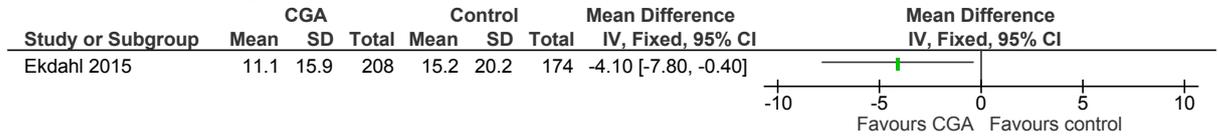


Figure 176: Unscheduled care (hospitalisation), 12 months

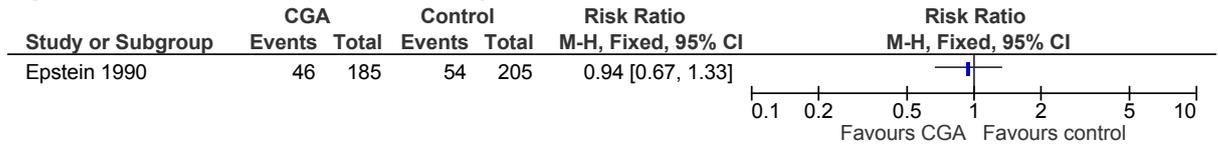


Figure 177: Unscheduled care (hospitalisations per patient), 24 months

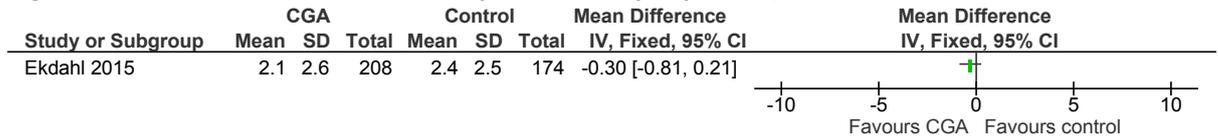


Figure 178: Unscheduled care (admission to care facility, 1-7 years)

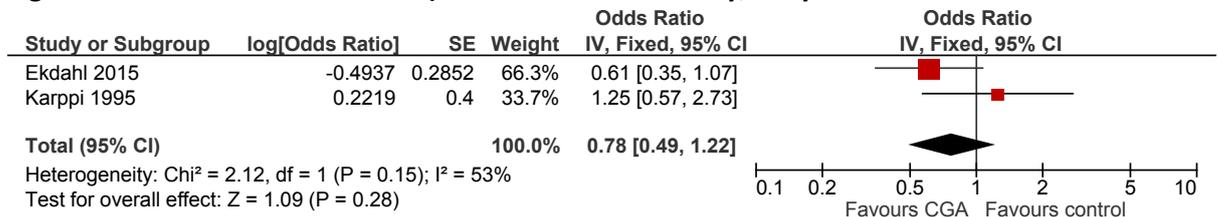
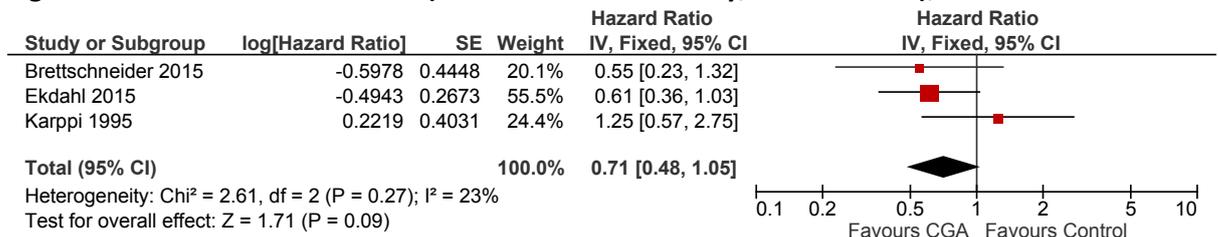


Figure 179: Unscheduled care (admission to care facility, time to event), 12-24 months



K.7 Self-management

K.7.1 Self-management versus usual care (participants with comorbid physical health conditions)

Figure 180: Health related quality of life

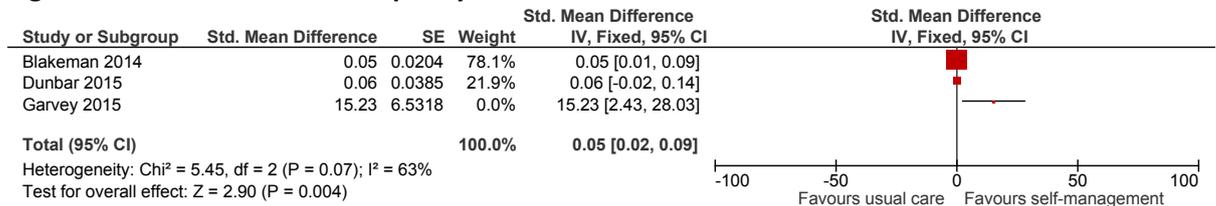


Figure 181: Self-rated health

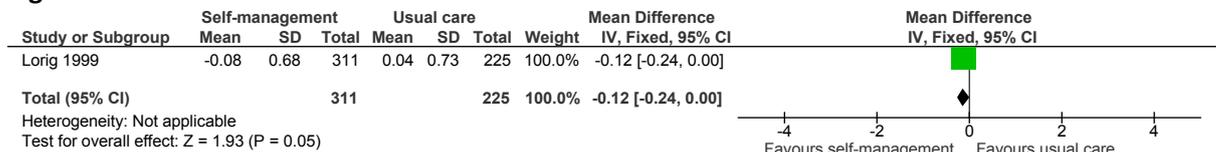


Figure 182: Disability

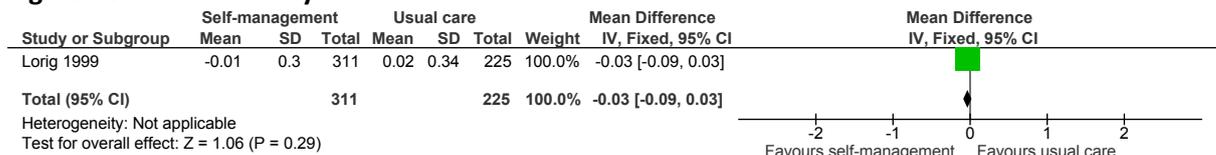


Figure 183: Psychological wellbeing

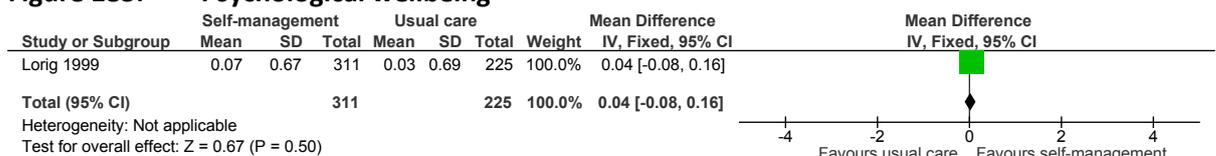


Figure 184: Positive and active engagement with life

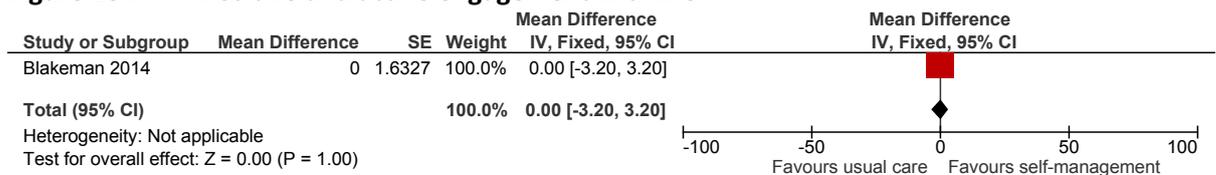


Figure 185: Role activities limitations

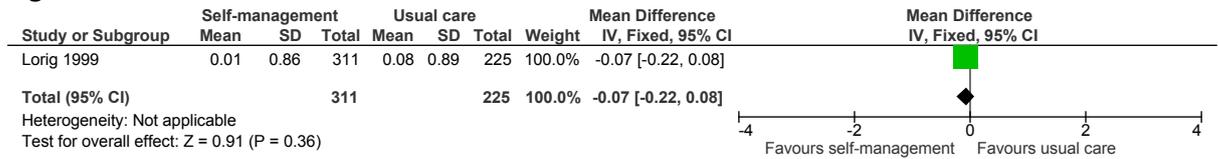


Figure 186: Social role activities

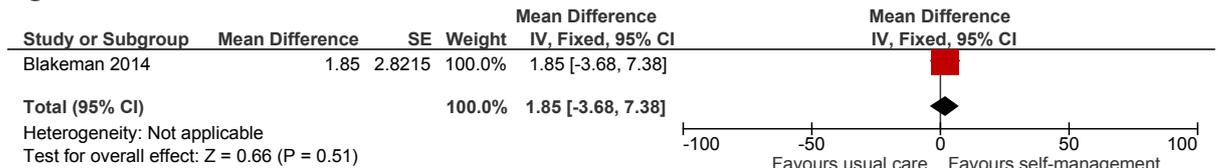


Figure 187: Mortality



Figure 188: Great difficulty with ADLs

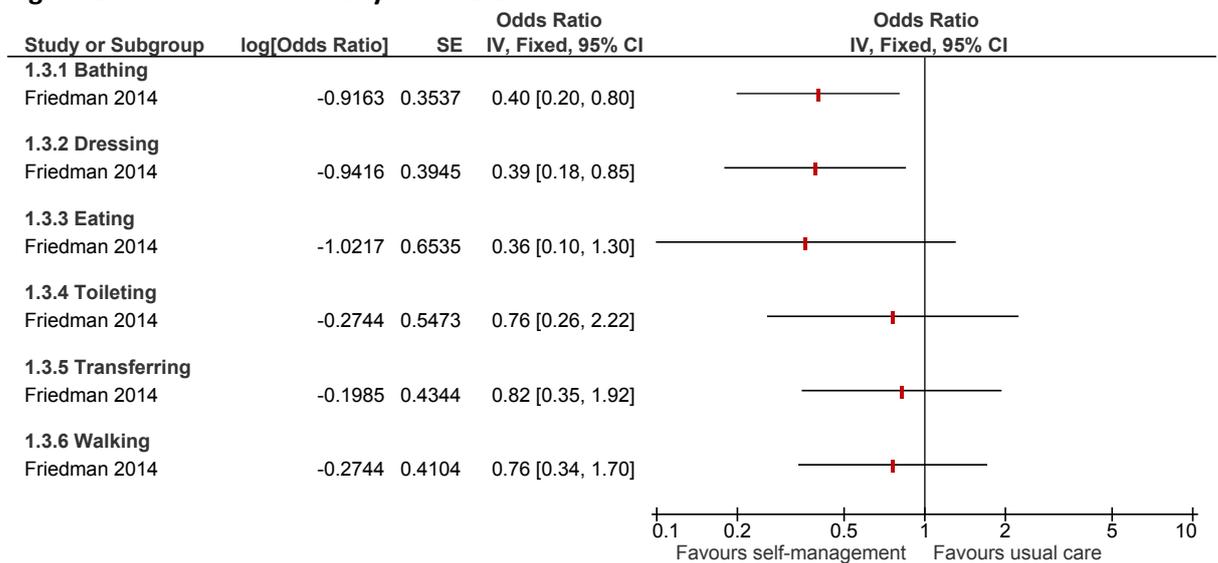


Figure 189: Some difficulty with ADLs

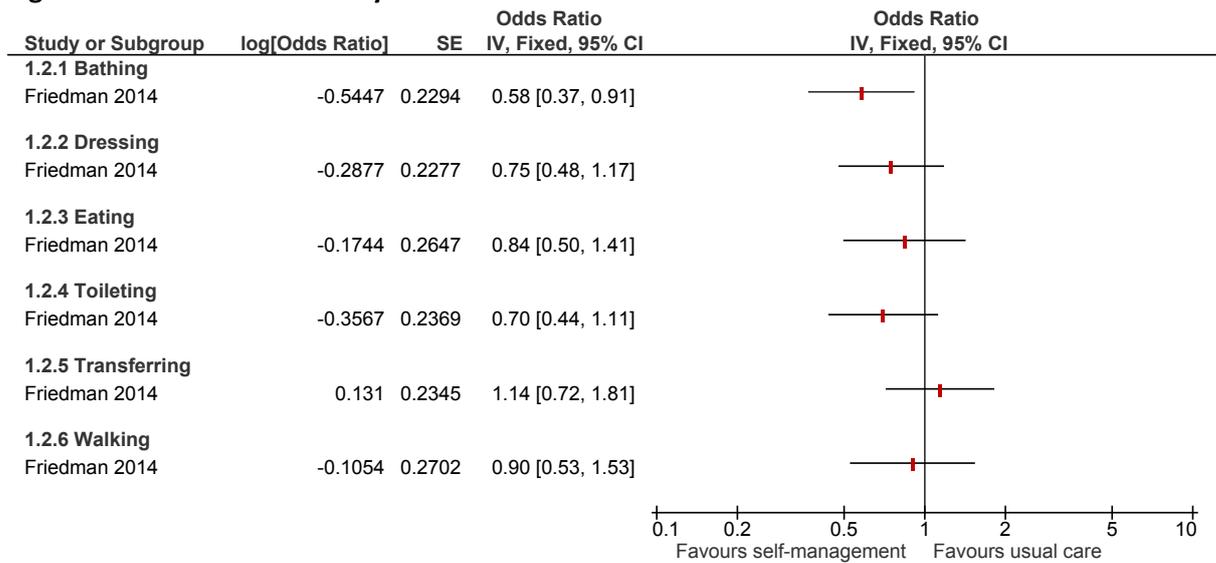


Figure 190: Health distress

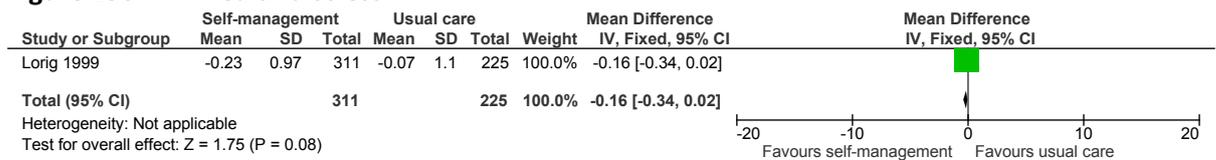


Figure 191: Nottingham Extended Activities of Daily Living (NEADL) (2 weeks)

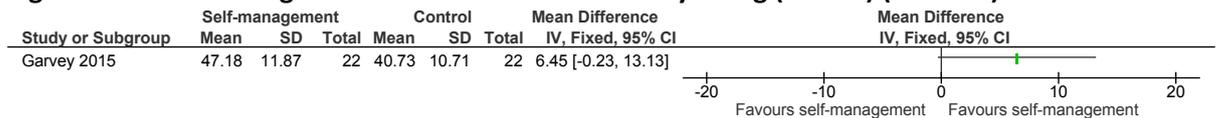


Figure 192: Canadian Occupational Performance Measure (COPM): satisfaction (2 weeks)

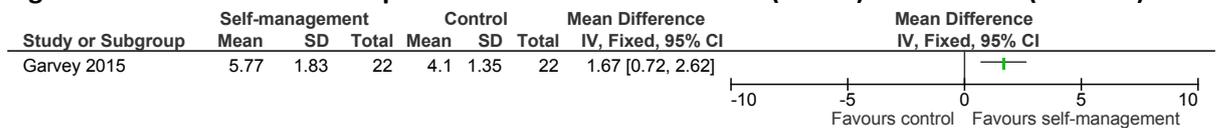


Figure 193: Canadian Occupational Performance Measure (COPM): performance (2 weeks)

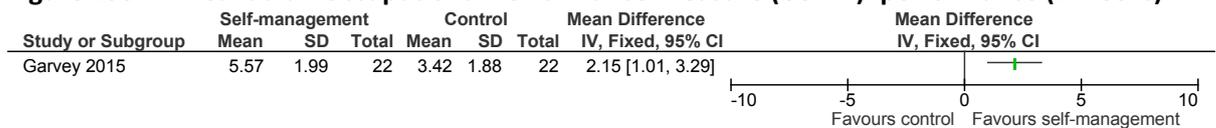


Figure 194: 6 minute walk test

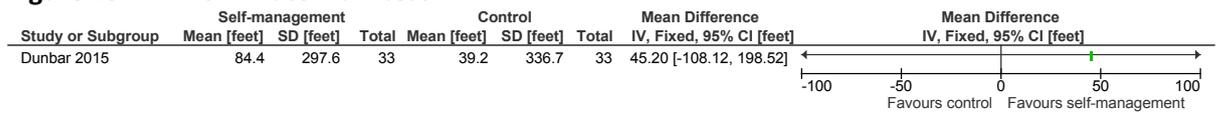


Figure 195: Community Healthy Activities Model Program for Seniors (CHAMPS) score >6 (6 months)

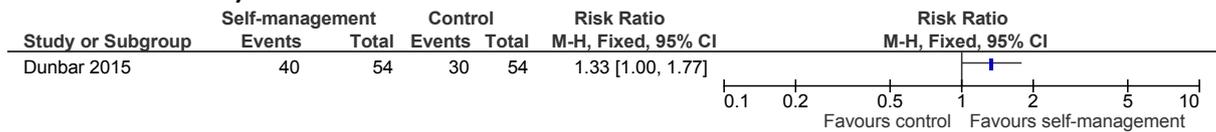


Figure 196: Hospital admissions (6 months)

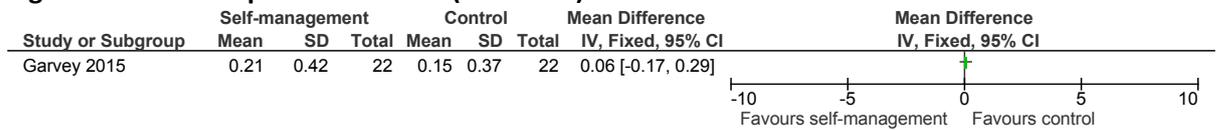
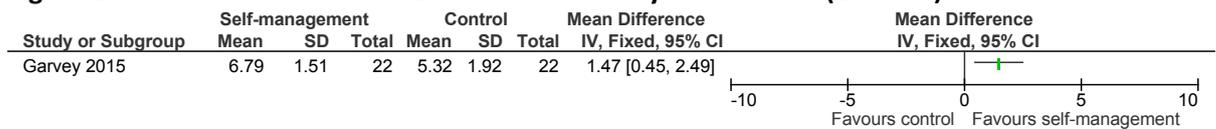


Figure 197: Stanford Chronic Disease Self-Efficacy 6-item Scale (2 weeks)



K.7.2 Self-management versus usual care (participants with comorbid physical and mental health conditions)

Figure 198: Health related quality of life

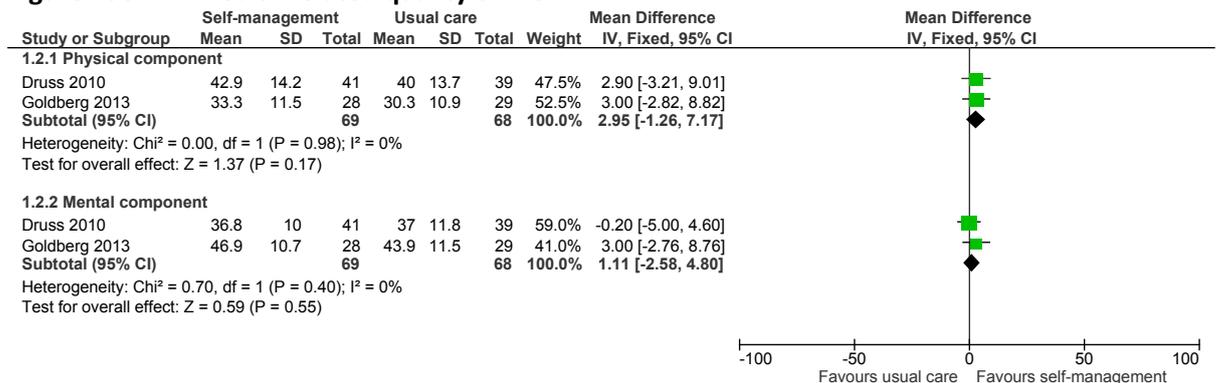


Figure 199: Health related quality of life

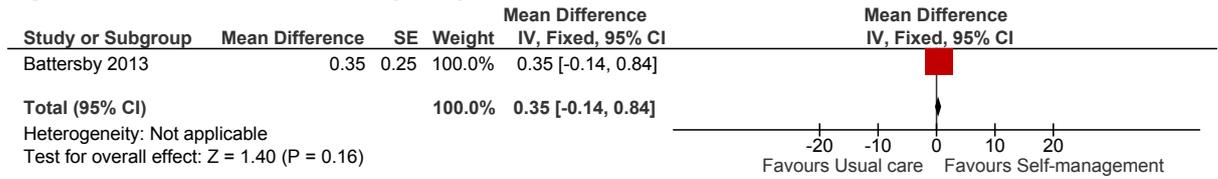


Figure 200: Physical activity

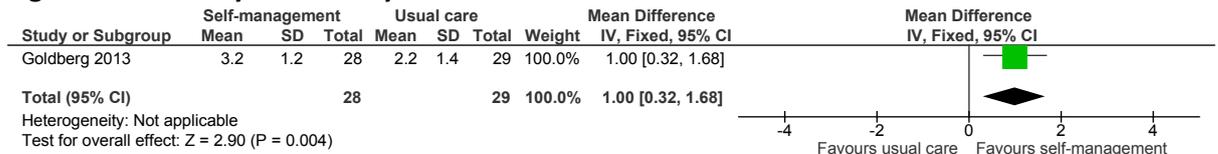


Figure 201: Walking (minutes/week)

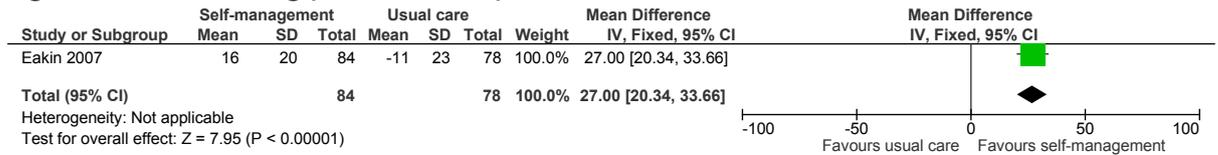


Figure 202: Moderate/vigorous physical activity (minutes/week)

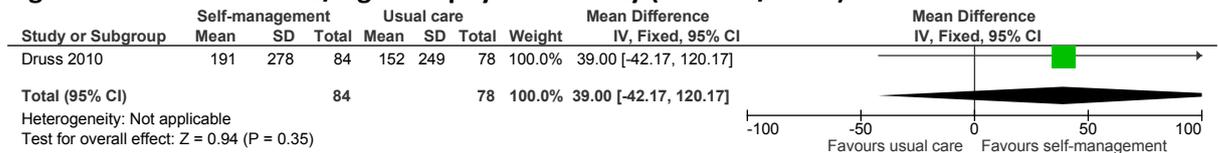


Figure 203: Use of emergency department

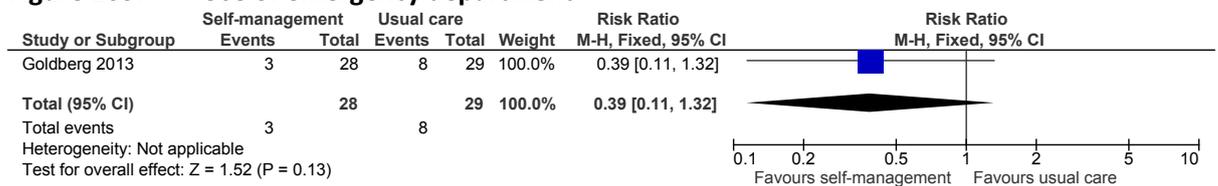


Figure 204: Self-efficacy

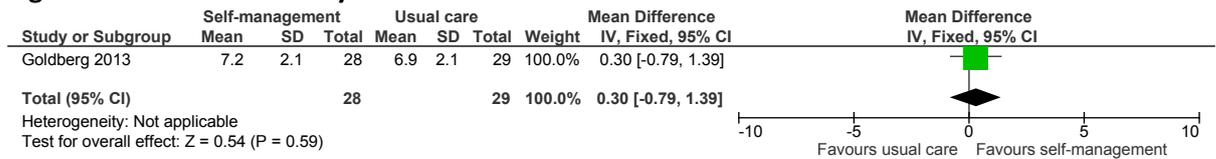
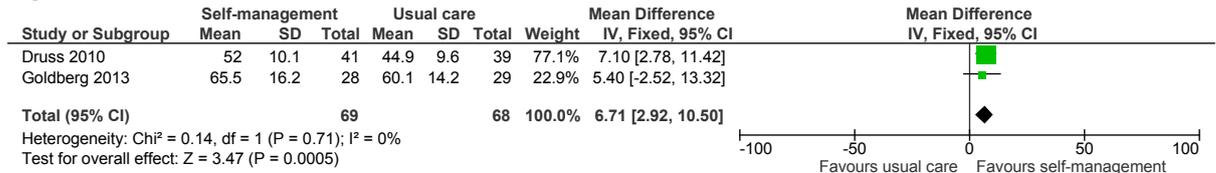


Figure 205: Patient activation



K.7.3 Self-management to improve management of treatment versus usual care (participants with physical health conditions, including participants diagnosed with dementia)

Figure 206: Self-rated health

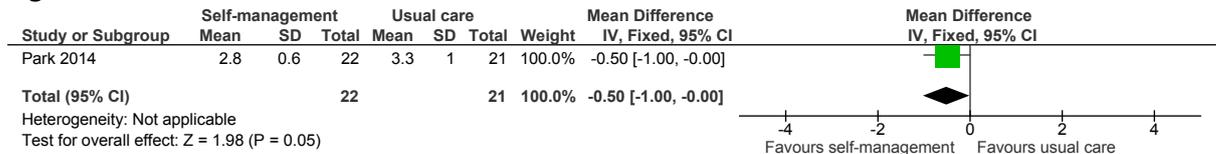
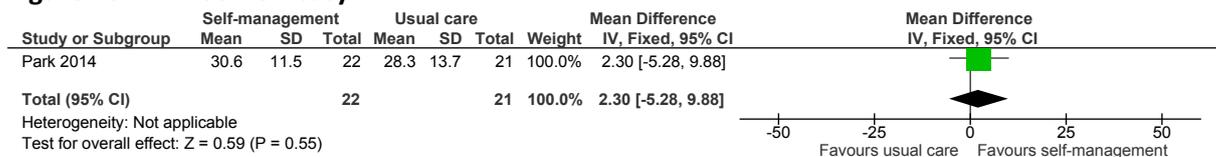
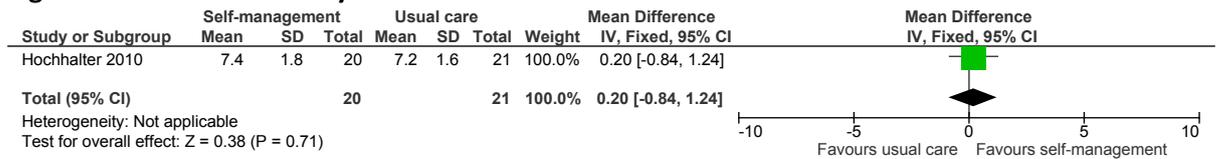


Figure 207: Self-efficacy



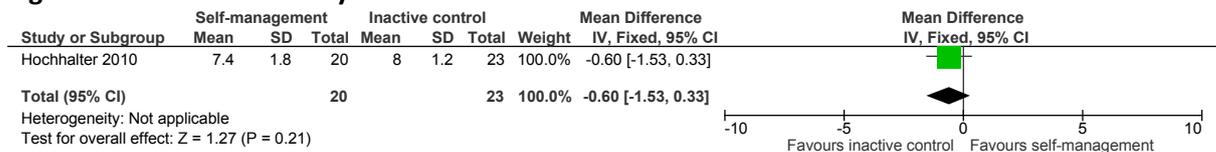
K.7.4 Self-management to improve management of treatment versus usual care (participants with comorbid physical and mental health conditions)

Figure 208: Self-efficacy



K.7.5 Self-management to improve management of treatment versus control intervention (participants with comorbid physical and mental health conditions)

Figure 209: Self-efficacy



K.8 Format of encounters

K.8.1 Telemonitoring versus usual care

Figure 210: Mortality (6 months)

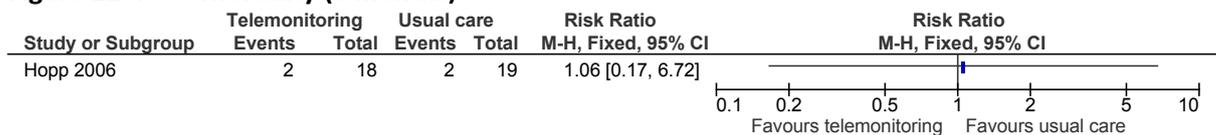


Figure 211: Quality of life (physical component); SF-36V, scale from 0 to 100, better indicated by higher values (6 months)

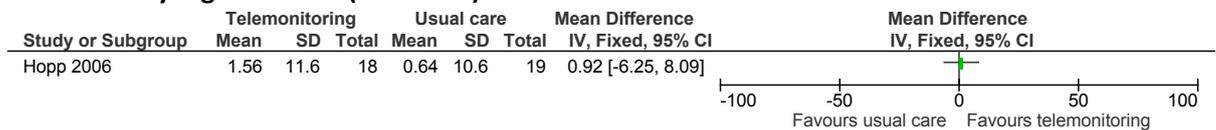


Figure 212: Quality of life (mental component); SF-36V, scale from 0 to 100, better indicated by higher values (6 months)

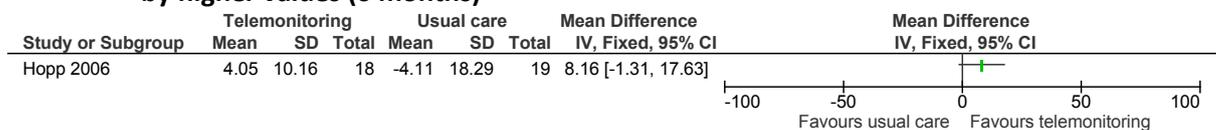


Figure 213: ED (6 months)

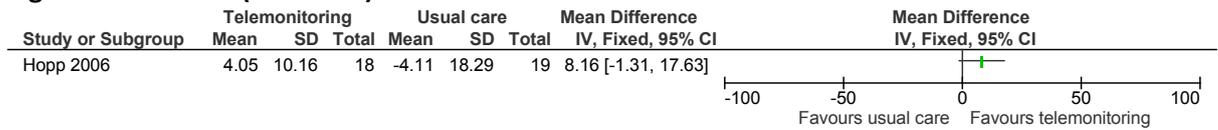


Figure 214: Hospital admissions (6 months)

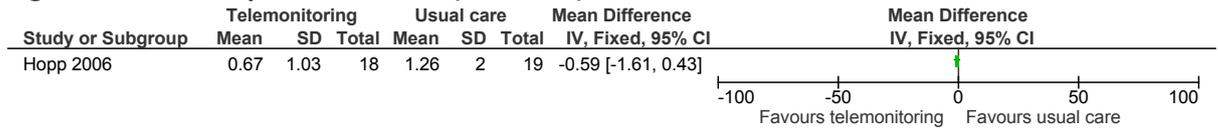


Figure 215: Hospital days (6 months)

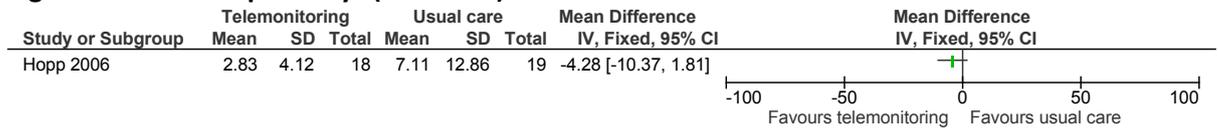
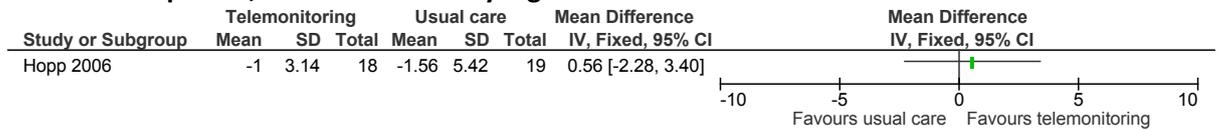


Figure 216: Patient satisfaction; General Home Care Satisfaction Scale, range of scores not reported, better indicated by higher values



K.8.2 Telemonitoring with alerts versus usual care

Figure 217: Mortality (1 year)

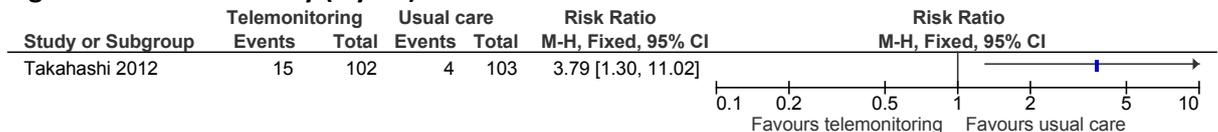


Figure 218: Quality of life (physical component); SF-12, scale from 0 to 100, better indicated by higher values (1 year)

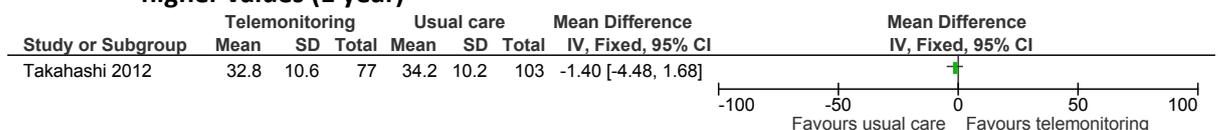


Figure 219: Quality of life (mental component); SF-12, scale from 0 to 100, better indicated by higher values (1 year)

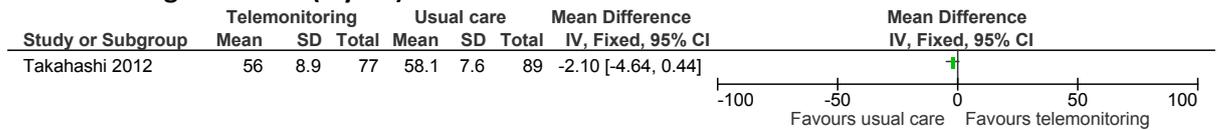


Figure 220: Functioning; Barthel ADL index, scale from 0 to 100, better indicated by higher values (1 year)

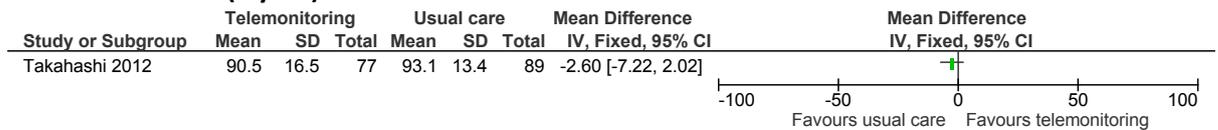


Figure 221: ED visits (1 year)

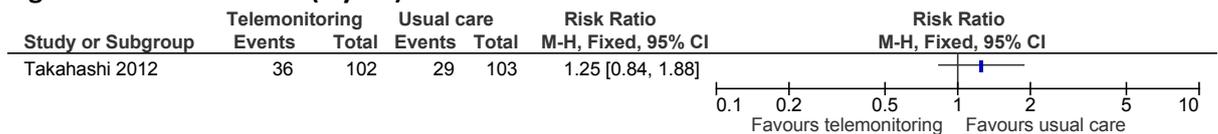


Figure 222: ED visits (1 year)

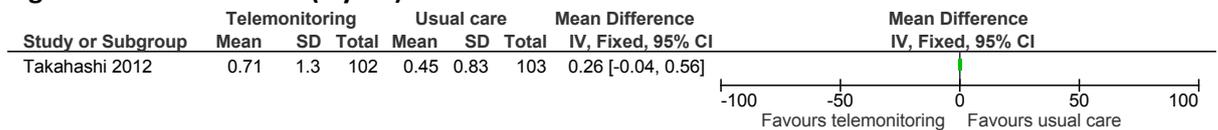


Figure 223: Hospital admissions (1 year)

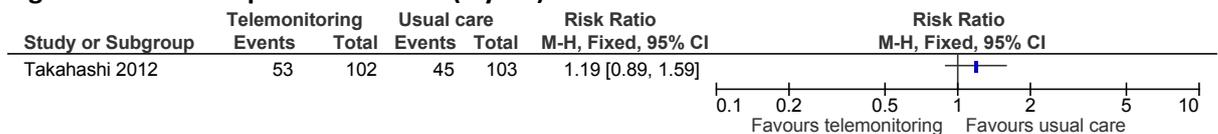


Figure 224: Hospital admissions (1 year)

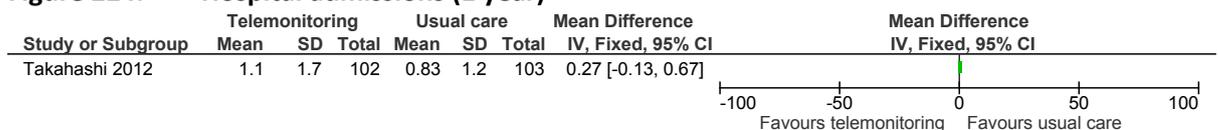


Figure 225: Length of hospital stay, days (1 year)

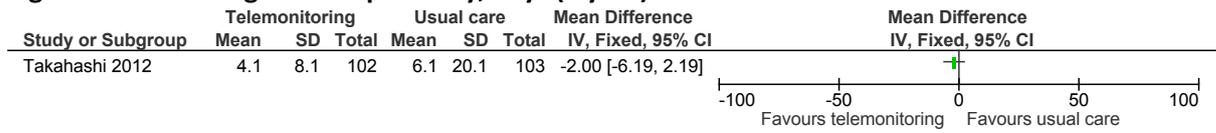


Figure 226: Hospice visits (1 year)

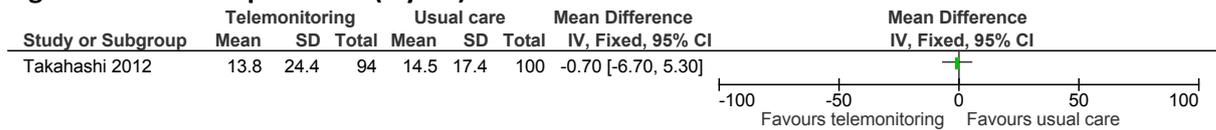


Figure 227: Length of hospice stay, days (1 year)

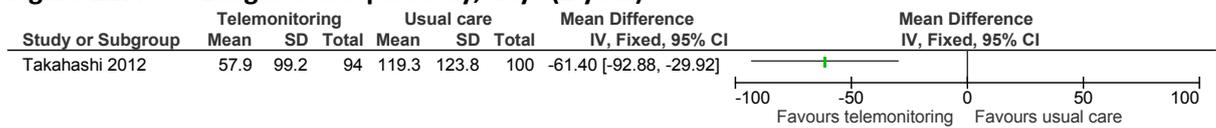
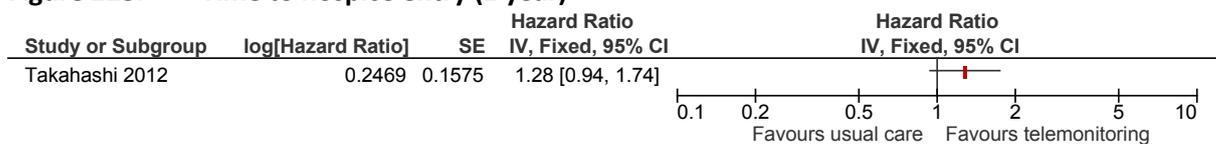


Figure 228: Time to hospice entry (1 year)



K.8.3 Telemonitoring with alerts (plus case management) versus usual care (plus case management)

Figure 229: Functional level; OARS Multidimensional Functional assessment, scale from 0 to 75, better indicated by higher values (6 months)

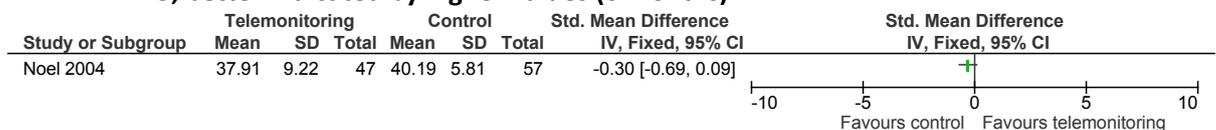


Figure 230: Cognitive status; OARS Multidimensional Functional assessment, scale from 0 to 50, better indicated by higher values (6 months)

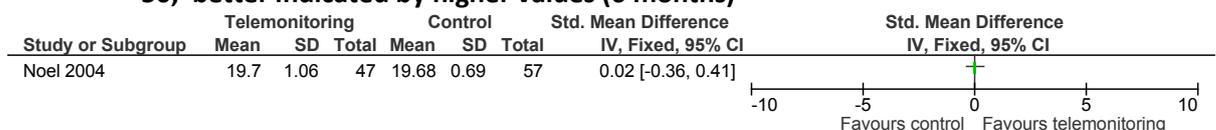


Figure 231: Patient satisfaction; OARS Multidimensional Functional assessment, scale from 0 to 140, better indicated by higher values (6 months)

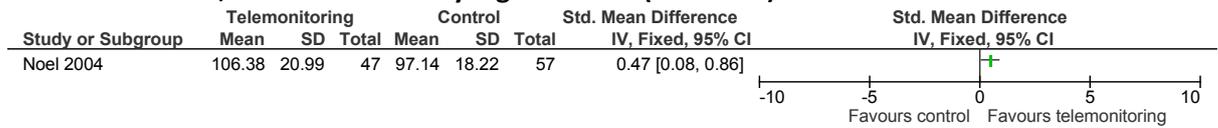
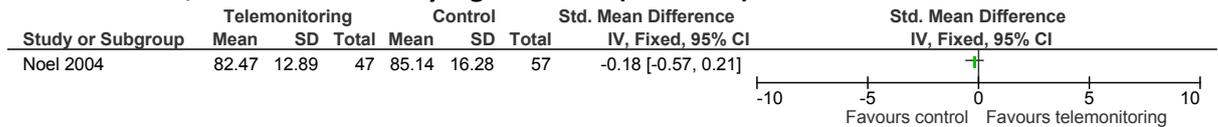


Figure 232: Self-rated health; OARS Multidimensional Functional assessment, scale from 0 to 185, better indicated by higher values (6 months)



K.8.4 Telemonitoring (plus self-management) versus usual care (plus psychoeducation)

Figure 233: Quality of life (mental component); SF-12, scale from 0 to 100, better indicated by higher values (6 months)

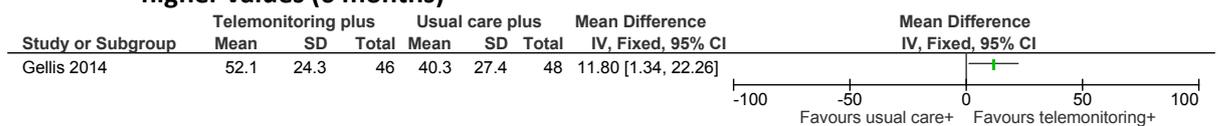


Figure 234: ED visits (6 months)

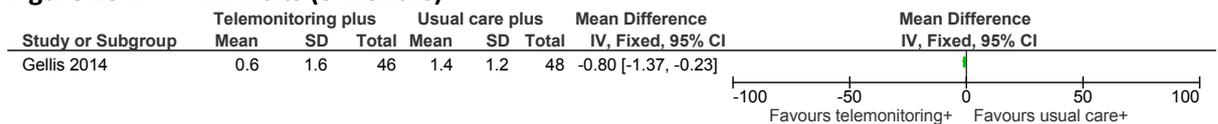


Figure 235: Episodes of care (6 months)

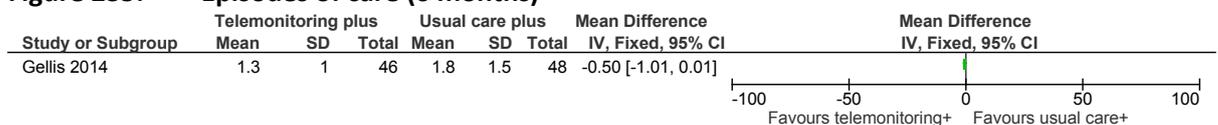


Figure 236: Length of hospital stay, days (6 months)

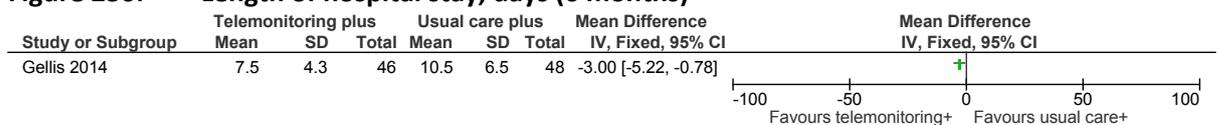
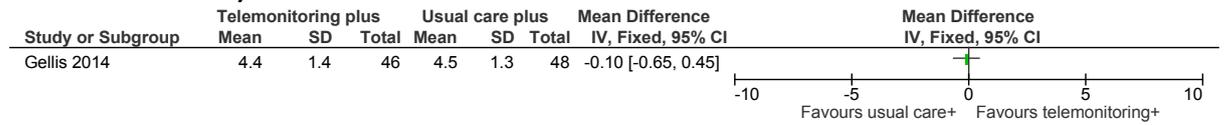


Figure 237: Patient satisfaction; scale not reported, better indicated by higher values (6 months)



Appendix L: Excluded clinical studies

L.1 Principles/Barriers of care

L.1.1 Principles of care

Table 254: Guidelines excluded from the clinical review

Reference	Reason for exclusion
AGS 2012D	Not a guideline
Anon 2004	Not a guideline
Anon 2005	Not a guideline
Anon 2005A	Incorrect design
Anon 2006A	Not a guideline (commissioning framework)
Anon 2008	Not a guideline
Anon 2010B	Not multimorbidity focused
Anon 2011E	Not a guideline
Anon 2011F	Not a guideline
Anon 2011I	Not a guideline
Anon 2012E	Not a guideline
Anon 2012F	Not a guideline
Anon 2012G	Not a guideline
Anon 2012K	Not a guideline
Anon 2012L	Not a guideline
Anon 2012M	Not a guideline
Anon 2012R	Not a guideline
Anon 2013	Not a guideline
Anon 2013B	Not a guideline
Anon 2013D	Not a guideline
Anon 2013F	Commentary
Anon 2013M	Specific review of efficacy of intervention
Anon 2014	Commentary
Anon 2014C	Not a guideline
Anon 2014H	Not a guideline
Anon 2014I	Not a guideline
Anon 2015A	Not a guideline
Anon 2015B	Not a guideline
Braithwaite 2009	Not a guideline
Cheng 2014	Abstract only
Cleary 2008	Low quality guideline
Dauden 2013	Recommendations specific to single, non-representative condition
Dumbreck 2015	Not a guideline
Fanciullo 2011	Not a guideline
Green 2013	Commentary

Reference	Reason for exclusion
Guthrie 2012	Commentary
Parekh 2014	Not a guideline
Reeve 2015	Commentary
Roland 2013	Commentary
Tinetti 2004	Not a guideline
Vanweel 2006	Not a guideline
Wyatt 2014	Not a guideline

L.1.2 Barriers of care

Table 255: Studies excluded from the clinical review

Reference	Reason for exclusion
Ahmed 2009 ¹⁶	Incorrect study design
Alderson 2014 ²⁶	Focus on single condition
Alfaro Lara 2012 ²⁹	Incorrect study design
Ancker 2014 ⁴⁶	Population does not match protocol
Ancker 2015 ⁴⁷	Focus not on barriers and facilitators to optimal care for people with multimorbidity
Ancker 2015A ⁴⁸	Checked for themes – no new themes identified
Annema 2009 ⁵⁵	Population does not match protocol
Aspin 2012 ⁶⁶	Population does not match protocol
Atkin 2005 ⁶⁹	Checked for themes – no new themes identified
Baker 2014 ⁸⁵	Population does not match protocol
Baughan 1983 ¹⁰⁵	Incorrect study design
Bayliss 2003 ¹⁰⁷	Included in systematic review (Koch 2015)
Belcher 2006 ¹¹⁷	Population does not match protocol
Beverly 2011 ¹²⁷	Checked for themes – no new themes identified
Beverly 2014 ¹²⁸	Checked for themes – no new themes identified
Bjorkelund 2013 ¹³⁸	Literature review
Blake 2009 ¹⁴⁴	Population does not match protocol
Blakeman 2012 ¹⁴⁶	Population does not match protocol
Bonavita 2008 ¹⁵⁶	Not relevant
Bower 2011 ¹⁷⁶	Included in systematic review
Bower 2012 ^{175,176}	Checked for themes – no new themes identified
Bower 2013 ¹⁷⁴	Incorrect study design
Bower 2014 ¹⁷³	Literature review
Bratzke 2015 ¹⁸³	Literature review
Bravo 2012 ¹⁸⁵	Incorrect study design
Burgers 2010 ²⁰³	Incorrect study design
Burke 2006A ²⁰⁴	Population does not match protocol
Caplan 2012 ²¹⁶	Population does not match protocol
Carder 2003 ²¹⁷	Population does not match protocol

Reference	Reason for exclusion
Chadwick 2012 ²³⁰	Literature review
Chapman 2009 ²⁴¹	Population does not match protocol
Cheraghi-Sohi 2013 ²⁵⁵	Literature review
Chew-Graham 2002 ²⁵⁷	Checked for themes – no new themes identified
Clarke 2014 ²⁷⁴	Literature review
Cook 2013 ²⁸⁷	Population does not match protocol
Coventry 2011 ³⁰¹	Population does not match protocol
Cramm 2013 ³⁰⁵	Incorrect study design
Crotty 2015 ³⁰⁸	Checked for themes – no new themes identified
Daker-White 2014 ³²⁰	Protocol – corresponding paper not currently published
Davis 2012 ³²⁹	Population does not match protocol
Demain 2015 ³⁴³	Incorrect population
Doos 2014 ³⁶⁷	Checked for themes – no new themes identified
Ehrlich 2015 ³⁸⁷	Incorrect study design
Ekdahl 2011 ³⁹⁰	Incorrect study design
Ekdahl 2012 ³⁹²	Population does not match protocol
Ekerstad 2010 ³⁹³	Incorrect study design
Eton 2015 ⁴¹¹	Checked for themes – no new themes identified
Fortin 2010 ⁴³⁵	Checked for themes – no new themes identified
Franz 2010 ⁴⁴⁵	Population does not match protocol
Freund 2013 ⁴⁵¹	Population does not match protocol
Fried 2011A ⁴⁵⁶	Included in systematic review (Sinnott 2013)
Fuji 2013 ⁴⁶²	Population does not match protocol
Giandinoto 2014 ⁴⁸⁰	Literature review
Gulliford 2011 ⁵²²	Incorrect study design
Gusdal 2011 ⁵²³	Incorrect study design
Gustafsson 2013A ⁵²⁴	Checked for themes – no new themes identified
Haapamaki 2008 ⁵²⁹	Incorrect study design
Halava 2014 ⁵³⁵	Incorrect study design
Halm 2000 ⁵³⁶	Incorrect study design
Halvorsen 2008 ⁵³⁷	Population does not match protocol
Hansen 2014A ⁵⁴³	Incorrect study design
Harries 2007 ⁵⁴⁶	Population does not match protocol
Harris 2013A ⁵⁴⁷	Literature review
Harrold 2013 ⁵⁵⁰	Incorrect study design
Haverhals 2011 ⁵⁵³	Checked for themes – no new themes identified
Heatley 2009 ⁵⁵⁷	Literature review
Heijmans 2015 ⁵⁶¹	Incorrect study design
Heisler 2007 ⁵⁶³	Incorrect study design
Helfrich 2014 ⁵⁶⁴	Incorrect study design
Helminen 2009 ⁵⁶⁵	Incorrect study design
Helstad 2004 ⁵⁶⁶	Incorrect study design
Henning-Smith 2013 ⁵⁷⁰	Incorrect study design

Reference	Reason for exclusion
Henry 2008 ⁵⁷¹	Incorrect study design
Hershkovitz 2001 ⁵⁷³	Incorrect study design
Hewitson 2014 ⁵⁷⁴	Incorrect study design
Heyrani 2012 ⁵⁷⁵	Incorrect study design
Hill-Briggs 2002 ⁵⁷⁸	Incorrect study design
Hinder 2012 ⁵⁸⁰	Population does not match protocol
Ho 2015 ⁵⁸⁵	Checked for themes – no new themes identified
Hoang 2009 ⁵⁹¹	Incorrect study design
Holmboe 2008 ⁵⁹⁷	Incorrect study design
Hong 2005 ⁵⁹⁹	Incorrect study design
Horrocks 2004 ⁶⁰³	Population does not match protocol
Houle 2012 ⁶⁰⁴	Incorrect study design
Howes 2010 ⁶⁰⁵	Population does not match protocol
Howes 2012 ⁶⁰⁶	Population does not match protocol
Hoyt 2006 ⁶⁰⁷	Population does not match protocol
Huber 2011 ⁶¹²	Population does not match protocol
Hung 2015 ⁶¹³	Population does not match protocol
Hwang 2011A ⁶¹⁸	Incorrect study design
Incalzi 2006 ⁶²³	Incorrect study design
Ionescu-Ittu 2007 ⁶²⁵	Incorrect study design
Ito 2013 ⁶²⁷	Literature review
Jager 2015 ⁶³⁰	Incorrect study design
Janke 2015 ⁶³⁴	Checked for themes – no new themes identified
Jansa 2010 ⁶³⁶	Incorrect study design
Jatrana 2009 ⁶³⁸	Incorrect study design
Jatrana 2011 ⁶³⁹	Incorrect study design
Jeon 2009 ⁶⁴¹	Population does not match protocol
Jerant 2005 ⁶⁴⁷	Included in systematic review (Koch 2015)
Joen 2010 ⁶⁴²	Population does not match protocol
Joen 2010A ⁶⁴³	Literature review
Johnson 2014 ⁶⁵¹	Incorrect study design
Johnston 2011 ⁶⁵³	Population does not match protocol
Johnston 2012 ⁶⁵²	Incorrect study design
Joo 2013 ⁶⁵⁹	Population does not match protocol
Joubert 2010 ⁶⁶²	Incorrect study design
Junius-Walker 2012A ⁶⁶⁵	Checked for themes – no new themes identified
Justice 2012 ⁶⁶⁶	Incorrect study design
Kenning 2013 ⁶⁸⁷	Checked for themes – no new themes identified
Kenning 2015 ⁶⁸⁶	Incorrect study design
Kenning 2015A ⁶⁸⁸	Focus not on barriers to optimal care for people with multimorbidity
Kerr 2007 ⁶⁸⁹	Incorrect study design
Knowles 2013 ⁷⁰³	Focus not on barriers and facilitators to optimal care for people with multimorbidity

Reference	Reason for exclusion
Knowles 2015 ⁷⁰²	Focus not on barriers and facilitators to optimal care for people with multimorbidity
Krein 2007 ⁷¹³	Incorrect study design
Kronish 2013 ⁷¹⁶	Incorrect study design
Kuluski 2015 ⁷¹⁸	Checked for themes – no new themes identified
Lai 2013 ⁷²⁶	Incorrect study design
Lam 2011 ⁷²⁸	Incorrect study design
Lamba 2012 ⁷³⁰	Incorrect study design
Lambie 2006 ⁷³¹	Incorrect study design
Langer 2013 ⁷³⁶	Literature review
Lasser 2008 ⁷³⁹	Population does not match protocol
Lee 2013B ⁷⁴³	Incorrect study design
Lee 2013E ⁷⁴⁹	Incorrect study design
Leendertse 2013 ⁷⁵⁰	Incorrect study design
Lekas 2012 ⁷⁵³	Population does not match protocol
Lenihan 2013 ⁷⁵⁵	Incorrect study design
Lenzen 2005 ⁷⁵⁶	Incorrect study design
Lenzi 2014 ⁷⁵⁷	Incorrect study design
Loeb 2015 ⁷⁷⁵	Incorrect population
Loza 2015 ⁷⁸²	Literature review
Lu 2011A ⁷⁸⁴	Incorrect study design
Luijks 2012 ⁷⁹⁰	Included in systematic review (Sinnott 2013)
Lupari 2011 ⁷⁹²	Literature review
MacLaughlin 2005 ⁷⁹⁸	Literature review
Manias 2007 ⁸⁰⁴	Population does not match protocol
Mann 2014 ⁸⁰⁵	Incorrect study design
Markenson 2011 ⁸¹²	Incorrect study design
Marrett 2012 ⁸¹⁴	Incorrect study design
Martinez-Garcia 2013 ⁸¹⁸	Incorrect study design
Marzolini 2013 ⁸²¹	Incorrect study design
Mathew 2014 ⁸²³	Incorrect study design
McCarthy 2007 ⁸³¹	Incorrect study design
McEntee 2009 ⁸³⁵	Literature review
Mehta 2008 ⁸⁴³	Incorrect study design
Meranius 2015 ¹¹⁵⁶	Checked for themes – no new themes identified
Meranius 2015 ⁸⁴⁷	Checked for themes – no new themes identified
Mercer 2007 ⁸⁴⁹	Incorrect study design
Mercer 2012 ⁸⁴⁸	Incorrect study design
Min 2007 ⁸⁶⁰	Incorrect study design
Mira 2013 ⁸⁶²	Incorrect study design
Mira 2014A ⁸⁶¹	Incorrect study design
Mishuris 2014 ⁸⁶³	Population does not match protocol
Mitchell 2008B ⁸⁶⁶	Incorrect study design

Reference	Reason for exclusion
Monane 1997 ⁸⁷³	Literature review
Monroe 2013 ⁸⁷⁴	Population does not match
Morris 2011 ⁸⁸⁰	Included in systematic review (Koch 2015)
Morrissey 2007 ⁸⁸¹	Literature review
O'Brien 2011 ⁹¹⁴	Included in systematic review (Sinnott 2013)
O'Keeffe 2001 ⁹¹⁹	Population does not match protocol
Paddison 2015 ⁹³⁹	Incorrect study design
Parke 2013 ⁹⁴⁵	Population does not match protocol
Paterson 2004 ⁹⁵⁰	Population does not match protocol
Petersen 1998 ⁹⁶⁴	Incorrect study design
Peters-Klimm 2012 ⁹⁶²	Population does not match protocol
Petkov 2010 ⁹⁶⁵	Population does not match protocol
Philips 2014A ⁹⁶⁷	Population does not match protocol
Poitras 2012 ⁹⁸²	Incorrect study design
Presseau 2009 ⁹⁹⁰	Population does not match protocol
Putnam 2004 ⁹⁹⁴	Population does not match protocol
Raven 2012 ¹⁰¹⁰	Population does not match protocol
Reed 2007 ¹⁰¹⁴	Population does not match protocol
Ridgeway 2014 ¹⁰¹⁹	Checked for themes – no new themes identified
Ritholz 2011 ¹⁰²²	Population does not match protocol
Robertson 2013 ¹⁰²⁸	Population does not match protocol
Roe 2009 ¹⁰³⁹	Population does not match protocol
Roland 2011 ¹⁰⁴⁰	Population does not match protocol
Rolfe 2010 ¹⁰⁴¹	Population does not match protocol
Ross 1994 ¹⁰⁴⁷	Population does not match protocol
Sada 2011 ¹⁰⁵⁶	Population does not match protocol
Santos Souza 2013 ¹⁰⁷⁷	Population does not match protocol
Schafer 2014 ¹⁰⁸²	Population does not match protocol
Schonfeld 2012 ¹⁰⁹³	Checked for themes – no new themes identified
Schuling 2012 ¹⁰⁹⁸	Included in systematic review (Sinnott 2013)
Shigaki 2010 ¹¹¹⁶	Checked for themes – no new themes identified
Simmonds 2013 ¹¹²²	Checked for themes – no new themes identified
Sinnott 2015 ¹¹²⁴	Checked for themes – no new themes identified
Sledge 2011 ¹¹²⁷	Population does not match protocol
Smith 2010 ¹¹²⁹	Included in systematic review (Sinnott 2013)
Søndergaard 2015 ¹¹³⁶	Incorrect study design
Stanhope 2014 ¹¹⁴⁴	Population does not match protocol
Stanners 2012 ¹¹⁴⁵	Checked for themes – no new themes identified
Tjia 2008A ¹¹⁹⁷	Population does not match protocol
Townsend 2006 ¹²¹⁰	Included in systematic review (Koch 2015)
Townsend 2012 ¹²⁰⁷	Checked for themes – no new themes identified
Townsend 2013 ¹²⁰⁸	Protocol – corresponding paper identified
Townsend 2015 ¹²⁰⁶	Not relevant

Reference	Reason for exclusion
Van der Kluit ¹²²⁸	Literature review
Van Durme 2014 ¹²³¹	Population does not match protocol
Van Hasselt 2013 ¹²³²	Population does not match protocol
Vik 2009 ¹²⁴⁸	Population does not match protocol
Walsh 2010 ¹²⁷⁴	Incorrect study design
Waterworth 2015 ¹²⁸⁷	Checked for themes – no new themes identified
Waterworth 2015A ¹²⁸⁶	Checked for themes – no new themes identified
Wensing 2014 ¹²⁹⁷	Population does not match protocol
Whitson 2011 ¹³⁰²	Checked for themes – no new themes identified
Williams 2005 ¹³⁰⁸	Population does not match protocol
Williams 2007 ¹³⁰⁶	Checked for themes – no new themes identified
Williams 2014A ¹³⁰⁷	Checked for themes – no new themes identified
Wilson 2013 ¹³¹⁰	Population does not match protocol
Yen 2011 ¹³²⁶	Population does not match protocol
Zulman 2015 ¹³⁵⁵	Checked for themes – no new themes identified

L.2 Identification

L.2.1 Unplanned hospital admissions

Table 22: Studies excluded from the clinical review

Reference	Reason for exclusion
Almagro 2012 ³⁶	Incorrect population
Almagro 2014 ³⁷	Incorrect population
Alvarez 2012 ⁴¹	Incorrect population
Amarasingham 2015 ⁴²	Incorrect population
Ando 2012 ⁵¹	Incorrect population
Angleman 2015 ⁵³	No relevant statistical outcomes reported
Antonelliinc 1997 ⁵⁶	Incorrect population
Antonelliinc 2007 ⁵⁷	No relevant statistical outcomes reported
Antoniou 2014 ⁵⁹	Incorrect population
Arfken 1998 ⁶²	No relevant statistical outcomes reported
Arminanza 2013 ⁶⁴	Incorrect population
Asao 2014 ⁶⁵	Incorrect population
Austin 2011 ⁷⁵	Incorrect population
Austin 2011A ⁷⁶	Incorrect population
Austin 2012 ⁷³	Incorrect population
Austin 2012A ⁷⁴	No relevant statistical outcomes reported
Austin 2015 ⁷²	Systematic review checked for references
Austin 2015A ⁷⁷	Incorrect population
Baker 2012 ⁸⁴	Tool not validated
Bang 2013 ⁹⁰	No relevant statistical outcomes reported
Bansal 2015 ⁹¹	Incorrect population

Reference	Reason for exclusion
Baser 2008 ⁹⁸	Incorrect population
Basic 2015 ⁹⁹	Incorrect population
Bateman 2013 ¹⁰¹	Incorrect population
Bateman 2015 ¹⁰⁰	No relevant outcomes reported
Bayliss 2005 ¹⁰⁶	Incorrect population
Beland 2012 ¹¹⁶	No relevant outcomes reported
Beloosesky 2011 ¹¹⁸	No relevant statistical outcomes reported
Bernabeu-Wittel 2011A ¹²⁴	No relevant outcomes reported
Bernardini 2004 ¹²⁵	Incorrect population
Bien 2015 ¹³³	No tool
Billings 2012 ¹³⁴	Tool not validated
Billings 2013 ¹³⁵	No relevant statistical outcomes reported
Boeckxstaens 2015A ¹⁵²	Incorrect study design
Bottle 2006 ¹⁶⁴	Tool not validated
Bottle 2011 ¹⁶³	Incorrect population
Boult 1993 ¹⁶⁶	No relevant outcomes reported
Boult 1995 ¹⁶⁷	Included in systematic review (Wallace 2013)
Boxer 2010 ¹⁷⁸	No relevant statistical outcomes reported
Bravo 2002 ¹⁸⁴	Tool not validated
Brevetti 2008 ¹⁹¹	No relevant statistical outcomes reported
Buntinx 2002 ²⁰²	No relevant statistical outcomes reported
Buurman 2011 ²⁰⁶	Incorrect population
Byles 2005 ²⁰⁷	No relevant statistical outcomes reported
Calvo-Espinos 2015 ²¹²	Incorrect population
Canoui 2011 ²¹⁵	No relevant outcomes reported
Carey 2004 ²¹⁹	Incorrect population
Carey 2008 ²¹⁸	Incorrect population
Carey 2013 ²²⁰	Incorrect population
Castelli 2014 ²²³	Incorrect population
Cei 2015 ²²⁷	Tool not validated
Chae 2011 ²³¹	Incorrect population
Chan 2010 ²³³	Incorrect population
Chan 2012 ²³⁵	No relevant outcomes reported
Chan 2014A ²³⁴	No relevant outcomes reported
Chang 2015 ²³⁸	No relevant statistical outcomes reported
Chapman 2013A ²⁴²	No relevant statistical outcomes reported
Chapman 2015 ²⁴⁰	Incorrect population
Charlson 1988 ²⁴⁵	Incorrect population
Charlson 1994 ²⁴⁴	No relevant statistical outcomes reported
Chaudhry 2003 ²⁴⁶	Incorrect population
Chen 2010B ²⁴⁹	No relevant statistical outcomes reported
Chen 2014C ²⁴⁸	Incorrect population
Chenore 2013 ²⁵⁴	Incorrect population

Reference	Reason for exclusion
Chiang 2012 ²⁵⁸	No relevant statistical outcomes reported
Chirions 2007 ²⁵⁹	Tool not validated
Cho 2013 ²⁶⁰	Incorrect population
Clark 1995 ²⁷¹	Incorrect population
Clarke 2011 ²⁷³	No relevant statistical outcomes reported
Conde-Martel 2012 ²⁸⁴	Incorrect population
Conde-Martel 2013 ²⁸³	No relevant statistical outcomes reported
Condon 2012 ²⁸⁵	Incorrect population
Conway 2015A ²⁸⁶	Incorrect population
Corsinovi 2009 ²⁹⁴	No tool
Crooks 2015 ³⁰⁷	Incorrect population
Cui 2015 ³¹¹	Incorrect population
D'hoore 1993 ³¹⁹	Incorrect population
D'hoore 1996 ³¹⁸	Incorrect population
Darcy 2005 ³¹⁷	Incorrect population
Davies 2012 ³²⁸	Incorrect population
Davis 2002 ³³⁰	Incorrect population
de Torres 2014 ³³⁴	Tool not validated
Dent 2015 ³⁴⁵	No relevant outcomes reported
Di Bari 2006 ³⁵²	Base model not validated
Di Bari 2010 ³⁵⁰	No relevant statistical outcomes reported
Di Bari 2012 ³⁵¹	No relevant outcomes reported
Dias 2015 ³⁵⁵	No relevant statistical outcomes reported
Diez-Manglano 2015 ³⁵⁷	No relevant outcomes reported
Di Lorio 1998 ³⁵³	No relevant statistical outcomes reported
Di Lorio 2004 ³⁵⁴	Incorrect population
Divo 2012 ³⁵⁹	Tool not validated
Dominick 2005 ³⁶²	Incorrect population
Dong 2013 ³⁶⁴	Incorrect population
Dorr 2006 ³⁶⁹	No relevant statistical outcomes reported
Drame 2008A ³⁷⁴	Incorrect population
Dugoff 2014 ³⁷⁹	Incorrect population
El Hajji 2015 ³⁹⁵	Incorrect population
Ensrud 2009A ⁴⁰²	Tool not validated
Espauella 2007 ⁴⁰⁷	No relevant statistical outcomes reported
Fabbian 2013 ⁴¹⁵	No relevant statistical outcomes reported
Falasca 2011 ⁴¹⁸	Incorrect population
Fischer 2006 ⁴²⁵	No relevant outcomes reported
Flacker 2003 ⁴²⁸	Incorrect population
Floege 2015 ⁴³⁰	Incorrect population
Formiga 2011 ⁴³²	No relevant statistical outcomes reported
Formiga 2013 ⁴³¹	No relevant statistical outcomes reported
Fortin 2005A ⁴³⁴	No relevant outcomes reported

Reference	Reason for exclusion
Fortin 2006 ⁴³⁷	No relevant outcomes reported
Fortin 2011 ⁴³⁶	No relevant outcomes reported
Franchi 2013 ⁴⁴²	No relevant statistical outcomes reported
Fried 2001 ⁴⁵²	Incorrect population
Fried 2003 ⁴⁵³	Incorrect population
Frisoli 2015 ⁴⁶⁰	No tool
Gabriel 1994A ⁴⁶³	No relevant statistical outcomes reported
Gagne 2011 ⁴⁶⁵	Incorrect population
Gallucci 2014 ⁴⁶⁷	No relevant statistical outcomes reported
Ganna 2015 ⁴⁶⁹	Incorrect population
George 2006 ⁴⁷⁷	No relevant statistical outcomes reported
Ghali 1996 ⁴⁷⁸	Incorrect population
Graf 2015 ⁵⁰⁶	Tool not validated
Greene 1990 ⁵¹²	No tool
Greene 2015 ⁵¹¹	Incorrect population
Grimmer 2014 ⁵¹⁶	No relevant outcomes reported
Groll 2005 ⁵¹⁸	Incorrect population
Groll 2006 ⁵¹⁷	Incorrect population
Grunau 2006 ⁵¹⁹	Incorrect population
Guaraldi 2015 ⁵²⁰	Incorrect population
Hansel 2004 ⁵⁴¹	Incorrect population
Harel 2014 ⁵⁴⁵	No relevant outcomes reported
Helvik 2013 ⁵⁶⁷	No relevant statistical outcomes reported
Hemmelgarn 2003 ⁵⁶⁹	Incorrect population
Hindmarsh 2014 ⁵⁸¹	No relevant statistical outcomes reported
Hiorth 2014 ⁵⁸²	No relevant outcomes reported
Ho 2007 ⁵⁸⁶	Incorrect population
Ho 2014B ⁵⁸⁹	No relevant statistical outcomes reported
Hoogerdujin 2010 ⁶⁰⁰	No relevant outcomes reported
Hsiao 2015 ⁶⁰⁸	No relevant statistical outcomes reported
Huang 2014D ⁶¹⁰	No relevant statistical outcomes reported
Huntley 2012 ⁶¹⁴	Systematic review checked for references
Hutchings 2013 ⁶¹⁵	Protocol
Hutchinson 2013 ⁶¹⁶	No relevant statistical outcomes reported
Hutchinson 2015 ⁶¹⁷	Incorrect population
Ingalzi 1997 ⁶²²	Tool not validated
Inoye 2003 ⁶²⁴	Incorrect population
Jang 2010 ⁶³¹	No relevant statistical outcomes reported
Jepsen 2008 ⁶⁴⁴	Incorrect population
Jepsen 2014A ⁶⁴⁵	Incorrect population
Jiang 2005 ⁶⁴⁹	Incorrect population
Jones 2005 ⁶⁵⁴	No relevant outcomes reported
Jong 2002 ⁶⁵⁵	No relevant outcomes reported

Reference	Reason for exclusion
Jonsen 2011 ⁶⁵⁸	Incorrect population
Jotheeswaran 2015 ⁶⁶¹	No relevant statistical outcomes reported
Jung 2014 ⁶⁶⁴	Incorrect population
Kan 2013 ⁶⁶⁸	Incorrect population
Kanis 1999 ⁶⁶⁹	No relevant outcomes reported
Kaplan 1974 ⁶⁷¹	Incorrect population
Khan 2010A ⁶⁹⁰	Incorrect population
Kieszak 1999 ⁶⁹²	No relevant statistical outcomes reported
Kil 2012 ⁶⁹³	Incorrect population
Kim 2014D ⁶⁹⁶	Acute care (post-operation)
Lee 2006 ⁷⁴⁷	Incorrect population
Lee 2015A ⁷⁴⁶	Literature review
Levine 2007 ⁷⁶⁰	Incorrect population
Levy 2015 ⁷⁶¹	Incorrect population
Low 2015 ⁷⁸¹	Incorrect population
Lu 2011 ⁷⁸³	Base model not validated
Luo 2015 ⁷⁹¹	No relevant outcomes reported
Manzano 2011 ⁸⁰⁸	No relevant statistical outcomes reported
Matsuzawa 2013 ⁸²⁶	Incorrect population
Martinez-Velilla 2014 ⁸¹⁹	No relevant outcomes reported
Matzen 2012 ⁸²⁸	Incorrect population
McGee 2008 ⁸³⁶	No relevant statistical outcomes reported
Menendez 2015B ⁸⁴⁵	Incorrect population
Metcalfe 2015 ⁸⁵¹	Incorrect population
Min 2009 ⁸⁵⁹	No relevant outcomes reported
Mosley 2009 ⁸⁸²	Included in systematic review (Wallace 2013)
Neuhaus 2013 ⁹⁰²	Incorrect population
Ng 2012 ⁹⁰³	No relevant outcomes reported
O'Caoimh 2015 ⁹¹⁵	Incorrect population
O'Caoimh 2015A ⁹¹⁶	Incorrect population
Orueta 2013 ⁹³⁰	Incorrect study design
Pacala 1997 ⁹³⁶	Insufficient data
Parkerson 2001 ⁹⁴⁷	Incorrect population
Pedone 2016 ⁹⁵⁴	Incorrect population
Pijpers 2012 ⁹⁶⁹	Review checked for references
Pilotto 2008 ⁹⁷¹	No relevant outcomes reported
Pilotto 2010 ⁹⁷⁰	No relevant outcomes reported
Pilotto 2012A ⁹⁷³	Incorrect population
Pilotto 2012B ⁹⁷⁴	Incorrect population
Pilotto 2013 ⁹⁷²	Incorrect population
Pilotto 2015 ⁹⁷⁶	Incorrect study design
Pilotto 2015B ⁹⁷⁵	Protocol
Polanczyk 1998 ⁹⁸³	Incorrect population

Reference	Reason for exclusion
Porock 2005 ⁹⁸⁶	No relevant outcomes reported
Poses 1996 ⁹⁸⁷	Incorrect population
Putnam 2002 ⁹⁹³	Incorrect population
Quach 2009 ⁹⁹⁵	Acute care (ICU)
Quail 2011 ⁹⁹⁶	Incorrect population
Quan 2011 ⁹⁹⁷	Incorrect population
Radley 2008 ¹⁰⁰²	No relevant outcomes reported
Radner 2015 ¹⁰⁰³	Incorrect population
Radovanovic 2014 ¹⁰⁰⁴	Incorrect population
Ravindrarajah 2013 ¹⁰¹¹	Incorrect population
Rector 2006 ¹⁰¹²	Disease-specific tool
Rius 2008 ¹⁰²⁵	Incorrect population
Roberts 2012 ¹⁰²⁷	No relevant outcomes reported
Roberts 2015 ¹⁰²⁶	Incorrect population
Robey-Williams 2007 ¹⁰²⁹	No relevant outcomes reported
Rockwood 2005 ¹⁰³⁴	No relevant outcomes reported
Rodriguez-Pascual 2012 ¹⁰³⁸	No relevant statistical outcomes reported
Romano 2000 ¹⁰⁴⁴	No relevant statistical outcomes reported
Romero-Ortuno 2013 ¹⁰⁴⁵	Incorrect population
Royston 2004 ¹⁰⁴⁸	Incorrect population
Rozzini 2002 ¹⁰⁴⁹	Tool not validated
Ruiz-Laiglesia 2014 ¹⁰⁵³	Incorrect population
Sanchis 2014 ¹⁰⁷⁴ Sanchis 2014	No relevant outcomes reported
Sabin 1999 ¹⁰⁵⁵	No relevant statistical outcomes reported
Sager 1996 ¹⁰⁵⁷	Incorrect population
Salvi 2008 ¹⁰⁶⁴	Acute care (cancer)
Sampalis 2009 ¹⁰⁶⁷	Incorrect population
Sampson 2012 ¹⁰⁶⁸	Incorrect population
Sanabria 2008 ¹⁰⁶⁹	Acute care (cancer)
Sancarolo 2011 ¹⁰⁷⁰	No relevant outcomes reported
Sancarolo 2012 ¹⁰⁷¹	No relevant outcomes reported
Sanchis 2011 ¹⁰⁷⁵	Incorrect population
Sanchis 2014 ¹⁰⁷⁴	No relevant outcomes reported
Schneeweiss 2000 ¹⁰⁸⁶	Review
Schneeweiss 2003 ¹⁰⁸⁸	Incorrect population
Schneeweiss 2004 ¹⁰⁸⁹	Tool not validated
Schonberg 2009 ¹⁰⁹²	Incorrect population
Schoufour 2015A ¹⁰⁹⁴	Incorrect population
Senni 2006 ¹¹⁰⁵	Incorrect population
Senni 2013 ¹¹⁰⁴	Incorrect population
Sessler 2010 ¹¹⁰⁶	External validation not in multimorbid population
Shamliyan 2013 ¹¹¹⁰	Systematic review checked for references
Shelton 2000 ¹¹¹²	Incorrect population

Reference	Reason for exclusion
Shih 2015 ¹¹¹⁷	Model not validated
Sidorov 2002 ¹¹²⁰	No relevant outcomes reported
Simon 2012A ¹¹²³	Acute care (cancer)
Sirola 2011 ¹¹²⁵	Incorrect population
Soares 2011 ¹¹³²	No relevant outcomes reported
Solberg 2007 ¹¹³³	Incorrect population
Solomon 2011 ¹¹³⁴	No relevant outcomes reported
Soubeyran 2012 ¹¹³⁹	Acute care (cancer)
Southerland 2014 ¹¹⁴⁰	Incorrect population
Stausberg 2015 ¹¹⁴⁶	Incorrect population
Steiner 1997 ¹¹⁴⁷	No relevant outcomes reported
Stukenborg 2001 ¹¹⁵⁵	Incorrect population
Sundarajan 2007 ¹¹⁵⁸	Incorrect population
Tal 2011 ¹¹⁶⁷	No relevant statistical outcomes reported
Tan 2013 ¹¹⁶⁸	Incorrect population
Tang 2015 ¹¹⁷¹	Incorrect population
Tapper 2015A ¹¹⁷⁶	Disease-specific tool
Tarazona-Santalbina 2012 ¹¹⁷⁷	No relevant statistical outcomes reported
Tate 2014 ¹¹⁷⁸	Incorrect population
Teno 2000 ¹¹⁸¹	Incorrect population
Tessier 2008 ¹¹⁸²	No relevant outcomes reported
Testa 2009 ¹¹⁸³	Incorrect population
Tetsche 2008 ¹¹⁸⁴	Acute care (cancer)
Theou 2013 ¹¹⁸⁵	Incorrect population
Thompson 2010 ¹¹⁸⁶	Acute care (trauma)
Thompson 2013 ¹¹⁸⁷	Incorrect population
Tierney 2004 ¹¹⁹²	No relevant statistical outcomes reported
Tierney 2007 ¹¹⁹³	No relevant outcomes reported
Tilling 2001 ¹¹⁹⁴	No relevant outcomes reported
Ting 2014 ¹¹⁹⁶	Acute care (trauma)
Tobacman 1994 ¹¹⁹⁹	Review
Torres 2004 ¹²⁰⁴	No relevant statistical outcomes reported
Torres 2006 ¹²⁰³	Base model not validated
Toson 2015 ¹²⁰⁵	Tool not validated
Tsui 2015 ¹²¹⁶	No relevant outcomes reported
Van Doorn 2001 ¹²³⁰	Incorrect population
Van Kempen 2015 ¹²³⁴	Incorrect population
Van Manen 2002 ¹²³⁵	Incorrect population
Van Walraven 2014 ¹²³⁶	Incorrect population
Van Walraven 2015 ¹²³⁶	Incorrect population
Velghe 2014 ¹²³⁹	Acute care (cancer)
Verdalles 2010 ¹²⁴³	Incorrect population
Vidan 2014 ¹²⁴⁶	No relevant statistical outcomes reported

Reference	Reason for exclusion
Vischer 2012 ¹²⁵¹	No relevant statistical outcomes reported
Visser 2004 ¹²⁵²	No relevant statistical outcomes reported
Vitry 2009 ¹²⁵³	No relevant outcomes reported
Vojta 2001 ¹²⁵⁷	No relevant outcomes reported
Volpato 2007 ¹²⁵⁹	No relevant outcomes reported
Von Korff 1992 ¹²⁶²	Incorrect population
Wagner 2006 ¹²⁶⁵	Included in systematic review (Wallace 2013)
Wagner 2011 ¹²⁶⁶	Incorrect population
Walker 2005 ¹²⁷⁰	No relevant statistical outcomes reported
Wallace 2014 ¹²⁷²	No relevant outcomes reported
Walter 2001 ¹²⁷⁶	Acute care (cancer)
Walter 2001A ¹²⁷⁵	Incorrect population
Wang 2013 ¹²⁷⁹	Incorrect population
Wang 2014A ¹²⁷⁷	Incorrect population
Watkin 2012 ¹²⁸⁸	Incorrect population
Weiss 2015 ¹²⁹⁶	Incorrect population
Wong 2011A ¹³¹⁶	No relevant outcomes reported
Wong 2014 ¹³¹⁵	No relevant outcomes reported
Woo 2012 ¹³¹⁷	Incorrect population
Wu 2013 ¹³²²	Incorrect population
Yan 2005 ¹³²⁴	Base model not validated
Yang 2014G ¹³²⁵	Incorrect population
Yourman 2012 ¹³²⁹	Systematic review checked for references
Yurkovich 2015 ¹³³²	Systematic review checked for references
Zampieri 2014 ¹³³³	Acute care (ICU)
Zekry 2009 ¹³³⁶	Derivation study, no validation
Zekry 2010 ¹³⁴⁰	No relevant statistical outcomes reported
Zekry 2010A ¹³⁴¹	No relevant statistical outcomes reported
Zekry 2012 ¹³³⁵	No relevant outcomes reported
Zekry 2012A ¹³³⁸	Tool not externally validated
Zekry 2013 ¹³³⁷	No relevant outcomes reported
Zeng 2015 ¹³⁴³	Acute care (ICU)
Zhu 2008 ¹³⁴⁶	Base model not validated
Zoghbi 2004 ¹³⁴⁷	Incorrect population

L.2.2 Health-related quality of life

Table 256: Studies excluded from the clinical review

Reference	Reason for exclusion
Abbatecola 2011 ⁴	No relevant outcomes reported
Almagro 2012 ³⁶	Incorrect population
Almagro 2014 ³⁷	Incorrect population
Alvarez 2012 ⁴¹	Incorrect population
Amarasingham 2015 ⁴²	Incorrect population

Reference	Reason for exclusion
Ando 2012 ⁵¹	Incorrect population
Angleman 2015 ⁵³	No relevant statistical outcomes reported
Antonelliinc 1997 ⁵⁶	Incorrect population
Antonelliinc 2007 ⁵⁷	No relevant statistical outcomes reported
Antoniou 2014 ⁵⁹	Incorrect population
Arfken 1998 ⁶²	No relevant statistical outcomes reported
Arminanza 2013 ⁶⁴	Incorrect population
Asao 2014 ⁶⁵	Incorrect population
Austin 2011 ⁷⁵	Incorrect population
Austin 2011A ⁷⁶	Incorrect population
Austin 2012 ⁷³	Incorrect population
Austin 2012A ⁷⁴	No relevant statistical outcomes reported
Austin 2015 ⁷²	Systematic review checked for references
Austin 2015A ⁷⁷	Incorrect population
Baker 2012 ⁸⁴	Tool not validated
Bang 2013 ⁹⁰	No relevant statistical outcomes reported
Bansal 2015 ⁹¹	Incorrect population
Baser 2008 ⁹⁸	Incorrect population
Basic 2015 ⁹⁹	Incorrect population
Bateman 2013 ¹⁰¹	Incorrect population
Bateman 2015 ¹⁰⁰	No relevant outcomes reported
Bayliss 2005 ¹⁰⁶	Incorrect population
Beland 2012 ¹¹⁶	No relevant outcomes reported
Beloosesky 2011 ¹¹⁸	No relevant statistical outcomes reported
Bernabeu-Wittel 2011A ¹²⁴	No relevant outcomes reported
Bernardini 2004 ¹²⁵	Incorrect population
Bien 2015 ¹³³	No tool
Billings 2012 ¹³⁴	Derivation study, no validation
Billings 2013 ¹³⁵	No relevant statistical outcomes reported
Boeckxstans 2015 ¹⁵¹	No relevant outcomes reported
Boeckxstaens 2015A ¹⁵²	Incorrect study design
Bottle 2006 ¹⁶⁴	Tool not validated
Bottle 2011 ¹⁶³	Incorrect population
Boult 1993 ¹⁶⁶	No relevant outcomes reported
Boult 1995 ¹⁶⁷	No relevant outcomes reported
Boxer 2010 ¹⁷⁸	No relevant statistical outcomes reported
Bravo 2002 ¹⁸⁴	Tool not validated
Brevetti 2008 ¹⁹¹	No relevant statistical outcomes reported
Buntinx 2002 ²⁰²	No relevant statistical outcomes reported
Buurman 2011 ²⁰⁶	Incorrect population
Byles 2005 ²⁰⁷	No relevant statistical outcomes reported
Calvo-Espinosa 2015 ²¹²	Incorrect population
Canoui 2011 ²¹⁵	No relevant outcomes reported

Reference	Reason for exclusion
Carey 2004 ²¹⁹	Incorrect population
Carey 2008 ²¹⁸	Incorrect population
Carey 2013 ²²⁰	Incorrect population
Castelli 2014 ²²³	Incorrect population
Cei 2015 ²²⁷	Tool not validated
Chae 2011 ²³¹	Incorrect population
Chan 2010 ²³³	Incorrect population
Chan 2012 ²³⁵	No relevant outcomes reported
Chan 2014A ²³⁴	No relevant outcomes reported
Chang 2015 ²³⁸	No relevant statistical outcomes reported
Chapman 2013A ²⁴²	No relevant statistical outcomes reported
Chapman 2015 ²⁴⁰	Incorrect population
Charlson 1988 ²⁴⁵	Incorrect population
Charlson 1994 ²⁴⁴	No relevant statistical outcomes reported
Chaudhry 2003 ²⁴⁶	Incorrect population
Chen 2010B ²⁴⁹	No relevant statistical outcomes reported
Chen 2014C ²⁴⁸	Incorrect population
Chenore 2013 ²⁵⁴	Incorrect population
Chiang 2012 ²⁵⁸	No relevant statistical outcomes reported
Chirions 2007 ²⁵⁹	Tool not validated
Cho 2013 ²⁶⁰	Incorrect population
Clark 1995 ²⁷¹	Incorrect population
Clarke 2011 ²⁷³	No relevant statistical outcomes reported
Coleman 1998 ²⁸¹	No relevant outcomes reported
Conde-Martel 2012 ²⁸⁴	Incorrect population
Conde-Martel 2013 ²⁸³	No relevant statistical outcomes reported
Condon 2012 ²⁸⁵	Incorrect population
Conway 2015A ²⁸⁶	Incorrect population
Corsinovi 2009 ²⁹⁴	No tool
Crooks 2015 ³⁰⁷	Incorrect population
Cui 2015 ³¹¹	Incorrect population
D'hoore 1993 ³¹⁹	Incorrect population
D'hoore 1996 ³¹⁸	Incorrect population
Daniels 2012 ³²²	No relevant outcomes reported
Darcy 2005 ³¹⁷	Incorrect population
Davies 2012 ³²⁸	Incorrect population
Davis 2002 ³³⁰	Incorrect population
de Torres 2014 ³³⁴	Tool not validated
Dent 2015 ³⁴⁵	No relevant outcomes reported
Di Bari 2006 ³⁵²	Base model not validated
Di Bari 2010 ³⁵⁰	No relevant statistical outcomes reported
Di Bari 2012 ³⁵¹	No relevant outcomes reported
Dias 2015 ³⁵⁵	No relevant statistical outcomes reported

Reference	Reason for exclusion
Diez-Manglano 2015 ³⁵⁷	No relevant outcomes reported
Di Lorio 1998 ³⁵³	No relevant statistical outcomes reported
Di Lorio 2004 ³⁵⁴	Incorrect population
Divo 2012 ³⁵⁹	Tool not validated
Dominick 2005 ³⁶²	Incorrect population
Donate-Martinez 2014 ³⁶³	No relevant outcomes reported
Dong 2013 ³⁶⁴	Incorrect population
Donnan 2008 ³⁶⁶	No relevant outcomes reported
Dorr 2006 ³⁶⁹	No relevant statistical outcomes reported
Drame 2008A ³⁷⁴	Incorrect population
Dugoff 2014 ³⁷⁹	Incorrect population
El Hajji 2015 ³⁹⁵	Incorrect population
Ensrud 2009A ⁴⁰²	Tool not validated
Espauella 2007 ⁴⁰⁷	No relevant statistical outcomes reported
Fabbian 2013 ⁴¹⁵	No relevant statistical outcomes reported
Falasca 2011 ⁴¹⁸	Incorrect population
Fischer 2006 ⁴²⁵	No relevant outcomes reported
Flacker 2003 ⁴²⁸	Incorrect population
Floege 2015 ⁴³⁰	Incorrect population
Formiga 2011 ⁴³²	No relevant statistical outcomes reported
Formiga 2013 ⁴³¹	No relevant statistical outcomes reported
Fortin 2006 ⁴³⁷	No relevant outcomes reported
Fortin 2011 ⁴³⁶	Incorrect population
Franchi 2013 ⁴⁴²	No relevant statistical outcomes reported
Fried 2001 ⁴⁵²	Incorrect population
Fried 2003 ⁴⁵³	Incorrect population
Frisoli 2015 ⁴⁶⁰	No tool
Gabriel 1994A ⁴⁶³	No relevant statistical outcomes reported
Gagne 2011 ⁴⁶⁵	Incorrect population
Gallucci 2014 ⁴⁶⁷	No relevant statistical outcomes reported
Ganna 2015 ⁴⁶⁹	Incorrect population
George 2006 ⁴⁷⁷	No relevant statistical outcomes reported
Ghali 1996 ⁴⁷⁸	Incorrect population
Graf 2015 ⁵⁰⁶	Tool not validated
Greene 1990 ⁵¹²	No tool
Greene 2015 ⁵¹¹	Incorrect population
Groll 2005 ⁵¹⁸	Incorrect population
Groll 2006 ⁵¹⁷	Incorrect population
Grunau 2006 ⁵¹⁹	Incorrect population
Guaraldi 2015 ⁵²⁰	Incorrect population
Hansel 2004 ⁵⁴¹	Incorrect population
Harel 2014 ⁵⁴⁵	No relevant outcomes reported
Helvik 2013 ⁵⁶⁷	No relevant statistical outcomes reported

Reference	Reason for exclusion
Hemmelgarn 2003 ⁵⁶⁹	Incorrect population
Hindmarsh 2014 ⁵⁸¹	No relevant statistical outcomes reported
Hiorth 2014 ⁵⁸²	No relevant outcomes reported
Hippisley-Cox 2013 ⁵⁸³	No relevant outcomes reported
Ho 2007 ⁵⁸⁶	Incorrect population
Ho 2014B ⁵⁸⁹	No relevant statistical outcomes reported
Hoogerdujin 2010 ⁶⁰⁰	No relevant outcomes reported
Hsiao 2015 ⁶⁰⁸	No relevant statistical outcomes reported
Huang 2014D ⁶¹⁰	No relevant statistical outcomes reported
Huntley 2012 ⁶¹⁴	Systematic review checked for references
Hutchings 2013 ⁶¹⁵	Protocol
Hutchinson 2013 ⁶¹⁶	No relevant statistical outcomes reported
Hutchinson 2015 ⁶¹⁷	Incorrect population
Ingalzi 1997 ⁶²²	Tool not validated
Inoye 2003 ⁶²⁴	Incorrect population
Jang 2010 ⁶³¹	No relevant statistical outcomes reported
Jensen 2001 ⁶⁴⁰	No relevant outcomes reported
Jepsen 2008 ⁶⁴⁴	Incorrect population
Jepsen 2014A ⁶⁴⁵	Incorrect population
Jiang 2005 ⁶⁴⁹	Incorrect population
Jones 2005 ⁶⁵⁴	No relevant outcomes reported
Jong 2002 ⁶⁵⁵	Incorrect population
Jonsen 2011 ⁶⁵⁸	Incorrect population
Jotheeswaran 2015 ⁶⁶¹	No relevant statistical outcomes reported
Jung 2014 ⁶⁶⁴	Incorrect population
Kan 2013 ⁶⁶⁸	Incorrect population
Kanis 1999 ⁶⁶⁹	No relevant outcomes reported
Kaplan 1974 ⁶⁷¹	Incorrect population
Khan 2010A ⁶⁹⁰	Incorrect population
Kieszak 1999 ⁶⁹²	No relevant statistical outcomes reported
Kil 2012 ⁶⁹³	Incorrect population
Kim 2014D ⁶⁹⁶	Acute care (post-operation)
Lee 2006 ⁷⁴⁷	Incorrect population
Lee 2015A ⁷⁴⁶	Literature review
Levine 2007 ⁷⁶⁰	Incorrect population
Levy 2015 ⁷⁶¹	Incorrect population
Low 2015 ⁷⁸¹	Incorrect population
Lu 2011 ⁷⁸³	Base model not validated
Luo 2015 ⁷⁹¹	No relevant outcomes reported
Manzano 2011 ⁸⁰⁸	No relevant statistical outcomes reported
Matsuzawa 2013 ⁸²⁶	Incorrect population
Martinez-Velilla 2014 ⁸¹⁹	No relevant outcomes reported
Matzen 2012 ⁸²⁸	Incorrect population

Reference	Reason for exclusion
Mazzaglia 2007 ⁸²⁹	No relevant outcomes reported
McGee 2008 ⁸³⁶	No relevant statistical outcomes reported
Menendez 2015B ⁸⁴⁵	Incorrect population
Metcalfe 2015 ⁸⁵¹	Incorrect population
Min 2009 ⁸⁵⁹	No relevant outcomes reported
Mosley 2009 ⁸⁸²	No relevant outcomes reported
Neuhaus 2013 ⁹⁰²	Incorrect population
Ng 2012 ⁹⁰³	No relevant outcomes reported
O'Caoimh 2015 ⁹¹⁵	Incorrect population
O'Caoimh 2015A ⁹¹⁶	Incorrect population
Orueta 2013 ⁹³⁰	Incorrect study design
Pacala 1997 ⁹³⁶	Insufficient data
Parkerson 2001 ⁹⁴⁷	Incorrect population
Pedone 2016 ⁹⁵⁴	Incorrect population
Pijpers 2012 ⁹⁶⁹	Review checked for references
Pilotto 2008 ⁹⁷¹	No relevant outcomes reported
Pilotto 2010 ⁹⁷⁰	No relevant outcomes reported
Pilotto 2012A ⁹⁷³	Incorrect population
Pilotto 2012B ⁹⁷⁴	Incorrect population
Pilotto 2013 ⁹⁷²	Incorrect population
Pilotto 2015 ⁹⁷⁶	Incorrect study design
Pilotto 2015B ⁹⁷⁵	Protocol
Polanczyk 1998 ⁹⁸³	Incorrect population
Porock 2005 ⁹⁸⁶	No relevant outcomes reported
Poses 1996 ⁹⁸⁷	Incorrect population
Putnam 2002 ⁹⁹³	Incorrect population
Quach 2009 ⁹⁹⁵	Acute care (ICU)
Quail 2011 ⁹⁹⁶	Incorrect population
Quan 2011 ⁹⁹⁷	Incorrect population
Radley 2008 ¹⁰⁰²	No relevant outcomes reported
Radner 2015 ¹⁰⁰³	Incorrect population
Radovanovic 014 ¹⁰⁰⁴	Incorrect population
Ravindrarajah 2013 ¹⁰¹¹	Incorrect population
Rector 2006 ¹⁰¹²	Disease-specific tool
Ritt 2015 ¹⁰²³	No relevant outcomes reported
Rius 2008 ¹⁰²⁵	Incorrect population
Roberts 2012 ¹⁰²⁷	No relevant outcomes reported
Roberts 2015 ¹⁰²⁶	Incorrect population
Robey-Williams 2007 ¹⁰²⁹	No relevant outcomes reported
Rockwood 2005 ¹⁰³⁴	No relevant outcomes reported
Rodriguez-Pascual 2012 ¹⁰³⁸	No relevant statistical outcomes reported
Romano 2000 ¹⁰⁴⁴	Incorrect population
Romero-Ortuno 2013 ¹⁰⁴⁵	Tool not validated

Reference	Reason for exclusion
Royston 2004 ¹⁰⁴⁸	Incorrect population
Rozzini 2002 ¹⁰⁴⁹	No relevant statistical outcomes reported
Ruiz-Laiglesia 2014 ¹⁰⁵³	Incorrect population
Sanchis 2014 ¹⁰⁷⁴ anchis 2014	No relevant outcomes reported
Sabin 1999 ¹⁰⁵⁵	Acute care (cancer)
Sager 1996 ¹⁰⁵⁷	No relevant outcomes reported
Salvi 2008 ¹⁰⁶⁴	No relevant statistical outcomes reported
Sampalis 2009 ¹⁰⁶⁷	Incorrect population
Sampson 2012 ¹⁰⁶⁸	Incorrect population
Sanabria 2008 ¹⁰⁶⁹	Acute care (cancer)
Sancarolo 2011 ¹⁰⁷⁰	No relevant outcomes reported
Sancarolo 2012 ¹⁰⁷¹	No relevant outcomes reported
Sanchis 2011 ¹⁰⁷⁵	Incorrect population
Sanchis 2014 ¹⁰⁷⁴	No relevant outcomes reported
Schneeweiss 2000 ¹⁰⁸⁶	Review
Schneeweiss 2001 ¹⁰⁸⁷	No relevant outcomes reported
Schneeweiss 2003 ¹⁰⁸⁸	Incorrect population
Schneeweiss 2004 ¹⁰⁸⁹	Base model not validated
Schonberg 2009 ¹⁰⁹²	Incorrect population
Schoufour 2015A ¹⁰⁹⁴	Incorrect population
Senni 2006 ¹¹⁰⁵	Incorrect population
Senni 2013 ¹¹⁰⁴	Incorrect population
Sessler 2010 ¹¹⁰⁶	Incorrect population
Shamliyan 2013 ¹¹¹⁰	Systematic review checked for references
Shelton 2000 ¹¹¹²	Incorrect population
Shih 2015 ¹¹¹⁷	Tool not validated
Sidorov 2002 ¹¹²⁰	No relevant outcomes reported
Simon 2012A ¹¹²³	Acute care (cancer)
Sirola 2011 ¹¹²⁵	Incorrect population
Soares 2011 ¹¹³²	No relevant outcomes reported
Solberg 2007 ¹¹³³	Incorrect population
Solomon 2011 ¹¹³⁴	No relevant outcomes reported
Soong 2015 ¹¹³⁷	No relevant outcomes reported
Soubeyran 2012 ¹¹³⁹	Acute care (cancer)
Southerland 2014 ¹¹⁴⁰	Incorrect population
Stausberg 2015 ¹¹⁴⁶	Incorrect population
Steiner 1997 ¹¹⁴⁷	No relevant outcomes reported
Stukenborg 2001 ¹¹⁵⁵	Incorrect population
Sundarajan 2007 ¹¹⁵⁸	Incorrect population
Susser 2008 ¹¹⁵⁹	No relevant outcomes reported
Tal 2011 ¹¹⁶⁷	No relevant statistical outcomes reported
Tan 2013 ¹¹⁶⁸	Incorrect population
Tang 2015 ¹¹⁷¹	Incorrect population

Reference	Reason for exclusion
Tapper 2015A ¹¹⁷⁶	Disease-specific tool
Tarazona-Santalbina 2012 ¹¹⁷⁷	No relevant statistical outcomes reported
Tate 2014 ¹¹⁷⁸	Incorrect population
Teno 2000 ¹¹⁸¹	Incorrect population
Tessier 2008 ¹¹⁸²	No relevant outcomes reported
Testa 2009 ¹¹⁸³	Incorrect population
Tetsche 2008 ¹¹⁸⁴	Acute care (cancer)
Theou 2013 ¹¹⁸⁵	Incorrect population
Thompson 2010 ¹¹⁸⁶	Acute care (trauma)
Thompson 2013 ¹¹⁸⁷	Incorrect population
Tierney 2004 ¹¹⁹²	No relevant statistical outcomes reported
Tierney 2007 ¹¹⁹³	No relevant outcomes reported
Tilling 2001 ¹¹⁹⁴	No relevant outcomes reported
Ting 2014 ¹¹⁹⁶	Acute care (trauma)
Tobacman 1994 ¹¹⁹⁹	Review
Torres 2004 ¹²⁰⁴	No relevant statistical outcomes reported
Torres 2006 ¹²⁰³	Base model not validated
Toson 2015 ¹²⁰⁵	Tool not validated
Tsui 2015 ¹²¹⁶	No relevant outcomes reported
Van Doorn 2001 ¹²³⁰	Incorrect population
Van Kempen 2015 ¹²³⁴	Incorrect population
Van Manen 2002 ¹²³⁵	Incorrect population
Van Walraven 2014 ¹²³⁶	Incorrect population
Van Walraven 2015 ¹²³⁶	Incorrect population
Velghe 2014 ¹²³⁹	Acute care (cancer)
Verdalles 2010 ¹²⁴³	Incorrect population
Vidan 2014 ¹²⁴⁶	No relevant statistical outcomes reported
Vischer 2012 ¹²⁵¹	No relevant statistical outcomes reported
Visser 2004 ¹²⁵²	No relevant statistical outcomes reported
Vitry 2009 ¹²⁵³	No relevant outcomes reported
Vojta 2001 ¹²⁵⁷	No relevant outcomes reported
Volpato 2007 ¹²⁵⁹	No relevant outcomes reported
Von Korff 1992 ¹²⁶²	Incorrect population
Wagner 2006 ¹²⁶⁵	No relevant outcomes reported
Wagner 2011 ¹²⁶⁶	Incorrect population
Walker 2005 ¹²⁷⁰	No relevant statistical outcomes reported
Wallace 2013 ¹²⁷¹	No relevant outcomes reported
Wallace 2014 ¹²⁷²	No relevant outcomes reported
Wallis 2015 ¹²⁷³	No relevant outcomes reported
Walter 2001 ¹²⁷⁶	Acute care (cancer)
Walter 2001A ¹²⁷⁵	Incorrect population
Wang 2013 ¹²⁷⁹	Incorrect population
Wang 2014A ¹²⁷⁷	Incorrect population

Reference	Reason for exclusion
Watkin 2012 ¹²⁸⁸	Incorrect population
Weiss 2015 ¹²⁹⁶	Incorrect population
Widagdo 2015 ¹³⁰³	No relevant outcomes reported
Wong 2011A ¹³¹⁶	No relevant outcomes reported
Wong 2014 ¹³¹⁵	No relevant outcomes reported
Woo 2012 ¹³¹⁷	Incorrect population
Wu 2013 ¹³²²	Incorrect population
Yan 2005 ¹³²⁴	Base model not validated
Yang 2014G ¹³²⁵	Incorrect population
Yourman 2012 ¹³²⁹	Systematic review checked for references
Yurkovich 2015 ¹³³²	Systematic review checked for references
Zampieri 2014 ¹³³³	Acute care (ICU)
Zekry 2009 ¹³³⁶	Tool not validated
Zekry 2010 ¹³⁴⁰	No relevant statistical outcomes reported
Zekry 2010A ¹³⁴¹	No relevant statistical outcomes reported
Zekry 2012 ¹³³⁵	No relevant outcomes reported
Zekry 2012A ¹³³⁸	Tool not externally validated
Zekry 2012B ¹³³⁹	No relevant outcomes reported
Zekry 2013 ¹³³⁷	No relevant outcomes reported
Zeng 2014 ¹³⁴⁴	No relevant outcomes reported
Zeng 2015 ¹³⁴³	Acute care (ICU)
Zhu 2008 ¹³⁴⁶	Base model not validated
Zoghbi 2004 ¹³⁴⁷	Incorrect population

L.2.3 Admission to care facility

Table 8: Studies excluded from the clinical review

Reference	Reason for exclusion
Abbatecola 2011 ⁴	No relevant outcomes reported
Almagro 2012 ³⁶	Incorrect population
Almagro 2014 ³⁷	Incorrect population
Alvarez 2012 ⁴¹	Incorrect population
Amarasingham 2015 ⁴²	Incorrect population
Ando 2012 ⁵¹	Incorrect population
Angleman 2015 ⁵³	No relevant statistical outcomes reported
Antonelliinc 1997 ⁵⁶	Incorrect population
Antonelliinc 2007 ⁵⁷	No relevant statistical outcomes reported
Antoniou 2014 ⁵⁹	Incorrect population
Arfken 1998 ⁶²	No relevant statistical outcomes reported
Arminanza 2013 ⁶⁴	Incorrect population
Asao 2014 ⁶⁵	Incorrect population
Austin 2011 ⁷⁵	Incorrect population
Austin 2011A ⁷⁶	Incorrect population
Austin 2012 ⁷³	Incorrect population

Reference	Reason for exclusion
Austin 2012A ⁷⁴	No relevant statistical outcomes reported
Austin 2015 ⁷²	Systematic review checked for references
Austin 2015A ⁷⁷	Incorrect population
Baker 2012 ⁸⁴	Tool not validated
Bang 2013 ⁹⁰	No relevant statistical outcomes reported
Bansal 2015 ⁹¹	Incorrect population
Baser 2008 ⁹⁸	Incorrect population
Basic 2015 ⁹⁹	Incorrect population
Bateman 2013 ¹⁰¹	Incorrect population
Bateman 2015 ¹⁰⁰	No relevant outcomes reported
Bayliss 2005 ¹⁰⁶	Incorrect population
Beland 2012 ¹¹⁶	No relevant outcomes reported
Beloosesky 2011 ¹¹⁸	No relevant statistical outcomes reported
Bernabeu-Wittel 2011A ¹²⁴	No relevant outcomes reported
Bernardini 2004 ¹²⁵	Incorrect population
Bien 2015 ¹³³	No tool
Billings 2012 ¹³⁴	Tool not validated
Billings 2013 ¹³⁵	No relevant statistical outcomes reported
Boeckxstans 2015 ¹⁵¹	No relevant outcomes reported
Boeckxstaens 2015A ¹⁵²	Incorrect study design
Bottle 2006 ¹⁶⁴	Tool not validated
Bottle 2011 ¹⁶³	Incorrect population
Boult 1993 ¹⁶⁶	No relevant outcomes reported
Boult 1995 ¹⁶⁷	No relevant outcomes reported
Boxer 2010 ¹⁷⁸	No relevant statistical outcomes reported
Bravo 2002 ¹⁸⁴	Tool not validated
Brevetti 2008 ¹⁹¹	No relevant statistical outcomes reported
Buntinx 2002 ²⁰²	No relevant statistical outcomes reported
Buurman 2011 ²⁰⁶	Incorrect population
Byles 2005 ²⁰⁷	No relevant statistical outcomes reported
Calvo-Espinos 2015 ²¹²	Incorrect population
Canoui 2011 ²¹⁵	No relevant outcomes reported
Carey 2004 ²¹⁹	Incorrect population
Carey 2008 ²¹⁸	Incorrect population
Carey 2013 ²²⁰	Incorrect population
Castelli 2014 ²²³	Incorrect population
Cei 2015 ²²⁷	Tool not validated
Chae 2011 ²³¹	Incorrect population
Chan 2010 ²³³	Incorrect population
Chan 2012 ²³⁵	No relevant outcomes reported
Chan 2014A ²³⁴	No relevant outcomes reported
Chang 2015 ²³⁸	No relevant statistical outcomes reported

Reference	Reason for exclusion
Chapman 2013A ²⁴²	No relevant statistical outcomes reported
Chapman 2015 ²⁴⁰	Incorrect population
Charlson 1988 ²⁴⁵	Incorrect population
Charlson 1994 ²⁴⁴	No relevant statistical outcomes reported
Chaudhry 2003 ²⁴⁶	Incorrect population
Chen 2010B ²⁴⁹	No relevant statistical outcomes reported
Chen 2014C ²⁴⁸	Incorrect population
Chenore 2013 ²⁵⁴	Incorrect population
Chiang 2012 ²⁵⁸	No relevant statistical outcomes reported
Chirions 2007 ²⁵⁹	Tool not validated
Cho 2013 ²⁶⁰	Incorrect population
Clark 1995 ²⁷¹	Incorrect population
Clarke 2011 ²⁷³	No relevant statistical outcomes reported
Coleman 1998 ²⁸¹	No relevant outcomes reported
Conde-Martel 2012 ²⁸⁴	Incorrect population
Conde-Martel 2013 ²⁸³	No relevant statistical outcomes reported
Condon 2012 ²⁸⁵	Incorrect population
Conway 2015A ²⁸⁶	Incorrect population
Corsinovi 2009 ²⁹⁴	No tool
Crooks 2015 ³⁰⁷	Incorrect population
Cui 2015 ³¹¹	Incorrect population
D'hoore 1993 ³¹⁹	Incorrect population
D'hoore 1996 ³¹⁸	Incorrect population
Daniels 2012 ³²²	No relevant outcomes reported
Darcy 2005 ³¹⁷	Incorrect population
Davies 2012 ³²⁸	Incorrect population
Davis 2002 ³³⁰	Incorrect population
de Torres 2014 ³³⁴	Tool not validated
Dent 2015 ³⁴⁵	No relevant outcomes reported
Di Bari 2006 ³⁵²	Base model not validated
Di Bari 2010 ³⁵⁰	No relevant statistical outcomes reported
Di Bari 2012 ³⁵¹	No relevant outcomes reported
Dias 2015 ³⁵⁵	No relevant statistical outcomes reported
Diez-Manglano 2015 ³⁵⁷	No relevant outcomes reported
Di Lorio 1998 ³⁵³	No relevant statistical outcomes reported
Di Lorio 2004 ³⁵⁴	Incorrect population
Divo 2012 ³⁵⁹	Tool not validated
Dominick 2005 ³⁶²	Incorrect population
Donate-Martinez 2014 ³⁶³	No relevant outcomes reported
Dong 2013 ³⁶⁴	Incorrect population

Reference	Reason for exclusion
Donnan 2008 ³⁶⁶	No relevant outcomes reported
Dorr 2006 ³⁶⁹	No relevant outcomes reported
Drame 2008A ³⁷⁴	Incorrect population
Dugoff 2014 ³⁷⁹	Incorrect population
El Hajji 2015 ³⁹⁵	Incorrect population
Ensrud 2009A ⁴⁰²	Tool not validated
Espauella 2007 ⁴⁰⁷	No relevant statistical outcomes reported
Fabbian 2013 ⁴¹⁵	No relevant statistical outcomes reported
Falasca 2011 ⁴¹⁸	Incorrect population
Fischer 2006 ⁴²⁵	No relevant outcomes reported
Flacker 2003 ⁴²⁸	Incorrect population
Floege 2015 ⁴³⁰	Incorrect population
Formiga 2011 ⁴³²	No relevant statistical outcomes reported
Formiga 2013 ⁴³¹	No relevant statistical outcomes reported
Fortin 2005A ⁴³⁴	No relevant outcomes reported
Fortin 2006 ⁴³⁷	No relevant outcomes reported
Fortin 2011 ⁴³⁶	Incorrect population
Franchi 2013 ⁴⁴²	No relevant statistical outcomes reported
Fried 2001 ⁴⁵²	Incorrect population
Fried 2003 ⁴⁵³	Incorrect population
Frisoli 2015 ⁴⁶⁰	No tool
Gabriel 1994A ⁴⁶³	No relevant statistical outcomes reported
Gagne 2011 ⁴⁶⁵	Incorrect population
Gallucci 2014 ⁴⁶⁷	No relevant statistical outcomes reported
Ganna 2015 ⁴⁶⁹	Incorrect population
George 2006 ⁴⁷⁷	No relevant statistical outcomes reported
Ghali 1996 ⁴⁷⁸	Incorrect population
Graf 2015 ⁵⁰⁶	Tool not validated
Greene 1990 ⁵¹²	No tool
Greene 2015 ⁵¹¹	Incorrect population
Grimmer 2014 ⁵¹⁶	No relevant outcomes reported
Groll 2005 ⁵¹⁸	Incorrect population
Groll 2006 ⁵¹⁷	Incorrect population
Grunau 2006 ⁵¹⁹	Incorrect population
Guaraldi 2015 ⁵²⁰	Incorrect population
Hansel 2004 ⁵⁴¹	Incorrect population
Harel 2014 ⁵⁴⁵	No relevant outcomes reported
Helvik 2013 ⁵⁶⁷	No relevant statistical outcomes reported

Reference	Reason for exclusion
Hemmelgarn 2003 ⁵⁶⁹	Incorrect population
Hindmarsh 2014 ⁵⁸¹	No relevant statistical outcomes reported
Hiorth 2014 ⁵⁸²	No relevant outcomes reported
Hippisley-Cox 2013 ⁵⁸³	No relevant outcomes reported
Ho 2007 ⁵⁸⁶	Incorrect population
Ho 2014B ⁵⁸⁹	No relevant statistical outcomes reported
Hoogerdujin 2010 ⁶⁰⁰	No relevant outcomes reported
Hsiao 2015 ⁶⁰⁸	No relevant statistical outcomes reported
Huang 2014D ⁶¹⁰	No relevant statistical outcomes reported
Huntley 2012 ⁶¹⁴	Systematic review
Hutchings 2013 ⁶¹⁵	Protocol
Hutchinson 2013 ⁶¹⁶	No relevant statistical outcomes reported
Hutchinson 2015 ⁶¹⁷	Incorrect population
Ingalzi 1997 ⁶²²	Tool not validated
Inoye 2003 ⁶²⁴	Incorrect population
Jang 2010 ⁶³¹	No relevant statistical outcomes reported
Jensen 2001 ⁶⁴⁰	No relevant outcomes reported
Jepsen 2008 ⁶⁴⁴	Incorrect population
Jepsen 2014A ⁶⁴⁵	Incorrect population
Jiang 2005 ⁶⁴⁹	Incorrect population
Jong 2002 ⁶⁵⁵	Incorrect population
Jonsen 2011 ⁶⁵⁸	Incorrect population
Jotheeswaran 2015 ⁶⁶¹	No relevant statistical outcomes reported
Jung 2014 ⁶⁶⁴	Incorrect population
Kan 2013 ⁶⁶⁸	Incorrect population
Kanis 1999 ⁶⁶⁹	No relevant outcomes reported
Kaplan 1974 ⁶⁷¹	Incorrect population
Khan 2010A ⁶⁹⁰	Incorrect population
Kieszak 1999 ⁶⁹²	No relevant statistical outcomes reported
Kil 2012 ⁶⁹³	Incorrect population
Kim 2014D ⁶⁹⁶	Acute care (post-operation)
Lee 2006 ⁷⁴⁷	Incorrect population
Lee 2015A ⁷⁴⁶	Literature review
Levine 2007 ⁷⁶⁰	Incorrect population
Levy 2015 ⁷⁶¹	Incorrect population
Low 2015 ⁷⁸¹	Incorrect population
Lu 2011 ⁷⁸³	Base model not validated
Luo 2015 ⁷⁹¹	No relevant outcomes reported
Manzano 2011 ⁸⁰⁸	No relevant statistical outcomes reported
Matsuzawa 2013 ⁸²⁶	Incorrect population
Martinez-Velilla 2014 ⁸¹⁹	No relevant outcomes reported
Matzen 2012 ⁸²⁸	Incorrect population
Mazzaglia 2007 ⁸²⁹	No relevant outcomes reported

Reference	Reason for exclusion
McGee 2008 ⁸³⁶	No relevant statistical outcomes reported
Menendez 2015B ⁸⁴⁵	Incorrect population
Metcalfe 2015 ⁸⁵¹	Incorrect population
Min 2009 ⁸⁵⁹	No relevant outcomes reported
Mosley 2009 ⁸⁸²	No relevant outcomes reported
Neuhaus 2013 ⁹⁰²	Incorrect population
Ng 2012 ⁹⁰³	No relevant outcomes reported
O'Caoimh 2015 ⁹¹⁵	Incorrect population
O'Caoimh 2015A ⁹¹⁶	Incorrect population
Orueta 2013 ⁹³⁰	Incorrect study design
Pacala 1997 ⁹³⁶	Insufficient data
Parkerson 2001 ⁹⁴⁷	Incorrect population
Pedone 2016 ⁹⁵⁴	Incorrect population
Pijpers 2012 ⁹⁶⁹	Review checked for references
Pilotto 2008 ⁹⁷¹	No relevant outcomes reported
Pilotto 2010 ⁹⁷⁰	No relevant outcomes reported
Pilotto 2012A ⁹⁷³	Incorrect population
Pilotto 2012B ⁹⁷⁴	Incorrect population
Pilotto 2013 ⁹⁷²	Incorrect population
Pilotto 2015 ⁹⁷⁶	Incorrect study design
Pilotto 2015B ⁹⁷⁵	Protocol
Polanczyk 1998 ⁹⁸³	Incorrect population
Porock 2005 ⁹⁸⁶	No relevant outcomes reported
Poses 1996 ⁹⁸⁷	Incorrect population
Putnam 2002 ⁹⁹³	Incorrect population
Quach 2009 ⁹⁹⁵	Acute care (ICU)
Quail 2011 ⁹⁹⁶	Incorrect population
Quan 2011 ⁹⁹⁷	Incorrect population
Radley 2008 ¹⁰⁰²	No relevant outcomes reported
Radner 2015 ¹⁰⁰³	Incorrect population
Radovanovic 014 ¹⁰⁰⁴	Incorrect population
Ravindrarajah 2013 ¹⁰¹¹	Incorrect population
Rector 2006 ¹⁰¹²	Disease-specific tool
Ritt 2015 ¹⁰²³	No relevant outcomes reported
Rius 2008 ¹⁰²⁵	Incorrect population
Roberts 2012 ¹⁰²⁷	No relevant outcomes reported
Roberts 2015 ¹⁰²⁶	Incorrect population
Robey-Williams 2007 ¹⁰²⁹	No relevant outcomes reported
Rodriguez-Pascual 2012 ¹⁰³⁸	No relevant statistical outcomes reported
Romano 2000 ¹⁰⁴⁴	Incorrect population
Romero-Ortuno 2013 ¹⁰⁴⁵	Tool not validated
Royston 2004 ¹⁰⁴⁸	Incorrect population

Reference	Reason for exclusion
Rozzini 2002 ¹⁰⁴⁹	No relevant statistical outcomes reported
Ruiz-Laiglesia 2014 ¹⁰⁵³	Incorrect population
Sanchis 2014 ¹⁰⁷⁴ Sanchis 2014	No relevant outcomes reported
Sabin 1999 ¹⁰⁵⁵	Acute care (cancer)
Sager 1996 ¹⁰⁵⁷	No relevant outcomes reported
Salvi 2008 ¹⁰⁶⁴	No relevant statistical outcomes reported
Sampalis 2009 ¹⁰⁶⁷	Incorrect population
Sampson 2012 ¹⁰⁶⁸	Incorrect population
Sanabria 2008 ¹⁰⁶⁹	Acute care (cancer)
Sancarlo 2011 ¹⁰⁷⁰	No relevant outcomes reported
Sancarlo 2012 ¹⁰⁷¹	No relevant outcomes reported
Sanchis 2011 ¹⁰⁷⁵	Incorrect population
Sanchis 2014 ¹⁰⁷⁴	No relevant outcomes reported
Schneeweiss 2000 ¹⁰⁸⁶	Review
Schneeweiss 2001 ¹⁰⁸⁷	No relevant outcomes reported
Schneeweiss 2003 ¹⁰⁸⁸	Incorrect population
Schneeweiss 2004 ¹⁰⁸⁹	Base model not validated
Schonberg 2009 ¹⁰⁹²	Incorrect population
Schoufour 2015A ¹⁰⁹⁴	Incorrect population
Senni 2006 ¹¹⁰⁵	Incorrect population
Senni 2013 ¹¹⁰⁴	Incorrect population
Sessler 2010 ¹¹⁰⁶	Incorrect population
Shamliyan 2013 ¹¹¹⁰	Systematic review checked for references
Shelton 2000 ¹¹¹²	Incorrect population
Shih 2015 ¹¹¹⁷	Tool not validated
Sidorov 2002 ¹¹²⁰	No relevant outcomes reported
Simon 2012A ¹¹²³	Acute care (cancer)
Sirola 2011 ¹¹²⁵	Incorrect population
Soares 2011 ¹¹³²	No relevant outcomes reported
Solberg 2007 ¹¹³³	Incorrect population
Solomon 2011 ¹¹³⁴	No relevant outcomes reported
Soubeyran 2012 ¹¹³⁹	Acute care (cancer)
Southerland 2014 ¹¹⁴⁰	Incorrect population
Stausberg 2015 ¹¹⁴⁶	Incorrect population
Steiner 1997 ¹¹⁴⁷	No relevant outcomes reported
Stukenborg 2001 ¹¹⁵⁵	Incorrect population
Sundarajan 2007 ¹¹⁵⁸	Incorrect population
Susser 2008 ¹¹⁵⁹	No relevant outcomes reported
Tal 2011 ¹¹⁶⁷	No relevant statistical outcomes reported
Tan 2013 ¹¹⁶⁸	Incorrect population
Tang 2015 ¹¹⁷¹	Incorrect population

Reference	Reason for exclusion
Tapper 2015A ¹¹⁷⁶	Disease-specific tool
Tarazona-Santalbina 2012 ¹¹⁷⁷	No relevant statistical outcomes reported
Tate 2014 ¹¹⁷⁸	Incorrect population
Teno 2000 ¹¹⁸¹	Incorrect population
Tessier 2008 ¹¹⁸²	No relevant outcomes reported
Testa 2009 ¹¹⁸³	Incorrect population
Tetsche 2008 ¹¹⁸⁴	Acute care (cancer)
Theou 2013 ¹¹⁸⁵	Incorrect population
Thompson 2010 ¹¹⁸⁶	Acute care (trauma)
Thompson 2013 ¹¹⁸⁷	Incorrect population
Tierney 2004 ¹¹⁹²	No relevant statistical outcomes reported
Tierney 2007 ¹¹⁹³	No relevant outcomes reported
Tilling 2001 ¹¹⁹⁴	No relevant outcomes reported
Ting 2014 ¹¹⁹⁶	Acute care (trauma)
Tobacman 1994 ¹¹⁹⁹	Review
Torres 2004 ¹²⁰⁴	No relevant statistical outcomes reported
Torres 2006 ¹²⁰³	Base model not validated
Toson 2015 ¹²⁰⁵	Tool not validated
Tsui 2015 ¹²¹⁶	No relevant outcomes reported
Van Doorn 2001 ¹²³⁰	Incorrect population
Van Kempen 2015 ¹²³⁴	Incorrect population
Van Manen 2002 ¹²³⁵	Incorrect population
Van Walraven 2014 ¹²³⁶	Incorrect population
Van Walraven 2015 ¹²³⁶	Incorrect population
Velghe 2014 ¹²³⁹	Acute care (cancer)
Verdalles 2010 ¹²⁴³	Incorrect population
Vidan 2014 ¹²⁴⁶	No relevant statistical outcomes reported
Vischer 2012 ¹²⁵¹	No relevant statistical outcomes reported
Visser 2004 ¹²⁵²	No relevant statistical outcomes reported
Vitry 2009 ¹²⁵³	No relevant outcomes reported
Vojta 2001 ¹²⁵⁷	No relevant outcomes reported
Volpato 2007 ¹²⁵⁹	No relevant outcomes reported
Von Korff 1992 ¹²⁶²	Incorrect population
Wagner 2006 ¹²⁶⁵	No relevant outcomes reported
Wagner 2011 ¹²⁶⁶	Incorrect population
Walker 2005 ¹²⁷⁰	No relevant statistical outcomes reported
Wallace 2013 ¹²⁷¹	No relevant outcomes reported
Wallace 2014 ¹²⁷²	No relevant outcomes reported
Wallis 2015 ¹²⁷³	No relevant outcomes reported
Walter 2001 ¹²⁷⁶	Acute care (cancer)
Walter 2001A ¹²⁷⁵	Incorrect population
Wang 2013 ¹²⁷⁹	Incorrect population
Wang 2014A ¹²⁷⁷	Incorrect population

Reference	Reason for exclusion
Watkin 2012 ¹²⁸⁸	Incorrect population
Weiss 2015 ¹²⁹⁶	Incorrect population
Wong 2011A ¹³¹⁶	No relevant outcomes reported
Wong 2014 ¹³¹⁵	No relevant outcomes reported
Woo 2012 ¹³¹⁷	Incorrect population
Wu 2013 ¹³²²	Incorrect population
Yan 2005 ¹³²⁴	Base model not validated
Yang 2014G ¹³²⁵	Incorrect population
Yourman 2012 ¹³²⁹	Systematic review checked for references
Yurkovich 2015 ¹³³²	Systematic review checked for references
Zampieri 2014 ¹³³³	Acute care (ICU)
Zekry 2009 ¹³³⁶	Tool not validated
Zekry 2010 ¹³⁴⁰	No relevant statistical outcomes reported
Zekry 2010A ¹³⁴¹	No relevant statistical outcomes reported
Zekry 2012 ¹³³⁵	No relevant outcomes reported
Zekry 2012A ¹³³⁸	Tool not externally validated
Zekry 2012B ¹³³⁹	No relevant outcomes reported
Zekry 2013 ¹³³⁷	No relevant outcomes reported
Zeng 2014 ¹³⁴⁴	No relevant outcomes reported
Zeng 2015 ¹³⁴³	Acute care (ICU)
Zhu 2008 ¹³⁴⁶	Base model not validated
Zoghbi 2004 ¹³⁴⁷	Incorrect population

L.2.4 Life expectancy risk tools

Table 257: Studies excluded from the clinical review

Reference	Reason for exclusion
Almagro 2012 ³⁶	Incorrect population
Almagro 2014 ³⁷	Incorrect population
Alvarez 2012 ⁴¹	Incorrect population
Amarasingham 2015 ⁴²	Incorrect population
Ando 2012 ⁵¹	Incorrect population
Angleman 2015 ⁵³	No relevant statistical outcomes reported
Antonelliinc 1997 ⁵⁶	Incorrect population
Antonelliinc 2007 ⁵⁷	No relevant statistical outcomes reported
Antoniou 2014 ⁵⁹	Incorrect population
Arfken 1998 ⁶²	No relevant statistical outcomes reported
Arminanza 2013 ⁶⁴	Incorrect population
Asao 2014 ⁶⁵	Incorrect population
Austin 2011 ⁷⁵	Incorrect population
Austin 2011A ⁷⁶	Incorrect population
Austin 2012 ⁷³	Incorrect population
Austin 2012A ⁷⁴	No relevant statistical outcomes reported

Reference	Reason for exclusion
Austin 2015 ⁷²	Systematic review checked for references
Austin 2015A ⁷⁷	Incorrect population
Baker 2012 ⁸⁴	Tool not validated
Bang 2013 ⁹⁰	No relevant statistical outcomes reported
Bansal 2015 ⁹¹	Incorrect population
Baser 2008 ⁹⁸	Incorrect population
Basic 2015 ⁹⁹	Incorrect population
Bateman 2013 ¹⁰¹	Incorrect population
Bateman 2015 ¹⁰⁰	No relevant outcomes reported
Bayliss 2005 ¹⁰⁶	Incorrect population
Beloosesky 2011 ¹¹⁸	No relevant statistical outcomes reported
Bernardini 2004 ¹²⁵	Incorrect population
Bien 2015 ¹³³	No tool
Billings 2012 ¹³⁴	Tool not validated
Billings 2013 ¹³⁵	No relevant statistical outcomes reported
Boeckxstaens 2015A ¹⁵²	Incorrect study design
Bottle 2006 ¹⁶⁴	Tool not validated
Bottle 2011 ¹⁶³	Incorrect population
Boult 1995 ¹⁶⁷	No relevant outcomes reported
Boxer 2010 ¹⁷⁸	No relevant statistical outcomes reported
Bravo 2002 ¹⁸⁴	Tool not validated
Brevetti 2008 ¹⁹¹	No relevant statistical outcomes reported
Buntinx 2002 ²⁰²	No relevant statistical outcomes reported
Buurman 2011 ²⁰⁶	Incorrect population
Byles 2005 ²⁰⁷	No relevant statistical outcomes reported
Calvo-Espinos 2015 ²¹²	Incorrect population
Canoui 2011 ²¹⁵	No relevant outcomes reported
Carey 2004 ²¹⁹	Incorrect population
Carey 2008 ²¹⁸	Incorrect population
Carey 2013 ²²⁰	Incorrect population
Castelli 2014 ²²³	Incorrect population
Cei 2015 ²²⁷	Tool not validated
Chae 2011 ²³¹	Incorrect population
Chan 2010 ²³³	Incorrect population
Chang 2015 ²³⁸	No relevant statistical outcomes reported
Chapman 2013A ²⁴²	No relevant statistical outcomes reported
Chapman 2015 ²⁴⁰	Incorrect population
Charlson 1988 ²⁴⁵	Incorrect population
Charlson 1994 ²⁴⁴	No relevant statistical outcomes reported
Chaudhry 2003 ²⁴⁶	Incorrect population
Chen 2010B ²⁴⁹	No relevant statistical outcomes reported
Chen 2014C ²⁴⁸	Incorrect population

Reference	Reason for exclusion
Chenore 2013 ²⁵⁴	Incorrect population
Chiang 2012 ²⁵⁸	No relevant statistical outcomes reported
Chirions 2007 ²⁵⁹	Tool not validated
Cho 2013 ²⁶⁰	Incorrect population
Clark 1995 ²⁷¹	Incorrect population
Clarke 2011 ²⁷³	No relevant statistical outcomes reported
Coleman 1998 ²⁸¹	No relevant outcomes reported
Conde-Martel 2012 ²⁸⁴	Incorrect population
Conde-Martel 2013 ²⁸³	No relevant statistical outcomes reported
Condon 2012 ²⁸⁵	Incorrect population
Conway 2015A ²⁸⁶	Incorrect population
Corsinovi 2009 ²⁹⁴	No tool
Crooks 2015 ³⁰⁷	Incorrect population
Cui 2015 ³¹¹	Incorrect population
D'hoore 1993 ³¹⁹	Incorrect population
D'hoore 1996 ³¹⁸	Incorrect population
Darcy 2005 ³¹⁷	Incorrect population
Davies 2012 ³²⁸	Incorrect population
Davis 2002 ³³⁰	Incorrect population
de Torres 2014 ³³⁴	Tool not validated
Dent 2015 ³⁴⁵	No relevant outcomes reported
Di Bari 2006 ³⁵²	Base model not validated
Di Bari 2010 ³⁵⁰	No relevant statistical outcomes reported
Di Bari 2012 ³⁵¹	No relevant outcomes reported
Dias 2015 ³⁵⁵	No relevant statistical outcomes reported
Di Lorio 1998 ³⁵³	No relevant statistical outcomes reported
Di Lorio 2004 ³⁵⁴	Incorrect population
Divo 2012 ³⁵⁹	Tool not validated
Dominick 2005 ³⁶²	Incorrect population
Donate-Martinez 2014 ³⁶³	No relevant outcomes reported
Dong 2013 ³⁶⁴	Incorrect population
Donnan 2008 ³⁶⁶	No relevant outcomes reported
Dorr 2006 ³⁶⁹	No relevant statistical outcomes reported
Drame 2008A ³⁷⁴	Incorrect population
Dugoff 2014 ³⁷⁹	Incorrect population
El Hajji 2015 ³⁹⁵	Incorrect population
Ensrud 2009A ⁴⁰²	Tool not validated
Espauella 2007 ⁴⁰⁷	No relevant statistical outcomes reported
Fabbian 2013 ⁴¹⁵	No relevant statistical outcomes reported
Falasca 2011 ⁴¹⁸	Incorrect population

Reference	Reason for exclusion
Fischer 2006 ⁴²⁵	No relevant outcomes reported
Flacker 2003 ⁴²⁸	Incorrect population
Floege 2015 ⁴³⁰	Incorrect population
Formiga 2011 ⁴³²	No relevant statistical outcomes reported
Formiga 2013 ⁴³¹	No relevant statistical outcomes reported
Fortin 2005A ⁴³⁴	No relevant outcomes reported
Fortin 2006 ⁴³⁷	No relevant outcomes reported
Fortin 2011 ⁴³⁶	Incorrect population
Franchi 2013 ⁴⁴²	No relevant statistical outcomes reported
Fried 2001 ⁴⁵²	Incorrect population
Fried 2003 ⁴⁵³	Incorrect population
Frisoli 2015 ⁴⁶⁰	No tool
Gabriel 1994A ⁴⁶³	No relevant statistical outcomes reported
Gagne 2011 ⁴⁶⁵	Incorrect population
Gallucci 2014 ⁴⁶⁷	No relevant statistical outcomes reported
Ganna 2015 ⁴⁶⁹	Incorrect population
George 2006 ⁴⁷⁷	No relevant statistical outcomes reported
Ghali 1996 ⁴⁷⁸	Incorrect population
Graf 2015 ⁵⁰⁶	Tool not validated
Greene 1990 ⁵¹²	No tool
Greene 2015 ⁵¹¹	Incorrect population
Grimmer 2014 ⁵¹⁶	No relevant outcomes reported
Groll 2005 ⁵¹⁸	Incorrect population
Groll 2006 ⁵¹⁷	Incorrect population
Grunau 2006 ⁵¹⁹	Incorrect population
Guaraldi 2015 ⁵²⁰	Incorrect population
Hansel 2004 ⁵⁴¹	Incorrect population
Harel 2014 ⁵⁴⁵	No relevant outcomes reported
Helvik 2013 ⁵⁶⁷	No relevant statistical outcomes reported
Hemmelgarn 2003 ⁵⁶⁹	Incorrect population
Hindmarsh 2014 ⁵⁸¹	No relevant statistical outcomes reported
Hiorth 2014 ⁵⁸²	No relevant outcomes reported
Hippisley-Cox 2013 ⁵⁸³	No relevant outcomes reported
Ho 2007 ⁵⁸⁶	Incorrect population
Ho 2014B ⁵⁸⁹	No relevant statistical outcomes reported
Hoogerdujin 2010 ⁶⁰⁰	No relevant outcomes reported
Hsiao 2015 ⁶⁰⁸	No relevant statistical outcomes reported
Huang 2014D ⁶¹⁰	No relevant statistical outcomes reported
Huntley 2012 ⁶¹⁴	Systematic review checked for references
Hutchings 2013 ⁶¹⁵	Protocol
Hutchinson 2013 ⁶¹⁶	No relevant statistical outcomes reported

Reference	Reason for exclusion
Hutchinson 2015 ⁶¹⁷	Incorrect population
Ingalzi 1997 ⁶²²	Tool not validated
Inoye 2003 ⁶²⁴	Incorrect population
Jang 2010 ⁶³¹	No relevant statistical outcomes reported
Jensen 2001 ⁶⁴⁰	No relevant outcomes reported
Jepsen 2008 ⁶⁴⁴	Incorrect population
Jepsen 2014A ⁶⁴⁵	Incorrect population
Jiang 2005 ⁶⁴⁹	Incorrect population
Jong 2002 ⁶⁵⁵	Incorrect population
Jonsen 2011 ⁶⁵⁸	Incorrect population
Jotheeswaran 2015 ⁶⁶¹	No relevant statistical outcomes reported
Jung 2014 ⁶⁶⁴	Incorrect population
Kan 2013 ⁶⁶⁸	Incorrect population
Kanis 1999 ⁶⁶⁹	No relevant outcomes reported
Kaplan 1974 ⁶⁷¹	Incorrect population
Khan 2010A ⁶⁹⁰	Incorrect population
Kieszak 1999 ⁶⁹²	No relevant statistical outcomes reported
Kil 2012 ⁶⁹³	Incorrect population
Kim 2014D ⁶⁹⁶	Acute care (post-operation)
Lee 2006 ⁷⁴⁷	Incorrect population
Lee 2015A ⁷⁴⁶	Literature review
Levine 2007 ⁷⁶⁰	Incorrect population
Levy 2015 ⁷⁶¹	Incorrect population
Low 2015 ⁷⁸¹	Incorrect population
Lu 2011 ⁷⁸³	Base model not validated
Luo 2015 ⁷⁹¹	No relevant outcomes reported
Manzano 2011 ⁸⁰⁸	No relevant statistical outcomes reported
Matsuzawa 2013 ⁸²⁶	Incorrect population
Matzen 2012 ⁸²⁸	Incorrect population
McGee 2008 ⁸³⁶	No relevant statistical outcomes reported
Menendez 2015B ⁸⁴⁵	Incorrect population
Metcalfe 2015 ⁸⁵¹	Incorrect population
Mosley 2009 ⁸⁸²	No relevant outcomes reported
Neuhaus 2013 ⁹⁰²	Incorrect population
O'Caoimh 2015 ⁹¹⁵	Incorrect population
O'Caoimh 2015A ⁹¹⁶	Incorrect population
Orueta 2013 ⁹³⁰	Incorrect study design
Pacala 1997 ⁹³⁶	Insufficient data
Parkerson 2001 ⁹⁴⁷	Incorrect population
Pedone 2016 ⁹⁵⁴	Incorrect population
Pijpers 2012 ⁹⁶⁹	Review checked for references
Pilotto 2010 ⁹⁷⁰	No relevant outcomes reported

Reference	Reason for exclusion
Pilotto 2012A ⁹⁷³	Incorrect population
Pilotto 2012B ⁹⁷⁴	Incorrect population
Pilotto 2013 ⁹⁷²	Incorrect population
Pilotto 2015 ⁹⁷⁶	Incorrect study design
Pilotto 2015B ⁹⁷⁵	Protocol
Polanczyk 1998 ⁹⁸³	Incorrect population
Porock 2005 ⁹⁸⁶	No relevant outcomes reported
Poses 1996 ⁹⁸⁷	Incorrect population
Putnam 2002 ⁹⁹³	Incorrect population
Quach 2009 ⁹⁹⁵	Acute care (ICU)
Quail 2011 ⁹⁹⁶	Incorrect population
Quan 2011 ⁹⁹⁷	Incorrect population
Radner 2015 ¹⁰⁰³	Incorrect population
Radovanovic 014 ¹⁰⁰⁴	Incorrect population
Ravindrarajah 2013 ¹⁰¹¹	Incorrect population
Rector 2006 ¹⁰¹²	Disease-specific tool
Ritt 2015 ¹⁰²³	No relevant outcomes reported
Rius 2008 ¹⁰²⁵	Incorrect population
Roberts 2012 ¹⁰²⁷	No relevant outcomes reported
Roberts 2015 ¹⁰²⁶	Incorrect population
Robey-Williams 2007 ¹⁰²⁹	No relevant outcomes reported
Rodriguez-Pascual 2012 ¹⁰³⁸	No relevant statistical outcomes reported
Romano 2000 ¹⁰⁴⁴	Incorrect population
Romero-Ortuno 2013 ¹⁰⁴⁵	Tool not validated
Royston 2004 ¹⁰⁴⁸	Incorrect population
Rozzini 2002 ¹⁰⁴⁹	No relevant statistical outcomes reported
Ruiz-Laiglesia 2014 ¹⁰⁵³	Incorrect population
Sanchis 2014 ¹⁰⁷⁴ anchis 2014	No relevant outcomes reported
Sabin 1999 ¹⁰⁵⁵	Acute care (cancer)
Sager 1996 ¹⁰⁵⁷	No relevant outcomes reported
Salvi 2008 ¹⁰⁶⁴	No relevant statistical outcomes reported
Sampalis 2009 ¹⁰⁶⁷	Incorrect population
Sampson 2012 ¹⁰⁶⁸	Incorrect population
Sanabria 2008 ¹⁰⁶⁹	Acute care (cancer)
Sanchis 2011 ¹⁰⁷⁵	Incorrect population
Sanchis 2014 ¹⁰⁷⁴	No relevant outcomes reported
Schneeweiss 2000 ¹⁰⁸⁶	Review
Schneeweiss 2003 ¹⁰⁸⁸	Incorrect population
Schneeweiss 2004 ¹⁰⁸⁹	Base model not validated
Schonberg 2009 ¹⁰⁹²	Incorrect population
Schoufour 2015A ¹⁰⁹⁴	Incorrect population
Senni 2006 ¹¹⁰⁵	Incorrect population

Reference	Reason for exclusion
Senni 2013 ¹¹⁰⁴	Incorrect population
Sessler 2010 ¹¹⁰⁶	Incorrect population
Shamliyan 2013 ¹¹¹⁰	Systematic review checked for references
Shelton 2000 ¹¹¹²	Incorrect population
Shih 2015 ¹¹¹⁷	Model not validated
Sidorov 2002 ¹¹²⁰	No relevant outcomes reported
Simon 2012A ¹¹²³	Acute care (cancer)
Sirola 2011 ¹¹²⁵	Incorrect population
Soares 2011 ¹¹³²	No relevant outcomes reported
Solberg 2007 ¹¹³³	Incorrect population
Solomon 2011 ¹¹³⁴	No relevant outcomes reported
Soong 2015 ¹¹³⁷	No relevant outcomes reported
Soubeyran 2012 ¹¹³⁹	Acute care (cancer)
Southerland 2014 ¹¹⁴⁰	Incorrect population
Stausberg 2015 ¹¹⁴⁶	Incorrect population
Steiner 1997 ¹¹⁴⁷	No relevant outcomes reported
Stukenborg 2001 ¹¹⁵⁵	Incorrect population
Sundarajan 2007 ¹¹⁵⁸	Incorrect population
Susser 2008 ¹¹⁵⁹	No relevant outcomes reported
Tal 2011 ¹¹⁶⁷	No relevant statistical outcomes reported
Tan 2013 ¹¹⁶⁸	Incorrect population
Tang 2015 ¹¹⁷¹	Incorrect population
Tapper 2015A ¹¹⁷⁶	Disease-specific tool
Tarazona-Santalbina 2012 ¹¹⁷⁷	No relevant statistical outcomes reported
Tate 2014 ¹¹⁷⁸	Incorrect population
Teno 2000 ¹¹⁸¹	Incorrect population
Tessier 2008 ¹¹⁸²	No relevant outcomes reported
Testa 2009 ¹¹⁸³	Incorrect population
Tetsche 2008 ¹¹⁸⁴	Acute care (cancer)
Theou 2013 ¹¹⁸⁵	Incorrect population
Thompson 2010 ¹¹⁸⁶	Acute care (trauma)
Thompson 2013 ¹¹⁸⁷	Incorrect population
Tierney 2004 ¹¹⁹²	No relevant statistical outcomes reported
Tierney 2007 ¹¹⁹³	No relevant outcomes reported
Tilling 2001 ¹¹⁹⁴	No relevant outcomes reported
Ting 2014 ¹¹⁹⁶	Acute care (trauma)
Tobacman 1994 ¹¹⁹⁹	Review
Torres 2004 ¹²⁰⁴	No relevant statistical outcomes reported
Torres 2006 ¹²⁰³	Base model not validated
Toson 2015 ¹²⁰⁵	Tool not validated
Tsui 2015 ¹²¹⁶	No relevant outcomes reported

Reference	Reason for exclusion
Van Doorn 2001 ¹²³⁰	Incorrect population
Van Kempen 2015 ¹²³⁴	Incorrect population
Van Manen 2002 ¹²³⁵	Incorrect population
Van Walraven 2014 ¹²³⁶	Incorrect population
Van Walraven 2015 ¹²³⁶	Incorrect population
Velghe 2014 ¹²³⁹	Acute care (cancer)
Verdalles 2010 ¹²⁴³	Incorrect population
Vidan 2014 ¹²⁴⁶	No relevant statistical outcomes reported
Vischer 2012 ¹²⁵¹	No relevant statistical outcomes reported
Visser 2004 ¹²⁵²	No relevant statistical outcomes reported
Vitry 2009 ¹²⁵³	No relevant outcomes reported
Vojta 2001 ¹²⁵⁷	No relevant outcomes reported
Volpato 2007 ¹²⁵⁹	No relevant outcomes reported
Von Korff 1992 ¹²⁶²	Incorrect population
Wagner 2006 ¹²⁶⁵	No relevant outcomes reported
Wagner 2011 ¹²⁶⁶	Incorrect population
Walker 2005 ¹²⁷⁰	No relevant statistical outcomes reported
Wallace 2013 ¹²⁷¹	No relevant outcomes reported
Wallace 2014 ¹²⁷²	No relevant outcomes reported
Wallis 2015 ¹²⁷³	No relevant outcomes reported
Walter 2001 ¹²⁷⁶	Acute care (cancer)
Walter 2001A ¹²⁷⁵	Incorrect population
Wang 2013 ¹²⁷⁹	Incorrect population
Wang 2014A ¹²⁷⁷	Incorrect population
Watkin 2012 ¹²⁸⁸	Incorrect population
Weiss 2015 ¹²⁹⁶	Incorrect population
Wong 2011A ¹³¹⁶	No relevant outcomes reported
Wong 2014 ¹³¹⁵	No relevant outcomes reported
Woo 2012 ¹³¹⁷	Incorrect population
Wu 2013 ¹³²²	Incorrect population
Yan 2005 ¹³²⁴	Base model not validated
Yang 2014G ¹³²⁵	Incorrect population
Yourman 2012 ¹³²⁹	Systematic review checked for references
Yurkovich 2015 ¹³³²	Systematic review checked for references
Zampieri 2014 ¹³³³	Acute care (ICU)
Zekry 2009 ¹³³⁶	Tool not externally validated
Zekry 2010 ¹³⁴⁰	No relevant statistical outcomes reported
Zekry 2010A ¹³⁴¹	No relevant statistical outcomes reported
Zekry 2012 ¹³³⁵	No relevant outcomes reported
Zekry 2012A ¹³³⁸	Tool not externally validated
Zekry 2013 ¹³³⁷	No relevant outcomes reported
Zeng 2015 ¹³⁴³	Acute care (ICU)
Zhu 2008 ¹³⁴⁶	Base model not validated

Reference	Reason for exclusion
Zoghbi 2004 ¹³⁴⁷	Incorrect population

L.2.5 Polypharmacy: unplanned hospital admissions

Table 258: Studies excluded from the clinical review

Reference	Reason for exclusion
Ahmad 2005 ¹⁴	No relevant outcomes reported
Ahmed 2014A ¹⁵	No relevant outcomes reported
Ahto 2007 ¹⁷	Adjusted data only
Al Hamid 2014 ²²	Systematic review - checked for references
Al Snih 2006 ²³	Adjusted data only
Albert 2010 ²⁴	No relevant outcomes reported
Alexopoulou 2008 ²⁸	No relevant outcomes reported
Alhawassi 2014 ³⁰	Systematic review - checked for references
Aljishi 2014 ³¹	Incorrect population
Appleton 2014 ⁶⁰	Incorrect population
Baandrup 2010 ⁷⁸	No relevant risk factor
Beer 2011 ¹¹¹	Adjusted data only
Bharucha 2004 ¹²⁹	Adjusted data only
Blix 2004 ¹⁴⁹	Not in English
Borenstein 2013 ¹⁶¹	Incorrect population
Buajordet 2001 ¹⁹⁹	No relevant outcomes reported
Campbell 2004 ²¹³	Systematic review - checked for references
Castro 2014 ²²⁶	No relevant outcomes reported
Chang 2005 ²³⁷	No relevant outcomes reported
Chang 2012A ²³⁹	No relevant outcomes reported
Chen 2012C ²⁵¹	Incorrect population
Chen 2014F ²⁵²	No relevant outcomes reported
Chen 2015C ²⁵³	No relevant outcomes reported
Cherubini 2012 ²⁵⁶	No relevant outcomes reported
Chrischilles 2007 ²⁶⁵	No relevant outcomes reported
Dale 2001 ³²¹	No relevant outcomes reported
De Buysier 2014 ³³²	Outcome <1 year
Dequito 2011 ³⁴⁶	No relevant outcomes reported
Devi 2012 ³⁴⁹	No relevant outcomes reported
Díez-Manglano 2015 ³⁵⁸	No relevant outcomes reported
Doran 2009 ³⁶⁸	Adjusted data only
Erceg 2013 ⁴⁰⁵	Incorrect study design
Espino 2006 ⁴⁰⁸	No relevant outcomes reported
Evans 2010 ⁴¹³	No relevant outcomes reported
Evans 2011 ⁴¹⁴	No relevant outcomes reported
Field 2001 ⁴²³	No relevant outcomes reported
Field 2004 ⁴²⁴	No relevant outcomes reported
Forster 2005 ⁴³³	No relevant outcomes reported

Reference	Reason for exclusion
Franic 2006 ⁴⁴⁴	No relevant risk factor
Fried 2014 ⁴⁵⁵	Systematic review – checked for references
Gandhi 2000 ⁴⁶⁸	No relevant outcomes reported
Garcia-Ptacek 2014 ⁴⁷⁰	Adjusted data only
Giuli 2014 ⁴⁹²	Incorrect study design
Glynn 2001 ⁴⁹³	No relevant outcomes reported
Gnjidic 2012 ⁴⁹⁴	No relevant outcomes reported
Gomez 2015 ⁵⁰⁰	No relevant outcomes reported
Green 2007 ⁵⁰⁸	No relevant outcomes reported
Hafner 2002 ⁵³⁰	No relevant outcomes reported
Haile 2013 ⁵³¹	No relevant outcomes reported
Hajjar 2007 ⁵³²	Literature review
Hak 2001 ⁵³⁴	Incorrect population
Hamilton 2011 ⁵³⁹	No relevant outcomes reported
Hanlon 2006 ⁵⁴⁰	No relevant outcomes reported
Heininger-Rothbucher 2001 ⁵⁶²	No relevant outcomes reported
Helvik 2010 ⁵⁶⁸	Incorrect study design
Holland 2000 ⁵⁹⁶	Not relevant
Iwata 2006 ⁶²⁸	No relevant outcomes reported
Janzen 2013 ⁶³⁷	No relevant outcomes reported
Jensen 2001 ⁶⁴⁰	No relevant risk factor reported
Jorgensen 2001 ⁶⁶⁰	Incorrect study design
Jyrkka 2009 ⁶⁶⁷	No relevant outcomes reported
Kannegaard 2010 ⁶⁷⁰	Incorrect population
Kaplan 2001A ⁶⁷²	No relevant outcomes reported
Kohler 2015 ⁷⁰⁸	No relevant outcomes reported
Kongkaew 2013 ⁷⁰⁹	Adjusted data only
Krause 2007 ⁷¹²	No relevant outcomes reported
Lachs 2002 ⁷²⁵	Adjusted data only
Lattazio 2012A ⁷⁴¹	No relevant outcomes reported
Leendertse 2008 ⁷⁵¹	Incorrect population
Leung 2013 ⁷⁵⁹	No relevant outcomes reported
Liao 2013 ⁷⁶⁶	No relevant outcomes reported
Lifshitz 2012 ⁷⁶⁸	No relevant outcomes reported
Lima-Costa 2011 ⁷⁷¹ ;	Adjusted data only
Luppa 2010 ⁷⁹³	Systematic review – checked for references
Macedo 2011 ⁷⁹⁶	No relevant outcomes reported
Maciejewski 2014 ⁷⁹⁷	No relevant risk factor
Maggiore 2014 ⁸⁰⁰	Adjusted data only
Malhorta 2001 ⁸⁰²	No relevant risk factor
Mandavi 2012 ⁸⁰³	No relevant outcomes reported
Mannesse 2000 ⁸⁰⁶	Incorrect study design
Mansur 2008 ⁸⁰⁷	No relevant risk factor

Reference	Reason for exclusion
Marcum 2012A ⁸⁰⁹	No relevant outcomes reported
Marinella 2000 ⁸¹¹	No relevant outcomes reported
Marusic 2014 ⁸²⁰	No relevant outcomes reported
Matthew 2012 ⁸²⁴	No relevant outcomes reported
Md Yusof 2010 ⁸⁴²	No relevant outcomes reported
Mercier 2010 ⁸⁵⁰	No relevant risk factor
Modi 2005 ⁸⁶⁸	No relevant risk factor
Morandi 2013 ⁸⁷⁶	Adjusted data only
Nguyen 2006 ⁹⁰⁴	No relevant outcomes reported
Nishtala 2014 ⁹⁰⁷	Incorrect study design
Nivya 2015 ⁹⁰⁸	Systematic review – checked for references
Nobili 2011B ⁹⁰⁹	No relevant outcomes reported
O'Connor 2012 ⁹¹⁷	No relevant outcomes reported
Obreli Neto 2012 ⁹²¹	No relevant outcomes reported
Olesen 2014C ⁹²³	Incorrect study design
Onder 2002 ⁹²⁶	Incorrect study design
Onder 2013 ⁹²⁵	No relevant outcomes reported
Oza 2014 ⁹³⁵	No relevant outcomes reported
Palacios-Cena 2013 ⁹⁴¹	No relevant risk factor
Pardo Cabello 2009 ⁹⁴²	No relevant outcomes reported
Passarelli 2005 ⁹⁴⁸	No relevant outcomes reported
Patel 2012 ⁹⁴⁹	Adjusted data only
Payne 2009 ⁹⁵¹	No relevant risk factor
Payne 2014 ⁹⁵²	Incorrect population
Perkins 2004 ⁹⁵⁷	No relevant outcomes reported
Preyde 2011 ⁹⁹²	Systematic review – checked for references
Queneau 2007 ⁹⁹⁸	No relevant outcomes reported
Radhakrishnan 2013 ¹⁰⁰¹	Incorrect study design
Richardson 2011 ¹⁰¹⁸	No relevant outcomes reported
Richardson 2014 ¹⁰¹⁸	No relevant outcomes reported
Romana 2012 ¹⁰⁴³	No relevant outcomes reported
Ruiz 2008 ¹⁰⁵²	No relevant outcomes reported
Salvi 2012A ¹⁰⁶⁶	Literature review
Sanchez Munoz-Torrero 2010 ¹⁰⁷²	No relevant outcomes reported
Sato 2013 ¹⁰⁷⁸	No relevant outcomes reported
Schuler 2008 ¹⁰⁹⁷	No relevant outcomes reported
Shah 2013a ¹¹⁰⁸	Adjusted data only
Sharifaskari 2005 ¹⁰⁵⁸	Incorrect population
Silva 2009 ¹¹²¹	No relevant outcomes reported
Snyder 2014 ¹¹³¹	No relevant outcomes reported
Szeto 2006 ¹¹⁶²	Incorrect population
Tangherlini 2010 ¹¹⁷²	No relevant outcomes reported

Reference	Reason for exclusion
Tangiisuran 2012 ¹¹⁷³	No relevant outcomes reported
Uggerby 2011 ¹²¹⁹	No relevant risk factor
Urbina 2015 ¹²²²	No relevant outcomes reported
Vaciuniene 2010 ¹²²⁵	Incorrect population
Van den Bemt 2000 ¹²²⁷	No relevant outcomes reported
Venkat 2011 ¹²⁴¹	Adjusted data only
Vetrano 2014 ¹²⁴⁵	No relevant outcomes reported
Voisin 2010 ¹²⁵⁶	No relevant risk factor
Volk 2012 ¹²⁵⁸	Incorrect population
Wang 2015B ¹²⁸⁰	No relevant outcomes reported
Wimmer 2014 ¹³¹²	No relevant outcomes reported
Wimmer 2014A ¹³¹¹	Risk tool
Wu 2012A ¹³²¹	No relevant outcomes reported
Zed 2008 ¹³³⁴	Incorrect population
Zopf 2008 ¹³⁵⁰	No relevant outcomes reported
Zopf 2008A ¹³⁵¹	No relevant outcomes reported
Zuckerman 2006 ¹³⁵²	No relevant outcomes reported

L.2.6 Polypharmacy: health-related quality of life

Table 259: Studies excluded from the clinical review

Reference	Reason for exclusion
Ahmad 2005 ¹⁴	No relevant outcomes reported
Ahmed 2014A ¹⁵	No relevant outcomes reported
Ahto 2007 ¹⁷	Adjusted data only
Al Hamid 2014 ²²	Systematic review - checked for references
Al Snih 2006 ²³	Adjusted data only
Albert 2010 ²⁴	No relevant outcomes reported
Alexopoulou 2008 ²⁸	No relevant outcomes reported
Alhawassi 2014 ³⁰	Systematic review - checked for references
Aljishi 2014 ³¹	Incorrect population
Appleton 2014 ⁶⁰	Incorrect population
Baandrup 2010 ⁷⁸	No relevant risk factor
Beer 2011 ¹¹¹	Adjusted data only
Bharucha 2004 ¹²⁹	Adjusted data only
Blix 2004 ¹⁴⁹	Not in English
Borenstein 2013 ¹⁶¹	Incorrect population
Buajordet 2001 ¹⁹⁹	No relevant outcomes reported
Campbell 2004 ²¹³	Systematic review - checked for references
Castro 2014 ²²⁶	No relevant outcomes reported
Chang 2005 ²³⁷	No relevant outcomes reported
Chang 2012A ²³⁹	No relevant outcomes reported
Chen 2012C ²⁵¹	Incorrect population
Chen 2014F ²⁵²	No relevant outcomes reported

Reference	Reason for exclusion
Chen 2015 ^{C253}	No relevant outcomes reported
Cherubini 2012 ²⁵⁶	No relevant outcomes reported
Chrischilles 2007 ²⁶⁵	No relevant outcomes reported
Dale 2001 ³²¹	No relevant outcomes reported
De Buyser 2014 ³³²	Outcome <1 year
Dequito 2011 ³⁴⁶	No relevant outcomes reported
Devi 2012 ³⁴⁹	No relevant outcomes reported
Díez-Manglano 2015 ³⁵⁸	No relevant outcomes reported
Doran 2009 ³⁶⁸	Adjusted data only
Erceg 2013 ⁴⁰⁵	Incorrect study design
Espino 2006 ⁴⁰⁸	No relevant outcomes reported
Evans 2010 ⁴¹³	No relevant outcomes reported
Evans 2011 ⁴¹⁴	No relevant outcomes reported
Field 2001 ⁴²³	No relevant outcomes reported
Field 2004 ⁴²⁴	No relevant outcomes reported
Forster 2005 ⁴³³	No relevant outcomes reported
Franic 2006 ⁴⁴⁴	No relevant risk factor
Fried 2014 ⁴⁵⁵	Systematic review – checked for references
Gandhi 2000 ⁴⁶⁸	No relevant outcomes reported
Garcia-Ptacek 2014 ⁴⁷⁰	Adjusted data only
Giuli 2014 ⁴⁹²	Incorrect study design
Glynn 2001 ⁴⁹³	No relevant outcomes reported
Gnjidic 2012 ⁴⁹⁴	No relevant outcomes reported
Gomez 2015 ⁵⁰⁰	No relevant outcomes reported
Green 2007 ⁵⁰⁸	No relevant outcomes reported
Hafner 2002 ⁵³⁰	No relevant outcomes reported
Haile 2013 ⁵³¹	No relevant outcomes reported
Hajjar 2007 ⁵³²	Literature review
Hak 2001 ⁵³⁴	Incorrect population
Hamilton 2011 ⁵³⁹	No relevant outcomes reported
Hanlon 2006 ⁵⁴⁰	No relevant outcomes reported
Heininger-Rothbucher 2001 ⁵⁶²	No relevant outcomes reported
Helvik 2010 ⁵⁶⁸	Incorrect study design
Holland 2000 ⁵⁹⁶	Not relevant
Iwata 2006 ⁶²⁸	No relevant outcomes reported
Janzen 2013 ⁶³⁷	No relevant outcomes reported
Jensen 2001 ⁶⁴⁰	No relevant risk factor reported
Jorgensen 2001 ⁶⁶⁰	Incorrect study design
Jyrkka 2009 ⁶⁶⁷	No relevant outcomes reported
Kannegaard 2010 ⁶⁷⁰	Incorrect population
Kaplan 2001A ⁶⁷²	No relevant outcomes reported
Kohler 2015 ⁷⁰⁸	No relevant outcomes reported
Kongkaew 2013 ⁷⁰⁹	Adjusted data only

Reference	Reason for exclusion
Krause 2007 ⁷¹²	No relevant outcomes reported
Lachs 2002 ⁷²⁵	Adjusted data only
Lattazio 2012A ⁷⁴¹	No relevant outcomes reported
Leendertse 2008 ⁷⁵¹	Incorrect population
Leung 2013 ⁷⁵⁹	No relevant outcomes reported
Liao 2013 ⁷⁶⁶	No relevant outcomes reported
Lifshitz 2012 ⁷⁶⁸	No relevant outcomes reported
Lima-Costa 2011 ⁷⁷¹ ;	Adjusted data only
Luppa 2010 ⁷⁹³	Systematic review – checked for references
Macedo 2011 ⁷⁹⁶	No relevant outcomes reported
Maciejewski 2014 ⁷⁹⁷	No relevant risk factor
Maggiore 2014 ⁸⁰⁰	Adjusted data only
Malhorta 2001 ⁸⁰²	No relevant risk factor
Mandavi 2012 ⁸⁰³	No relevant outcomes reported
Mannesse 2000 ⁸⁰⁶	Incorrect study design
Mansur 2008 ⁸⁰⁷	No relevant risk factor
Marcum 2012A ⁸⁰⁹	No relevant outcomes reported
Marinella 2000 ⁸¹¹	No relevant outcomes reported
Marusic 2014 ⁸²⁰	No relevant outcomes reported
Matthew 2012 ⁸²⁴	No relevant outcomes reported
Md Yusof 2010 ⁸⁴²	No relevant outcomes reported
Mercier 2010 ⁸⁵⁰	No relevant risk factor
Modi 2005 ⁸⁶⁸	No relevant risk factor
Morandi 2013 ⁸⁷⁶	Adjusted data only
Nguyen 2006 ⁹⁰⁴	No relevant outcomes reported
Nishtala 2014 ⁹⁰⁷	Incorrect study design
Nivya 2015 ⁹⁰⁸	Systematic review – checked for references
Nobili 2011B ⁹⁰⁹	No relevant outcomes reported
O'Connor 2012 ⁹¹⁷	No relevant outcomes reported
Obreli Neto 2012 ⁹²¹	No relevant outcomes reported
Olesen 2014C ⁹²³	Incorrect study design
Onder 2002 ⁹²⁶	Incorrect study design
Onder 2013 ⁹²⁵	No relevant outcomes reported
Oza 2014 ⁹³⁵	No relevant outcomes reported
Palacios-Cena 2013 ⁹⁴¹	No relevant risk factor
Pardo Cabello 2009 ⁹⁴²	No relevant outcomes reported
Passarelli 2005 ⁹⁴⁸	No relevant outcomes reported
Patel 2012 ⁹⁴⁹	Adjusted data only
Payne 2009 ⁹⁵¹	No relevant risk factor
Payne 2014 ⁹⁵²	Incorrect population
Perkins 2004 ⁹⁵⁷	No relevant outcomes reported
Pozzi 2010 ⁹⁸⁹	No relevant outcomes reported
Preyde 2011 ⁹⁹²	Systematic review – checked for references

Reference	Reason for exclusion
Queneau 2007 ⁹⁹⁸	No relevant outcomes reported
Radhakrishnan 2013 ¹⁰⁰¹	Incorrect study design
Richardson 2011 ¹⁰¹⁸	No relevant outcomes reported
Richardson 2014 ¹⁰¹⁸	No relevant outcomes reported
Romana 2012 ¹⁰⁴³	No relevant outcomes reported
Ruiz 2008 ¹⁰⁵²	No relevant outcomes reported
Salvi 2012A ¹⁰⁶⁶	Literature review
Sanchez Munoz-Torrero 2010 ¹⁰⁷²	No relevant outcomes reported
Sato 2013 ¹⁰⁷⁸	No relevant outcomes reported
Schuler 2008 ¹⁰⁹⁷	No relevant outcomes reported
Shah 2013a ¹¹⁰⁸	Adjusted data only
Sharifaskari 2005 ¹⁰⁵⁸	Incorrect population
Silva 2009 ¹¹²¹	No relevant outcomes reported
Snyder 2014 ¹¹³¹	No relevant outcomes reported
Spector 2013 ¹¹⁴¹	No relevant outcomes reported
Szeto 2006 ¹¹⁶²	Incorrect population
Tangherlini 2010 ¹¹⁷²	No relevant outcomes reported
Tangiisuran 2012 ¹¹⁷³	No relevant outcomes reported
Uggerby 2011 ¹²¹⁹	No relevant risk factor
Urbina 2015 ¹²²²	No relevant outcomes reported
Vaciuniene 2010 ¹²²⁵	Incorrect population
Van den Bemt 2000 ¹²²⁷	No relevant outcomes reported
Venkat 2011 ¹²⁴¹	Adjusted data only
Vetrano 2014 ¹²⁴⁵	No relevant outcomes reported
Voisin 2010 ¹²⁵⁶	No relevant risk factor
Volk 2012 ¹²⁵⁸	Incorrect population
Wang 2015B ¹²⁸⁰	No relevant outcomes reported
Wimmer 2014 ¹³¹²	No relevant outcomes reported
Wimmer 2014A ¹³¹¹	Risk tool
Wu 2012A ¹³²¹	No relevant outcomes reported
Zed 2008 ¹³³⁴	Incorrect population
Zopf 2008 ¹³⁵⁰	No relevant outcomes reported
Zopf 2008A ¹³⁵¹	No relevant outcomes reported
Zuckerman 2006 ¹³⁵²	No relevant outcomes reported

L.2.7 Polypharmacy: admission to care facilities

Table 260: Studies excluded from the clinical review

Reference	Reason for exclusion
Ahmad 2005 ¹⁴	No relevant outcomes reported
Ahmed 2014A ¹⁵	No relevant outcomes reported
Ahto 2007 ¹⁷	Adjusted data only
Al Hamid 2014 ²²	Systematic review - checked for references

Reference	Reason for exclusion
Al Snih 2006 ²³	Adjusted data only
Albert 2010 ²⁴	No relevant outcomes reported
Alexopoulou 2008 ²⁸	No relevant outcomes reported
Alhawassi 2014 ³⁰	Systematic review - checked for references
Aljishi 2014 ³¹	Incorrect population
Appleton 2014 ⁶⁰	Incorrect population
Baandrup 2010 ⁷⁸	No relevant risk factor
Beer 2011 ¹¹¹	Adjusted data only
Bharucha 2004 ¹²⁹	Adjusted data only
Blix 2004 ¹⁴⁹	Not in English
Borenstein 2013 ¹⁶¹	Incorrect population
Buajordet 2001 ¹⁹⁹	No relevant outcomes reported
Campbell 2004 ²¹³	Systematic review - checked for references
Castro 2014 ²²⁶	No relevant outcomes reported
Chang 2005 ²³⁷	No relevant outcomes reported
Chang 2012A ²³⁹	No relevant outcomes reported
Chen 2012C ²⁵¹	Incorrect population
Chen 2014F ²⁵²	No relevant outcomes reported
Chen 2015C ²⁵³	No relevant outcomes reported
Cherubini 2012 ²⁵⁶	No relevant outcomes reported
Chrischilles 2007 ²⁶⁵	No relevant outcomes reported
Dale 2001 ³²¹	No relevant outcomes reported
De Buyser 2014 ³³²	Outcome <1 year
Dequito 2011 ³⁴⁶	No relevant outcomes reported
Devi 2012 ³⁴⁹	No relevant outcomes reported
Díez-Manglano 2015 ³⁵⁸	No relevant outcomes reported
Doran 2009 ³⁶⁸	Adjusted data only
Erceg 2013 ⁴⁰⁵	Incorrect study design
Espino 2006 ⁴⁰⁸	No relevant outcomes reported
Evans 2010 ⁴¹³	No relevant outcomes reported
Evans 2011 ⁴¹⁴	No relevant outcomes reported
Field 2001 ⁴²³	No relevant outcomes reported
Field 2004 ⁴²⁴	No relevant outcomes reported
Forster 2005 ⁴³³	No relevant outcomes reported
Franic 2006 ⁴⁴⁴	No relevant risk factor
Fried 2014 ⁴⁵⁵	Systematic review – checked for references
Gandhi 2000 ⁴⁶⁸	No relevant outcomes reported
Garcia-Ptacek 2014 ⁴⁷⁰	Adjusted data only
Giuli 2014 ⁴⁹²	Incorrect study design
Glynn 2001 ⁴⁹³	No relevant outcomes reported
Gnjidic 2012 ⁴⁹⁴	No relevant outcomes reported
Gomez 2015 ⁵⁰⁰	No relevant outcomes reported
Green 2007 ⁵⁰⁸	No relevant outcomes reported

Reference	Reason for exclusion
Hafner 2002 ⁵³⁰	No relevant outcomes reported
Haile 2013 ⁵³¹	No relevant outcomes reported
Hajjar 2007 ⁵³²	Literature review
Hak 2001 ⁵³⁴	Incorrect population
Hamilton 2011 ⁵³⁹	No relevant outcomes reported
Hanlon 2006 ⁵⁴⁰	No relevant outcomes reported
Heininger-Rothbucher 2001 ⁵⁶²	No relevant outcomes reported
Helvik 2010 ⁵⁶⁸	Incorrect study design
Holland 2000 ⁵⁹⁶	Not relevant
Iwata 2006 ⁶²⁸	No relevant outcomes reported
Janzen 2013 ⁶³⁷	No relevant outcomes reported
Jensen 2001 ⁶⁴⁰	No relevant risk factor reported
Jorgensen 2001 ⁶⁶⁰	Incorrect study design
Jyrkka 2009 ⁶⁶⁷	No relevant outcomes reported
Kannegaard 2010 ⁶⁷⁰	Incorrect population
Kaplan 2001A ⁶⁷²	No relevant outcomes reported
Kohler 2015 ⁷⁰⁸	No relevant outcomes reported
Kongkaew 2013 ⁷⁰⁹	Adjusted data only
Krause 2007 ⁷¹²	No relevant outcomes reported
Lachs 2002 ⁷²⁵	Adjusted data only
Lattazio 2012A ⁷⁴¹	No relevant outcomes reported
Leendertse 2008 ⁷⁵¹	Incorrect population
Leung 2013 ⁷⁵⁹	No relevant outcomes reported
Liao 2013 ⁷⁶⁶	No relevant outcomes reported
Lifshitz 2012 ⁷⁶⁸	No relevant outcomes reported
Lima-Costa 2011 ⁷⁷¹ ;	Adjusted data only
Luppa 2010 ⁷⁹³	Systematic review – checked for references
Macedo 2011 ⁷⁹⁶	No relevant outcomes reported
Maciejewski 2014 ⁷⁹⁷	No relevant risk factor
Maggiore 2014 ⁸⁰⁰	Adjusted data only
Malhorta 2001 ⁸⁰²	No relevant risk factor
Mandavi 2012 ⁸⁰³	No relevant outcomes reported
Mannesse 2000 ⁸⁰⁶	Incorrect study design
Mansur 2008 ⁸⁰⁷	No relevant risk factor
Marcum 2012A ⁸⁰⁹	No relevant outcomes reported
Marinella 2000 ⁸¹¹	No relevant outcomes reported
Marusic 2014 ⁸²⁰	No relevant outcomes reported
Matthew 2012 ⁸²⁴	No relevant outcomes reported
Md Yusof 2010 ⁸⁴²	No relevant outcomes reported
Mercier 2010 ⁸⁵⁰	No relevant risk factor
Modi 2005 ⁸⁶⁸	No relevant risk factor
Morandi 2013 ⁸⁷⁶	Adjusted data only
Nguyen 2006 ⁹⁰⁴	No relevant outcomes reported

Reference	Reason for exclusion
Nishtala 2014 ⁹⁰⁷	Incorrect study design
Nivya 2015 ⁹⁰⁸	Systematic review – checked for references
Nobili 2011B ⁹⁰⁹	No relevant outcomes reported
O'Connor 2012 ⁹¹⁷	No relevant outcomes reported
Obreli Neto 2012 ⁹²¹	No relevant outcomes reported
Olesen 2014C ⁹²³	Incorrect study design
Onder 2002 ⁹²⁶	Incorrect study design
Onder 2013 ⁹²⁵	No relevant outcomes reported
Oza 2014 ⁹³⁵	No relevant outcomes reported
Palacios-Cena 2013 ⁹⁴¹	No relevant risk factor
Pardo Cabello 2009 ⁹⁴²	No relevant outcomes reported
Passarelli 2005 ⁹⁴⁸	No relevant outcomes reported
Patel 2012 ⁹⁴⁹	Adjusted data only
Payne 2009 ⁹⁵¹	No relevant risk factor
Payne 2014 ⁹⁵²	Incorrect population
Perkins 2004 ⁹⁵⁷	No relevant outcomes reported
Pozzi 2010 ⁹⁸⁹	No relevant outcomes reported
Preyde 2011 ⁹⁹²	Systematic review – checked for references
Queneau 2007 ⁹⁹⁸	No relevant outcomes reported
Radhakrishnan 2013 ¹⁰⁰¹	Incorrect study design
Richardson 2011 ¹⁰¹⁸	No relevant outcomes reported
Richardson 2014 ¹⁰¹⁸	No relevant outcomes reported
Romana 2012 ¹⁰⁴³	No relevant outcomes reported
Ruiz 2008 ¹⁰⁵²	No relevant outcomes reported
Salvi 2012A ¹⁰⁶⁶	Literature review
Sanchez Munoz-Torrero 2010 ¹⁰⁷²	No relevant outcomes reported
Sato 2013 ¹⁰⁷⁸	No relevant outcomes reported
Schuler 2008 ¹⁰⁹⁷	No relevant outcomes reported
Shah 2013a ¹¹⁰⁸	Adjusted data only
Sharifaskari 2005 ¹⁰⁵⁸	Incorrect population
Silva 2009 ¹¹²¹	No relevant outcomes reported
Snyder 2014 ¹¹³¹	No relevant outcomes reported
Spector 2013 ¹¹⁴¹	No relevant outcomes reported
Szeto 2006 ¹¹⁶²	Incorrect population
Tangherlini 2010 ¹¹⁷²	No relevant outcomes reported
Tangiisuran 2012 ¹¹⁷³	No relevant outcomes reported
Uggerby 2011 ¹²¹⁹	No relevant risk factor
Urbina 2015 ¹²²²	No relevant outcomes reported
Vaciuniene 2010 ¹²²⁵	Incorrect population
Van den Bemt 2000 ¹²²⁷	No relevant outcomes reported
Venkat 2011 ¹²⁴¹	Adjusted data only
Vetrano 2014 ¹²⁴⁵	No relevant outcomes reported

Reference	Reason for exclusion
Voisin 2010 ¹²⁵⁶	No relevant risk factor
Volk 2012 ¹²⁵⁸	Incorrect population
Wang 2015B ¹²⁸⁰	No relevant outcomes reported
Wimmer 2014 ¹³¹²	No relevant outcomes reported
Wimmer 2014A ¹³¹¹	Risk tool
Wu 2012A ¹³²¹	No relevant outcomes reported
Zed 2008 ¹³³⁴	Incorrect population
Zopf 2008 ¹³⁵⁰	No relevant outcomes reported
Zopf 2008A ¹³⁵¹	No relevant outcomes reported

L.2.8 Polypharmacy: mortality

Table 261: Studies excluded from the clinical review

Reference	Reason for exclusion
Ahmed 2014A ¹⁵	No relevant outcomes reported
Ahto 2007 ¹⁷	Adjusted data only
Al Hamid 2014 ²²	Systematic review - checked for references
Al Snih 2006 ²³	Adjusted data only
Albert 2010 ²⁴	No relevant outcomes reported
Alexopoulou 2008 ²⁸	No relevant outcomes reported
Alhawassi 2014 ³⁰	Systematic review - checked for references
Aljishi 2014 ³¹	Incorrect population
Appleton 2014 ⁶⁰	Incorrect population
Baandrup 2010 ⁷⁸	No relevant risk factor
Beer 2011 ¹¹¹	Adjusted data only
Bharucha 2004 ¹²⁹	Adjusted data only
Blix 2004 ¹⁴⁹	Not in English
Borenstein 2013 ¹⁶¹	Incorrect population
Buajordet 2001 ¹⁹⁹	No relevant outcomes reported
Campbell 2004 ²¹³	Systematic review - checked for references
Castro 2014 ²²⁶	No relevant outcomes reported
Chang 2005 ²³⁷	No relevant outcomes reported
Chang 2012A ²³⁹	No relevant outcomes reported
Chen 2012C ²⁵¹	Incorrect population
Chen 2014F ²⁵²	No relevant outcomes reported
Chen 2015C ²⁵³	No relevant outcomes reported
Cherubini 2012 ²⁵⁶	No relevant outcomes reported
Chrischilles 2007 ²⁶⁵	No relevant outcomes reported
Dale 2001 ³²¹	No relevant outcomes reported
De Buyser 2014 ³³²	Outcome <1 year
Dequito 2011 ³⁴⁶	No relevant outcomes reported
Devi 2012 ³⁴⁹	No relevant outcomes reported

Reference	Reason for exclusion
Díez-Manglano 2015 ³⁵⁸	No relevant outcomes reported
Doran 2009 ³⁶⁸	Adjusted data only
Erceg 2013 ⁴⁰⁵	Incorrect study design
Evans 2010 ⁴¹³	No relevant outcomes reported
Evans 2011 ⁴¹⁴	No relevant outcomes reported
Field 2001 ⁴²³	No relevant outcomes reported
Field 2004 ⁴²⁴	No relevant outcomes reported
Forster 2005 ⁴³³	No relevant outcomes reported
Franic 2006 ⁴⁴⁴	No relevant risk factor
Fried 2014 ⁴⁵⁵	Systematic review – checked for references
Gandhi 2000 ⁴⁶⁸	No relevant outcomes reported
Garcia-Ptacek 2014 ⁴⁷⁰	Adjusted data only
Giuli 2014 ⁴⁹²	Incorrect study design
Glynn 2001 ⁴⁹³	No relevant outcomes reported
Green 2007 ⁵⁰⁸	No relevant outcomes reported
Hafner 2002 ⁵³⁰	No relevant outcomes reported
Haile 2013 ⁵³¹	No relevant outcomes reported
Hajjar 2007 ⁵³²	Literature review
Hak 2001 ⁵³⁴	Incorrect population
Hamilton 2011 ⁵³⁹	No relevant outcomes reported
Hanlon 2006 ⁵⁴⁰	No relevant outcomes reported
Heininger-Rothbucher 2001 ⁵⁶²	No relevant outcomes reported
Helvik 2010 ⁵⁶⁸	Incorrect study design
Holland 2000 ⁵⁹⁶	Not relevant
Iwata 2006 ⁶²⁸	No relevant outcomes reported
Janzen 2013 ⁶³⁷	No relevant outcomes reported
Jensen 2001 ⁶⁴⁰	No relevant risk factor reported
Jorgensen 2001 ⁶⁶⁰	Incorrect study design
Kannegaard 2010 ⁶⁷⁰	Incorrect population
Kaplan 2001A ⁶⁷²	No relevant outcomes reported
Kohler 2015 ⁷⁰⁸	No relevant outcomes reported
Kongkaew 2013 ⁷⁰⁹	Adjusted data only
Lachs 2002 ⁷²⁵	Adjusted data only
Lattazio 2012A ⁷⁴¹	No relevant outcomes reported
Leendertse 2008 ⁷⁵¹	Incorrect population
Leung 2013 ⁷⁵⁹	No relevant outcomes reported
Liao 2013 ⁷⁶⁶	No relevant outcomes reported
Lifshitz 2012 ⁷⁶⁸	No relevant outcomes reported
Lima-Costa 2011 ⁷⁷¹ ;	Adjusted data only
Luppa 2010 ⁷⁹³	Systematic review – checked for references
Macedo 2011 ⁷⁹⁶	No relevant outcomes reported
Maciejewski 2014 ⁷⁹⁷	No relevant risk factor
Maggiore 2014 ⁸⁰⁰	Adjusted data only

Reference	Reason for exclusion
Malhorta 2001 ⁸⁰²	No relevant risk factor
Mandavi 2012 ⁸⁰³	No relevant outcomes reported
Mannesse 2000 ⁸⁰⁶	Incorrect study design
Mansur 2008 ⁸⁰⁷	No relevant risk factor
Marcum 2012A ⁸⁰⁹	No relevant outcomes reported
Marinella 2000 ⁸¹¹	No relevant outcomes reported
Marusic 2014 ⁸²⁰	No relevant outcomes reported
Matthew 2012 ⁸²⁴	No relevant outcomes reported
Mercier 2010 ⁸⁵⁰	No relevant risk factor
Modi 2005 ⁸⁶⁸	No relevant risk factor
Morandi 2013 ⁸⁷⁶	Adjusted data only
Nguyen 2006 ⁹⁰⁴	No relevant outcomes reported
Nishtala 2014 ⁹⁰⁷	Incorrect study design
Nivya 2015 ⁹⁰⁸	Systematic review – checked for references
Nobili 2011B ⁹⁰⁹	No relevant outcomes reported
O'Connor 2012 ⁹¹⁷	No relevant outcomes reported
Obreli Neto 2012 ⁹²¹	No relevant outcomes reported
Olesen 2014C ⁹²³	Incorrect study design
Onder 2002 ⁹²⁶	Incorrect study design
Onder 2013 ⁹²⁵	No relevant outcomes reported
Oza 2014 ⁹³⁵	No relevant outcomes reported
Palacios-Cena 2013 ⁹⁴¹	No relevant risk factor
Pardo Cabello 2009 ⁹⁴²	No relevant outcomes reported
Passarelli 2005 ⁹⁴⁸	No relevant outcomes reported
Patel 2012 ⁹⁴⁹	Adjusted data only
Payne 2009 ⁹⁵¹	No relevant risk factor
Payne 2014 ⁹⁵²	Incorrect population
Perkins 2004 ⁹⁵⁷	No relevant outcomes reported
Preyde 2011 ⁹⁹²	Systematic review – checked for references
Queneau 2007 ⁹⁹⁸	No relevant outcomes reported
Radhakrishnan 2013 ¹⁰⁰¹	Incorrect study design
Richardson 2014 ¹⁰¹⁸	No relevant outcomes reported
Romana 2012 ¹⁰⁴³	No relevant outcomes reported
Ruiz 2008 ¹⁰⁵²	No relevant outcomes reported
Salvi 2012A ¹⁰⁶⁶	Literature review
Sanchez Munoz-Torrero 2010 ¹⁰⁷²	No relevant outcomes reported
Sato 2013 ¹⁰⁷⁸	No relevant outcomes reported
Schuler 2008 ¹⁰⁹⁷	No relevant outcomes reported
Shah 2013a ¹¹⁰⁸	Adjusted data only
Sharifaskari 2005 ¹⁰⁵⁸	Incorrect population
Silva 2009 ¹¹²¹	No relevant outcomes reported
Snyder 2014 ¹¹³¹	No relevant outcomes reported

Reference	Reason for exclusion
Spector 2013 ¹¹⁴¹	No relevant outcomes reported
Szeto 2006 ¹¹⁶²	Incorrect population
Tangherlini 2010 ¹¹⁷²	No relevant outcomes reported
Tangiisuran 2012 ¹¹⁷³	No relevant outcomes reported
Uggerby 2011 ¹²¹⁹	No relevant risk factor
Urbina 2015 ¹²²²	No relevant outcomes reported
Vaciuniene 2010 ¹²²⁵	Incorrect population
Van den Bemt 2000 ¹²²⁷	No relevant outcomes reported
Venkat 2011 ¹²⁴¹	Adjusted data only
Vetrano 2014 ¹²⁴⁵	No relevant outcomes reported
Voisin 2010 ¹²⁵⁶	No relevant risk factor
Volk 2012 ¹²⁵⁸	Incorrect population
Wimmer 2014 ¹³¹²	No relevant outcomes reported
Wimmer 2014A ¹³¹¹	Risk tool
Wu 2012A ¹³²¹	No relevant outcomes reported
Zed 2008 ¹³³⁴	Incorrect population
Zopf 2008 ¹³⁵⁰	No relevant outcomes reported
Zopf 2008A ¹³⁵¹	No relevant outcomes reported
Zuckerman 2006 ¹³⁵²	No relevant outcomes reported

L.3 Frailty

Table 262: Studies excluded from the clinical review

Reference	Reason for exclusion
Abellan Van Kan 2009 ⁵	Systematic review: citations checked
Abellan Van Kan 2011 ⁶	Incorrect study design
Baitar 2013 ⁸³	Incorrect population (cancer)
Barreto 2012 ⁹⁶	Incorrect study design
Basic 2015 ⁹⁹	Incorrect study design
Bielderma 2013 ¹³²	Incorrect study design
Boxer 2010 ¹⁷⁸	Incorrect study design
Brown 2000 ¹⁹⁶	Incorrect study design
Cesari 2014a ²²⁹	Incorrect study design
Chan 2010 ²³³	Incorrect study design
Chang 2015 ²³⁸	Incorrect study design
Clegg 2015 ²⁷⁵	Systematic review: citations checked
Coelho 2015 ²⁷⁸	Incorrect study design
Dayhoff 1998 ³³¹	Incorrect reference standard
De Vries ³³⁸	Incorrect study design
De Witte 2013 ³⁴⁰	Incorrect study design

Reference	Reason for exclusion
Drubbel 2013 ³⁷⁶	Incorrect study design
Frisoli 2015 ⁴⁶⁰	Incorrect study design
Greene 1990 ⁵¹²	Incorrect study design
Greene 2014a ⁵¹⁰	Incorrect study design
Guaraldi 2015 ⁵²⁰	Incorrect study design
Hamaker 2012 ⁵³⁸	Systematic review not relevant
Hilmer 2009 ⁵⁷⁹	Incorrect study design
Jones 2005 ⁶⁵⁴	Incorrect study design
Jotheeswaran 2015 ⁶⁶¹	Incorrect study design
Jung 2014 ⁶⁶⁴	Incorrect study design
Kellen 2010 ⁶⁸¹	Incorrect population (cancer)
Kenig 2014 ⁶⁸³	Incorrect population (cancer)
Kenig 2015 ⁶⁸⁴	Incorrect population (cancer)
Kiely 2009 ⁶⁹¹	Incorrect study design
Kristjansson 2012 ⁷¹⁴	Incorrect study design
Lee 2015 ⁷⁴⁴	Incorrect study design
Luo 2015 ⁷⁹¹	Incorrect study design
Luce 2012 ⁷⁸⁶	Incorrect population (cancer)
Luciani 2010 ⁷⁸⁷	Incorrect population (cancer)
Matthews 2004 ⁸²⁷	Incorrect study design
Metzelthin 2010 ⁸⁵³	Incorrect study design
Mitnitski 2011a ⁸⁶⁷	Incorrect study design
Mohile 2007 ⁸⁶⁹	Incorrect population (cancer)
Molina-Garrido 2011 ⁸⁷⁰	Incorrect population (cancer)
Molina-Garrido 2012a ⁸⁷¹	Incorrect reference standard
O’Caoimh 2015 ⁹¹⁵	Incorrect study design
O’Caoimh 2015a ⁹¹⁶	Incorrect study design
Oo 2013 ⁹²⁷	Incorrect study design
Oo 2015 ⁹²⁸	Abstract only
Owusu 2011 ⁹³⁴	Incorrect population (cancer)
Pedone 2016 ⁹⁵⁴	Incorrect study design
Pijpers 2012 ⁹⁶⁹	Incorrect study design
Ravindrarajah 2013 ¹⁰¹¹	Incorrect study design
Ritt 2015 ¹⁰²³	Incorrect study design
Rockwood 2007 ¹⁰³²	Incorrect study design
Rockwood 2007a ¹⁰³³	Incorrect study design
Rockwood 2014 ¹⁰³⁶	Incorrect study design
Rockwood 2015 ¹⁰³⁵	Incorrect study design
Rolfson 2006 ¹⁰⁴²	Incorrect study design
Romero-Ortuno 2010 ¹⁰⁴⁶	Incorrect study design
Romero-Ortuno 2013a ¹⁰⁴⁵	Incorrect study design
Salvi 2012 ¹⁰⁶⁵	Incorrect reference standard
Sampaio 2014 ¹¹⁰⁷	Incorrect study design

Reference	Reason for exclusion
Schoufour 2015a ¹⁰⁹⁴	Incorrect study design
Schwenk 2015 ¹¹⁰⁰	Incorrect index test
Theou 2013 ¹¹⁸⁵	Incorrect study design
Tocchi 2014 ¹²⁰⁰	Incorrect study design
Wallis 2015 ¹²⁷³	Incorrect study design
Widagdo 2015a ¹³⁰³	Incorrect study design
Woo 2012 ¹³¹⁷	Incorrect study design
Vellas 2013 ¹²⁴⁰	Incorrect study design
van Kempen 2015 ¹²³⁴	Incorrect study design
Zeng 2015 ¹³⁴³	Incorrect study design

L.4 Delivering an approach to care that takes account of multimorbidity

L.4.1 Treatment burden

Table 263: Studies excluded from the clinical review

Reference	Reason for exclusion
Demain 2015 ³⁴³	Incorrect study design
Eton 2012 ⁴¹⁰	Incorrect study design (qualitative)
Eton 2013 ⁴⁰⁹	Incorrect study design (qualitative systematic review)
Eton 2015 ⁴¹¹	Incorrect study design
Gallacher 2011 ⁴⁶⁶	Incorrect study design (qualitative)
Guex 2010 ⁵²¹	Abstract
Jani 2013 ⁶³²	Incorrect study design (qualitative literature review)
Karampampa 2012 ⁶⁷³	Not relevant
Kuluski 2015 ⁷¹⁸	Incorrect study design
Sav 2013 ¹⁰⁷⁹	Incorrect study design (qualitative)
Sav 2013A ¹⁰⁸¹	Incorrect study design (qualitative)
Sav 2015 ¹⁰⁸⁰	Checked for references
Wister 2015 ¹³¹³	Incorrect study design

L.4.2 Ranking

None.

L.4.3 Stopping antihypertensive treatment

Table 264: Studies excluded from the clinical review

Study	Exclusion reason
Abraczinskas 2001 ⁷	Not review population
Abraham 2013 ⁹	Incorrect interventions
Adams 2013 ¹²	Incorrect interventions

Study	Exclusion reason
Alderman 1986 ²⁵	No comparison
Almas 2006 ³⁸	Incorrect interventions
An 2013 ⁴⁵	Incorrect interventions
Atella 2006 ⁶⁷	Incorrect interventions
Bailey 2010 ⁸²	Incorrect interventions
Bramley 2006 ¹⁸¹	Incorrect interventions
Breekveldt-postma 2008 ¹⁸⁶	Incorrect interventions
Breitscheidel 2012 ¹⁸⁷	No outcomes of interest
Burke 2006 ²⁰⁵	No relevant outcomes reported
Carter 2010 ²²¹	Incorrect interventions
Chapman 2010 ²⁴³	Incorrect interventions
Chen 2004 ²⁴⁷	Incorrect interventions
Christe 2014 ²⁶⁶	Study design (cohort)
Corrao 2011 ²⁹⁰	Incorrect interventions
Corrao 2012 ²⁹¹	Incorrect interventions
Correa Leite 2014 ²⁹²	Study design (cohort)
Cummings 2013 ³¹³	Incorrect interventions
Daugherty 2012 ³²⁷	Incorrect interventions
Davis 1993	Incorrect interventions
Dragomir 2010 ³⁷³	Incorrect interventions
Ekbom 1994 ³⁸⁹	Study design (cohort)
Fotherby 1994 ⁴³⁸	Inappropriate comparison
Fotherby 1994 ⁴³⁹	No relevant outcomes reported
Freis 1989 ⁴⁴⁹	Inappropriate comparison
Goncalves 2011 ⁵⁰¹	No comparison. Not guideline condition.
Hajjar 2013 ⁵³³	Inappropriate comparison
Hansen 1983 ⁵⁴²	No comparison
Hoer 2007 ⁵⁹³	No relevant outcomes reported
Kochar 1990 ⁷⁰⁶	Inappropriate comparison
Kostis 1998 ⁷¹⁰	Inappropriate comparison
Lalic 2013 ⁷²⁷	Incorrect interventions
Langford 1984 ⁷³⁷	Relevant outcome not reported
Lucas 1995 ⁷⁸⁵	Participants on antihypertensives for less than 1 year
Macdonald 2007 ⁷⁹⁵	Inappropriate comparison
Martin 2010 ⁸¹⁶	Incorrect interventions
Matsumura 2013 ⁸²⁵	Incorrect interventions
Muntner 2013 ⁸⁸⁶	Incorrect interventions
Nelson 2001 ⁸⁹⁹	No relevant outcomes reported
Nelson 2002 ⁹⁰⁰	Inappropriate comparison
Nelson 2003 ⁹⁰¹	Inappropriate comparison
Rajgopal 2014 ¹⁰⁰⁶	Incorrect population
Ramli 2012 ¹⁰⁰⁷	Incorrect interventions
Schmieder 1997 ¹⁰⁸⁴	No relevant outcomes reported

Study	Exclusion reason
Schmitt 2010 ¹⁰⁸⁵	Incorrect interventions
Schobel 1992 ¹⁰⁹⁰	Literature review
Schroeder 2006 ¹⁰⁹⁶	Incorrect interventions
Teichert 2007 ¹¹⁸⁰	Minimum duration of antihypertensives 30 days
Thorpe 2009 ¹¹⁸⁹	Incorrect interventions
Van Wijk 2007 ¹²³⁷	Incorrect interventions
Veronesi 2007 ¹²⁴⁴	Incorrect interventions
Wassertheil-smoller 1982 ¹²⁸⁴	Relevant outcomes not reported
Webster 1974 ¹²⁹¹	Case study
Wentzlaff 2011 ¹²⁹⁸	Participants on antihypertensives for less than 1 year before discontinuation
Wuerzner 2003 ¹³²³	Incorrect interventions
Zeltser 2004 ¹³⁴²	No relevant outcomes reported

L.4.4 Stopping drugs for osteoporosis

Table 265: Studies excluded from the clinical review

Study	Exclusion reason
Bagger 2003 ⁸¹	No relevant outcomes
Bauer 2014 ¹⁰⁴	Incorrect study design
Bone 2004 ¹⁵⁸	Incorrect study design
Bone 2011 ¹⁵⁷	Incorrect comparison: stopping vs. never treated
Brown 2013 ¹⁹⁵	Incorrect study design
Brown 2014 ¹⁹⁴	Incorrect study design
Cosman 2014 ²⁹⁵	Incorrect study design
Fitzpatrick 2014 ⁴²⁷	Incorrect interventions (Ronacaleret)
Fraser 2011 ⁴⁴⁶	Systematic review: study designs inappropriate
Greenspan 2002 ⁵¹³	Incorrect comparison
Greenspan 2008 ⁵¹⁴	Not review population (Acute illness (cancer))
Neele 2002 ⁸⁹⁷	Incorrect interventions (Raloxifene or oestrogen)
Uusi-rasi 2004 ¹²²⁴	Incorrect comparison
Voskaridou 2008 ¹²⁶³	Incorrect comparison

Wasnich 2004 ¹²⁸³	No relevant outcomes
Watts 2008 ¹²⁹⁰	Incorrect comparison

L.4.5 Stopping statins

Table 266: Studies excluded from the clinical review

Study	Exclusion reason
Andersohn 2010 ⁵⁰	Systematic review cross checked for references
Anon 1984 ¹	Incorrect interventions. Comparison between different rates of compliance with no 'stopping' group.
Anon 1997 ¹¹¹³	Non-randomised study
Aubert 2010 ⁷¹	Incorrect interventions. No non-stopping group.
Bitton 2013 ¹³⁷	Systematic review cross checked for references
Blackburn 2005 ¹⁴³	Not guideline condition. Non-adherence <60%.
Bouchard 2007 ¹⁶⁵	Incorrect interventions. No non-stopping group.
Burke 2006 ²⁰⁵	Does not report outcome specified in protocol
Carter 2010 ²²¹	Incorrect interventions
Choudhry 2014 ²⁶¹	Adherence versus non-adherence groups not compared
Chowdhury 2013 ²⁶⁴	Systematic review (could not check included studies as information could not be accessed)
Colivicchi 2007 ²⁸²	Non-randomised study
Corrao 2010 ²⁸⁹	Non-randomised study
Croft 1986 ³⁰⁶	Incorrect interventions
Cubeddu 2006 ³⁰⁹	Literature review cross checked for references
Daskalopoulou 2008 ³²⁵	Incorrect intervention. Non-statin users used as reference group. No continued versus stop comparison.
Daskalopoulou 2015 ³²⁶	Incorrect interventions
De vera 2011 ³³⁶	Non-randomised study
De vera 2012 ³³⁷	Non-randomised study
De vera 2014 ³³⁵	Systematic review cross checked for studies
Degli esposti 2012 ³⁴¹	Non-randomised study
Dowlatshahi 2012 ³⁷²	Pre admission statin versus no statin
Egstrup 1988 ³⁸⁶	Incorrect intervention
Ekbom 1994-1 ³⁸⁹	Incorrect intervention
Ekbom 1994-2 ³⁸⁹	Incorrect intervention
Endres 2006 ⁴⁰¹	Literature review cross checked for references
Ensrud 2004 ⁴⁰³	Incorrect intervention
Fagerberg 1992 ⁴¹⁶	Incorrect intervention
Fallouh 2012 ⁴¹⁹	Literature review cross checked for references
Fletcher 1988 ⁴²⁹	Incorrect intervention
Fotherby 1994 ⁴³⁹	Not guideline condition
Frishman 1982 ⁴⁵⁹	Incorrect intervention

Study	Exclusion reason
Garfinkel 2007 ⁴⁷³	No stopping versus continuing comparison
Garfinkel 2010 ⁴⁷²	No stopping versus continuing comparison
Gislason 2007 ⁴⁸⁸	Non-randomised study
Goldman 2006 ⁴⁹⁸	Incorrect interventions. No non-stopping group.
Gomez sandoval 2011 ⁴⁹⁹	Systematic review cross checked for studies
Gorwit 1995 ⁵⁰³	Incorrect intervention
Gottlieb 1984 ⁵⁰⁵	Incorrect intervention
Gottlieb 1985 ⁵⁰⁴	Incorrect intervention
Greenberg 1986 ⁵⁰⁹	Incorrect intervention
Heeschen 2002 ⁵⁶⁰	Same data as 2003 paper
Heeschen 2003 ⁵⁵⁹	Non-randomised study
Ho 2006 ⁵⁸⁸	Non-randomised study
Ho 2008 ⁵⁸⁷	Non-adherence defined as <80%
Hopper 2014 ⁶⁰²	Systematic review cross checked for included studies
Huan-Loh ⁶⁰⁹	Non-randomised study
Iyer 2008 ⁶²⁹	Systematic review cross checked for studies
Kim 2015 ⁶⁹⁵	Incorrect intervention
Klungel 2002 ⁷⁰⁰	Non-adherence <60%
Kumbhani 2013 ⁷²⁰	Non-randomised study
Le manach 2007 ⁷⁴²	Abstract
Lee 2014 ⁷⁴⁸	No relevant outcome data
Lesaffre 2003 ⁷⁵⁸	Non-adherence <80%
Maland 1983 ⁸⁰¹	Incorrect intervention
Mcginnis 2009 ⁸³⁷	Non-adherence <80%
Mcgowan 2004 ⁸³⁸	No baseline data or adjusted analysis
Metra 2007 ⁸⁵²	Incorrect intervention
Middeke 1990 ⁸⁵⁶	Incorrect intervention
Nombela 2006 ⁹¹²	Abstract
Olsson 1988 ⁹²⁴	Incorrect intervention
Overgaard 1990 ⁹³³	Incorrect intervention
Packer 1993 ⁹³⁷	Incorrect intervention
Penning-van beest 2007 ⁹⁵⁶	Incorrect intervention
Perreault 2008 ⁹⁵⁹	Non-randomised study
Perreault 2009 ⁹⁶⁰	Non-randomised study
Perreault 2009 ⁹⁵⁸	Non-randomised study
Pittman 2011 ⁹⁷⁷	Comparison not stopping versus continuing statins
Rasmussen 2007 ¹⁰⁰⁹	Non-randomised study
Reeve 2013 ¹⁰¹⁵	Abstract
Reeve 2013 ¹⁰¹⁵	No intervention
Reeve 2014 ¹⁰¹⁶	No intervention
Risselada 2009 ¹⁰²¹	Incorrect interventions. No outcomes of interest.
Saito 2002 ¹⁰⁶⁰	Non-randomised study
Scheitz 2013 ¹⁰⁸³	Systematic review cross checked for references

Study	Exclusion reason
Shalev 2009-1 ¹¹⁰⁹	Non-randomised study
Shalev 2009-2 ¹¹⁰⁹	Non-randomised study
Sheperd 1997 ¹¹¹³	Incorrect interventions. Non-adherence group less than 80%.
Shepherd 2008 ¹¹¹⁴	No stopping versus continuing statin comparison
Shin 2014 ¹¹¹⁸	Non-randomised study
Slejko 2014 ¹¹²⁸	Comparison not continuing versus stopping statins
Spencer 2004 ¹¹⁴³	Incorrect intervention
Spencer 2004 ¹¹⁴²	No continuing versus stopping group
Stockler 2015 ¹¹⁵¹	Commentary
Thomsen 1987 ¹¹⁸⁸	Incorrect intervention
Tjia 2012 ¹¹⁹⁸	No intervention
Tong 2015 ¹²⁰¹	Non-randomised study
Tuppin 2010 ¹²¹⁷	Non-adherence <80%
Vinogradova 2015 ¹²⁵⁰	Protocol only
Watts 2008 ¹²⁹⁰	Incorrect intervention
Wei 2002 ¹²⁹²	Non-randomised study
Wei 2008 ¹²⁹³	Non-adherence <80%
West of Scotland coronary prevention study group 1999 ¹²⁹⁹	Incorrect interventions. No non-stopping group.

L.5 Interventions

L.5.1 Models of care

Table 267: Studies excluded from the clinical review

Study	Exclusion reason
Abraha 2015 ⁸	Systematic review is not relevant to review question or unclear PICO
Achey 2014 ¹⁰	Systematic review is not relevant to review question or unclear PICO
Agarwal 2015 ¹³	Protocol only
Ai 2014 ¹⁸	Systematic review is not relevant to review question or unclear PICO
Aizen 2015 ²¹	Intervention was condition specific
Alexopoulos 2014 ²⁷	Intervention focused on specific condition
Allen 1986 ³³	Incorrect interventions
Allen 2014 ³⁵	Systematic review is not relevant to review question or unclear PICO
Amris 2014 ⁴⁴	Intervention specific to single condition
Anders 2012 ⁴⁹	Not in English
Andrade 2015 ⁵²	Intervention was condition specific
Anon 2014 ²¹⁴	Incorrect interventions
Anon 2015 ³	Not published
Anon 2015 ³⁴²	Systematic review is not relevant to review question or unclear PICO
Anon 2015 ¹⁰⁰³	Incorrect interventions
Anon 2015 ²	Non-randomised study

Study	Exclusion reason
Anon 2015 ¹¹⁵⁷	Non-randomised study
Arbaje 2010 ⁶¹	Intervention is short term only without reorganising care
Arija 2012 ⁶³	Incorrect interventions
Atienza 2004 ⁶⁸	Not guideline condition. <80% MM
Atlantis 2014 ⁷⁰	Systematic review cross checked for references
Bachman 1987 ⁷⁹	Incorrect interventions
Bader 2014 ⁸⁰	Poster only
Bakker 2011 ⁸⁷	Abstract
Bakker 2011 ⁸⁶	Systematic review
Bakker 2013 ⁸⁸	Incorrect interventions. Incorrect intervention (Psychology focused)
Balaban 2015 ⁸⁹	Not review population. Not guideline condition
Barnes 2012 ⁹⁴	Not guideline condition
Battersby 2013 ¹⁰³	Incorrect interventions
Battersby 2015 ¹⁰²	Not guideline condition
Baynouna 2010 ¹⁰⁸	Incorrect interventions
Becker 1987 ¹¹⁰	Commentary
Bekelman 2015 ¹¹⁴	Intervention specific to single condition
Benavent-caballer 2014 ¹¹⁹	Incorrect interventions
Bendayan 2014 ¹²⁰	Systematic review
Berkhof 2015 ¹²³	Intervention specific to single condition
Berry 2013 ¹²⁶	No outcomes of interest
Bibas 2014 ¹³⁰	Systematic review is not relevant to review question or unclear PICO
Bielaszka-duvernay 2011 ¹³¹	Short report on trial reported elsewhere
Billington 2015 ¹³⁶	Intervention specific to single condition
Blakeman 2014 ¹⁴⁵	Self-management and Expert Patient Programme review
Bleich 2015 ¹⁴⁷	Systematic review is not relevant to review question or unclear PICO
Bleijenberg 2013 ¹⁴⁸	Incorrect study design (focus group/questionnaire)
Bogner 2008 ¹⁵³	No outcomes of interest
Bogner 2010 ¹⁵⁴	No relevant outcomes reported
Bogner 2012 ¹⁵⁵	No relevant outcomes reported
Bonnefoy 2012 ¹⁵⁹	Incorrect interventions
Bosner 2012 ¹⁶²	Incorrect interventions
Bove 2015 ¹⁷²	Intervention specific to single condition
Brannstrom 2014 ¹⁸²	Intervention specific to single condition
Briskman 2012 ¹⁹²	Not relevant
Brovold 2013 ¹⁹³	Incorrect interventions
Brown 2012 ¹⁹⁷	Not guideline condition
Bruhn 2013 ¹⁹⁸	Not guideline condition
Buckingham 2015 ²⁰⁰	Intervention specific to single condition
Cadore 2014 ²⁰⁸	Incorrect interventions
Cady 2015 ²⁰⁹	Not review population
Caillet 2014 ²¹⁰	Systematic review
Calderon-larranaga 2012 ²¹¹	Not relevant

Study	Exclusion reason
Ceramidas 2013 ²²⁸	Incorrect interventions
Chan 2015 ²³²	Protocol only
Chen 2010 ²⁵⁰	Not an RCT
Chouinard 2013 ²⁶²	Not an RCT
Chung 2013 ²⁶⁷	Incorrect interventions. No control arm
Ciechanowski 2006 ²⁶⁸	Incorrect interventions
Clark 2012 ²⁷²	Incorrect interventions
Clark 2015 ²⁷⁰	Intervention specific to single condition
Coleman 2001 ²⁸⁰	Not guideline condition
Corser 2011 ²⁹³	Self-management review
Coulter 2015 ²⁹⁶	Systematic review is not relevant to review question or unclear PICO
Counsell 2006 ²⁹⁷	No relevant outcomes reported
Coventry 2015 ³⁰³	Intervention only targets depression
Cudney 2012 ³¹⁰	Incorrect interventions
Cunliffe 2004 ³¹⁴	Incorrect interventions
De heer 2013 ³³³	Trial protocol
De vries 2010 ³³⁹	Incorrect interventions
Dennis 2013 ³⁴⁴	Incorrect interventions
Deschodt 2011 ³⁴⁸	Not an RCT
Deschodt 2015 ³⁴⁷	Non-randomised CGA trial
Dickinson 2014 ³⁵⁶	Intervention specific to single condition
Dorresteyn 2011 ³⁷⁰	Incorrect interventions
Dougados 2015 ³⁷¹	Intervention specific to single condition
Drennan 2014 ³⁷⁵	Protocol only
Due 2014 ³⁷⁸	Not guideline condition
Dunbar 2015 ³⁸¹	Condition specific intervention
Eakin 2007 ³⁸²	Incorrect interventions. Intervention: self-management
Edelman 2010 ³⁸³	Narrow care plan, focusing on one condition only
Evangelista 2015 ⁴¹²	Intervention specific to single condition
Fairhall 2012 ⁴¹⁷	Incorrect interventions
Ferrer 2014 ⁴²²	Incorrect interventions
Fox 2010 ⁴⁴⁰	Incorrect interventions
Franek 2013 ⁴⁴³	Systematic review cross checked for references
Friedman 2014 ⁴⁵⁷	Incorrect interventions
Fu 2003 ⁴⁶¹	Self-management and Expert Patient Programme review
Garvey 2015 ⁴⁷⁴	Incorrect interventions
Gensichen 2005 ⁴⁷⁶	Protocol, intervention specific to single condition
Gharacholou 2012 ⁴⁷⁹	Not guideline condition
Gibson 2012 ⁴⁸²	Not guideline condition
Gill 2001 ⁴⁸⁵	Incorrect interventions
Gill 2003 ⁴⁸⁴	Incorrect interventions
Giovannetti 2012 ⁴⁸⁷	Background information
Gitlin 2006 ⁴⁹¹	Incorrect interventions. Interventions: self-management

Study	Exclusion reason
Gnjidic 2014 ⁴⁹⁵	Abstract
Gray 2010 ⁵⁰⁷	Not guideline condition. Aged >50 years. Mean MM: 1.4.
Gustafsson 2012 ⁵²⁶	Incorrect interventions
Gustafsson 2013 ⁵²⁵	Incorrect interventions
Hansen 2011 ⁵⁴⁴	Systematic review cross checked for references
Harris 2011 ⁵⁴⁸	Incorrect interventions
Health 2013 ⁵⁵⁶	Systematic review cross checked for references
Health 2013 ⁵⁵⁴	Systematic review cross checked for references
Health 2013 ⁵⁵⁵	Systematic review cross checked for references
Hebert 2010 ⁵⁵⁸	Not an RCT
Hernandez 2015 ⁵⁷²	Intervention was condition specific
Hirani 2014 ⁵⁸⁴	Incorrect interventions
Hochhalter 2010 ⁵⁹²	Incorrect interventions. Interventions: self-management
Holmes 2013 ⁵⁹⁸	Not relevant
Huang 2013 ⁶¹¹	Systematic review cross checked for references
Ijff 2007 ⁶¹⁹	Intervention specific to single condition
Imai 2013 ⁶²⁰	Protocol
Imhof 2012 ⁶²¹	Incorrect intervention
Janig 2014 ⁶³³	Not in English
Jerant 2009 ⁶⁴⁶	Self-management and Expert Patient Programme review
Jonker 2015 ⁶⁵⁶	Not guideline condition
Jonkers 2012 ⁶⁵⁷	Incorrect interventions
Katon 2004 ⁶⁷⁹	Intervention only targets single condition
Katon 2008 ⁶⁷⁸	Intervention for single conditions only
Katon 2012 ⁶⁸⁰	Cost-effectiveness paper, clinical paper checked
Kenealy 2015 ⁶⁸²	Intervention specific to single condition
Kennedy 2007 ⁶⁸⁵	Self-management and Expert Patient Programme review
Kinder 2006 ⁶⁹⁷	Intervention only targets single condition
Kirchberger 2015 ⁶⁹⁸	Intervention was condition specific
Kivipelto 2013 ⁶⁹⁹	Incorrect interventions
Knight 2014 ⁷⁰¹	Incorrect interventions
Koberich 2015 ⁷⁰⁴	Intervention specific to single condition
Kogan 2013 ⁷⁰⁷	Incorrect interventions
Krska 2001 ⁷¹⁷	Incorrect interventions. Intervention: medication review
Kumar 2007 ⁷¹⁹	Systematic review cross checked for references
Kushner 2015 ⁷²¹	Incorrect interventions
Kwok 2008 ⁷²³	Not guideline condition
Laakkonen 2012 ⁷²⁴	Proof of concept paper
Lam 2010 ⁷²⁹	Not guideline condition
Lamers 2010 ⁷³²	Incorrect interventions
Lang 2012 ⁷³⁵	People who only have multiple mental health problems and no physical health problems
Lapane 2011 ⁷³⁸	Incorrect interventions

Study	Exclusion reason
Lassere 2015 ⁷⁴⁰	Protocol only
Lee 2014 ⁷⁴⁵	No relevant outcomes
Lee 2015 ⁷⁴⁴	Intervention specific to single condition
Lewin 2014 ⁷⁶²	Flawed randomisation strategy
Li 2015 ⁷⁶⁵	Commentary
Linden 2014 ⁷⁷²	Intervention specific to single condition
Lisby 2010 ⁷⁷³	Incorrect interventions
Litaker 2003 ⁷⁷⁴	Narrow care plan, focusing on one condition only
Loffler 2014 ⁷⁷⁶	Protocol
Lorig 1999 ⁷⁸⁰	Incorrect interventions. Intervention: self-management
Lorig 2003 ⁷⁷⁸	Self-management and Expert Patient Programme review
Luck 2013 ⁷⁸⁸	Not appropriate intervention. No outcomes of interest
Marek 2013 ⁸¹⁰	Incorrect interventions
Markle-reid 2013 ⁸¹³	Not an RCT
Masters 2013 ⁸²²	Self-management review
Mccall 2011 ⁸³⁰	Incorrect interventions
Mcdowell 2015 ⁸³⁴	Intervention specific to single condition
Mcmartin 2013 ⁸⁴⁰	Systematic review cross checked for references
Mcvey 1989 ⁸⁴¹	Inappropriate comparison
Melis 2005 ⁸⁴⁴	Study protocol
Mistiaen 2007 ⁸⁶⁴	Systematic review cross checked for references
Mitchell 2014 ⁸⁶⁵	Intervention specific to single condition
Moller 2014 ⁸⁷²	Intervention is single condition specific
Morgan 2009 ⁸⁷⁷	Description of study
Morgan 2013 ⁸⁷⁹	Intervention only targets single condition
Morgan 2015 ⁸⁷⁸	Non-randomised study
Mosquera 2014 ⁸⁸³	Not review population
Mueser 2012 ⁸⁸⁴	Self-management review
Munding 2000 ⁸⁸⁵	Not guideline condition
Naylor 2011 ⁸⁹⁵	Population unclear
Nicolaidis-bouman 2004 ⁹⁰⁵	Study protocol
Nykanen 2014 ⁹¹³	Incorrect interventions
Ory 2013 ⁹³¹	Self-management review
Overend 2014 ⁹³²	Intervention specific to single condition
Pedone 2015 ⁹⁵⁵	Condition specific intervention
Petersen 2014 ⁹⁶³	Intervention specific to single condition
Phillips 2004 ⁹⁶⁶	Not guideline condition
Pickett 2014 ⁹⁶⁸	Intervention specific to single condition
Pizzi 2014 ⁹⁷⁸	Intervention specific to single condition
Plant 2015 ⁹⁷⁹	Not review population
Ploeg 2010 ⁹⁸⁰	Incorrect interventions
Pope 2011 ⁹⁸⁵	Incorrect interventions
Powell 1990 ⁹⁸⁸	Abstract

Study	Exclusion reason
Prestmo 2015 ⁹⁹¹	Intervention was condition specific
Ramli 2014 ¹⁰⁰⁸	Intervention specific to single condition
Ringbaek 2015 ¹⁰²⁰	Intervention specific to single condition
Ritter 2011 ¹⁰²⁴	Self-management review
Rytter 2010 ¹⁰⁵⁴	Discharge planning. Incorrect interventions
Sahlen 2006 ¹⁰⁵⁹	Not guideline condition
Sajatovic 2011 ¹⁰⁶¹	Self-management review
Salisbury 2012 ¹⁰⁶²	Review paper
Saltz 1988 ¹⁰⁶³	Incorrect interventions
Schraeder 2008 ¹⁰⁹⁵	Non-randomised study
Scott 2010 ¹¹⁰¹	Systematic review cross checked for references
Sharpe 2014 ¹¹¹¹	Intervention specific to single condition
Shepperd 2010 ¹¹¹⁵	Systematic review is not relevant to review question or unclear PICO
Smith 2010 ¹¹²⁹	Qualitative study
Stewart 2014 ¹¹⁴⁹	Intervention specific to single condition
Stokes 2015 ¹¹⁵²	Systematic review is not relevant to review question or unclear PICO
Stuck 2007 ¹¹⁵⁴	Protocol
Tanajewski 2015 ¹¹⁶⁹	CEA on previously extracted trial, no new outcomes
Tanner 2015 ¹¹⁷⁴	Intervention specific to single condition
Tao 2012 ¹¹⁷⁵	Not an RCT
Tierce-hazard 2014 ¹¹⁹¹	Commentary
Timmer 2014 ¹¹⁹⁵	Systematic review is not relevant to review question or unclear PICO
Upshur 2015 ¹²²¹	Intervention specific to single condition
Van hout 2005 ¹²³³	Protocol
Vanderlip 2015 ¹²³⁸	Commentary
Vera 2010 ¹²⁴²	Intervention aimed at single condition
Vind 2010 ¹²⁴⁹	Incorrect interventions
Watson 2015 ¹²⁸⁹	Protocol
Williams 2004 ¹³⁰⁹	Intervention only targets single condition
Worrall 2006 ¹³¹⁸	Systematic review cross checked for references
Yu 2015 ¹³³¹	Intervention specific to single condition
Zhao 2009 ¹³⁴⁵	Not guideline condition

L.5.2 Holistic assessment

Table 268: Studies excluded from the clinical review

Study	Exclusion reason
Abraha 2015 ⁸	Systematic review is not relevant to review question or unclear PICO
Achey 2014 ¹⁰	Systematic review is not relevant to review question or unclear PICO
Agarwal 2015 ¹³	Protocol only
Ai 2014 ¹⁸	Systematic review is not relevant to review question or unclear PICO
Aizen 2015 ²¹	Intervention was condition specific
Alexopoulos 2014 ²⁷	Intervention focused on specific condition
Allen 1986 ³³	Incorrect interventions

Study	Exclusion reason
Allen 2014 ³⁵	Systematic review is not relevant to review question or unclear PICO
Amris 2014 ⁴⁴	Intervention specific to single condition
Anders 2012 ⁴⁹	Not in English
Andrade 2015 ⁵²	Intervention was condition specific
Anon 2014 ²¹⁴	Incorrect interventions
Anon 2015 ³	Not published
Anon 2015 ³⁴²	Systematic review is not relevant to review question or unclear PICO
Anon 2015 ¹⁰⁰³	Incorrect interventions
Anon 2015 ²	Non-randomised study
Anon 2015 ¹¹⁵⁷	Non-randomised study
Arbaje 2010 ⁶¹	Intervention is short term only without reorganising care
Arija 2012 ⁶³	Incorrect interventions
Atienza 2004 ⁶⁸	Not guideline condition. <80% MM
Atlantis 2014 ⁷⁰	Systematic review cross checked for references
Bachman 1987 ⁷⁹	Incorrect interventions
Bader 2014 ⁸⁰	Poster only
Bakker 2011 ⁸⁷	Abstract
Bakker 2011 ⁸⁶	Systematic review
Bakker 2013 ⁸⁸	Incorrect interventions. Incorrect intervention (Psychology focused)
Balaban 2015 ⁸⁹	Not review population. Not guideline condition
Barnes 2012 ⁹⁴	Not guideline condition
Battersby 2013 ¹⁰³	Incorrect interventions
Battersby 2015 ¹⁰²	Not guideline condition
Baynouna 2010 ¹⁰⁸	Incorrect interventions
Becker 1987 ¹¹⁰	Commentary
Bekelman 2015 ¹¹⁴	Intervention specific to single condition
Benavent-caballer 2014 ¹¹⁹	Incorrect interventions
Bendayan 2014 ¹²⁰	Systematic review
Berkhof 2015 ¹²³	Intervention specific to single condition
Berry 2013 ¹²⁶	No outcomes of interest
Bibas 2014 ¹³⁰	Systematic review is not relevant to review question or unclear PICO
Bielaszka-duvernay 2011 ¹³¹	Short report on trial reported elsewhere
Billington 2015 ¹³⁶	Intervention specific to single condition
Blakeman 2014 ¹⁴⁵	Self-management and Expert Patient Programme review
Bleich 2015 ¹⁴⁷	Systematic review is not relevant to review question or unclear PICO
Bleijenberg 2013 ¹⁴⁸	Incorrect study design (focus group/questionnaire)
Bogner 2008 ¹⁵³	No outcomes of interest
Bogner 2010 ¹⁵⁴	No relevant outcomes reported
Bogner 2012 ¹⁵⁵	No relevant outcomes reported
Bonnefoy 2012 ¹⁵⁹	Incorrect interventions
Bosner 2012 ¹⁶²	Incorrect interventions
Bove 2015 ¹⁷²	Intervention specific to single condition
Brannstrom 2014 ¹⁸²	Intervention specific to single condition

Study	Exclusion reason
Briskman 2012 ¹⁹²	Not relevant
Brovold 2013 ¹⁹³	Incorrect interventions
Brown 2012 ¹⁹⁷	Not guideline condition
Bruhn 2013 ¹⁹⁸	Not guideline condition
Buckingham 2015 ²⁰⁰	Intervention specific to single condition
Cadore 2014 ²⁰⁸	Incorrect interventions
Cady 2015 ²⁰⁹	Not review population
Caillet 2014 ²¹⁰	Systematic review
Calderon-larranaga 2012 ²¹¹	Not relevant
Ceramidas 2013 ²²⁸	Incorrect interventions
Chan 2015 ²³²	Protocol only
Chen 2010 ²⁵⁰	Not an RCT
Chouinard 2013 ²⁶²	Not an RCT
Chung 2013 ²⁶⁷	Incorrect interventions. No control arm
Ciechanowski 2006 ²⁶⁸	Incorrect interventions
Clark 2012 ²⁷²	Incorrect interventions
Clark 2015 ²⁷⁰	Intervention specific to single condition
Coleman 2001 ²⁸⁰	Not guideline condition
Corser 2011 ²⁹³	Self-management review
Coulter 2015 ²⁹⁶	Systematic review is not relevant to review question or unclear PICO
Counsell 2006 ²⁹⁷	No relevant outcomes reported
Coventry 2015 ³⁰³	Intervention only targets depression
Cudney 2012 ³¹⁰	Incorrect interventions
Cunliffe 2004 ³¹⁴	Incorrect interventions
De heer 2013 ³³³	Trial protocol
De vries 2010 ³³⁹	Incorrect interventions
Dennis 2013 ³⁴⁴	Incorrect interventions
Deschodt 2011 ³⁴⁸	Not an RCT
Deschodt 2015 ³⁴⁷	Non-randomised CGA trial
Dickinson 2014 ³⁵⁶	Intervention specific to single condition
Dorresteyn 2011 ³⁷⁰	Incorrect interventions
Dougados 2015 ³⁷¹	Intervention specific to single condition
Drennan 2014 ³⁷⁵	Protocol only
Due 2014 ³⁷⁸	Not guideline condition
Dunbar 2015 ³⁸¹	Condition specific intervention
Eakin 2007 ³⁸²	Incorrect interventions. Intervention: self-management
Edelman 2010 ³⁸³	Narrow care plan, focusing on one condition only
Evangelista 2015 ⁴¹²	Intervention specific to single condition
Fairhall 2012 ⁴¹⁷	Incorrect interventions
Ferrer 2014 ⁴²²	Incorrect interventions
Fox 2010 ⁴⁴⁰	Incorrect interventions
Franek 2013 ⁴⁴³	Systematic review cross checked for references
Friedman 2014 ⁴⁵⁷	Incorrect interventions

Study	Exclusion reason
Fu 2003 ⁴⁶¹	Self-management and Expert Patient Programme review
Garvey 2015 ⁴⁷⁴	Incorrect interventions
Gensichen 2005 ⁴⁷⁶	Protocol, intervention specific to single condition
Gharacholou 2012 ⁴⁷⁹	Not guideline condition
Gibson 2012 ⁴⁸²	Not guideline condition
Gill 2001 ⁴⁸⁵	Incorrect interventions
Gill 2003 ⁴⁸⁴	Incorrect interventions
Giovannetti 2012 ⁴⁸⁷	Background information
Gitlin 2006 ⁴⁹¹	Incorrect interventions. Interventions: self-management
Gnjidic 2014 ⁴⁹⁵	Abstract
Gray 2010 ⁵⁰⁷	Not guideline condition. Aged >50 years. Mean MM: 1.4.
Gustafsson 2012 ⁵²⁶	Incorrect interventions
Gustafsson 2013 ⁵²⁵	Incorrect interventions
Hansen 2011 ⁵⁴⁴	Systematic review cross checked for references
Harris 2011 ⁵⁴⁸	Incorrect interventions
Health 2013 ⁵⁵⁶	Systematic review cross checked for references
Health 2013 ⁵⁵⁴	Systematic review cross checked for references
Health 2013 ⁵⁵⁵	Systematic review cross checked for references
Hebert 2010 ⁵⁵⁸	Not an RCT
Hernandez 2015 ⁵⁷²	Intervention was condition specific
Hirani 2014 ⁵⁸⁴	Incorrect interventions
Hochhalter 2010 ⁵⁹²	Incorrect interventions. Interventions: self-management
Holmes 2013 ⁵⁹⁸	Not relevant
Huang 2013 ⁶¹¹	Systematic review cross checked for references
Ijff 2007 ⁶¹⁹	Intervention specific to single condition
Imai 2013 ⁶²⁰	Protocol
Imhof 2012 ⁶²¹	Incorrect intervention
Janig 2014 ⁶³³	Not in English
Jerant 2009 ⁶⁴⁶	Self-management and Expert Patient Programme review
Jonker 2015 ⁶⁵⁶	Not guideline condition
Jonkers 2012 ⁶⁵⁷	Incorrect interventions
Katon 2004 ⁶⁷⁹	Intervention only targets single condition
Katon 2008 ⁶⁷⁸	Intervention for single conditions only
Katon 2012 ⁶⁸⁰	Cost-effectiveness paper, clinical paper checked
Kenealy 2015 ⁶⁸²	Intervention specific to single condition
Kennedy 2007 ⁶⁸⁵	Self-management and Expert Patient Programme review
Kinder 2006 ⁶⁹⁷	Intervention only targets single condition
Kirchberger 2015 ⁶⁹⁸	Intervention was condition specific
Kivipelto 2013 ⁶⁹⁹	Incorrect interventions
Knight 2014 ⁷⁰¹	Incorrect interventions
Koberich 2015 ⁷⁰⁴	Intervention specific to single condition
Kogan 2013 ⁷⁰⁷	Incorrect interventions
Krska 2001 ⁷¹⁷	Incorrect interventions. Intervention: medication review

Study	Exclusion reason
Kumar 2007 ⁷¹⁹	Systematic review cross checked for references
Kushner 2015 ⁷²¹	Incorrect interventions
Kwok 2008 ⁷²³	Not guideline condition
Laakkonen 2012 ⁷²⁴	Proof of concept paper
Lam 2010 ⁷²⁹	Not guideline condition
Lamers 2010 ⁷³²	Incorrect interventions
Lang 2012 ⁷³⁵	People who only have multiple mental health problems and no physical health problems
Lapane 2011 ⁷³⁸	Incorrect interventions
Lassere 2015 ⁷⁴⁰	Protocol only
Lee 2014 ⁷⁴⁵	No relevant outcomes
Lee 2015 ⁷⁴⁴	Intervention specific to single condition
Lewin 2014 ⁷⁶²	Flawed randomisation strategy
Li 2015 ⁷⁶⁵	Commentary
Linden 2014 ⁷⁷²	Intervention specific to single condition
Lisby 2010 ⁷⁷³	Incorrect interventions
Litaker 2003 ⁷⁷⁴	Narrow care plan, focusing on one condition only
Loffler 2014 ⁷⁷⁶	Protocol
Lorig 1999 ⁷⁸⁰	Incorrect interventions. Intervention: self-management
Lorig 2003 ⁷⁷⁸	Self-management and Expert Patient Programme review
Luck 2013 ⁷⁸⁸	Not appropriate intervention. No outcomes of interest
Marek 2013 ⁸¹⁰	Incorrect interventions
Markle-reid 2013 ⁸¹³	Not an RCT
Masters 2013 ⁸²²	Self-management review
Mccall 2011 ⁸³⁰	Incorrect interventions
Mcdowell 2015 ⁸³⁴	Intervention specific to single condition
Mcmartin 2013 ⁸⁴⁰	Systematic review cross checked for references
Mcvey 1989 ⁸⁴¹	Inappropriate comparison
Melis 2005 ⁸⁴⁴	Study protocol
Mistiaen 2007 ⁸⁶⁴	Systematic review cross checked for references
Mitchell 2014 ⁸⁶⁵	Intervention specific to single condition
Moller 2014 ⁸⁷²	Intervention is single condition specific
Morgan 2009 ⁸⁷⁷	Description of study
Morgan 2013 ⁸⁷⁹	Intervention only targets single condition
Morgan 2015 ⁸⁷⁸	Non-randomised study
Mosquera 2014 ⁸⁸³	Not review population
Mueser 2012 ⁸⁸⁴	Self-management review
Mundinger 2000 ⁸⁸⁵	Not guideline condition
Naylor 2011 ⁸⁹⁵	Population unclear
Nicolaides-bouman 2004 ⁹⁰⁵	Study protocol
Nykanen 2014 ⁹¹³	Incorrect interventions
Ory 2013 ⁹³¹	Self-management review
Overend 2014 ⁹³²	Intervention specific to single condition

Study	Exclusion reason
Pedone 2015 ⁹⁵⁵	Condition specific intervention
Petersen 2014 ⁹⁶³	Intervention specific to single condition
Phillips 2004 ⁹⁶⁶	Not guideline condition
Pickett 2014 ⁹⁶⁸	Intervention specific to single condition
Pizzi 2014 ⁹⁷⁸	Intervention specific to single condition
Plant 2015 ⁹⁷⁹	Not review population
Ploeg 2010 ⁹⁸⁰	Incorrect interventions
Pope 2011 ⁹⁸⁵	Incorrect interventions
Powell 1990 ⁹⁸⁸	Abstract
Prestmo 2015 ⁹⁹¹	Intervention was condition specific
Ramli 2014 ¹⁰⁰⁸	Intervention specific to single condition
Ringbaek 2015 ¹⁰²⁰	Intervention specific to single condition
Ritter 2011 ¹⁰²⁴	Self-management review
Rytter 2010 ¹⁰⁵⁴	Discharge planning. Incorrect interventions
Sahlen 2006 ¹⁰⁵⁹	Not guideline condition
Sajatovic 2011 ¹⁰⁶¹	Self-management review
Salisbury 2012 ¹⁰⁶²	Review paper
Saltz 1988 ¹⁰⁶³	Incorrect interventions
Schraeder 2008 ¹⁰⁹⁵	Non-randomised study
Scott 2010 ¹¹⁰¹	Systematic review cross checked for references
Sharpe 2014 ¹¹¹¹	Intervention specific to single condition
Shepperd 2010 ¹¹¹⁵	Systematic review is not relevant to review question or unclear PICO
Smith 2010 ¹¹²⁹	Qualitative study
Stewart 2014 ¹¹⁴⁹	Intervention specific to single condition
Stokes 2015 ¹¹⁵²	Systematic review is not relevant to review question or unclear PICO
Stuck 2007 ¹¹⁵⁴	Protocol
Tanajewski 2015 ¹¹⁶⁹	CEA on previously extracted trial, no new outcomes
Tanner 2015 ¹¹⁷⁴	Intervention specific to single condition
Tao 2012 ¹¹⁷⁵	Not an RCT
Tierce-hazard 2014 ¹¹⁹¹	Commentary
Timmer 2014 ¹¹⁹⁵	Systematic review is not relevant to review question or unclear PICO
Upshur 2015 ¹²²¹	Intervention specific to single condition
Van hout 2005 ¹²³³	Protocol
Vanderlip 2015 ¹²³⁸	Commentary
Vera 2010 ¹²⁴²	Intervention aimed at single condition
Vind 2010 ¹²⁴⁹	Incorrect interventions
Watson 2015 ¹²⁸⁹	Protocol
Williams 2004 ¹³⁰⁹	Intervention only targets single condition
Worrall 2006 ¹³¹⁸	Systematic review cross checked for references
Yu 2015 ¹³³¹	Intervention specific to single condition
Zhao 2009 ¹³⁴⁵	Not guideline condition

L.6 Self-management

Table 269: Studies excluded from the clinical review

Study	Exclusion reason
Amoako 2008 ⁴³	Intervention targeted at single condition only
Bekelman 2013 ¹¹³	Trial protocol
Belaiche 2012 ¹¹⁵	Incorrect interventions
Beretta 2014 ¹²¹	Incorrect interventions
Blixen 2015 ¹⁵⁰	Incorrect study design
Bozorgmehr 2014 ¹⁸⁰	Trial protocol
Chow 2014 ²⁶³	Incorrect interventions
Chung 2013 ²⁶⁷	Incorrect interventions
Cimpean 2011 ²⁶⁹	Systematic review
Coburn 2012 ²⁷⁷	Incorrect interventions
Corbi 2015 ²⁸⁸	Incorrect study design
Corser 2011 ²⁹³	Incorrect study design
Cully 2014 ³¹²	Trial protocol
De Heer 2013 ³³³	Trial protocol
Dobscha 2008 ³⁶⁰	Not guideline condition
Dobscha 2009 ³⁶¹	Not guideline condition
Dougados 2015 ³⁷¹	Not guideline condition
Eikelenboom 2013 ³⁸⁸	Trial protocol
Elissen 2012 ³⁹⁶	Not guideline condition
Elzen 2007 ³⁹⁹	Not guideline condition
Emmons 2014 ⁴⁰⁰	Not guideline condition
Ersek 2003 ⁴⁰⁶	Intervention targeted at single condition only
Fitzner 2013 ⁴²⁶	Incorrect study design
Fraccaro 2015 ⁴⁴¹	No relevant
Freedland 2015 ⁴⁴⁷	Incorrect intervention
Fu 2003 ⁴⁶¹	Not guideline condition
Gitlin 2006 ⁴⁹¹	Incorrect interventions
Goeppinger 2007 ⁴⁹⁶	Inappropriate comparison
Goodrich 2012 ⁵⁰²	Incorrect study design
Griffiths 2005 ⁵¹⁵	Not guideline condition
Gustavsson 2010 ⁵²⁷	Not guideline condition
Gutiérrez 2009 ⁵²⁸	Intervention targeted at single condition only
Harrison 2012 ⁵⁴⁹	Inappropriate comparison
Haugli 2003 ⁵⁵²	Not guideline condition
Hickman 2015 ⁵⁷⁷	No relevant outcomes
Janke 2014 ⁶³⁵	Trial protocol
Jerant 2009 ⁶⁴⁶	Not guideline condition
Johansson 2012 ⁶⁵⁰	Not guideline condition

Study	Exclusion reason
Jonker 2015 ⁶⁵⁶	Incorrect population
Karhula 2015 ⁶⁷⁴	Incorrect population
Katon 2004 ⁶⁷⁹	Intervention targeted at single condition only
Kennedy 2007 ⁶⁸⁵	Not guideline condition
Kilbourne 2009 ⁶⁹⁴	Not guideline condition
Kogan 2013 ⁷⁰⁷	Incorrect study design
Lenferink 2013 ⁷⁵⁴	Trial protocol
Lorig 2001 ⁷⁷⁷	Not guideline condition
Lorig 2003 ⁷⁷⁸	Not guideline condition
Lorig 2006 ⁷⁷⁹	Not guideline condition
Lynch 2014 ⁷⁹⁴	Inappropriate comparison
Masters 2013 ⁸²²	Incorrect interventions
Mccusker 2012 ⁸³²	No comparison
McCusker 2015 ⁸³³	Incorrect population
Mcgregor 2011 ⁸³⁹	Incorrect interventions
Millard 2013 ⁸⁵⁷	Not guideline condition. Systematic review.
Morgan 2009 ⁸⁷⁷	Incorrect interventions
Mueser 2012 ⁸⁸⁴	No comparison
Naik 2012 ⁸⁸⁷	No comparison
Nelson 2014 ⁸⁹⁸	Intervention targeted at single condition only
Nobis 2013 ⁹¹⁰	Trial protocol
O'hara 2002 ⁹¹⁸	Not guideline condition
Ory 2013 ⁹³¹	No comparison
Packer 2012 ⁹³⁸	Inappropriate comparison
Padwal 2013 ⁹⁴⁰	Trial protocol
Peters-klimm 2007 ⁹⁶¹	Not guideline condition
Plow 2014 ⁹⁸¹	Not guideline condition
Popa-velea 2014 ⁹⁸⁴	Review
Quinones 2014 ⁹⁹⁹	Systematic review
Rae-grant 2011 ¹⁰⁰⁵	Not guideline condition
Reed 2011 ¹⁰¹³	Trial protocol
Ritter 2011 ¹⁰²⁴	Incorrect study design
Sajatovic 2011 ¹⁰⁶¹	No comparison
Sanchez 2012 ¹⁰⁷³	Not guideline condition
Sease 2013 ¹¹⁰²	Inappropriate comparison
Shively 2013 ¹¹¹⁹	Intervention targeted at single condition only
Steultjens esther 2003 ¹¹⁴⁸	Systematic review. Not guideline condition.
Stockl 2010 ¹¹⁵⁰	Not guideline condition
Stringer 2011 ¹¹⁵³	Incorrect study design
Swerissen 2006 ¹¹⁶¹	Not guideline condition
Tang 2012 ¹¹⁷⁰	Intervention targeted at single condition only
Toobert 2011 ¹²⁰²	Not guideline condition
Turner 2014 ¹²¹⁸	Not guideline condition

Study	Exclusion reason
Utriyaprasit 2010 ¹²²³	Not guideline condition
Van bastelaar 2008 ¹²²⁶	Trial protocol
Van der voort 2011 ¹²²⁹	Not guideline condition
Vera 2010 ¹²⁴²	Incorrect interventions
Vieira 2013 ¹²⁴⁷	Incorrect interventions
Vlaeyen 1996 ¹²⁵⁴	Not guideline condition
Voeller 2005 ¹²⁵⁵	Not guideline condition
Von korff 2011 ¹²⁶⁰	Inappropriate comparison
Von korff 2012 ¹²⁶¹	Incorrect interventions
Wakabayashi 2011 ¹²⁶⁷	Intervention targeted at single condition only
Wang 2003 ¹²⁷⁸	Not guideline condition
Warrington 2003 ¹²⁸¹	Intervention targeted at single condition only
Warsi 2004 ¹²⁸²	Systematic review
Wasson 1984 ¹²⁸⁵	Not guideline condition
Weinstock 2011 ¹²⁹⁵	Intervention targeted at single condition only
Woltmann 2012 ¹³¹⁴	Not guideline condition
Wong 2014 ¹³¹⁵	Not guideline condition
Wu 2012 ¹³²⁰	Not guideline condition
Yohannes 2010 ¹³²⁷	Systematic review. Incorrect interventions.
Zonneveld 2009 ¹³⁴⁸	Not guideline condition
Zonneveld 2012 ¹³⁴⁹	Not guideline condition
Zwisler 2005 ¹³⁵⁶	Not guideline condition

L.7 Format of encounters

Table 270: Studies excluded from the clinical review

Study	Exclusion reason
Adams 2010 ¹¹	Not guideline condition
Aimonino 2001 ²⁰	Incorrect intervention
Aimonino Ricauda 1998 ¹⁹	Incorrect intervention
Altiner 2013 ⁴⁰	Protocol
Angstman 2009 ⁵⁴	Not guideline condition
Antoniades 2012 ⁵⁸	Not guideline condition
Barberan-Garcia 2014 ⁹²	Incorrect intervention
Bartels 2004 ⁹⁷	Review
Beretta 2014 ¹²¹	Incorrect intervention
Black 2013 ¹³⁹	Incorrect intervention
Bowles 2011 ¹⁷⁷	Incorrect population
Breslow 2004 ¹⁸⁹	Not guideline condition
Breslow 2004a ¹⁸⁸	Comment
Buist 2014 ²⁰¹	Incorrect intervention
Cartier 2013 ²²²	Review

Study	Exclusion reason
Castelnuovo 2010 ²²⁵	Protocol
Castelnuovo 2011 ²²⁴	No relevant outcomes
Chan 2011 ²³⁶	Not guideline condition
Cole 2002 ²⁷⁹	Single condition focused
Coventry 2013 ³⁰²	Protocol
Coventry 2015 ³⁰³	Incorrect intervention
Cully 2014 ³¹²	Protocol
Dar 2009 ³²³	Not guideline condition
Darkins 2008 ³²⁴	No comparison
Deheer 2013 ³³³	Protocol
Dobscha 2009 ³⁶¹	Not guideline condition
Edelman 2010 ³⁸³	Incorrect intervention
Edelstein 1993 ³⁸⁴	Incorrect interventions
Feltzcornelis 2013 ⁴²¹	Incorrect interventions
Flodgren 2015	Systematic review – checked for references
Friedman 1996 ⁴⁵⁸	Not guideline condition
Gardner 2014 ⁴⁷¹	Incorrect interventions
Giordano 2013 ⁴⁸⁶	Single condition focused
Harris 2011A ⁵⁴⁸	Not guideline condition
Hirani 2014 ⁵⁸⁴	Not guideline condition
Ho 2014 ⁵⁹⁰	Incorrect study design
Hofmann 2015 ⁵⁹⁴	Incorrect population
Jia 2009 ⁶⁴⁸	Not guideline condition
Junius-Walker 2012 ⁶⁶⁵	No relevant outcomes
Krahn 2006 ⁷¹¹	Single condition focused
Kroenke 2013 ⁷¹⁵	Not guideline condition
Lewis 2010 ⁷⁶³	Incorrect population
Liddy 2008 ⁷⁶⁷	No comparison
Marsteller 2010 ⁸¹⁵	No relevant outcomes reported
Martin 2011 ⁸¹⁷	Not guideline condition
Menon 2001 ⁸⁴⁶	Mental health only
Nakamura 1999 ⁸⁸⁸	Incorrect intervention
Nassar 2014 ⁸⁸⁹	Incorrect intervention
O'Neil 2011 ⁹²⁰	Protocol
Rabow 2004 ¹⁰⁰⁰	Not guideline condition
Ricauda 2004 ¹⁰¹⁷	Not guideline condition
Rochette 2010 ¹⁰³⁰	Protocol
Rochette 2013 ¹⁰³¹	Not guideline condition
Schwarz 2008 ¹⁰⁹⁹	Single condition focused
Slaets 1997 ¹¹²⁶	Incorrect interventions
Soran 2008 ¹¹³⁸	Incorrect population
Sweeney 2007 ¹¹⁶⁰	Incorrect intervention
Taggart 2009 ¹¹⁶³	Qualitative study

Study	Exclusion reason
Takahashi 2010 ¹¹⁶⁴	Protocol
Taveira 2011 ¹¹⁷⁹	Incorrect interventions
Tibaldi 2004 ¹¹⁹⁰	Not guideline condition
Trief 2006 ¹²¹⁵	Single condition focused
Wade 2005 ¹²⁶⁴	Incorrect interventions
Wakefield 2011 ¹²⁶⁸	No relevant outcomes reported
Wakefield 2012 ¹²⁶⁹	No relevant outcomes reported
Weinerman 2005 ¹²⁹⁴	Not guideline condition
Weinstock 2011 ¹²⁹⁵	Single condition focused
White 2010 ¹³⁰⁰	No comparison
Whitford 2007 ¹³⁰¹	Protocol
Williams 2010 ¹³⁰⁴	Protocol
Wrede 2013 ¹³¹⁹	No relevant outcomes
Yount 2014 ¹³²⁸	Inappropriate comparison
Yu 2014 ¹³³⁰	Protocol
Zuckerman 1992 ¹³⁵³	Not guideline condition
Zullig 2014 ¹³⁵⁴	No relevant outcomes reported

Appendix M: Excluded health economic studies

M.1 Principles/Barriers of care

M.1.1 Principles of care

Table 271: Studies excluded from the economic review

Reference	Reason for exclusion
None	

M.1.2 Barriers of care

Table 272: Studies excluded from the economic review

Reference	Reason for exclusion
None	

M.2 Identification

M.2.1 Unplanned hospital admissions

Table 273: Studies excluded from the economic review

Reference	Reason for exclusion
None	

M.2.2 Health-related quality of life

Table 274: Studies excluded from the economic review

Reference	Reason for exclusion
None	

M.2.3 Admission to care facility

Table 275: Studies excluded from the economic review

Reference	Reason for exclusion
None	

M.2.4 Life expectancy risk tools

Table 276: Studies excluded from the economic review

Reference	Reason for exclusion
None	

M.2.5 Polypharmacy: unplanned hospital admissions

Table 277: Studies excluded from the economic review

Reference	Reason for exclusion
None	

M.2.6 Polypharmacy: health-related quality of life

Table 278: Studies excluded from the economic review

Reference	Reason for exclusion
None	

M.2.7 Polypharmacy: admission to care facilities

Table 279: Studies excluded from the economic review

Reference	Reason for exclusion
None	

M.2.8 Polypharmacy: mortality

Table 280: Studies excluded from the economic review

Reference	Reason for exclusion
None	

M.3 Frailty

Table 281: Studies excluded from the economic review

Reference	Reason for exclusion
None	

M.4 Delivering an approach to care that takes account of multimorbidity

M.4.1 Treatment burden

Table 282: Studies excluded from the economic review

Reference	Reason for exclusion
None	

M.4.2 Ranking

Table 283: Studies excluded from the economic review

Reference	Reason for exclusion
None	

M.4.3 Stopping antihypertensive treatment

Table 284: Studies excluded from the economic review

Reference	Reason for exclusion
None	

M.4.4 Stopping drugs for osteoporosis

Table 285: Studies excluded from the economic review

Reference	Reason for exclusion
None	

M.4.5 Stopping statins

Table 286: Studies excluded from the economic review

Reference	Reason for exclusion
None	

M.5 Interventions

M.5.1 Models of care

Table 287: Studies excluded from the economic review

Reference	Reason for exclusion
Gage 2013 ⁴⁶⁴	This study was selectively excluded due to a combination of applicability and methodological limitations. UK resource use and unit cost data (2008-9) may not reflect current NHS context. Health outcomes not expressed as QALYs. Time horizon may not be sufficient to capture all benefits and costs if benefits persist beyond 9 months. Within-trial analysis and so does not reflect full body of available evidence for this comparison; Gage2013 is not included in the clinical review as it is a case study, participants are not randomised and therefore have significantly different characteristics between comparators. No sensitivity analyses undertaken.

M.5.2 Holistic assessment

Table 288: Studies excluded from the economic review

Reference	Reason for exclusion
Nikolaus 1999 ⁹⁰⁶	This study was assessed as not applicable. German resources use and costs from before 1999 judged unlikely to be applicable to current UK NHS context.

M.6 Self-management

Table 289: Studies excluded from the economic review

Reference	Reason for exclusion
Battersby 2013 ¹⁰³	This study was assessed as partially applicable with very serious limitations. Only part of the intervention costs included. Costs for full time horizon not reported – no downstream healthcare utilisation costs included. Source of unit costs not reported.
Blakeman 2014 ¹⁴⁵	This study was assessed as not applicable. Costs included out of pocket costs and cost of lost productivity and it is not possible to present NHS/PSS costs only.

M.7 Format of encounters

Table 290: Studies excluded from the economic review

Reference	Reason for exclusion
Pare 2013 ⁹⁴³	This study was identified but excluded due to a combination of combination of limited applicability and serious methodological limitations. It was felt that the study had limited applicability as it may not reflect a UK NHS content, since it was taken from a Canadian healthcare perspective and health outcomes were not expressed in QALYs. In addition the study was deemed to be of limited quality for it to be used to make any recommendation. First, the study was not included in the clinical review since it is not an RCT, and therefore does not reflect clinical evidence. Second, it was considered a follow-up period of less than one year would not fully capture all the downstream cost/effects of the intervention. Second, many of the health outcomes required from the review protocol were not reported: HRQoL, mortality, functional outcomes. Third, uncertainty was not adequately taken into account through its omission of sensitivity analyses. Finally, health service use has seasonal elements which were not taken into account in the study which would influence its results.

Appendix N: Cost-effectiveness analysis: holistic assessment compared to usual care

N.1 Introduction

A systematic review was conducted to assess the effectiveness of holistic assessment (HA) where this was categorised as low intensity and high intensity according to the format of the assessment and in the number and seniority of clinicians conducting the assessment in the included studies. High intensity studies were those that required highly trained individuals performing interview/examination based assessments over longer periods of time or included formal multidisciplinary meetings to formulate care plans. Low intensity studies typically involved a largely standardised questionnaire based assessment and care plan formulation involving 1 or 2 individuals familiar with the person (for example, the nurse who performed the assessment and a GP). The clinical review showed that community low intensity Holistic Assessment (HA) is clinically effective at lowering mortality for people with multimorbidity.

Therefore an economic model was prioritised to assess whether the increase in effectiveness associated with low intensity holistic assessment in a community setting justifies the incremental costs. The question that the model tries to address is:

What is the cost-effectiveness of community (low intensity) holistic assessment to improve continuity of care and outcomes in people with multimorbidity?

N.2 In the clinical review, high intensity HA was found not to significantly improve outcomes compared to usual care and for this reason it was not considered in the model. Methods

N.2.1 Model overview

N.2.1.1 Comparators

The model compared community low intensity HA to no HA (usual care). The GDG defined HA as a comprehensive assessment of a person that considers their physical health, mental health, social conditions and functional capabilities, which is then followed by the development of a care plan that seeks to address needs identified. This differs from usual care which is a more reactive process involving primary or community care services and social care. The details of the intervention (HA) were obtained from the clinical study which contributed the most to the clinical outcomes, that is, the study which had the highest weight in the meta-analysis on mortality. In this study (Frese 2012)⁴⁵⁰ people in the HA arm received an assessment from a nurse, followed by the formulation and agreement of a care plan which is jointly done by a GP and a nurse. The usual care arm received no assessment or care plan. Few patients in the clinical study had a repeated HA, therefore in a sensitivity analysis we assumed the HA was repeated every year for the first three years.

N.2.1.2 Population

The population considered in the analysis reflected the inclusion criteria of the studies in the clinical review (older adults (>65 years) with multimorbidity in the community). Based on the main study

included in the clinical review,⁴⁵⁰ the average age was set to 80 as the population in the study consisted in patients older than 70 and the average age of the cohort was 80. The initial age was changed in a sensitivity analysis.

N.2.1.3 Time horizon, perspective, discount rates used

The time horizon reflects the duration of the effect of the intervention. Therefore, because a difference in mortality between HA and usual care was observed in the clinical review, a lifetime horizon is used for the analysis. The analysis follows the standard assumptions of the NICE reference case⁸⁹⁴ including discounting at 3.5% for costs and health effects, and incremental analysis is conducted. A sensitivity analysis using a discount rate of 3.5% for costs and 1.5% for health benefits is conducted. Other scenarios will include varying individual parameters which are expected to be driving the result.

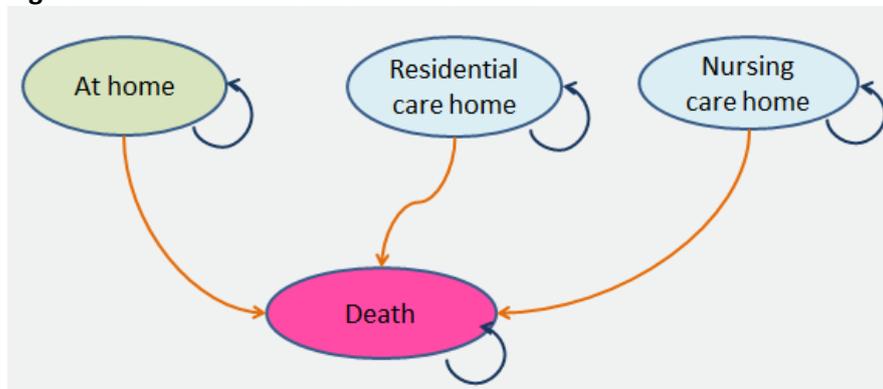
N.2.2 Approach to modelling

In order to take into account natural mortality and a possible repetition of holistic assessment, a Markov model was developed with a one-month cycle length to account for the high mortality rate. The main outcome considered in the model was mortality which the clinical review found was different between the two arms. No difference in quality of life (QoL) was found from the clinical review and this outcome was assumed to be independent from the intervention received.

N.2.2.1 Model structure

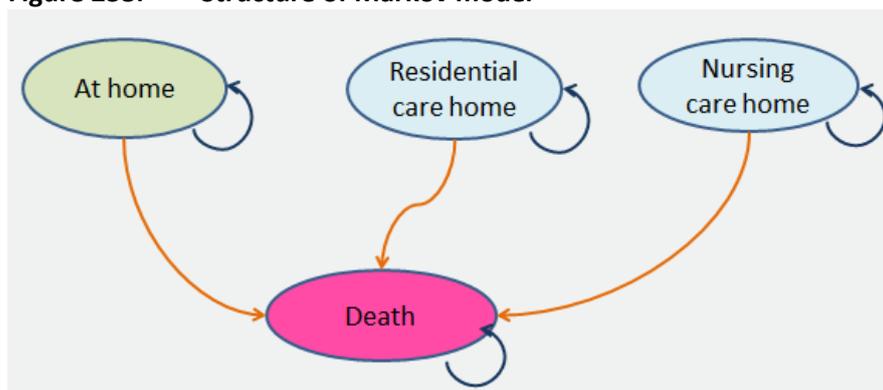
The structure of the model is set out in

Figure 238: Structure of Markov model



. The model is mainly based on the mortality data which showed a clinically important difference between arms and also takes into account the possible residency status of the individual, therefore within both arms of the model people start either at home, in a residential care home, or in a nursing care home. They will then move to the 'Death' state according to the intervention-specific probability. There is no other possible transition between 'at home', 'residential care home', and 'nursing care home' states because no evidence was found to inform these transition probabilities. Mortality specific to the residency status of individuals could not be incorporated into the model and this was considered independent from the setting.

Figure 238: Structure of Markov model



Costs and QALYs are accrued in each cycle based on the proportion of individuals in each health state, and according to the cost of the intervention in cycle 0.

N.2.2.2 Uncertainty

The model was built probabilistically to take account of the uncertainty around input parameter point estimates. A probability distribution was defined for each model input parameter. When the model was run, a value for each input was randomly selected simultaneously from its respective probability distribution; mean costs and mean QALYs were calculated using these values. The model was run 10,000 times and results were summarised.

The way in which distributions are defined reflects the nature of the data, so for example utilities were given a beta distribution, which is bounded by 0 and 1, reflecting that a quality of life weighting will not be outside this range. All of the variables that were probabilistic in the model and their distributional parameters are detailed in Table 291 and in the relevant input summary tables in Section N.2.3. Probability distributions in the analysis were parameterised using error estimates from data sources.

Table 291: Description of the type and properties of distributions used in the probabilistic sensitivity analysis

Parameter	Type of distribution	Properties of distribution
Utility	Beta	Bounded between 0 and 1. Derived from mean and sample size (n). Alpha and Beta values were calculated as follows: Alpha = mean × n Beta = n – Alpha
Disutility	Gamma	Bounded at 0, positively skewed. Derived from mean and its standard error. Alpha and Lambda values were calculated as follows: Alpha = (mean/SE) ² Lambda = mean/SE ²
Hazard ratio	Lognormal	The natural log of the mean was calculated as follows: Mean = ln(mean cost) – SE ² /2 Where the natural log of the standard error was calculated by: SE = [ln(upper 95% CI) – ln(lower 95% CI)]/(1.96×2)
Probabilities and	Beta	Bounded between 0 and 1. Derived using event data given

Parameter	Type of distribution	Properties of distribution
proportions		in the clinical studies. Alpha and Beta values were calculated as follows: Alpha = (number of events) Beta = (sample size) – (number of events)
Resource use	Lognormal	The natural log of the mean was calculated as follows: Mean = $\ln(\text{mean cost}) - SE^2/2$ Where the natural log of the standard error was calculated by: $SE = [\ln(\text{upper 95\% CI}) - \ln(\text{lower 95\% CI})]/(1.96 \times 2)$

The following variables were left deterministic (that is, they were not varied in the probabilistic analysis):

- the cost-effectiveness threshold (which was deemed to be fixed by NICE),
- the resource, including time and cost of staff, required to implement each strategy (assumed to be fixed according to national pay scales and programme content)

In addition, various deterministic sensitivity analyses were undertaken to test the robustness of model assumptions. In these, one or more inputs were changed and the analysis rerun to evaluate the impact on results and whether conclusions on which intervention should be recommended would change.

N.2.3 Model inputs

N.2.3.1 Summary table of model inputs

Model inputs were based on clinical evidence identified in the systematic review undertaken for the guideline, supplemented by additional data sources as required. Model inputs were validated with clinical members of the GDG. A summary of the model inputs used in the base-case (primary) analysis is provided in **Table 292** below. More details about sources, calculations and rationale for selection can be found in the sections following this summary table.

Table 292: Overview of parameters and parameter distributions used in the model

Parameter description	Point estimate	Probability distribution	Distribution parameters	Source
Patients characteristics				
Initial age	80			Frese 2012 ⁴⁵⁰
Proportion of patients living in their own home	0.923		$\alpha=1464, \beta=122$	Richardson 2011 ¹⁰¹⁸
Proportion of patients living in nursing home	0.0385		Residual from parameter above divided by 2	Residual from parameter above divided by 2
Proportion of patient living in residential care home	0.0385			Assumption: same proportion of people living in nursing home
Proportion of male/female	0.36/0.64	Beta	Male: $\alpha=576, \beta=1010$ Female calculated as a residual	Richardson 2011 ¹⁰¹⁸
Number of conditions on average in patients with	4			Barnett 2012 ⁹⁵ - see paragraph N.2.3.2

Parameter description	Point estimate	Probability distribution	Distribution parameters	Source
multimorbidity				
Number of drugs on average in patients with multimorbidity	5			Based on number of conditions – see paragraph N.2.3.2
Number of drugs on average in general population	3			Barnett 2012 ⁹⁵ - see paragraph N.2.3.2
Cost (£)				
Cost of HA	£140			See paragraph N.2.3.6.1
Cost nursing home per month	£615			See paragraph N.2.3.6.2
Cost residential care home per month	£128			See paragraph N.2.3.6.2
Cost own home per month	£21.38			See paragraph N.2.3.6.2
Baseline Risk				
Mortality rate	Dependent on age, gender, and MM status			England Life Table ⁹²²
HR – increase in mortality for each additional drug taken	1.177	Lognormal	$\mu = 0.163, \sigma = 0.021$	Ahmad 2005 ¹⁴ - See paragraph N.2.3.3
Effectiveness				
HR mortality (HA vs usual care)	0.78	Lognormal	$\mu = -0.251, \sigma = 0.078$	Frese 2012 ⁴⁵⁰
Quality of life				
Utility in people with multimorbidity living in their own home	0.58	Beta	$\alpha=399.93, \beta=293.07$	Heyworth 2009 ⁵⁷⁶ - see paragraph N.2.3.5
Disutility in people in residential/nursing care home	0.13	Gamma	$\alpha=19.14, \lambda =147.24$	Rodriguez-Blazquez 2012 ¹⁰³⁷ - see paragraph N.2.3.5
Model specification				
Discount rate (health effects and costs)	3.5%			NICE Reference Case ⁸⁹⁴

Abbreviations: HA = holistic assessment; HR=hazard ratio.

N.2.3.2 Initial cohort settings

Using data from the UK study by Richardson et al (2011)¹⁰¹⁸ for the polypharmacy cohort in the study, it was assumed that 92.3% of the population would start in the community and the remaining 7.7% would start in a care home (equally split between a residential and nursing care home). When both groups in the study were considered (polypharmacy and no polypharmacy) the proportion of people living at home was 96%. This was not very different from 2011 Census data which showed that 97% people aged 65 or more live in a household. In the base case we used the data from the polypharmacy group as this was thought to be more representative of a multimorbid population and it would also be in line with a conservative approach (that is, would favour usual care instead of HA as future costs would be lower in the own home state).

The split between male and female (36% vs 64%) was obtained from the same study by Richardson et al (2011).¹⁰¹⁸

The population in the model was defined in terms of number of conditions or number of medications, these two characteristics being linked. The link was created using the data from Barnett et al. (2012)⁹⁵, a cross-sectional study where a database of 1,751,841 people registered with 314 medical practices in Scotland was used to extract data on multimorbidity. In the subgroup of people aged 65 and over, those with multimorbidity (defined as two or more conditions) had an average of 5 prescriptions, while those without multimorbidity had an average of 3 prescriptions. Each number of conditions was linked to a given number of medications prescribed and vice versa, as reported in Table 293.

Table 293: Link between number of conditions and number of drugs prescribed

Number of conditions	Number of drugs taken(a)
0	0
1	2
2	3
3	4
4	5
5	6
6	7
7	8
8	8
9	9
10	10
11	10
12	11
13	11
14	11
15	12
16	14
17	15

(a) Based on mid-point of a range

The definition of these two characteristics was necessary to estimate the baseline mortality risk for people in our model as this was thought to be different from the general population mortality. This is described in more detail in the next section.

N.2.3.3 Baseline event rates

To make the model more applicable to a UK setting, baseline mortality was taken from the UK National Life Tables provided by the Office of National Statistics (ONS),⁹²² and then adjusted to account for this being a population with multimorbidity. This was done by using polypharmacy as a continuous predictor, as the clinical review conducted for this guideline on the mortality risk based on polypharmacy showed an increased risk for each additional drug. The study by Ahmad 2005¹⁴ reported a hazard ratio of 1.18 for mortality rate for each additional medication. This was applied to the overall mortality rate as follows:

$$m_{rate_{MM}} = m_{rate_{GP}} \times HR_{drugs}^{\left(\frac{N_{drugs_{MM}}}{N_{drugs_{GP}}}\right)}$$

where

m_rateMM is the mortality rate in the MM population in the model

m_rateGP is the mortality rate in the general population as reported in the Life Tables

HR_drugs is the increase in mortality for each additional drug as reported in Ahmad 2005

N_drugs_MM and N_drugs_GP are respectively the mean number of drug prescribed in the MM and in the general population as described in the previous paragraph.

The approach to estimate the baseline mortality rate in a population with MM was varied in a sensitivity analysis (see paragraph N.2.5).

The baseline mortality for the general population was linked to the age of the individual throughout the model.

N.2.3.4 Relative treatment effects

Once baseline mortality rate for a multimorbid population had been calculated, the mortality rate (and associated transition probability) for the HA arm was calculated by applying the HR of 0.78 from the Frese 2012 study.⁴⁵⁰ This study was selected to inform the effectiveness data in the model as the intervention described in this study reflected the type of HA that the GDG considered for recommendation as it is a low intensity intervention with a potential impact on effectiveness; furthermore this study had the longest of follow-up and was the main contributor to the measure of clinical effectiveness in the clinical review. When this study was combined with the other long-term follow up (>24 months) study by Senior et al (2014),¹¹⁰³ the resulting HR was very similar (0.79).

In a sensitivity analysis the impact of the relative treatment effect was assessed by varying the mortality HR estimate.

The study by Frese et al (2012)⁴⁵⁰ reported also an outcome combining the residency status and mortality of patients; however it was impossible to elicit from these data any changes in residency status (that is, admission to residential or nursing care homes). Therefore this parameter was assumed to be constant and if patients started the model in a setting no transition to a different one was allowed.

N.2.3.5 Utilities

Since no suitable quality of life (QoL) data was found within the clinical review, an additional search was conducted to find what QoL a general multimorbid population would be experiencing.

Priority was given to studies which were conducted in the UK and which reported EQ5D as the utility measure. Two studies were identified which met these criteria (Heyworth et al (2009)⁵⁷⁶ and Parker 2014⁹⁴⁶); eventually the study by Heyworth et al (2009)⁵⁷⁶ was deemed more appropriate for the modelling purpose as the other one by Parker et al (2014)⁹⁴⁶ reported EQ5D estimated through regression for defined groups of conditions and according to age, gender, smoking status and deprivation index, which did not allow for an overall value to be estimated.

In the selected study, data are specific to the number of chronic conditions. In the base case this is linked to the average number of conditions in the MM population as defined in the population setting (see paragraph N.2.3.2). The EQ5D scores associated with the number of chronic conditions are reported in Table 294.

Table 294: Weighted EQ5D scores for people with MM

# chronic conditions	# people	EQ5D	Weighted EQ5D for general MM population
0	2934	0.83	-
1	1209	0.69	-
2	510	0.61	0.4489
3	164	0.5	0.1183
4	15	0.39	0.0084
5	4	0.25	0.0014
Average EQ5D score for MM population			0.5771

In a different analysis the mean EQ5D score for people with MM (2 or more chronic conditions) was estimated using a weighted average. The table above also report this value which was used in a sensitivity analysis for a general MM population, with no specific definition of number of conditions.

The values reported above were attached to the 'At home' health state. A further search was conducted to find the QoL experienced among a multimorbid population who were in a care home setting. For people in a residential or nursing care home we used a 'disutility' estimated from the study by Rodriguez-Blazquez et al (2012)¹⁰³⁷. In this study, the average EQ5D score in people older than 78 living at home was 0.71, while the score in institutionalised patients was 0.58. The difference between the score in the two groups (0.13) was applied to the QoL of the 'at home' state to obtain the QoL value for individuals in the nursing or residential care home state in the model.

N.2.3.6 Resource use and costs

N.2.3.6.1 Intervention cost

The cost of the intervention was based on the description of holistic assessment provided in the main clinical study⁴⁵⁰ supplemented by GDG opinion when the health care professional time was not available from the study or when the intervention did not match what would happen in the NHS setting.

The intervention described in the study consisted in home visits with comprehensive geriatric assessment (CGA), using the STEP-tool (standardised assessment of elderly people in primary care in Europe; a combination of a structured questionnaire and a structured physical examination) and Barthel-Index, Lambeth questionnaire, Tinetti-gait score, Hamilton Depression scale, MMSE, Hierarchic Dementia scale, clock drawing test and COOP-Charts, followed by recommendations for the general practitioner. The CGA was performed by a trained medical student and took up to 1 hour. Recommendations were made by geriatrician trainees under the supervision of experienced geriatricians.

The GDG advised that in the UK the following health care professionals would be involved with the two components of the intervention:

- A. Assessment would be conducted by a community nurse and would require 1 hour. The main change from the intervention described in the study is that a nurse does the assessment instead of a trained medical student.
- B. Development of a care plan would be done by a GP and a nurse and would require 30 minutes each.

Based on the above definition of the intervention, the costing for each component and the resulting total cost are reported in Table 295 below.

Table 295: Cost of holistic assessment

Component	Health care professional involved	Cost per hour (a)	Time required	Total cost
Assessment	Community nurse – band 6	£57 (b)	1 hour	£57
Formulation of care plan	Community nurse – band 6	£57 (b)	0.5 hour	£28.5
	GP	£109 (c)	0.5 hours	£54.5
TOTAL				£140

(a) Source: PSSRU 2014³¹⁶

(b) Cost of one hour of patient-related work

(c) Cost of general medical service contract activity, excluding travel time costs and direct care staff costs.

The estimated cost of £140 for each HA was applied to each individual in the HA arm in the model, while no cost was applied to the usual care arm since the intervention is assumed to be implemented in addition to usual care.

Carrying out the intervention may lead to additional cost if a need for further care or a change in management is identified as a consequence of the holistic assessment. The quantification of these costs was discussed extensively with the GDG and it was agreed that there was no point estimate or range that could be used with any degree of certainty. This is because each individual patient may require expensive further care or none at all and it was difficult to decide on the cost of different levels of care and the proportion of people receiving it.

We also checked details about further care in the clinical studies included in the clinical review and we found that the only significant outcome was admission to care facilities which was lower for the HA arm. We also considered the economic analysis in the social care guideline⁸⁹¹ where the significant results showed a reduced use in acute care service in the second year of the intervention, a greater community healthcare service use in the two years of the intervention (mental health and rehabilitation), lower cost in the third year of the intervention. In conclusion, no data was found showing an increase in management costs.

Due to these difficulties, we decided to assess the impact of this cost in a threshold analysis where we varied the additional cost from £0 to any positive value. This is described in the sensitivity analysis section N.2.5.

The cost of the intervention was added at the beginning of the model (cycle 0) as a one off cost, with the exception of a sensitivity analysis whereby the intervention was assumed to be repeated every two years (see paragraph N.2.5). The cost of the change in management which was evaluated in a sensitivity analysis was added to each cycle, therefore the threshold analysis identified the cost per month at which the intervention would not be cost effective (see paragraph N.2.5).

N.2.3.6.2 Health states

Alive individuals in the model can be in three different health states which are independent from the intervention. A health-related cost was attached to each of them based on the health care resources used in different settings.

Own home

To estimate the average health care resource use for individuals in this health state, we obtained the average number of consultations with GP, practice nurse, and community nurse for people living in their own home from a Scottish national statistics dataset⁶²⁶ where data were reported separately

for different age and gender groups (data for the 'over 75' group were used in the model). These data are reported in Table 296 below.

Table 296: Resource use and cost for the 'own home' health state

	Average number of consultations per year per patient (male)	Probability distributions and parameters (male)	Average number of consultations per year per patient (female)	Probability distributions and parameters (female)	Cost per consultation
GP	5.3	Lognormal $\mu = 1.673, \sigma = 0.033$	5.5	Lognormal $\mu = 1.705, \sigma = 0.032$	£38 (a)
Practice nurse	4.3	Lognormal $\mu = 1.448, \sigma = 0.043$	3.5	Lognormal $\mu = 1.240, \sigma = 0.044$	£11.37 (b)
Community nurse	3.9	Lognormal $\mu = 1.358, \sigma = 0.125$	5.6	Lognormal $\mu = 1.717, \sigma = 0.118$	£39 (c)

(a) Average cost of GP visit lasting 11.7 minutes including direct care staff cost (PSSRU 2014)³¹⁶

(b) Average cost per hour contact is £44 and average minutes per consultation 15.5.

(c) Average cost for a face to face contact in district nursing services

The number of consultations was divided by 12 in each cycle of the model to account for the one-month cycle length.

Based on the data above the total monthly cost for this health state is £37.

Nursing care home and residential care home

People in these settings would use GP services and community nursing services. Although these data are not available in the recent PSSRU publications, they were reported in the PSSRU 2010³¹⁵ publication and were inflated to 2014 costs. For people in the nursing care home setting, the NHS contribution to nursing care (£110 per week) (PSSRU 2014)³¹⁶ was added to the cost of the state. Data used to calculate the cost of each monthly cycle are reported in Table 297 below.

Table 297: Resource use and cost for the 'nursing care home' and residential care home' health states

	Cost– Nursing care home	Cost– Residential care home
GP services (per week)	£31 (a)	£20 (a)
Community nurse (per week)	£0.81 (a)	£9.5 (a)
NHS contribution to nursing care (per week)	£110 (b)	-
Total per week	£141.81	£29.5
Total per month	£615	£128

(a) Source: PSSRU 2010³¹⁵ uplifted using inflation index from PSSRU 2014³¹⁶

(b) Source: PSSRU 2014³¹⁶

N.2.4 Computations

The model was constructed in TreeAge 2015 and was evaluated by cohort analysis. Time dependency was built in by cross referencing the cohorts age as a respective risk factor for mortality.

To calculate QALYs for each cycle, $Q(t)$, the time spent in the alive state of the model (1 month or 0.08 years) was weighted by a utility value that is dependent on the time spent in the model and the treatment effect. A half-cycle correction was not applied as the cycle length was already short (1 month). QALYs were discounted to reflect time preference (discount rate 3.5%). QALYs during the first cycle were not discounted. The total discounted QALYs were the sum of the discounted QALYs per cycle. The total discounted QALYs were the sum of the discounted QALYs per cycle.

Costs per cycle, $C(t)$, were calculated in the same way as QALYs. Costs were discounted to reflect time preference (discount rate 3.5%) in the same way as QALYs using the following formula:

$$\text{Discounted total} = \frac{\text{Total}}{(1+r)^n}$$

Where:
 r =discount rate per annum
 n =time (years)

N.2.5 Sensitivity analyses

As some parameters in the model were uncertain, the GDG wished to explore whether any modification of important inputs and assumptions in the base case analysis would have an effect on the results. The following sensitivity analyses were conducted:

SA1: Mortality HR from Richardson 2011

While in the base case the HR for mortality was estimated as a continuous variable based on the increase in number of drugs, in a sensitivity analysis the study from Richardson et al (2011)¹⁰¹⁸ used to estimate a fixed HR for mortality in people with MM compared to the general population. This was considered equal to the HR for people on polypharmacy (5 drugs or more) compared to the group of people with no polypharmacy. The HR used was 2.00 for men and 1.79 women. This was applied to baseline mortality rate for the general population to obtain the mortality in the MM population of the model.

SA2: Mortality HR from Jyrkka 2009 – 6 to 9 drugs

The study by Jyrkka et al (2009)⁶⁶⁷ was a non-UK study which reported the HR for mortality in people on 6 to 9 drugs compared to no polypharmacy and in people on 10 or more drugs compared to no polypharmacy (HR = 2.87). In SA2 the value for the group on 6 to 9 was used in the model (HR = 1.50).

SA3: Mortality HR from Jyrkka 2009 – 10 or more drugs

In SA3 the value for the group on 10 or more drugs from the same study⁶⁶⁷ was applied to the baseline mortality rate (HR = 2.87); this would represent a higher risk population.

SA4: Care setting

There was some uncertainty around the proportion of people living at home and how this could affect results. This proportion was varied from 0% to 100%.

SA5: Initial age

The initial age of individuals in the model was varied between 65 and 95.

SA6: Average QoL

While in the base case the utility values were number of conditions-specific, in SA6 we used an average utility score for people with multimorbidity, which is the weighted average reported in Table 294 (0.58).

SA7: Repeat HA

In the base case the intervention is assumed to take place just once in the patient's lifetime, according to the intervention described in the outcome paper.⁴⁵⁰ In a sensitivity analysis we assumed the intervention is repeated every year for the first 3 years, effectively adding its costs for three more years while keeping the same effectiveness as in the base case.

SA8: Cost of HA

The cost of HA as a whole (assessment and formulation of a plan) was doubled to take into account the possibility of a longer time spent by health care professionals in doing this. The total cost of HA used in SA8 is £280. In addition a threshold analysis was performed to assess the impact of the cost of the intervention on the results.

SA9: Cost of nursing care home

In the base case analysis we only incorporated the NHS cost for people in nursing care home; however if a broader perspective has to be adopted, this cost would be much higher. In SA9 we varied the monthly cost of nursing home up to £5,000.

SA10: Mortality HR for intervention

The base case mortality HR for the intervention group compared to usual care was obtained by Frese 2012.⁴⁵⁰ This study had several limitations and the GDG had serious concerns on the reliability of the estimated HR which was 0.78. This value was varied up to 0.999 in SA10.

SA11: Number of conditions

Since many parameters in the model are a function the number of conditions (mortality, QoL), this number was varied between 2 to 8 in SA11.

SA12: Cost of change in care

As described in N.2.3.6.1 no cost due to a change in management subsequent to the HA was included in the model due to difficulties in finding any meaningful value. However the potential cost consequences of HA were assessed in SA12 were an additional monthly cost was added to the individuals in the HA arm of the model. This value was varied in a threshold sensitivity analysis to assess the impact of the further costs on the results.

N.2.6 Model validation

The model was developed in consultation with the GDG; model structure, inputs and results were presented to and discussed with the GDG for clinical validation and interpretation.

The model was systematically checked by the health economist undertaking the analysis; this included inputting null and extreme values and checking that results were plausible given inputs. The model was peer reviewed by a second experienced health economist from the NCGC; this included systematic checking of the model calculations.

N.2.7 Estimation of cost effectiveness

The widely used cost-effectiveness metric is the incremental cost-effectiveness ratio (ICER). This is calculated by dividing the difference in costs associated with 2 alternatives by the difference in QALYs. The decision rule then applied is that if the ICER falls below a given cost per QALY threshold the result is considered to be cost effective. If both costs are lower and QALYs are higher the option is said to dominate and an ICER is not calculated.

$$ICER = \frac{Costs(B) - Costs(A)}{QALYs(B) - QALYs(A)}$$

Where: Costs(A) = total costs for option A; QALYs(A) = total QALYs for option A

Cost-effective if:
 • ICER < Threshold

N.2.8 Interpreting Results

NICE's report 'Social value judgements: principles for the development of NICE guidance'⁸⁹² sets out the principles that GDGs should consider when judging whether an intervention offers good value for money. In general, an intervention was considered to be cost effective if either of the following criteria applied (given that the estimate was considered plausible):

- The intervention dominated other relevant strategies (that is, it was both less costly in terms of resource use and more clinically effective compared with all the other relevant alternative strategies), or
- The intervention costs less than £20,000 per quality-adjusted life-year (QALY) gained compared with the next best strategy.

N.3 Results

N.3.1 Base case

The base case analysis was run both deterministically and probabilistically. The probabilistic results are reported in Table 298 below.

Table 298: Probabilistic base case analysis results (mean per patient)

	Mean cost	Mean QALYs	ICER (£/QALY)	Probability that strategy is most cost-effective [£20k per QALY]
Usual care	£4,704	2.3764		1%
Holistic Assessment	£5,484	2.7003		99%
<i>Incremental</i>	<i>£781</i>	<i>0.3239</i>	2,411	

The results show that HA is more costly but also more effective than usual care in the base case, that is when the parameters of the model were set as described in Table 292. The increase in cost is acceptable at the NICE threshold of £20,000 per QALY gained as the ICER is £2,411, well below this threshold.

The deterministic analysis results are very similar to the probabilistic analysis and they are reported in Table 299 below.

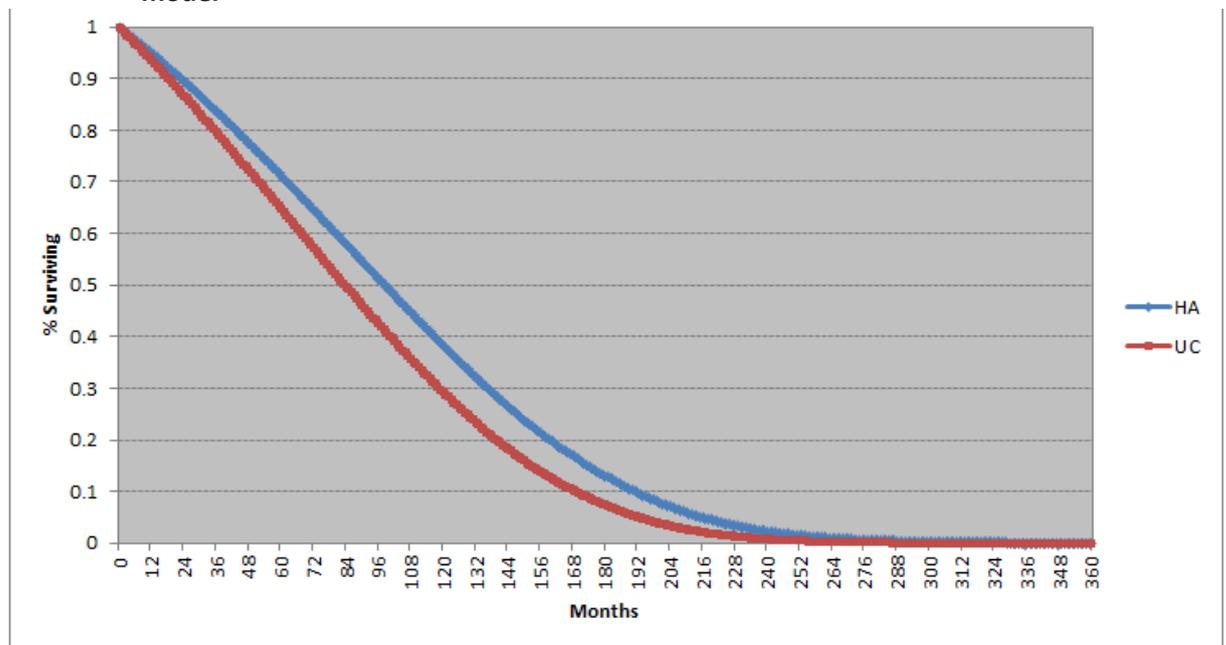
Table 299: Deterministic base case analysis results (mean per patient)

	Mean cost	Mean QALYs	ICER (£/QALY)	Undiscounted costs	Undiscounted life expectancy	Discounted life expectancy
--	-----------	------------	---------------	--------------------	------------------------------	----------------------------

	Mean cost	Mean QALYs	ICER (£/QALY)	Undiscounted costs	Undiscounted life expectancy	Discounted life expectancy
Usual care	£4,712	2.3775		£5,599	7.43	6.26
Holistic Assessment	£5,478	2.6934		£6,621	8.61	7.09
<i>Incremental</i>	<i>£766</i>	<i>0.3159</i>	2,425	<i>£1,022</i>	<i>1.18</i>	<i>0.83</i>

The main driver of the model is the effectiveness of HA in terms of reduction of mortality, which is the only effectiveness assumed for HA. The survival curves for the two arms of the model are shown in Figure 239 below. In this picture the red curve represents the proportion of individuals surviving at each time point (months) in the x axis while the blue curve represents the same for the HA arm.

Figure 239: Survival curve for the usual care (UC) and holistic assessment (HA) arms of the model



N.3.2 Sensitivity analyses

A series of sensitivity analyses were planned and conducted; details are reported in section N.2.5 and results are provided in the sections below. These were run deterministically as no difference was noted between the base case deterministic and probabilistic analysis.

SA1: Mortality HR from Richardson 2011

Table 300: SA1 - results (mean per patient)

	Mean cost	Mean QALYs	ICER (£/QALY)
Usual care	£3868	1.9519	
Holistic Assessment	£4577	2.2391	
<i>Incremental</i>	<i>£709</i>	<i>0.2872</i>	2469

SA2: Mortality HR from Jyrkka 2009 – 6 to 9 drugs

Table 301: SA2 - results (mean per patient)

	Mean cost	Mean QALYs	ICER (£/QALY)
Usual care	£4388	2.2142	
Holistic Assessment	£5133	2.5196	
<i>Incremental</i>	<i>£745</i>	<i>0.3055</i>	2440

SA3: Mortality HR from Jyrkka 2009 – 10 or more drugs

Table 302: SA3 - results (mean per patient)

	Mean cost	Mean QALYs	ICER (£/QALY)
Usual care	£2994	1.5107	
Holistic Assessment	£3628	1.7601	
<i>Incremental</i>	<i>£634</i>	<i>0.2494</i>	2543

SA4: Care setting

The proportion of people living in their own home was varied from 0% to 100%. The ICERs for HA compared to usual care on these two extreme values were respectively £17,800 and £1,570 per QALY. The difference is explained by the fact that people in the HA arm live for longer; therefore if they are in a 'more expensive' health state such as the nursing home state the intervention that increases survival is less cost effective as it does increase QALYs but also costs.

SA5: Initial age

The initial age of individuals in the model was varied between 65 and 95. The ICERs for HA compared to usual care on these two extreme values were respectively £2,337 and £2,735 per QALY. This shows that the initial age did not have much influence on the results.

SA6: Average QoL

Table 303: SA6 - results (mean per patient)

	Mean cost	Mean QALYs	ICER (£/QALY)
Usual care	£4712	3.5663	
Holistic Assessment	£5478	4.0401	
<i>Incremental</i>	<i>£766</i>	<i>0.4738</i>	1617

SA7: Repeat HA

Table 304: SA7 - results (mean per patient)

	Mean cost	Mean QALYs	ICER (£/QALY)
Usual care	£4712	2.3775	
Holistic Assessment	£5829	2.6934	
<i>Incremental</i>	<i>£1117</i>	<i>0.3159</i>	3536

SA8: Cost of HA

Table 305: SA8 - results (mean per patient)

	Mean cost	Mean QALYs	ICER (£/QALY)
Usual care	£4712	2.3775	
Holistic Assessment	£5618	2.6934	
<i>Incremental</i>	<i>£906</i>	<i>0.3159</i>	2868

The threshold analysis on the cost of the intervention showed that HA is cost effective as long as its cost does not exceed £5691. This would represent the cost of both components but does not include the cost of the change in management further to the HA.

SA9: Cost of nursing care home

In SA9 we varied the monthly cost of nursing home up to £5,000. The threshold analysis did not report any values within the range at which the main results would change. In the table below we report the results when the extreme value of £5000 per month was used.

Table 306: SA9 - results (mean per patient)

	Mean cost	Mean QALYs	ICER (£/QALY)
Usual care	£17386	2.3775	
Holistic Assessment	£19836	2.6934	
<i>Incremental</i>	<i>£2450</i>	<i>0.3159</i>	7756

SA10: Mortality HR for intervention

When the base case mortality HR for the intervention group compared to usual care (0.78) was applied, HA was cost effective; however in this threshold analysis HA was not cost effective anymore when the HR was 0.994 or above. This value is very close to 1, which shows that even a small improvement in mortality would make HA cost effective.

SA11: Number of conditions

Since many parameters in the model are a function the number of conditions (mortality, QoL), this number was varied between 2 to 8 in SA11.

The number of conditions in the model population was varied between 2 and 8. The ICERs for HA compared to usual care on these two extreme values were respectively £1529 and £3869 per QALY.

This is explained by the lower utility values with the higher number of conditions which makes the life-extending intervention less effective (fewer total QALYs).

SA12: Cost of change in care

In SA12 an additional monthly cost was added to the individuals in the HA arm of the model. This value has to be less than £556 per month (over a patient's lifetime) for HA to still be cost effective.

N.4 Discussion

N.4.1 Summary of results

In the base case analysis HA was shown to be highly cost effective, as to a small increase in costs (£781) corresponded an increase in QALYs (0.32) which largely justified the costs according to the £20,000 per QALY threshold (ICER was £2411 per QALY).

Many assumptions and parameters were tested in a series of sensitivity analyses; throughout these analyses HA remained cost effective under reasonable parameter values and the probabilistic analysis showed HA to be cost effective in 99% of the simulations. The sensitivity analysis on the relative effectiveness of HA compared to usual care (SA10) was deemed to be the most important SA conducted for the model as the main driver of the cost effectiveness results was the effectiveness of the intervention at reducing mortality. If the mortality HR is at least 0.994, which corresponds to a very small improvement in survival, HA is cost effective. Although this value is much higher than the base case value (0.78) this was considered by the GDG to be probably an overestimate as what it was expected from this intervention from a clinical point of you was possible a change in quality of life but no significant improvement in survival.

N.4.2 Limitations and interpretation

The model had potentially serious limitations which were mainly due to a lack of data or poor quality of data. We also had no data on the potential cost of a change in management as a consequence of holistic assessment. A sensitivity analysis highlighted this would have to be a considerable ongoing cost for HA not to be cost effective, therefore this was not considered a major limitation per se in the model.

The major limitation that made the GDG less confident in the model conclusions was the source of the effectiveness data. The only clinical outcome incorporated into the model was mortality and this was based mainly on one study⁴⁵⁰ as other studies did not have a long enough follow up time. This study had some important limitations: although the study was randomised, the authors employed a stratified randomisation procedure. The intervention group was composed of a stratified sample of patients randomly selected from 6 “health states” specified by the authors. The control group was composed of the remaining patients who had been recruited to the study. The result was that the control group was predominantly composed of patients from the “less healthy” health states compared to the intervention group. Although the authors adjusted their analyses for some potential confounding factors, including health states, the GDG had concerns that this would not completely address the risk of bias from the population differences at baseline.

Due to the low credibility on the effectiveness estimate and on any reduction in mortality generated by the intervention, the GDG were cautious on the main findings of the model.

N.4.3 Generalisability to other populations or settings

In our model we tried to set the parameters to reflect a population with multimorbidity, for example by increasing the general life expectancy for people in England based on the number of conditions and number of medications taken. The effectiveness estimate was based on a study not strictly on patients with **multimorbidity** but on an older population, which was considered a proxy for the guideline population.

In a sensitivity analysis we varied the average age of people in the clinical study (80) to a younger and older population and the results were constant, which meant the conclusions of the model would be applicable to any person with multimorbidity independently from their age.

N.4.4 Comparisons with published studies

Other three published studies^{799, 190, 391} based on RCTs (see the economic evidence review in the Holistic Assessment Chapter of the Full Guideline) only assessed the cost effectiveness of HA based on the quality of life outcome, while mortality was not considered in these studies. Their conclusion was that the improvement in quality of life was not significant and it did not justify the increase in costs.

N.4.5 Conclusions

The outcomes of the model were driven by the reduction of mortality observed in the holistic assessment arm. In the base case holistic assessment was more costly but also more effective than usual care; the probability of the intervention being cost effective was 99%. These conclusions were also stable to a series of sensitivity analyses which were conducted on the main parameters and assumptions. The only change in conclusion was observed when the Hazard Ratio for mortality was increased from 0.78 in the base case to 0.994 in a threshold analysis; at this value of HR holistic assessment would not be cost effective anymore.

Despite the stable results of the model, the GDG expressed their scepticism especially around the effectiveness estimate which was considered to be an overestimate. In fact, this intervention was expected to have a potential change in quality of life but no significant improvement in survival. Other RCTs and associated economic evaluations showed no improvement in quality of life and a cost ineffectiveness of holistic assessment when quality of life was the outcome considered. For this reason the GDG did not believe the clinical evidence informing the model was robust enough to make a recommendation in favour of holistic assessment for every patient with multimorbidity.

Although the intervention was costed at £140, if this was implemented for every patient with multimorbidity in England, this would lead to a high implementation cost and running cost overall.

N.4.6 Implications for future research

Given the lack of trust that the GDG had on the clinical evidence informing the effectiveness data of the model, an RCT with a long follow up time assessing both quality of life and mortality of HA compared to usual care would help to have more confidence in the results of an economic analysis based on these data. Also information about the impact of the intervention in subsequent care would be required in order to consider all the costs associated with the intervention and not only the cost of the intervention itself.

Appendix O: Research recommendations

O.1 Organisation of Care

O.1.1 Research Question:

What is the clinical and cost effectiveness of alternative approaches to organising primary care compared with usual care for people with multimorbidity?

O.1.2 Why is this important:

The guideline committee felt that primary care was well suited to managing multimorbidity, but agreed that this was often challenging partly because of how primary care is currently organised. However, there was inadequate high-quality research on alternative approaches to organising care for people with multimorbidity. Trials should be undertaken to examine the impact of different strategies on important clinical outcomes, quality of life and cost effectiveness. The committee believed that no single trial could likely address this research need, because there are many plausible interventions and many defined populations in which such interventions might be of value.

Large, well designed trials of alternative ways of organising general practice based primary care for people with multimorbidity would be of value in defined patient groups (for example, people with multimorbidity who find it difficult to manage their treatment or care or day-to-day activities, people with multiple providers or services involved in their care, people with both long-term physical and mental health problems, people with well-defined frailty, people frequently using unscheduled care, people prescribed multiple regular medicines, and people who are housebound or care home residents).

Such trials should have clear identification and justification of the planned target population, careful piloting and optimisation, and well-described interventions. They need to be sufficiently powered to provide evidence of clinically important effects of interventions on outcomes that are relevant to patients and health and social care services (for example, quality of life, hospital and care home admission, mortality).

O.1.3 Proposed format of research recommendations

Criterion	Explanation
Population	Adults with multimorbidity living in the community in their own homes or in residential care and nursing homes. Within this broad group, researchers should specify which patients the intervention will focus on and the rationale for this focus. Plausible rationales include place of residence (care home, housebound, non-housebound), frailty and poor function, polypharmacy, high unscheduled care or emergency hospital admission rates, and combined physical and mental health morbidity (recognising that many people will fit in more than one category). People in the terminal phase of illness should be excluded.
Intervention	The intervention should be clearly tailored to the population being targeted, but could contain different blends of components including for example: Patient-level for example, methods for identifying and engaging suitable patients (depending on the targeted population); self-management in interventions for example, PRISMS

Criterion	Explanation
	<p>Practitioner level for example, education and training around management of people with MM and polypharmacy (with emphasis on identification of treatment burden, shared decision-making around medication management; case-finding for anxiety and depression)</p> <p>Practice level for example, case management + key worker; tailored mechanisms for access (for example, accelerated urgent access, or directed access to a known clinician wherever possible); longer appointment time; proactive follow-up/call and recall; offering alternative means of consultation; discussion of patients at clinical meetings – with all multi-disciplinary team members; creation of new, general practice based multidisciplinary teams for targeted patients (for example, including pharmacists, specialist nurses [for example, geriatric or psychogeriatric], social workers) approaches such as regular involvement of a pharmacist in medicines management; liaison with specialist care.</p> <p>The potential components would therefore include changes to:</p> <ul style="list-style-type: none"> • access for the targeted population (for example enhanced speed of access; ensuring that patients see their preferred clinician wherever possible including for urgent care; access to rapid telephone or e-mail consultation). • consultation length (for example, routinely longer appointments or choice over consultation length to allow longer appointments where the patient believes this necessary) • consultation format (for example, group appointments) • the multidisciplinary team involved in practice-based review (for example, additional review by pharmacists, relevant specialist nurses including geriatrics/psychogeriatrics). • Allocation of a key worker/case manager/GP with responsibility • Regular structured assessment of mental health and well-being, with appropriate multidisciplinary intervention where required.
Comparator(s)	Routine NHS care.
Outcome	<p>Essential outcomes are quality of life and mortality to allow the evaluation of cost-effectiveness.</p> <p>It is important that adequate time is given to implement the intervention in each practice, since complex interventions involving reconfiguring existing systems typically require time to bed in, so too early evaluation may be falsely negative. Minimum follow-up should be one year, although two years would be preferable.</p>
Study Design	Appropriate development and optimisation of the intervention, with evaluation of the final intervention in a cluster randomised controlled trial with practice as the unit of randomisation, with an associated economic evaluation and parallel process evaluation of implementation.
Timeframe	Is there a timeframe in which the study needs to be completed? For example to inform a guidance review, or whether it is anticipated that the technology could be superseded before the results of any study are anticipated.

O.1.4 Potential criteria to support prioritisation of key research recommendations

Potential Criterion	Explanation
Importance to patients or the population	This is of high importance of the population A large proportion of the population have multimorbidity and this is even more common in people who are older and frail. New models of delivery of care are required.
Relevance to NICE guidance	Good quality evidence would inform updates of NICE guidance
Relevance to the NHS	This area is of importance to the NHS as a whole.
National priorities	Improving care of older people is a national priority and many older and frail people are multimorbid.
Current evidence base	There is very little evidence available on alternative ways of organising general practice services
Equality	Multimorbidity is more common at a younger age in less affluent population.
Feasibility	The proposed research is feasible but requires significant funding and organisation to ensure appropriate piloting and involvement of all relevant personnel. Mercer et al (BMC Medicine (2016) 14:88 DOI 10.1186/s12916-016-0634-2) have conducted a feasibility study which demonstrated plausible benefit and value for money for a larger trial for an intervention of longer consultation, relationship continuity, practitioner support and self- management support.
Other comments	

O.2 Holistic assessment in the community

O.2.1 Research Question

What is the clinical and cost effectiveness of a community holistic assessment and intervention for people living with high levels of multimorbidity?

O.2.2 Why is this important:

There was low quality evidence to indicate potential benefit from community assessments based on the principles of comprehensive geriatric assessment in older people. However, the studies were conducted outside the UK and were not aimed at all adults living with multimorbidity. The guideline committee believed that there was some evidence that holistic assessment and intervention in the community may be of benefit for older people, but that the evidence was of low quality and not adequate to inform strong recommendations.

Large, well-designed trials of holistic assessment and intervention in people with multimorbidity would be of value in defined patient groups in the community (for example, people in nursing homes, people who are housebound, people of all ages with well-defined frailty, people with high levels of multimorbidity or polypharmacy).

Such trials must be rigorous, with clear identification and justification of the planned target population, careful piloting and optimisation, and well-described interventions. They need to be sufficiently powered to provide evidence of clinically important effects of interventions on outcomes that are relevant to patients and health and social care services (for example, quality of life, hospital and care home admission, and mortality).

The guideline committee believed that no single trial could likely address this research need, since there are many plausible interventions and many defined populations in which such interventions might be of value. The committee believed that assessment should follow the principles of Comprehensive Geriatric Assessment or the Standardised Assessment of Elderly People in Europe (STEP) tool, and that interventions would likely involve a multidisciplinary team.

O.2.3 Proposed format of research recommendations

Criterion	Explanation																										
Population	<p>People living in the community with high levels of multimorbidity.</p> <p>Inclusion: Adults with multimorbidity living in the community in their own homes or in residential care and nursing homes. Within this broad group, researchers should specify which patients the intervention will focus on and the rationale for this focus. Plausible rationales include place of residence (care home, housebound, non-housebound), frailty and poor function, polypharmacy, high unscheduled care or emergency hospital admission rates, and combined physical and mental health morbidity (recognising that many people will fit in more than one category).</p> <p>Exclusion: People in the terminal phase of illness, People in hospital.</p>																										
Intervention	<p>The intervention should be clearly tailored to the population being targeted. Although there are many plausible intervention sub-components, the framework of Community Holistic Assessment and Interdisciplinary Intervention will include the principal components of holistic structured assessment and interdisciplinary care planning:</p> <p>A structured holistic assessment, based on the principles of Comprehensive Geriatric Assessment (CGA) and the Standardized Assessment of Elderly People in Primary care in Europe (STEP tool). An example of some of the subcomponents that should be considered for inclusion in the assessment is shown in the table below.</p> <p>A holistic individualised plan for treatment, rehabilitation, support and long term follow up. This is to include realistic shared goals, reviewing and optimising medications and specialist appointments, clear follow-up and review arrangements, and a communication plan with the patient and between professionals. The plan will result from an interdisciplinary discussion including the GP.</p> <p>Possible holistic assessment subcomponents</p> <table border="1"> <tbody> <tr> <td></td> <td>Perspectives, attitudes, values and priorities. The perceived burden of treatment. Ideas, concerns and expectations.</td> </tr> <tr> <td>The Patient</td> <td></td> </tr> <tr> <td>Medical/physical state</td> <td>Co-morbid conditions and disease severity</td> </tr> <tr> <td></td> <td>Medication Review</td> </tr> <tr> <td></td> <td>Nutritional status</td> </tr> <tr> <td></td> <td>Primary preventive issues</td> </tr> <tr> <td></td> <td>Assessment of frailty if appropriate</td> </tr> <tr> <td></td> <td>Problem list</td> </tr> <tr> <td>Mental Health</td> <td>Cognitive function</td> </tr> <tr> <td></td> <td>Depression and/or anxiety</td> </tr> <tr> <td>Functional capacity</td> <td>Activities of daily living</td> </tr> <tr> <td></td> <td>Gait and balance</td> </tr> <tr> <td></td> <td>Activity/exercise status</td> </tr> </tbody> </table>		Perspectives, attitudes, values and priorities. The perceived burden of treatment. Ideas, concerns and expectations.	The Patient		Medical/physical state	Co-morbid conditions and disease severity		Medication Review		Nutritional status		Primary preventive issues		Assessment of frailty if appropriate		Problem list	Mental Health	Cognitive function		Depression and/or anxiety	Functional capacity	Activities of daily living		Gait and balance		Activity/exercise status
	Perspectives, attitudes, values and priorities. The perceived burden of treatment. Ideas, concerns and expectations.																										
The Patient																											
Medical/physical state	Co-morbid conditions and disease severity																										
	Medication Review																										
	Nutritional status																										
	Primary preventive issues																										
	Assessment of frailty if appropriate																										
	Problem list																										
Mental Health	Cognitive function																										
	Depression and/or anxiety																										
Functional capacity	Activities of daily living																										
	Gait and balance																										
	Activity/exercise status																										

Criterion	Explanation														
	<table border="1"> <tr> <td data-bbox="603 237 938 277">Social circumstances</td> <td data-bbox="946 237 1473 277">Social network including visitors or daytime activities</td> </tr> <tr> <td data-bbox="603 284 938 324"></td> <td data-bbox="946 284 1473 324">Informal support available from family or friends</td> </tr> <tr> <td data-bbox="603 331 938 371"></td> <td data-bbox="946 331 1473 371">Eligibility for being offered care resources</td> </tr> <tr> <td data-bbox="603 378 938 418">Environment</td> <td data-bbox="946 378 1473 418">Home comfort, facilities and safety</td> </tr> <tr> <td data-bbox="603 425 938 465"></td> <td data-bbox="946 425 1473 465">Use or potential use of telehealth technology, aids and adaptations</td> </tr> <tr> <td data-bbox="603 472 938 512"></td> <td data-bbox="946 472 1473 512">Transport facilities</td> </tr> <tr> <td data-bbox="603 519 938 560"></td> <td data-bbox="946 519 1473 560">Accessibility to local resources</td> </tr> </table>	Social circumstances	Social network including visitors or daytime activities		Informal support available from family or friends		Eligibility for being offered care resources	Environment	Home comfort, facilities and safety		Use or potential use of telehealth technology, aids and adaptations		Transport facilities		Accessibility to local resources
Social circumstances	Social network including visitors or daytime activities														
	Informal support available from family or friends														
	Eligibility for being offered care resources														
Environment	Home comfort, facilities and safety														
	Use or potential use of telehealth technology, aids and adaptations														
	Transport facilities														
	Accessibility to local resources														
Comparator(s)	<p>Comparator</p> <p>The comparator would be treatment as usual with no extra assessment or multidisciplinary intervention beyond that which happens in usual care.</p>														
Outcome	<p>Outcomes</p> <p>Critical outcomes</p> <p>Health related quality of life</p> <p>Health and social care costs including GP time</p> <p>Admission to a care home (for those not already resident in a care home)</p> <p>Cost effectiveness</p> <p>Important outcomes</p> <p>Mood (measures of anxiety/depression)</p> <p>Function (measures of activities of daily living physical and cognitive function)</p> <p>Hospital admission</p> <p>Mortality</p> <p>Other resource use (for example, social care)</p>														
Study Design	<p>Structure</p> <p>Interventions will require development and careful piloting before evaluation in a phase 3 trial, following the principles of the MRC Framework for the development and evaluation of complex interventions.</p> <p>To avoid contamination within each practice setting it would be preferable to perform a cluster randomised trial with GP practices clustered to active and comparator groups. Consideration should be given to stratifying the sample according to age, care setting and frailty.</p> <p>It should be specified whether there is to be a single intervention or repeated interventions with a specified follow-up period.</p> <p>A comprehensive process evaluation will be undertaken that ideally clearly describes the following:</p> <p>The context in which the intervention is implemented</p> <p>The intervention intended to be delivered and actually delivered</p> <p>The population to which the intervention was intended to be delivered and actually delivered, including an assessment of the reach of the intervention (that is, the proportion of eligible patients who accept or receive the intervention, and reasons why not)</p> <p>A systematic examination of the success and failure of implementation and of effectiveness will be required. This process evaluation is likely to require mixed methods, and should follow the principles of the MRC guidance on process evaluation of trials of complex interventions.</p>														

Criterion	Explanation
Timeframe	The minimum follow-up period should be one year, although two years would be preferable. Longer follow-up would be desirable, but may be constrained by resources (although extended routine data follow-up should be feasible for at least some outcomes such as mortality and hospital or care home admission, and should be planned for if possible).

O.2.4 Potential criteria to support prioritisation of key research recommendations

Potential Criterion	Explanation
Importance to patients or the population	High. Growing numbers of people have multimorbidity in the context of ageing and frailty.
Relevance to NICE guidance	High: the research is essential to inform future updates of key recommendations in the guideline.
Relevance to the NHS	High: There has been increasing interest in delivering proactive holistic to older frail people and this model of care has already been rolled out in areas such as attempts to reduce unplanned hospital admissions. Evidence of the cost and cost effectiveness of these interventions is highly relevant to NHS.
National priorities	Improving care for older people is a core component of the NHS operating framework.
Current evidence base	There are no UK based studies examining these programmes in people in the community but health economic modelling indicated that such interventions may be cost effective..
Equality	Studies should include both older and frail people who are often omitted from studies but also younger less affluent groups who suffer from multimorbidity earlier than their more affluent counterparts.
Feasibility	The proposed research can likely be carried out within a realistic timescale. Pilot studies to establish the intervention may be required (for example as a single grant with staged funding). The expense needed to resolve the question would be warranted.
Other comments	None.

O.3 Stopping drugs

O.3.1 Review question:

What is the clinical and cost effectiveness of stopping preventive medicines in people with multimorbidity who may not benefit from continuing them?

O.3.2 Why is this important:

There is good evidence from randomised controlled trials of the medium term (2–10 years) benefit of medicines recommended in guidelines for preventing future morbidity or mortality, including treatments for hypertension, hyperglycaemia and osteoporosis. However, there is much less evidence about the balance of benefit and harm over longer periods of treatment. It is plausible that harms outweigh benefits in some people with multimorbidity (for example, because of higher rates of adverse events in older, frailer people prescribed multiple regular medicines, or because the expected benefit from continuing a preventive medicine is reduced when there is limited life expectancy or high risk of death from other morbidities). These people are unlikely to have been eligible or included in published trials showing initial benefit from preventive medicines. The systematic review undertaken by NICE in 2015 did not find any randomised controlled trials of stopping antihypertensive medicines in people with multimorbidity. The review found 1 small

randomised controlled trial of stopping statins in people with a life expectancy of 1 year, but the committee did not consider this provided enough evidence to make a recommendation. The review found several randomised controlled trials of stopping bisphosphonates (although not clearly in populations with multimorbidity) and a recommendation was made for to this, but no randomised controlled trials were found of stopping calcium and/or vitamin D. Recommendations based on robust evidence on the clinical and cost effectiveness of stopping preventive medicines in people with multimorbidity who may not benefit could have significant budgetary implications for the NHS. No ongoing trials have been identified.

The guideline committee considered that 1 or more large, well-designed trials of stopping preventive medicine in people with multimorbidity would be of value in defined patient groups in the community (for example, people in nursing homes, people who are housebound, people with well-defined frailty, people with high levels of multimorbidity or polypharmacy, people with limited life expectancy). Discontinuation could either be complete (all relevant medicines) or partial (for example, reduced intensity of hypotensive or hypoglycaemic treatment). Such trials have to be sufficiently powered to provide evidence of clinically important effects of interventions on outcomes that are relevant to patients and health and social care systems (for example, quality of life, hospital and care home admission and mortality). The committee believed that given the existing evidence, it would be of greater value to evaluate the effects of stopping discrete medicines or drug classes, rather than stopping all preventive medicines at the same time. The committee also believed that no single trial could likely address this research need, since there are many medicines that could be stopped and many defined populations in which this might be of value.

O.3.3 Proposed format of research recommendations

Criterion	Explanation
Population	People with multimorbidity who plausibly may not benefit from continued preventive medications, for example people in nursing homes, people who are housebound, people with well-defined frailty, people with high levels of multimorbidity or polypharmacy, people with limited life expectancy.
Intervention	Stopping or reducing the intensity of the targeted medications according to a well-described protocol suitable for routine use in primary care settings. Researchers will have to justify their choice of medications to target and whether the aim is complete cessation or reduced intensity aiming for a particular intermediate outcome target. It may be appropriate to carry out a pilot study to examine recruitment and feasibility before going to full trial.
Comparator(s)	Continuation of preventive medications at the same intensity.
Outcome	Critical outcomes for all studies are total mortality and quality of life. Important outcomes will vary depending on the targeted medication, but could include disease specific outcomes including disease specific mortality, hospitalisation, institutionalisation, and intermediate outcome control. Follow-up should be an absolute minimum of one year, and ideally a minimum of two years.
Study Design	Patient randomised controlled trial, consider use of equivalence or non-inferiority design depending on the primary outcome.
Timeframe	There is an urgent need for this type of research to inform future guidance including any update of NICE multimorbidity guideline.

O.3.4 Potential criteria to support prioritisation of key research recommendations

Potential Criterion	Explanation
Importance to patients or the population	High. Growing numbers of people are taking drugs for long-term prevention based on evidence that these drugs are effective in the first 3-10 years of treatment. Whether observed benefits are maintained as people age, become multimorbid, become frail or are co-prescribed many drugs for other conditions is unclear. Very large numbers of people are affected, and if net benefit is not maintained, then this would have significant impact on large numbers of vulnerable people.
Relevance to NICE guidance	High: the research is essential to inform future updates of key recommendations in the guideline.
Relevance to the NHS	High: the cost of preventive drugs is considerable, and if there are populations in which the drugs cause net harm, then this may have significant additional impact on the NHS.
National priorities	Improving care for older people is a core component of the NHS operating framework; improving care for older people with frailty, including more appropriate prescribing, is supported in specialty guidelines (e.g. BGS Fit for Frailty) and NHS England guidance (e.g. Safe, compassionate care for frail older people using an integrated care pathway). Also improving care for care home residents is a core component of NHS England New Models of Care Programme & 2011 BGS Working Party Inquiry.
Current evidence base	Limited. Randomised controlled trials of preventive medications typically focus on effectiveness in the first 2 to 10 years of treatment, and are largely carried out in younger, fitter and less multimorbid populations. For most conditions, there is at least some more recent evidence in relation to starting preventive medications in older populations, but there is uncertainty regarding continuing benefit. This is a particular issue in some groups of people with multimorbidity, including older people with frailty, care home residents and people receiving palliative care. These groups are typically at greater risk of medication-related side effects and may gain less benefit (or experience harm) from continuing preventive treatment.
Equality	The research recommendation focuses on particular populations who may not benefit from continued antihypertensive treatment.
Feasibility	The proposed research can likely be carried out within a realistic timescale, but pilot studies to evaluate feasibility including recruitment may be required (for example as a single grant with staged funding). The expense needed to resolve the question would be warranted. The main ethical issues would be around the potential vulnerability of the populations selected, including consideration of obtaining informed consent in the context of cognitive impairment/dementia.
Other comments	None.

O.4 Predicting life expectancy

O.4.1 Review Question:

Is it possible to analyse primary care data to identify characteristics that affect life expectancy and to develop algorithms and prediction tools for patients and healthcare providers to predict reduced life expectancy?

O.4.2 Why is this important?

Many people take preventive medicines which are likely to offer small benefits because of reduced life expectancy from other causes. Medicines and other treatments may therefore be adding to treatment burden without adding quality or length of life. The ability to identify people with reduced life expectancy could provide healthcare professionals and people with information that could inform decisions about starting or continuing long-term preventive treatments. Conversely younger people with multimorbidity and reduced life expectancy may benefit from additional preventive treatments. Because this information would be used most often in a primary care setting, the committee considered that a tool derived from information within primary care databases would be most useful.

O.4.3 Proposed format of research recommendations

Criterion	Explanation
Population	Adults (aged 18 years and above), although in practice the focus is likely to be on middle aged and older adults in whom reduced life expectancy is more common.
Risk tools	Multivariable risk tools comprised of variables available within routine primary care databases to identify people at risk of a reduced life expectancy. Validated thresholds for varying levels of risk of mortality should be provided.
Target condition or reference standard	All cause mortality after 12-months, and within the normal time horizon under which preventative treatment decisions are made (typically 3-10 years, as appropriate).
Outcomes	<p>Statistical outputs should include discrimination data, where the sensitivity and specificity of the tool at validated thresholds should be reported with their respective confidence intervals (i.e. not AUC data alone). Calibration data should also be reported, including the Hosmer-Lemeshow statistic and calibration plots and the adjusted and unadjusted pseudo R².</p> <p>The tool should prioritise high specificity (i.e. the ability of the tool to correctly identify people who are <i>not</i> at risk of a reduced life expectancy; true negatives). This is because the primary use of this tool will be to guide decisions on initiating or withdrawing treatment in people who may not live long enough to experience</p>

	<p>the benefit, and there may be the harm of withdrawing medication in people unnecessarily. However, the tool should also demonstrate at least moderate sensitivity (i.e. the ability of the tool to correctly identify people who are at risk of reduced life expectancy; true positives), in order to add meaningfully to clinical practice.</p> <p>Ideally, the tool should demonstrate accuracy in a broad population of people including in both younger and older adults, but this will depend on the technical performance of the tool in different age groups which should be specifically examined separately.</p>
Study Design	Development and external validation of a risk tool. External validation should ideally be geographical as well as temporal, and should be prioritised compared to validation within the same study population (i.e., split half validation). Studies conducted within the UK would be preferable, in order to be most applicable to the population and settings in the NHS.
Timeframe	To inform update of Multimorbidity guideline

O.4.4 Potential criteria to support prioritisation of key research recommendations

Potential Criterion	Explanation
Importance to patients or the population	High.
Relevance to NICE guidance	High: the research is essential to inform future updates of key recommendations in the guideline.
Relevance to the NHS	High: the cost of preventive drugs is considerable, and if there are populations in which some people have significantly reduced benefit, then this may have significant additional impact on the NHS.
National priorities	Improving care for older people is a core component of the NHS operating framework.
Current evidence base	Limited. A number of studies have developed and validated risk tools to predict mortality, however the evidence base is significantly limited. The systematic review undertaken by NICE in 2015 found that risk tools are evaluated by a very small number of studies, insufficient for meta-analysis. Studies report limited data on the performance of the tool; in particular, a significant number of studies do not report the sensitivity and specificity of the tools, which is the only data that can indicate the clinical implications of using the tool in practice (i.e. the number of true/false positives and negatives). The systematic review undertaken by NICE in 2015 also found that few studies report a validated threshold for the tool, which can be used to indicate risk of reduced life expectancy. Finally, the systematic review undertaken by NICE in 2015 found that no existing risk tool was able to demonstrate both adequate

	specificity and sensitivity for predicting mortality was available and validated in England..
Equality	The purpose of using this tool would be to ensure that treatment is tailored to individual needs, and there are no specific equality issues.
Feasibility	The proposed research can likely be carried out within a realistic timescale. Large databases of primary care data already exist and are used to develop prediction tools.
Other comments	None.

Appendix P: NICE technical team

NICE technical team members

Mark Baker	Guideline Lead
Jeremy Wight, Martin Allaby	Clinical Advisor
Toni Tan	Technical Lead
Bhash Naidoo	Health Economist
Caroline Keir	Guideline Commissioning Manager
Helen Dickinson	Guideline Coordinator
Anne Louise Clayton	Editor

Appendix Q: References

- 1 Abrupt withdrawal of verapamil in ischaemic heart disease. The Danish Study Group on Verapamil in Myocardial Infarction. *European Heart Journal*. 1984; 5(7):529-532
- 2 "It might actually 3.0 ANCC contact hours work this time": benefits and barriers to adapted 12-step facilitation therapy and mutual-help group attendance from the perspective of dually diagnosed individuals. *Journal of Addictions Nursing*. Baltimore, Maryland: Lippincott Williams & Wilkins. 2015; 26(3):120-128
- 3 Patient Centred Assessment Method (PCAM): improving nurse led biopsychosocial assessment of patients with long term conditions and co-morbid mental health needs. *Health Technology Assessment*, 2015
- 4 Abbatecola AM, Spazzafumo L, Corsonello A, Sirolla C, Bustacchini S, Guffanti E. Development and validation of the HOPE prognostic index on 24-month posthospital mortality and rehospitalization: Italian National Research Center on Aging (INRCA). *Rejuvenation Research*. 2011; 14(6):605-613
- 5 Abellan van Kan G, Rolland Y, Andrieu S, Bauer J, Beauchet O, Bonnefoy M et al. Gait speed at usual pace as a predictor of adverse outcomes in community-dwelling older people an International Academy on Nutrition and Aging (IANA) Task Force. *Journal of Nutrition, Health and Aging*. 2009; 13(10):881-889
- 6 Abellan van Kan G, Vellas B. Is the Mini Nutritional Assessment an appropriate tool to assess frailty in older adults? *Journal of Nutrition, Health and Aging*. 2011; 15(3):159-161
- 7 Abraczinskas DR, Ookubo R, Grace ND, Groszmann RJ, Bosch J, Garcia-Tsao G et al. Propranolol for the prevention of first esophageal variceal hemorrhage: a lifetime commitment? *Hepatology*. 2001; 34(6):1096-1102
- 8 Abraha I, Trotta F, Rimland JM, Cruz-Jentoft A, Lozano-Montoya I, Soiza RL et al. Efficacy of non-pharmacological interventions to prevent and treat delirium in older patients: a systematic overview. The SENATOR project ONTOP Series. *PLoS ONE*. 2015; 10(6):e0123090
- 9 Abraham I, Van Camp Y, Villa L, Denhaerynck K, Sun D, Vancayzeele S et al. Hierarchical modeling of patient and physician determinants of blood pressure outcomes in adherent vs nonadherent hypertensive patients: pooled analysis of 6 studies with 14,646 evaluable patients. *Journal of Clinical Hypertension*. 2013; 15(9):663-673
- 10 Achey MA, Beck CA, Beran DB, Boyd CM, Schmidt PN, Willis AW et al. Virtual house calls for Parkinson disease (Connect.Parkinson): study protocol for a randomized, controlled trial. *Trials*. 2014; 15:465
- 11 Adams AL, Schiff MA, Koepsell TD, Rivara FP, Leroux BG, Becker TM et al. Physician consultation, multidisciplinary care, and 1-year mortality in Medicare recipients hospitalized with hip and lower extremity injuries. *Journal of the American Geriatrics Society*. 2010; 58(10):1835-1842
- 12 Adams AS, Uratsu C, Dyer W, Magid D, O'Connor P, Beck A et al. Health system factors and antihypertensive adherence in a racially and ethnically diverse cohort of new users. *JAMA Internal Medicine*. 2013; 173(1):54-61

- 13 Agarwal G, McDonough B, Angeles R, Pirrie M, Marzanek F, McLeod B et al. Rationale and methods of a multicentre randomised controlled trial of the effectiveness of a Community Health Assessment Programme with Emergency Medical Services (CHAP-EMS) implemented on residents aged 55 years and older in subsidised seniors' housing buildings in Ontario, Canada. *BMJ Open*. 2015; 5(6):e008110
- 14 Ahmad R, Bath PA. Identification of risk factors for 15-year mortality among community-dwelling older people using Cox regression and a genetic algorithm. *Journals of Gerontology Series A, Biological Sciences and Medical Sciences*. 2005; 60(8):1052-1058
- 15 Ahmed B, Nanji K, Mujeeb R, Patel MJ. Effects of polypharmacy on adverse drug reactions among geriatric outpatients at a tertiary care hospital in Karachi: a prospective cohort study. *PLoS ONE*. 2014; 9(11):e112133
- 16 Ahmed S, Gogovor A, Berman E, Miloff M, Burnand B, Krelbaum M et al. Changing healthcare: stakeholder perceptions of the burden of chronic disease and the value of teams, measurements and communication. *Healthcare Quarterly*. 2009; 12(2):e1-e13
- 17 Ahto M, Isoaho R, Puolijoki H, Vahlberg T, Kivela SL. Stronger symptoms of depression predict high coronary heart disease mortality in older men and women. *International Journal of Geriatric Psychiatry*. 2007; 22(8):757-763
- 18 Ai AL, Carretta H, Beitsch LM, Watson L, Munn J, Mehriary S. Medication therapy management programs: promises and pitfalls. *Journal of Managed Care and Specialty Pharmacy*. 2014; 20(12):1162-1182
- 19 Aimonino Ricauda N, Fiorio Pla L, Marinello R, Molaschi M, Fabris F. Feasibility of an acute stroke home care service for elderly patients. *Archives of Gerontology and Geriatrics*. Elsevier. 1998; 26:17-22
- 20 Aimonino N, Molaschi M, Salerno D, Roglia D, Rocco M, Fabris F. The home hospitalization of frail elderly patients with advanced dementia. *Archives of Gerontology and Geriatrics Supplement*. 2001; 7:19-23
- 21 Aizen E, Lutsyk G, Wainer L, Carmeli S. Effectiveness of individualized fall prevention program in geriatric rehabilitation hospital setting: a cluster randomized trial. *Aging Clinical and Experimental Research*. 2015; 27(5):681-688
- 22 Al Hamid A, Ghaleb M, Aljadhey H, Aslanpour Z. A systematic review of hospitalization resulting from medicine-related problems in adult patients. *British Journal of Clinical Pharmacology*. 2014; 78(2):202-217
- 23 Al Snih S, Markides KS, Ray LA, Freeman JL, Ostir GV, Goodwin JS. Predictors of healthcare utilization among older Mexican Americans. *Ethnicity and Disease*. 2006; 16(3):640-646
- 24 Albert SM, Colombi A, Hanlon J. Potentially inappropriate medications and risk of hospitalization in retirees: analysis of a US retiree health claims database. *Drugs and Aging*. 2010; 27(5):407-415
- 25 Alderman MH, Davis TK, Gerber LM, Robb M. Antihypertensive drug therapy withdrawal in a general population. *Archives of Internal Medicine*. 1986; 146(7):1309-1311
- 26 Alderson SL, Foy R, Glidewell L, House AO. Patients understanding of depression associated with chronic physical illness: a qualitative study. *BMC Family Practice*. 2014; 15:37

- 27 Alexopoulos GS, Kiosses DN, Sirey JA, Kanellopoulos D, Seirup JK, Novitch RS et al. Untangling therapeutic ingredients of a personalized intervention for patients with depression and severe COPD. *American Journal of Geriatric Psychiatry*. 2014; 22(11):1316-1324
- 28 Alexopoulou A, Dourakis SP, Mantzoukis D, Pitsariotis T, Kandyli A, Deutsch M et al. Adverse drug reactions as a cause of hospital admissions: a 6-month experience in a single center in Greece. *European Journal of Internal Medicine*. 2008; 19(7):505-510
- 29 Alfaro Lara ER, Vega Coca MD, Galvan BM, Marin GR, Nieto Martin MD, Perez GC et al. Selection of tools for reconciliation, compliance and appropriateness of treatment in patients with multiple chronic conditions. *European Journal of Internal Medicine*. 2012; 23(6):506-512
- 30 Alhawassi TM, Krass I, Bajorek BV, Pont LG. A systematic review of the prevalence and risk factors for adverse drug reactions in the elderly in the acute care setting. *Clinical Interventions In Aging*. 2014; 9:2079-2086
- 31 Aljishi M, Parekh K. Risk factors for general medicine readmissions and association with mortality. *New Zealand Medical Journal*. 2014; 127(1394):42-50
- 32 Alkema GE, Wilber KH, Shannon GR, Allen D. Reduced mortality: the unexpected impact of a telephone-based care management intervention for older adults in managed care. *Health Services Research*. 2007; 42:1632-1650
- 33 Allen CM, Becker PM, McVey LJ, Saltz C, Feussner JR, Cohen HJ. A randomized, controlled clinical trial of a geriatric consultation team. Compliance with recommendations. *JAMA*. 1986; 255(19):2617-2621
- 34 Allen D, Badro V, Denyer-Willis L, Ellen Macdonald M, Pare A, Hutchinson T et al. Fragmented care and whole-person illness: Decision-making for people with chronic end-stage kidney disease. *Chronic Illness*. 2015; 11(1):44-55
- 35 Allen J, Hutchinson AM, Brown R, Livingston PM. Quality care outcomes following transitional care interventions for older people from hospital to home: a systematic review. *BMC Health Services Research*. 2014; 14:346
- 36 Almagro P, Cabrera FJ, Diez J, Boixeda R, Alonso Ortiz MB, Murio C et al. Comorbidities and short-term prognosis in patients hospitalized for acute exacerbation of COPD: the EPOC en Servicios de medicina interna (ESMI) study. *Chest*. 2012; 142(5):1126-1133
- 37 Almagro P, Soriano JB, Cabrera FJ, Boixeda R, Alonso-Ortiz MB, Barreiro B et al. Short- and medium-term prognosis in patients hospitalized for COPD exacerbation: the CODEX index. *Chest*. 2014; 145(5):972-980
- 38 Almas A, Hameed A, Ahmed B, Islam M. Compliance to antihypertensive therapy. *Journal of the College of Physicians and Surgeons--Pakistan*. 2006; 16(1):23-26
- 39 Altfeld SJ, Shier GE, Rooney M, Johnson TJ, Golden RL, Karavolos K et al. Effects of an enhanced discharge planning intervention for hospitalized older adults: a randomized trial. *Gerontologist*. 2013; 53(3):430-440
- 40 Altiner A, Schafer I, Mellert C, Loffler C, Mortsiefer A, Ernst A et al. Activating GENERAL practitioners dialogue with patients on their Agenda (MultiCare AGENDA) study protocol for a cluster randomized controlled trial. *BMC Family Practice*. 2012; 13:118

- 41 Alvarez V, Januel JM, Burnand B, Rossetti AO. Role of comorbidities in outcome prediction after status epilepticus. *Epilepsia*. 2012; 53(5):e89-e92
- 42 Amarasingham R, Velasco F, Xie B, Clark C, Ma Y, Zhang S et al. Electronic medical record-based multicondition models to predict the risk of 30 day readmission or death among adult medicine patients: validation and comparison to existing models. *BMC Medical Informatics and Decision Making*. 2015; 15:39
- 43 Amoako E, Skelly AH, Rossen EK. Outcomes of an intervention to reduce uncertainty among African American women with diabetes. *Western Journal of Nursing Research*. 2008; 30:928-942
- 44 Amris K, Waehrens EE, Christensen R, Bliddal H, Danneskiold-Samsøe B. Interdisciplinary rehabilitation of patients with chronic widespread pain: Primary endpoint of the randomized, nonblinded, parallel-group IMPROVE trial. *Pain*. 2014; 155(7):1356-1364
- 45 An J, Nichol MB. Multiple medication adherence and its effect on clinical outcomes among patients with comorbid type 2 diabetes and hypertension. *Medical Care*. 2013; 51(10):879-887
- 46 Ancker JS, Miller MC, Patel V, Kaushal R, HITEC Investigators. Sociotechnical challenges to developing technologies for patient access to health information exchange data. *Journal of the American Medical Informatics Association*. 2014; 21(4):664-670
- 47 Ancker JS, Witteman HO, Hafeez B, Provencher T, Van de Graaf M, Wei E. "You get reminded you're a sick person": personal data tracking and patients with multiple chronic conditions. *Journal of Medical Internet Research*. 2015; 17(8):e202
- 48 Ancker JS, Witteman HO, Hafeez B, Provencher T, Van de Graaf M, Wei E. The invisible work of personal health information management among people with multiple chronic conditions: qualitative interview study among patients and providers. *Journal of Medical Internet Research*. 2015; 17(6):e137
- 49 Anders J, Profener F, Dapp U, Golgert S, Daubmann A, Wegscheider K et al. Health and competence. detection and decoding using comprehensive assessments in the longitudinal urban cohort ageing study (LUCAS). *Zeitschrift Fur Gerontologie Und Geriatrie*. 2012; 45(4):271-278
- 50 Andersohn F. Adherence to statin therapy: the key to survival? *International Journal of Clinical Practice*. 2010; 64(7):843-847
- 51 Ando K, Doi T, Moody SY, Ohkuni Y, Sato S, Kaneko N. The effect of comorbidity on the prognosis of acute lung injury and acute respiratory distress syndrome. *Internal Medicine*. 2012; 51(14):1835-1840
- 52 Andrade AD, Anam R, Karanam C, Downey P, Ruiz JG. An overactive bladder online self-management program with embedded avatars: a randomized controlled trial of efficacy. *Urology*. 2015; 85(3):561-567
- 53 Angleman SB, Santoni G, Pilotto A, Fratiglioni L, Welmer A-K. Multidimensional prognostic index in association with future mortality and number of hospital days in a population-based sample of older adults: Results of the EU Funded MPI-AGE project. *PLoS ONE*. 2015; 10(7)
- 54 Angstman KB, Rohrer JE, Adamson SC, Chaudhry R. Impact of e-consults on return visits of primary care patients. *Health Care Manager*. 2009; 28(3):253-257

- 55 Annema C, Luttik M-L, Jaarsma T. Reasons for readmission in heart failure: Perspectives of patients, caregivers, cardiologists, and heart failure nurses. *Heart and Lung: Journal of Acute and Critical Care*. 2009; 38(5):427-434
- 56 Antonelli Inc, Fuso L, De Rosa M, Forastiere F, Rapiti E, Nardecchia B et al. Co-morbidity contributes to predict mortality of patients with chronic obstructive pulmonary disease. *European Respiratory Journal*. 1997; 10(12):2794-2800
- 57 Antonelli-Inc, Ancona C, Forastiere F, Belleudi V, Corsonello A, Perucci CA. Socioeconomic status and hospitalization in the very old: a retrospective study. *BMC Public Health*. 2007; 7:227
- 58 Antoniadou NC, Rochford PD, Pretto JJ, Pierce RJ, Gogler J, Steinkrug J et al. Pilot study of remote telemonitoring in COPD. *Telemedicine Journal and E-Health*. 2012; 18(8):634-640
- 59 Antoniou T, Ng R, Glazier RH, Kopp A, Austin PC. Comparison of comorbidity classification methods for predicting outcomes in a population-based cohort of adults with human immunodeficiency virus infection. *Annals of Epidemiology*. 2014; 24(7):532-537
- 60 Appleton SC, Abel GA, Payne RA. Cardiovascular polypharmacy is not associated with unplanned hospitalisation: evidence from a retrospective cohort study. *BMC Family Practice*. 2014; 15:58
- 61 Arbaje AI, Maron DD, Yu Q, Wendel VI, Tanner E, Boulton C et al. The geriatric floating interdisciplinary transition team. *Journal of the American Geriatrics Society*. 2010; 58(2):364-370
- 62 Arfken CL, Lichtenberg PA, Kuiken T. Special feature: Importance of comorbid illnesses in predicting mortality for geriatric rehabilitation. *Topics in Geriatric Rehabilitation*. 1998; 13(4):69-76
- 63 Arija V, Martin N, Canela T, Anguera C, Castelao AI, Garcia-Barco M et al. Nutrition education intervention for dependent patients: protocol of a randomized controlled trial. *BMC Public Health*. 2012; 12:373
- 64 Arminanzas C, Velasco L, Calvo N, Portilla R, Riancho JA, Valero C. CURB-65 as an initial prognostic score in Internal Medicine patients. *European Journal of Internal Medicine*. 2013; 24(5):416-419
- 65 Asao K, McEwen LN, Crosson JC, Waitzfelder B, Herman WH. Revisit frequency and its association with quality of care among diabetic patients: Translating Research Into Action for Diabetes (TRIAD). *Journal of Diabetes and Its Complications*. 2014; 28(6):811-818
- 66 Aspin C, Brown N, Jowsey T, Yen L, Leeder S. Strategic approaches to enhanced health service delivery for Aboriginal and Torres Strait Islander people with chronic illness: a qualitative study. *BMC Health Services Research*. 2012; 12:143
- 67 Atella V, Peracchi F, Depalo D, Rossetti C. Drug compliance, co-payment and health outcomes: evidence from a panel of Italian patients. *Health Economics*. 2006; 15(9):875-892
- 68 Atienza F, Anguita M, Martinez-Alzamora N, Osca J, Ojeda S, Almenar L et al. Multicenter randomized trial of a comprehensive hospital discharge and outpatient heart failure management program. *European Journal of Heart Failure*. 2004; 6(5):643-652

- 69 Atkin K, Holmes J, Martin C. Provision of care for older people with co-morbid mental illness in general hospitals: general nurses' perceptions of their training needs. *International Journal of Geriatric Psychiatry*. 2005; 20(11):1081-1083
- 70 Atlantis E, Fahey P, Foster J. Collaborative care for comorbid depression and diabetes: a systematic review and meta-analysis. *BMJ Open*. 2014; 4(4):e004706
- 71 Aubert RE, Yao J, Xia F, Garavaglia SB. Is there a relationship between early statin compliance and a reduction in healthcare utilization? *American Journal of Managed Care*. 2010; 16(6):459-466
- 72 Austin CA, Mohottige D, Sudore RL, Smith AK, Hanson LC. Tools to promote shared decision making in serious illness: a systematic review. *JAMA Internal Medicine*. 2015;
- 73 Austin PC, Shah BR, Newman A, Anderson GM. Using the Johns Hopkins' Aggregated Diagnosis Groups (ADGs) to predict 1-year mortality in population-based cohorts of patients with diabetes in Ontario, Canada. *Diabetic Medicine*. 2012; 29(9):1134-1141
- 74 Austin PC, Stanbrook MB, Anderson GM, Newman A, Gershon AS. Comparative ability of comorbidity classification methods for administrative data to predict outcomes in patients with chronic obstructive pulmonary disease. *Annals of Epidemiology*. 2012; 22(12):881-887
- 75 Austin PC, van Walraven C, Wodchis WP, Newman A, Anderson GM. Using the Johns Hopkins Aggregated Diagnosis Groups (ADGs) to predict mortality in a general adult population cohort in Ontario, Canada. *Medical Care*. 2011; 49(10):932-939
- 76 Austin PC, Walraven C. The mortality risk score and the ADG score: two points-based scoring systems for the Johns Hopkins aggregated diagnosis groups to predict mortality in a general adult population cohort in Ontario, Canada. *Medical Care*. 2011; 49(10):940-947
- 77 Austin SR, Wong YN, Uzzo RG, Beck JR, Egleston BL. Why summary comorbidity measures such as the Charlson Comorbidity Index and Elixhauser score work. *Medical Care*. 2015; 53(9):e65-e72
- 78 Baandrup L, Gasse C, Jensen VD, Glenthøj BY, Nordentoft M, Lublin H et al. Antipsychotic polypharmacy and risk of death from natural causes in patients with schizophrenia: a population-based nested case-control study. *Journal of Clinical Psychiatry*. 2010; 71(2):103-108
- 79 Bachman SS, Collard AF, Greenberg JN, Fountain E, Huebner TW, Kimball B et al. An innovative approach to geriatric acute care delivery: the Choate-Symmes experience. *Hospital and Health Services Administration*. 1987; 32(4):509-520
- 80 Bader P. Impact of nurse practitioner visits on readmission rates in skilled nursing homes Brandman University; 2014.
- 81 Bagger YZ, Tanko LB, Alexandersen P, Ravn P, Christiansen C. Alendronate has a residual effect on bone mass in postmenopausal Danish women up to 7 years after treatment withdrawal. *Bone*. 2003; 33(3):301-307
- 82 Bailey JE, Wan JY, Tang J, Ghani MA, Cushman WC. Antihypertensive medication adherence, ambulatory visits, and risk of stroke and death. *Journal of General Internal Medicine*. 2010; 25(6):495-503

- 83 Baitar A, Van Fraeyenhove F, Vandebroek A, De Droogh E, Galdermans D, Mebis J et al. Evaluation of the Groningen Frailty Indicator and the G8 questionnaire as screening tools for frailty in older patients with cancer. *Journal of Geriatric Oncology*. 2013; 4(1):32-38
- 84 Baker A, Leak P, Ritchie LD, Lee AJ, Fielding S. Anticipatory care planning and integration: a primary care pilot study aimed at reducing unplanned hospitalisation. *British Journal of General Practice*. 2012; 62(595):e113-e120
- 85 Baker W, Harris M, Battersby M. Health workers' views of a program to facilitate physical health care in mental health settings: implications for implementation and training. *Australasian Psychiatry*. 2014; 22(6):560-563
- 86 Bakker FC, Robben SHM, Olde Rikkert MGM. Effects of hospital-wide interventions to improve care for frail older inpatients: A systematic review. *BMJ Quality and Safety*. 2011; 20(8):680-691
- 87 Bakker TJEM, Duivenvoorden HJ, van der Lee J, Olde Rikkert MGM, Beekman ATF, Ribbe MW. Integrative psychotherapeutic nursing home program to reduce multiple psychiatric symptoms of cognitively impaired patients and caregiver burden: randomized controlled trial. *American Journal of Geriatric Psychiatry*. 2011; 19(6):507-520
- 88 Bakker TJEM, Duivenvoorden HJ, van der Lee J, Olde Rikkert MGM, Beekman ATF, Ribbe MW. Benefit of an integrative psychotherapeutic nursing home program to reduce multiple psychiatric symptoms of psychogeriatric patients and caregiver burden after six months of follow-up: a re-analysis of a randomized controlled trial. *International Psychogeriatrics*. 2013; 25(1):34-46
- 89 Balaban RB, Galbraith AA, Burns ME, Vialle-Valentin CE, Laroche MR, Ross-Degnan D. A patient navigator intervention to reduce hospital readmissions among high-risk safety-net patients: a randomized controlled trial. *Journal of General Internal Medicine*. 2015; 30(7):907-915
- 90 Bang JH, Hwang SH, Lee EJ, Kim Y. The predictability of claim-data-based comorbidity-adjusted models could be improved by using medication data. *BMC Medical Informatics and Decision Making*. 2013; 13:128
- 91 Bansal N, Katz R, De Boer IH, Peralta CA, Fried LF, Siscovick DS et al. Development and validation of a model to predict 5-year risk of death without ESRD among older adults with CKD. *Clinical Journal of the American Society of Nephrology*. 2015; 10(3):363-371
- 92 Barberan-Garcia A, Vogiatzis I, Solberg HS, Vilaro J, Rodriguez DA, Garasen HM et al. Effects and barriers to deployment of telehealth wellness programs for chronic patients across 3 European countries. *Respiratory Medicine*. 2014; 108(4):628-637
- 93 Bardach SH, Schoenberg NE. Primary care physicians' prevention counseling with patients with multiple morbidity. *Qualitative Health Research*. 2012; 22(12):1599-1611
- 94 Barnes DE, Palmer RM, Kresevic DM, Fortinsky RH, Kowal J, Chren MM et al. Acute care for elders units produced shorter hospital stays at lower cost while maintaining patients' functional status. *Health Affairs*. 2012; 31(6):1227-1236
- 95 Barnett K, Mercer SW, Norbury M, Watt G, Wyke S, Guthrie B. Epidemiology of multimorbidity and implications for health care, research, and medical education: a cross-sectional study. *The Lancet*. 2012; 380(9836):37-43

- 96 Barreto PDS, Greig C, Ferrandez A-M. Detecting and categorizing frailty status in older adults using a self-report screening instrument. *Archives of Gerontology and Geriatrics*. 2012; 54(3):e249-e254
- 97 Bartels SJ. Caring for the whole person: integrated health care for older adults with severe mental illness and medical comorbidity. *Journal of the American Geriatrics Society*. 2004; 52(s12):S249-S257
- 98 Baser O, Palmer L, Stephenson J. The estimation power of alternative comorbidity indices. *Value in Health*. 2008; 11(5):946-955
- 99 Basic D, Shanley C. Frailty in an older inpatient population: using the clinical frailty scale to predict patient outcomes. *Journal of Aging and Health*. 2015; 27(4):670-685
- 100 Bateman BT, Gagne JJ. The Obstetric Comorbidity Index predicts severe maternal morbidity. *BJOG*. 2015; 122(13):1756
- 101 Bateman BT, Mhyre JM, Hernandez-Diaz S, Huybrechts KF, Fischer MA, Creanga AA et al. Development of a comorbidity index for use in obstetric patients. *Obstetrics and Gynecology*. 2013; 122(5):957-965
- 102 Battersby M, Harris M, Smith D, Reed R, Woodman R. A pragmatic randomized controlled trial of the Flinders Program of chronic condition management in community health care services. *Patient Education and Counseling*. 2015; 98(11):1367-1375
- 103 Battersby MW, Beattie J, Pols RG, Smith DP, Condon J, Blunden S. A randomised controlled trial of the Flinders Program of chronic condition management in Vietnam veterans with co-morbid alcohol misuse, and psychiatric and medical conditions. *Australian and New Zealand Journal of Psychiatry*. 2013; 47(5):451-462
- 104 Bauer DC, Schwartz A, Palermo L, Cauley J, Hochberg M, Santora A et al. Fracture prediction after discontinuation of 4 to 5 years of alendronate therapy: the FLEX study. *JAMA Internal Medicine*. 2014; 174(7):1126-1134
- 105 Baughan DM, Revicki D, Nieman LZ. Management of problem patients with multiple chronic diseases. *Journal of Family Practice*. 1983; 17(2):233-239
- 106 Bayliss EA, Ellis JL, Steiner JF. Subjective assessments of comorbidity correlate with quality of life health outcomes: initial validation of a comorbidity assessment instrument. *Health and Quality of Life Outcomes*. 2005; 3:51
- 107 Bayliss EA, Steiner JF, Fernald DH, Crane LA, Main DS. Descriptions of barriers to self-care by persons with comorbid chronic diseases. *Annals of Family Medicine*. 2003; 1(1):15-21
- 108 Baynouna LM, Shamsan AI, Ali TA, Al Mukini LA, Al Kuwiti MH, Al Ameri TA et al. A successful chronic care program in Al Ain-United Arab Emirates. *BMC Health Services Research*. 2010; 10:47
- 109 Beck A, Scott J, Williams P, Robertson B, Jackson D, Gade G et al. A randomized trial of group outpatient visits for chronically ill older hmo members: The cooperative health care clinic. *Journal of the American Geriatrics Society*. 1997; 45(5):543-549

- 110 Becker PM, McVey LJ, Saltz CC, Feussner JR, Cohen HJ. Hospital-acquired complications in a randomized controlled clinical trial of a geriatric consultation team. *JAMA*. 1987; 257(17):2313-2317
- 111 Beer C, Hyde Z, Almeida OP, Norman P, Hankey GJ, Yeap BB et al. Quality use of medicines and health outcomes among a cohort of community dwelling older men: an observational study. *British Journal of Clinical Pharmacology*. 2011; 71(4):592-599
- 112 Behm L, Wilhelmson K, Falk K, Eklund K, Ziden L, Dahlin-Ivanoff S. Positive health outcomes following health-promoting and disease-preventive interventions for independent very old persons: long-term results of the three-armed RCT Elderly Persons in the Risk Zone. *Archives of Gerontology and Geriatrics*. 2014; 58(3):376-383
- 113 Bekelman DB, Plomondon ME, Sullivan MD, Nelson K, Hattler B, McBryde C et al. Patient-centered disease management (PCDM) for heart failure: study protocol for a randomised controlled trial. *BMC Cardiovascular Disorders*. 2013; 13:49
- 114 Bekelman DB, Plomondon ME, Carey EP, Sullivan MD, Nelson KM, Hattler B et al. Primary results of the patient-centered disease management (PCDM) for heart failure study: a randomized clinical trial. *JAMA Internal Medicine*. 2015; 175(5):725-732
- 115 Belaiche S, Romanet T, Allenet B, Calop J, Zaoui P. Identification of drug-related problems in ambulatory chronic kidney disease patients: a 6-month prospective study. *Journal of Nephrology*. 2012; 25:782-788
- 116 Beland SG, Tannenbaum C, Ducruet T, Preville M, Berbiche D, Moride Y. Effect of external variables on the performance of the geriatric comorbidity score derived from prescription claims in the community-dwelling elderly. *Drugs and Aging*. 2012; 29(11):891-897
- 117 Belcher VN, Fried TR, Agostini JV, Tinetti ME. Views of older adults on patient participation in medication-related decision making. *Journal of General Internal Medicine*. 2006; 21(4):298-303
- 118 Beloosesky Y, Weiss A, Mansur N. Validity of the Medication-based Disease Burden Index compared with the Charlson Comorbidity Index and the Cumulative Illness Rating Scale for geriatrics: a cohort study. *Drugs and Aging*. 2011; 28(12):1007-1014
- 119 Benavent-Caballer V, Rosado-Calatayud P, Segura-Orti E, Amer-Cuenca JJ, Lison JF. Effects of three different low-intensity exercise interventions on physical performance, muscle CSA and activities of daily living: A randomized controlled trial. *Experimental Gerontology*. 2014; 58:159-165
- 120 Bendayan M, Bibas L, Levi M, Mullie L, Forman DE, Afilalo J. Therapeutic interventions for frail elderly patients: part II. Ongoing and unpublished randomized trials. *Progress in Cardiovascular Diseases*. 2014; 57(2):144-151
- 121 Beretta S, Beghi E, Messina P, Gerardi F, Pescini F, La Licata A et al. Comprehensive educational plan for patients with epilepsy and comorbidity (EDU-COM): a pragmatic randomised trial. *Journal of Neurology, Neurosurgery and Psychiatry*. 2014; 85:889-894
- 122 Berglund H, Hasson H, Kjellgren K, Wilhelmson K. Effects of a continuum of care intervention on frail older persons' life satisfaction: a randomized controlled study. *Journal of Clinical Nursing*. 2015; 24(7-8):1079-1090

- 123 Berkhof FF, van den Berg JWK, Uil SM, Kerstjens HAM. Telemedicine, the effect of nurse-initiated telephone follow up, on health status and health-care utilization in COPD patients: a randomized trial. *Respirology*. 2015; 20(2):279-285
- 124 Bernabeu-Wittel M, Ollero-Baturone M, Moreno-Gavino L, Baron-Franco B, Fuertes A, Murcia-Zaragoza J et al. Development of a new predictive model for polypathological patients. The PROFUND index. *European Journal of Internal Medicine*. 2011; 22(3):311-317
- 125 Bernardini J, Callen S, Fried L, Piraino B. Inter-rater reliability and annual rescoring of the Charlson comorbidity index. *Advances in Peritoneal Dialysis*. 2004; 20:125-127
- 126 Berry LL, Rock BL, Smith Houskamp B, Brueggeman J, Tucker L. Care coordination for patients with complex health profiles in inpatient and outpatient settings. *Mayo Clinic Proceedings*. 2013; 88(2):184-194
- 127 Beverly EA, Wray LA, Chiu CJ, Weinger K. Perceived challenges and priorities in co-morbidity management of older patients with Type 2 diabetes. *Diabetic Medicine*. 2011; 28(7):781-784
- 128 Beverly E, Wray L, Ching-Ju C, LaCoe C. Older adults' perceived challenges with health care providers treating their type 2 diabetes and comorbid conditions. *Clinical Diabetes*. 2014; 32(1):12-17
- 129 Bharucha AJ, Pandav R, Shen C, Dodge HH, Ganguli M. Predictors of nursing facility admission: a 12-year epidemiological study in the United States. *Journal of the American Geriatrics Society*. 2004; 52(3):434-439
- 130 Bibas L, Levi M, Bendayan M, Mullie L, Forman DE, Afilalo J. Therapeutic interventions for frail elderly patients: part I. Published randomized trials. *Progress in Cardiovascular Diseases*. 2014; 57(2):134-143
- 131 Bielaszka-DuVernay C. Innovation profile: The 'GRACE' model: In-home assessments lead to better care for dual eligibles. *Health Affairs*. 2011; 30(3):431-434
- 132 Bielderma A, van der Schans CP, van Lieshout MR, de Greef MH, Boersma F, Krijnen WP et al. Multidimensional structure of the Groningen Frailty Indicator in community-dwelling older people. *BMC Geriatrics*. 2013; 13:86
- 133 Bien B, Bien-Barkowska K, Wojtkowicz A, Kasiukiewicz A, Wojszel ZB. Prognostic factors of long-term survival in geriatric inpatients. Should we change the recommendations for the oldest people? *Journal of Nutrition, Health and Aging*. 2015; 19(4):481-488
- 134 Billings J, Blunt I, Steventon A, Georghiou T, Lewis G, Bardsley M. Development of a predictive model to identify inpatients at risk of re-admission within 30 days of discharge (PARR-30). *BMJ Open*. 2012; 2(4)
- 135 Billings J, Georghiou T, Blunt I, Bardsley M. Choosing a model to predict hospital admission: an observational study of new variants of predictive models for case finding. *BMJ Open*. 2013; 3(8):e003352
- 136 Billington J, Coster S, Murrells T, Norman I. Evaluation of a nurse-led educational telephone intervention to support self-management of patients with chronic obstructive pulmonary disease: a randomized feasibility study. *COPD*. 2015; 12(4):395-403

- 137 Bitton A, Choudhry NK, Matlin OS, Swanton K, Shrank WH. The impact of medication adherence on coronary artery disease costs and outcomes: a systematic review. *American Journal of Medicine*. 2013; 126(4):357
- 138 Bjorkelund C, Maun A, Murante AM, Hoffman K, De Maeseneer J, Farkas-Pall Z. Impact of continuity on quality of primary care: from the perspective of citizens' preferences and multimorbidity - position paper of the European Forum for Primary Care. *Quality in Primary Care*. 2013; 21(3):193-204
- 139 Black DA, Taggart J, Jayasinghe UW, Proudfoot J, Crookes P, Beilby J et al. The Teamwork Study: enhancing the role of non-GP staff in chronic disease management in general practice. *Australian Journal of Primary Health*. 2013; 19:184-189
- 140 Black DM, Reid IR, Boonen S, Bucci-Rechtweg C, Cauley JA, Cosman F et al. The effect of 3 versus 6 years of zoledronic acid treatment of osteoporosis: a randomized extension to the HORIZON-Pivotal Fracture Trial (PFT). *Journal of Bone and Mineral Research*. 2012; 27(2):243-254
- 141 Black DM, Reid IR, Cauley JA, Cosman F, Leung PC, Lakatos P et al. The effect of 6 versus 9 years of zoledronic acid treatment in osteoporosis: a randomized second extension to the HORIZON-Pivotal Fracture Trial (PFT). *Journal of Bone and Mineral Research*. 2015; 30(5):934-944
- 142 Black DM, Schwartz AV, Ensrud KE, Cauley JA, Levis S, Quandt SA et al. Effects of continuing or stopping alendronate after 5 years of treatment: the Fracture Intervention Trial Long-term Extension (FLEX): a randomized trial. *JAMA*. 2006; 296(24):2927-2938
- 143 Blackburn DF, Dobson RT, Blackburn JL, Wilson TW. Cardiovascular morbidity associated with nonadherence to statin therapy. *Pharmacotherapy*. 2005; 25(8):1035-1043
- 144 Blake KB, Madhavan SS, Scott VG, Meredith Elswick BL. Medication therapy management services in West Virginia: pharmacists' perceptions of educational and training needs. *Research in Social and Administrative Pharmacy*. 2009; 5(2):182-188
- 145 Blakeman T, Blickem C, Kennedy A, Reeves D, Bower P, Gaffney H et al. Effect of information and telephone-guided access to community support for people with chronic kidney disease: randomised controlled trial. *PLoS ONE*. 2014; 9:e109135
- 146 Blakeman T, Protheroe J, Chew-Graham C, Rogers A, Kennedy A. Understanding the management of early-stage chronic kidney disease in primary care: a qualitative study. *British Journal of General Practice*. 2012; 62(597):e233-e242
- 147 Bleich SN, Sherrod C, Chiang A, Boyd C, Wolff J, Chang E et al. Systematic review of programs treating high-need and high-cost people with multiple chronic diseases or disabilities in the United States, 2008-2014. *Preventing Chronic Disease*. 2015; 12:E197
- 148 Bleijenberg N, Ten Dam VH, Steunenbergh B, Drubbel I, Numans ME, de Wit NJ et al. Exploring the expectations, needs and experiences of general practitioners and nurses towards a proactive and structured care programme for frail older patients: a mixed-methods study. *Journal of Advanced Nursing*. 2013; 69(10):2262-2273
- 149 Blix HS, Viktil KK, Reikvam A, Moger TA, Hjemaas BJ, Pretsch P et al. The majority of hospitalised patients have drug-related problems: results from a prospective study in general hospitals. *European Journal of Clinical Pharmacology*. 2004; 60(9):651-658

- 150 Blixen C, Perzynski A, Kanuch S, Dawson N, Kaiser D, Lawless ME et al. Training peer educators to promote self-management skills in people with serious mental illness (SMI) and diabetes (DM) in a primary health care setting. *Primary Health Care Research and Development*. 2015; 16(2):127-137
- 151 Boeckstaens P, Vaes B, Van Pottelbergh G, De Sutter A, Legrand D, Adriaensen W et al. Multimorbidity measures were poor predictors of adverse events in patients aged >80 years: a prospective cohort study. *Journal of Clinical Epidemiology*. 2015; 68(2):220-227
- 152 Boeckstaens P, Vaes B, Legrand D, Dalleur O, De Sutter A, Degryse JM. The relationship of multimorbidity with disability and frailty in the oldest patients: a cross-sectional analysis of three measures of multimorbidity in the BELFRAIL cohort. *European Journal of General Practice*. 2015; 21(1):39-44
- 153 Bogner HR, de Vries HF. Integration of depression and hypertension treatment: a pilot, randomized controlled trial. *Annals of Family Medicine*. 2008; 6(4):295-301
- 154 Bogner HR, de Vries HF. Integrating type 2 diabetes mellitus and depression treatment among African Americans: a randomized controlled pilot trial. *Diabetes Educator*. 2010; 36(2):284-292
- 155 Bogner HR, Morales KH, de Vries HF, Cappola AR. Integrated management of type 2 diabetes mellitus and depression treatment to improve medication adherence: a randomized controlled trial. *Annals of Family Medicine*. 2012; 10(1):15-22
- 156 Bonavita V, De Simone R. Towards a definition of comorbidity in the light of clinical complexity. *Neurological Sciences*. 2008; 29 Suppl 1:S99-102
- 157 Bone HG, Bolognese MA, Yuen CK, Kendler DL, Miller PD, Yang YC et al. Effects of denosumab treatment and discontinuation on bone mineral density and bone turnover markers in postmenopausal women with low bone mass. *Journal of Clinical Endocrinology and Metabolism*. 2011; 96(4):972-980
- 158 Bone HG, Hosking D, Devogelaer JP, Tucci JR, Emkey RD, Tonino RP et al. Ten years' experience with alendronate for osteoporosis in postmenopausal women. *New England Journal of Medicine*. 2004; 350(12):1189-1199
- 159 Bonnefoy M, Boutitie F, Mercier C, Gueyffier F, Carre C, Guetemme G et al. Efficacy of a home-based intervention programme on the physical activity level and functional ability of older people using domestic services: a randomised study. *Journal of Nutrition, Health and Aging*. 2012; 16(4):370-377
- 160 Boorsma M, Frijters DHM, Knol DL, Ribbe ME, Nijpels G, van Hout HPJ. Effects of multidisciplinary integrated care on quality of care in residential care facilities for elderly people: a cluster randomized trial. *CMAJ Canadian Medical Association Journal*. 2011; 183(11):E724-E732
- 161 Borenstein J, Aronow HU, Bolton LB, Choi J, Bresee C, Braunstein GD. Early recognition of risk factors for adverse outcomes during hospitalization among Medicare patients: a prospective cohort study. *BMC Geriatrics*. 2013; 13:72
- 162 Bosner S, Keller H, Wohner A, Wohner C, Sonnichsen A, Baum E et al. Prevention of falls by outdoor-walking in elderly persons at risk ("power") - A pilot study. *European Geriatric Medicine*. 2012; 3(1):28-32

- 163 Bottle A, Aylin P. Comorbidity scores for administrative data benefited from adaptation to local coding and diagnostic practices. *Journal of Clinical Epidemiology*. 2011; 64(12):1426-1433
- 164 Bottle A, Aylin P, Majeed A. Identifying patients at high risk of emergency hospital admissions: a logistic regression analysis. *Journal of the Royal Society of Medicine*. 2006; 99(8):406-414
- 165 Bouchard MH, Dragomir A, Blais L, Berard A, Pilon D, Perreault S. Impact of adherence to statins on coronary artery disease in primary prevention. *British Journal of Clinical Pharmacology*. 2007; 63(6):698-708
- 166 Boulton C, Dowd B, McCaffrey D, Boulton L, Hernandez R, Krulewicz H. Screening elders for risk of hospital admission. *Journal of the American Geriatrics Society*. 1993; 41(8):811-817
- 167 Boulton C, Pacala JT, Boulton LB. Targeting elders for geriatric evaluation and management: reliability, validity, and practicality of a questionnaire. *Aging (Milan, Italy)*. 1995; 7(3):159-164
- 168 Boulton C, Reider L, Frey K, Leff B, Boyd CM, Wolff JL et al. Early effects of "Guided Care" on the quality of health care for multimorbid older persons: a cluster-randomized controlled trial. *Journals of Gerontology Series A, Biological Sciences and Medical Sciences*. 2008; 63(3):321-327
- 169 Boulton C, Reider L, Leff B, Frick KD, Boyd CM, Wolff JL et al. The effect of guided care teams on the use of health services: results from a cluster-randomized controlled trial. *Archives of Internal Medicine*. 2011; 171:460-466
- 170 Boulton C, Leff B, Boyd CM, Wolff JL, Marsteller JA, Frick KD et al. A matched-pair cluster-randomized trial of guided care for high-risk older patients. *Journal of General Internal Medicine*. 2013; 28(5):612-621
- 171 Bouman A, van Rossum E, Evers S, Ambergen T, Kempen G, Knipschild P. Effects on health care use and associated cost of a home visiting program for older people with poor health status: a randomized clinical trial in the Netherlands. *Journals of Gerontology Series A, Biological Sciences and Medical Sciences*. 2008; 63(3):291-297
- 172 Bove DG, Overgaard D, Lomborg K, Lindhardt BO, Midtgaard J. Efficacy of a minimal home-based psychoeducative intervention versus usual care for managing anxiety and dyspnoea in patients with severe chronic obstructive pulmonary disease: a randomised controlled trial protocol. *BMJ Open*. 2015; 5(7):e008031
- 173 Bower P. Better management of multimorbidity: A critical look at the 'Ariadne principles'. *BMC Medicine*. 2014; 12(1)
- 174 Bower P, Hann M, Rick J, Rowe K, Burt J, Roland M et al. Multimorbidity and delivery of care for long-term conditions in the English National Health Service: baseline data from a cohort study. *Journal of Health Services Research and Policy*. 2013; 18(2 Suppl):29-37
- 175 Bower P, Harkness E, Macdonald W, Coventry P, Bundy C, Moss-Morris R. Illness representations in patients with multimorbid long-term conditions: qualitative study. *Psychology and Health*. 2012; 27(10):1211-1226
- 176 Bower P, Macdonald W, Harkness E, Gask L, Kendrick T, Valderas JM et al. Multimorbidity, service organization and clinical decision making in primary care: a qualitative study. *Family Practice*. 2011; 28(5):579-587

- 177 Bowles KH, Hanlon AL, Glick HA, Naylor MD, O'Connor M, Riegel B et al. Clinical effectiveness, access to, and satisfaction with care using a telehomecare substitution intervention: a randomized controlled trial. *International Journal of Telemedicine and Applications*. 2011; 2011:540138
- 178 Boxer R, Kleppinger A, Ahmad A, Annis K, Hager D, Kenny A. The 6-minute walk is associated with frailty and predicts mortality in older adults with heart failure. *Congestive Heart Failure*. 2010; 16(5):208-213
- 179 Boyd CM, Reider L, Frey K, Scharfstein D, Leff B, Wolff J et al. The effects of guided care on the perceived quality of health care for multi-morbid older persons: 18-month outcomes from a cluster-randomized controlled trial. *Journal of General Internal Medicine*. 2010; 25:235-242
- 180 Bozorgmehr K, Szecsenyi J, Ose D, Besier W, Mayer M, Krisam J et al. Practice network-based care management for patients with type 2 diabetes and multiple comorbidities (GEDIMAPlus): study protocol for a randomized controlled trial. *Trials*. 2014; 15:243
- 181 Bramley TJ, Gerbino PP, Nightengale BS, Frech-Tamas F. Relationship of blood pressure control to adherence with antihypertensive monotherapy in 13 managed care organizations. *Journal of Managed Care Pharmacy*. 2006; 12(3):239-245
- 182 Brannstrom M, Boman K. Effects of person-centred and integrated chronic heart failure and palliative home care. PREFER: a randomized controlled study. *European Journal of Heart Failure*. 2014; 16(10):1142-1151
- 183 Bratzke LC, Muehrer RJ, Kehl KA, Lee KS, Ward EC, Kwekkeboom KL. Self-management priority setting and decision-making in adults with multimorbidity: a narrative review of literature. *International Journal of Nursing Studies*. 2015; 52(3):744-755
- 184 Bravo G, Dubois MF, Hebert R, De Wals P, Messier L. A prospective evaluation of the Charlson Comorbidity Index for use in long-term care patients. *Journal of the American Geriatrics Society*. 2002; 50(4):740-745
- 185 Bravo G, Arcand M, Blanchette D, Boire-Lavigne AM, Dubois MF, Guay M et al. Promoting advance planning for health care and research among older adults: a randomized controlled trial. *BMC Medical Ethics*. 2012; 13:1
- 186 Breekveldt-Postma NS, Penning-van Beest FJA, Siiskonen SJ, Falvey H, Vincze G, Klungel OH et al. The effect of discontinuation of antihypertensives on the risk of acute myocardial infarction and stroke. *Current Medical Research and Opinion*. 2008; 24(1):121-127
- 187 Breitscheidel L, Ehlken B, Kostev K, Oberdiek MSA, Sandberg A, Schmieder RE. Real-life treatment patterns, compliance, persistence, and medication costs in patients with hypertension in Germany. *Journal of Medical Economics*. 2012; 15(1):155-165
- 188 Breslow MJ, Rosenfeld BA, Doerfler M. Erratum: Effect of multiple-site intensive care unit telemedicine program on clinical and economic outcomes: An alternative paradigm for intensivist staffing (*Critical Care Medicine* (2004) 32 (31-38)). *Critical Care Medicine*. 2004; 32(7):1632
- 189 Breslow MJ, Rosenfeld BA, Doerfler M, Burke G, Yates G, Stone DJ et al. Effect of a multiple-site intensive care unit telemedicine program on clinical and economic outcomes: an alternative paradigm for intensivist staffing. *Critical Care Medicine*. 2004; 32:31-38

- 190 Brettschneider C, Luck T, Fleischer S, Roling G, Beutner K, Lupp M et al. Cost-utility analysis of a preventive home visit program for older adults in Germany. *BMC Health Services Research*. 2015; 15:141
- 191 Brevetti G, Giugliano G, Oliva G, Lanero S, De Maio JI, Chiariello M. The impact of comorbidity burden on the cardiovascular risk in the Peripheral Arteriopathy and Cardiovascular Events study. *QJM*. 2008; 101(7):575-582
- 192 Briskman I, Bar G, Boaz M, Shargorodsky M. Impact of co-morbid mental illness on the diagnosis and management of patients hospitalized for medical conditions in a general hospital. *International Journal of Psychiatry in Medicine*. 2012; 43(4):339-348
- 193 Brovold T, Skelton DA, Bergland A. Older adults recently discharged from the hospital: effect of aerobic interval exercise on health-related quality of life, physical fitness, and physical activity. *Journal of the American Geriatrics Society*. 2013; 61(9):1580-1585
- 194 Brown JP, Reid IR, Wagman RB, Kendler D, Miller PD, Jensen JEB et al. Effects of up to 5 years of denosumab treatment on bone histology and histomorphometry: the FREEDOM study extension. *Journal of Bone and Mineral Research*. 2014; 29(9):2051-2056
- 195 Brown JP, Roux C, Torring O, Ho PR, Beck Jensen JE, Gilchrist N et al. Discontinuation of denosumab and associated fracture incidence: analysis from the Fracture Reduction Evaluation of Denosumab in Osteoporosis Every 6 Months (FREEDOM) trial. *Journal of Bone and Mineral Research*. 2013; 28(4):746-752
- 196 Brown M, Sinacore DR, Binder EF, Kohrt WM. Physical and performance measures for the identification of mild to moderate frailty. *Journals of Gerontology Series A, Biological Sciences and Medical Sciences*. 2000; 55(6):M350-M355
- 197 Brown R, Peikes D, Peterson G, Schore J, Razafundrakoto C. Six features of Medicare coordinated care demonstration programs that cut hospital admissions of high-risk patients. *Health Affairs*. 2012; 31(6):1156-1166
- 198 Bruhn H, Bond CM, Elliott AM, Hannaford PC, Lee AJ, McNamee P et al. Pharmacist-led management of chronic pain in primary care: results from a randomised controlled exploratory trial. *BMJ Open*. 2013; 3(4)
- 199 Buajordet I, Ebbesen J, Erikssen J, Brors O, Hilberg T. Fatal adverse drug events: the paradox of drug treatment. *Journal of Internal Medicine*. 2001; 250(4):327-341
- 200 Buckingham S, Kendall M, Ferguson S, Macnee W, Sheikh A, White P et al. HELPing older people with very severe chronic obstructive pulmonary disease (HELP-COPD): Mixed-method feasibility pilot randomised controlled trial of a novel intervention. *Npj Primary Care Respiratory Medicine*. 2015; 25
- 201 Buist DSM, Ross NK, Reid RJ, Grossman DC. Electronic health risk assessment adoption in an integrated healthcare system. *American Journal of Managed Care*. 2014; 20(1):62-69
- 202 Buntinx F, Niclaes L, Suetens C, Jans B, Mertens R, van den Akker M. Evaluation of Charlson's comorbidity index in elderly living in nursing homes. *Journal of Clinical Epidemiology*. 2002; 55(11):1144-1147

- 203 Burgers JS, Voerman GE, Grol R, Faber MJ, Schneider EC. Quality and coordination of care for patients with multiple conditions: results from an international survey of patient experience. *Evaluation and the Health Professions*. 2010; 33(3):343-364
- 204 Burke JA, Earley M, Dixon LD, Wilke A, Puczynski S. Patients with diabetes speak: exploring the implications of patients' perspectives for their diabetes appointments. *Health Communication*. 2006; 19(2):103-114
- 205 Burke TA, Sturkenboom MC, Lu Se, Wentworth CE, Lin Y, Rhoads GG. Discontinuation of antihypertensive drugs among newly diagnosed hypertensive patients in UK general practice. *Journal of Hypertension*. 2006; 24(6):1193-1200
- 206 Buurman BM, Hoogerduijn JG, de Haan RJ, Abu-Hanna A, Lagaay AM, Verhaar HJ et al. Geriatric conditions in acutely hospitalized older patients: prevalence and one-year survival and functional decline. *PLoS ONE*. 2011; 6(11):e26951
- 207 Byles JE, D'Este C, Parkinson L, O'Connell R, Treloar C. Single index of multimorbidity did not predict multiple outcomes. *Journal of Clinical Epidemiology*. 2005; 58(10):997-1005
- 208 Cadore EL, Casas-Herrero A, Zambom-Ferraresi F, Idoate F, Millor N, Gomez M et al. Multicomponent exercises including muscle power training enhance muscle mass, power output, and functional outcomes in institutionalized frail nonagenarians. *Age*. 2014; 36(2):773-785
- 209 Cady RG, Erickson M, Lunos S, Finkelstein SM, Looman W, Celebreeze M et al. Meeting the needs of children with medical complexity using a telehealth advanced practice registered nurse care coordination model. *Maternal and Child Health Journal*. 2015; 19(7):1497-1506
- 210 Caillet P, Laurent M, Bastuji-Garin S, Liuu E, Culine S, Lagrange JL et al. Optimal management of elderly cancer patients: usefulness of the Comprehensive Geriatric Assessment. *Clinical Interventions In Aging*. 2014; 9:1645-1660
- 211 Calderon-Larranaga A, Poblador-Plou B, Gonzalez-Rubio F, Gimeno-Feliu LA, Abad-Diez JM, Prados-Torres A. Multimorbidity, polypharmacy, referrals, and adverse drug events: Are we doing things well? *British Journal of General Practice*. 2012; 62(605):e821-e826
- 212 Calvo-Espinos C, De Gaona-Lana ER, Gonzalez-Anguren C, Lama-Gay M. Assessment of the impact of comorbidity on the survival of cancer patients treated by palliative care teams. *Palliative and Supportive Care*. 2015; 13(4):1049-1055
- 213 Campbell SE, Seymour DG, Primrose WR, ACMEPLUS Project. A systematic literature review of factors affecting outcome in older medical patients admitted to hospital. *Age and Ageing*. 2004; 33(2):110-115
- 214 Canady VA. *New Illinois crisis intervention center modeled like a BH emergency room*. *Mental Health Weekly*. Hoboken, New Jersey: John Wiley & Sons, Inc. 2014; 24(40):1-6
- 215 Canoui-Poitrine F, Bastuji-Garin S, Alonso E, Darcel G, Verstichel P, Caillet P et al. Risk and prognostic factors of epileptic status in the elderly: a case-control study. *Epilepsia*. 2011; 52(10):1849-1856
- 216 Caplan L, Haverhals LM. Barriers and facilitators for preventing adverse drug reactions of long latency: a qualitative study. *International Journal of Risk and Safety in Medicine*. 2012; 24(2):81-94

- 217 Carder PC, Vuckovic N, Green CA. Negotiating medications: patient perceptions of long-term medication use. *Journal of Clinical Pharmacy and Therapeutics*. 2003; 28(5):409-417
- 218 Carey EC, Covinsky KE, Lui LY, Eng C, Sands LP, Walter LC. Prediction of mortality in community-living frail elderly people with long-term care needs. *Journal of the American Geriatrics Society*. 2008; 56(1):68-75
- 219 Carey EC, Walter LC, Lindquist K, Covinsky KE. Development and validation of a functional morbidity index to predict mortality in community-dwelling elders. *Journal of General Internal Medicine*. 2004; 19(10):1027-1033
- 220 Carey IM, Shah SM, Harris T, DeWilde S, Cook DG. A new simple primary care morbidity score predicted mortality and better explains between practice variations than the Charlson index. *Journal of Clinical Epidemiology*. 2013; 66(4):436-444
- 221 Carter BL, Doucette WR, Franciscus CL, Ardery G, Kluesner KM, Chrischilles EA. Deterioration of blood pressure control after discontinuation of a physician-pharmacist collaborative intervention. *Pharmacotherapy*. 2010; 30(3):228-235
- 222 Cartier JM. A team-based approach to the care of depression in later life: where are we now? *Psychiatric Clinics of North America*. 2013; 36:651-660
- 223 Castelli R, Bucciarelli P, Porro F, Depetri F, Cugno M. Pulmonary embolism in elderly patients: prognostic impact of the Cumulative Illness Rating Scale (CIRS) on short-term mortality. *Thrombosis Research*. 2014; 134(2):326-330
- 224 Castelnuovo G, Manzoni GM, Cuzziol P, Cesa GL, Corti S, Tuzzi C et al. TECNOB Study: Ad interim results of a randomized controlled trial of a multidisciplinary telecare intervention for obese patients with type-2 diabetes. *Clinical Practice and Epidemiology in Mental Health [Electronic Resource]: CP and EMH*. 2011; 7:44-50
- 225 Castelnuovo G, Manzoni GM, Cuzziol P, Cesa GL, Tuzzi C, Villa V et al. TECNOB: study design of a randomized controlled trial of a multidisciplinary telecare intervention for obese patients with type-2 diabetes. *BMC Public Health*. 2010; 10:204
- 226 Castro VM, McCoy TH, Cagan A, Rosenfield HR, Murphy SN, Churchill SE et al. Stratification of risk for hospital admissions for injury related to fall: cohort study. *BMJ*. 2014; 349:g5863
- 227 Cei M, Mumoli N, Vitale J, Dentali F. A prognostic index for 1-year mortality can also predict in-hospital mortality of elderly medical patients. *Internal and Emergency Medicine*. 2015; 10(5):575-579
- 228 Ceramidas D, Glasgow N. Multi-morbidity: a system design challenge in delivering patient-centred care. *Australian Health Review*. 2013; 37(3):309-311
- 229 Cesari M, Demougeot L, Bocalon H, Guyonnet S, Abellan van Kan G, Vellas B et al. A self-reported screening tool for detecting community-dwelling older persons with frailty syndrome in the absence of mobility disability: The FiND questionnaire. *PLoS ONE*. 2014; 9(7)
- 230 Chadwick A, Street C, McAndrew S, Deacon M. Minding our own bodies: reviewing the literature regarding the perceptions of service users diagnosed with serious mental illness on barriers to accessing physical health care. *International Journal of Mental Health Nursing*. 2012; 21(3):211-219

- 231 Chae JW, Song CS, Kim H, Lee KB, Seo BS, Kim DI. Prediction of mortality in patients undergoing maintenance hemodialysis by Charlson Comorbidity Index using ICD-10 database. *Nephron Clinical Practice*. 2011; 117(4):c379-c384
- 232 Chan A, Matchar DB, Tsao MA, Harding S, Chiu C-T, Tay B et al. Self-Care for Older People (SCOPE): A cluster randomized controlled trial of self-care training and health outcomes in low-income elderly in Singapore. *Contemporary Clinical Trials*. 2015; 41:313-324
- 233 Chan DC, Tsou HH, Chen CY, Chen CY. Validation of the Chinese-Canadian study of health and aging clinical frailty scale (CSHA-CFS) telephone version. *Archives of Gerontology and Geriatrics*. 2010; 50(3):e74-e80
- 234 Chan TC, Luk JK, Chu LW, Chan FH. Validation study of Charlson Comorbidity Index in predicting mortality in Chinese older adults. *Geriatrics and Gerontology International*. 2014; 14(2):452-457
- 235 Chan TC, Shea YF, Luk KH, Chan HW, Chu LW. Development and validation of a prognostic index for 2-year mortality in Chinese older residents living in nursing homes. *Geriatrics and Gerontology International*. 2012; 12(3):555-562
- 236 Chan WS, Whitford DL, Conroy R, Gibney D, Hollywood B. A multidisciplinary primary care team consultation in a socio-economically deprived community: an exploratory randomised controlled trial. *BMC Health Services Research*. 2011; 11:15
- 237 Chang CM, Liu PYY, Yang YHK, Yang YC, Wu CF, Lu FH. Use of the Beers criteria to predict adverse drug reactions among first-visit elderly outpatients. *Pharmacotherapy*. 2005; 25(6):831-838
- 238 Chang SF, Lin PL. Frail phenotype and mortality prediction: a systematic review and meta-analysis of prospective cohort studies. *International Journal of Nursing Studies*. 2015; 52(8):1362-1374
- 239 Chang YP, Huang SK, Tao P, Chien CW. A population-based study on the association between acute renal failure (ARF) and the duration of polypharmacy. *BMC Nephrology*. 2012; 13:96
- 240 Chapman BP, Weiss A, Fiscella K, Muennig P, Kawachi I, Duberstein P. Mortality risk prediction: can comorbidity indices be improved with psychosocial data? *Medical Care*. 2015; 53(11):909-915
- 241 Chapman L, Smith A, Williams V, Oliver D. Community matrons: primary care professionals' views and experiences. *Journal of Advanced Nursing*. 2009; 65(8):1617-1625
- 242 Chapman MD, Le BH, Gorelik A. The Vulnerable Elders Survey and its prognostic relationship to survival in an older community-based palliative population. *BMJ Supportive and Palliative Care*. 2013; 3(3):335-342
- 243 Chapman RH, Yeaw J, Roberts CS. Association between adherence to calcium-channel blocker and statin medications and likelihood of cardiovascular events among US managed care enrollees. *BMC Cardiovascular Disorders*. 2010; 10:29
- 244 Charlson M, Szatrowski TP, Peterson J, Gold J. Validation of a combined comorbidity index. *Journal of Clinical Epidemiology*. 1994; 47(11):1245-1251

- 245 Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *Journal of Chronic Diseases*. 1987; 40(5):373-383
- 246 Chaudhry S, Jin L, Meltzer D. Use of a self-report-generated Charlson Comorbidity Index for predicting mortality. *Medical Care*. 2005; 43(6):607-615
- 247 Chen GJ, Smith RD, Ferrario CM. Association between antihypertensive agent use and hospital admissions in a managed care population. *American Journal of the Medical Sciences*. 2004; 327(6):310-314
- 248 Chen JY, Tsai SH, Chuang PH, Chang CH, Chuang CL, Chen HL et al. A comorbidity index for mortality prediction in Chinese patients with ESRD receiving hemodialysis. *Clinical Journal of American Society of Nephrology: CJASN*. 2014; 9(3):513-519
- 249 Chen LK, Peng LN, Lin MH, Lai HY, Hwang SJ, Lan CF. Predicting mortality of older residents in long-term care facilities: comorbidity or care problems? *Journal of the American Medical Directors Association*. 2010; 11(8):567-571
- 250 Chen L-K, Chen Y-M, Hwang S-J, Peng L-N, Lin M-H, Lee W-J et al. Effectiveness of community hospital-based post-acute care on functional recovery and 12-month mortality in older patients: A prospective cohort study. *Annals of Medicine*. 2010; 42(8):630-636
- 251 Chen YC, Fan JS, Hsu TF, Chen MH, Huang HH, Cheng KW et al. Detection of patients presenting with adverse drug events in the emergency department. *Internal Medicine Journal*. 2012; 42(6):651-657
- 252 Chen YC, Fan JS, Chen MH, Hsu TF, Huang HH, Cheng KW et al. Risk factors associated with adverse drug events among older adults in emergency department. *European Journal of Internal Medicine*. 2014; 25(1):49-55
- 253 Chen YC, Huang HH, Fan JS, Chen MH, Hsu TF, Yen DH-T et al. Comparing characteristics of adverse drug events between older and younger adults presenting to a Taiwan emergency department. *Medicine*. 2015; 94(7):e547
- 254 Chenore T, Pereira Gray DJ, Forrer J, Wright C, Evans PH. Emergency hospital admissions for the elderly: insights from the Devon Predictive Model. *Journal of Public Health*. 2013; 35(4):616-623
- 255 Cheraghi-Sohi S, Bower P, Kennedy A, Morden A, Rogers A, Richardson J et al. Patient priorities in osteoarthritis and comorbid conditions: a secondary analysis of qualitative data. *Arthritis Care and Research*. 2013; 65(6):920-927
- 256 Cherubini A, Eusebi P, Dell'Aquila G, Landi F, Gasperini B, Bacuccoli R et al. Predictors of hospitalization in Italian nursing home residents: the U.L.I.S.S.E. project. *Journal of the American Medical Directors Association*. 2012; 13(1):84-10
- 257 Chew-Graham CA, Hogg T. Patients with chronic physical illness and co-existing psychological morbidity: GPs' views on their role in detection and management. *Primary Care Psychiatry*.: LibraPharm Informa Healthcare. 2002; 8(2):35-40
- 258 Chiang C-H, Chou M-Y, Chou S-L, Liang C-K, Chen L-K, Yen DHT et al. Risk factors for frequent emergency department visits of veterans home residents in Northern Taiwan. *Journal of Clinical Gerontology and Geriatrics*. 2012; 3(4):118-121

- 259 Chirinos JA, Veerani A, Zambrano JP, Schob A, Perez G, Mendez AJ et al. Evaluation of comorbidity scores to predict all-cause mortality in patients with established coronary artery disease. *International Journal of Cardiology*. 2007; 117(1):97-102
- 260 Cho H, Klabunde CN, Yabroff KR, Wang Z, Meekins A, Lansdorp-Vogelaar I et al. Comorbidity-adjusted life expectancy: a new tool to inform recommendations for optimal screening strategies. *Annals of Internal Medicine*. 2013; 159(10):667-676
- 261 Choudhry NK, Glynn RJ, Avorn J, Lee JL, Brennan TA, Reisman L et al. Untangling the relationship between medication adherence and post-myocardial infarction outcomes: medication adherence and clinical outcomes. *American Heart Journal*. 2014; 167(1):51-58
- 262 Chouinard MC, Hudon C, Dubois MF, Roberge P, Loignon C, Tchouaket E et al. Case management and self-management support for frequent users with chronic disease in primary care: a pragmatic randomized controlled trial. *BMC Health Services Research*. 2013; 13:49
- 263 Chow SK, Wong FK. A randomized controlled trial of a nurse-led case management programme for hospital-discharged older adults with co-morbidities. *Journal of Advanced Nursing*. 2014; 70:2257-2271
- 264 Chowdhury R, Khan H, Heydon E, Shroufi A, Fahimi S, Moore C et al. Adherence to cardiovascular therapy: a meta-analysis of prevalence and clinical consequences. *European Heart Journal*. 2013; 34(38):2940-2948
- 265 Chrischilles E, Rubenstein L, Van Gilder R, Voelker M, Wright K, Wallace R. Risk factors for adverse drug events in older adults with mobility limitations in the community setting. *Journal of the American Geriatrics Society*. 2007; 55(1):29-34
- 266 Christe V, Waeber G, Vollenweider P, Marques-Vidal P. Antihypertensive drug treatment changes in the general population: the CoLaus study. *BMC Pharmacology and Toxicology*. 2014; 15(1):20
- 267 Chung H, Kim A, Neighbors C, Cummings J, Ricketts S, O'Grady M et al. Early experience of a pilot intervention for patients with depression and chronic medical illness in an urban ACO. *General Hospital Psychiatry*. 2013; 35(5):468-471
- 268 Ciechanowski PS, Russo JE, Katon WJ, Von Korff M, Simon GE, Lin EH et al. The association of patient relationship style and outcomes in collaborative care treatment for depression in patients with diabetes. *Medical Care*. 2006; 44(3):283-291
- 269 Cimpean D, Drake RE. Treating co-morbid chronic medical conditions and anxiety/depression. *Epidemiology and Psychiatric Science*. 2011; 20:141-150
- 270 Clark AP, McDougall G, Riegel B, Joiner-Rogers G, Innerarity S, Meraviglia M et al. Health status and self-care outcomes after an education-support intervention for people with chronic heart failure. *Journal of Cardiovascular Nursing*. 2015; 30(4 Suppl 1):S3-13
- 271 Clark DO, Von Korff M, Saunders K, Baluch WM, Simon GE. A chronic disease score with empirically derived weights. *Medical Care*. 1995; 33(8):783-795
- 272 Clark F, Jackson J, Carlson M, Chou CP, Cherry BJ, Jordan-Marsh M et al. Effectiveness of a lifestyle intervention in promoting the well-being of independently living older people: results of the Well Elderly 2 Randomised Controlled Trial. *Journal of Epidemiology and Community Health*. 2012; 66(9):782-790

- 273 Clarke B, Howlett J, Sapp J, Andreou P, Parkash R. The effect of comorbidity on the competing risk of sudden and nonsudden death in an ambulatory heart failure population. *Canadian Journal of Cardiology*. 2011; 27(2):254-261
- 274 Clarke LH, Bennett EV, Korotchenko A. Negotiating vulnerabilities: how older adults with multiple chronic conditions interact with physicians. *Canadian Journal on Aging*. 2014; 33(1):26-37
- 275 Clegg A, Rogers L, Young J. Diagnostic test accuracy of simple instruments for identifying frailty in community-dwelling older people: a systematic review. *Age and Ageing*. 2015; 44(1):148-152
- 276 Clegg A, Bates C, Young J, Ryan R, Nichols L, Ann Teale E et al. Development and validation of an electronic frailty index using routine primary care electronic health record data. *Age and Ageing*. 2016; 45(3):353-360
- 277 Coburn KD, Marcantonio S, Lazansky R, Keller M, Davis N. Effect of a community-based nursing intervention on mortality in chronically ill older adults: a randomized controlled trial. *PLoS Medicine*. 2012; 9(7):e1001265
- 278 Coelho T, Paul C, Gobbens RJJ, Fernandes L. Frailty as a predictor of short-term adverse outcomes. *PeerJ*. 2015; 3:e1121
- 279 Cole MG, McCusker J, Bellavance F, Primeau FJ, Bailey RF, Bonnycastle MJ et al. Systematic detection and multidisciplinary care of delirium in older medical inpatients: a randomized trial. *CMAJ Canadian Medical Association Journal*. 2002; 167(7):753-759
- 280 Coleman EA, Eilertsen TB, Kramer AM, Magid DJ, Beck A, Conner D. Reducing emergency visits in older adults with chronic illness. A randomized, controlled trial of group visits. *Effective Clinical Practice : ECP*. 2001; 4(2):49-57
- 281 Coleman EA, Wagner EH, Grothaus LC, Hecht J, Savarino J, Buchner DM. Predicting hospitalization and functional decline in older health plan enrollees: are administrative data as accurate as self-report? *Journal of the American Geriatrics Society*. 1998; 46(4):419-425
- 282 Colivicchi F, Bassi A, Santini M, Caltagirone C. Discontinuation of statin therapy and clinical outcome after ischemic stroke. *Stroke; a Journal of Cerebral Circulation*. 2007; 38(10):2652-2657
- 283 Conde-Martel A, Formiga F, Perez-Bocanegra C, Armengou-Arxe A, Muela-Molinero A, Sanchez-Sanchez C et al. Clinical characteristics and one-year survival in heart failure patients more than 85 years of age compared with younger. *European Journal of Internal Medicine*. 2013; 24(4):339-345
- 284 Conde-Martel A, Hemmersbach-Miller M, Marchena-Gomez J, Saavedra-Santana P, Betancor-Leon P. Five-year survival and prognostic factors in a cohort of hospitalized nonagenarians. *European Journal of Internal Medicine*. 2012; 23(6):513-518
- 285 Condon JR, You J, McDonnell J. Performance of comorbidity indices in measuring outcomes after acute myocardial infarction in Australian indigenous and non-indigenous patients. *Internal Medicine Journal*. 2012; 42(7):e165-e173
- 286 Conway R, Byrne D, O'Riordan D, Silke B. Emergency readmissions are substantially determined by acute illness severity and chronic debilitating illness: A single centre cohort study. *European Journal of Internal Medicine*. 2015; 26(1):12-17

- 287 Cook DA, Sorensen KJ, Wilkinson JM, Berger RA. Barriers and decisions when answering clinical questions at the point of care: a grounded theory study. *JAMA Internal Medicine*. 2013; 173(21):1962-1969
- 288 Corbi G, Gambassi G, Pagano G, Russomanno G, Conti V, Rengo G et al. Impact of an innovative educational strategy on medication appropriate use and length of stay in elderly patients. *Medicine*. 2015; 94(24)
- 289 Corrao G, Conti V, Merlino L, Catapano AL, Mancina G. Results of a retrospective database analysis of adherence to statin therapy and risk of nonfatal ischemic heart disease in daily clinical practice in Italy. *Clinical Therapeutics*. 2010; 32(2):300-310
- 290 Corrao G, Parodi A, Nicotra F, Zambon A, Merlino L, Cesana G et al. Better compliance to antihypertensive medications reduces cardiovascular risk. *Journal of Hypertension*. 2011; 29(3):610-618
- 291 Corrao G, Zambon A, Parodi A, Merlino L, Mancina G. Incidence of cardiovascular events in Italian patients with early discontinuations of antihypertensive, lipid-lowering, and antidiabetic treatments. *American Journal of Hypertension*. 2012; 25(5):549-555
- 292 Correa Leite ML, Firmo JOA, Loyola Filho AI, Lima-Costa MF. Discontinuation of anti-hypertensive drugs increases 11-year cardiovascular mortality risk in community-dwelling elderly (the Bambui Cohort Study of Ageing). *BMC Public Health*. 2014; 14:725
- 293 Corser W, Dontje K. Self-management perspectives of heavily comorbid primary care adults. *Professional Case Management*. 2011; 16(1):6-17
- 294 Corsinovi L, Bo M, Ricauda Aimonino N, Marinello R, Gariglio F, Marchetto C et al. Predictors of falls and hospitalization outcomes in elderly patients admitted to an acute geriatric unit. *Archives of Gerontology and Geriatrics*. 2009; 49(1):142-145
- 295 Cosman F, Cauley JA, Eastell R, Boonen S, Palermo L, Reid IR et al. Reassessment of fracture risk in women after 3 years of treatment with zoledronic acid: when is it reasonable to discontinue treatment? *Journal of Clinical Endocrinology and Metabolism*. 2014; 99(12):4546-4554
- 296 Coulter A, Entwistle VA, Eccles A, Ryan S, Shepperd S, Perera R. Personalised care planning for adults with chronic or long-term health conditions. *Cochrane Database of Systematic Reviews*. 2015; Issue 3:CD010523
- 297 Counsell SR, Callahan CM, Buttar AB, Clark DO, Frank KI. Geriatric Resources for Assessment and Care of Elders (GRACE): a new model of primary care for low-income seniors. *Journal of the American Geriatrics Society*. 2006; 54(7):1136-1141
- 298 Counsell SR, Callahan CM, Clark DO, Tu W, Buttar AB, Stump TE et al. Geriatric care management for low-income seniors: a randomized controlled trial. *JAMA*. 2007; 298(22):2623-2633
- 299 Courtney M, Edwards H, Chang A, Parker A, Finlayson K, Hamilton K. Fewer emergency readmissions and better quality of life for older adults at risk of hospital readmission: A randomized controlled trial to determine the effectiveness of a 24-week exercise and telephone follow-up program. *Journal of the American Geriatrics Society*. 2009; 57(3):395-402

- 300 Coventry PA, Fisher L, Kenning C, Bee P, Bower P. Capacity, responsibility, and motivation: a critical qualitative evaluation of patient and practitioner views about barriers to self-management in people with multimorbidity. *BMC Health Services Research*. 2014; 14:536
- 301 Coventry PA, Hays R, Dickens C, Bundy C, Garrett C, Cherrington A et al. Talking about depression: a qualitative study of barriers to managing depression in people with long term conditions in primary care. *BMC Family Practice*. 2011; 12:10
- 302 Coventry PA, Lovell K, Dickens C, Bower P, Chew-Graham C, Cherrington A et al. Update on the collaborative interventions for circulation and depression (COINCIDE) trial: changes to planned methodology of a cluster randomized controlled trial of collaborative care for depression in people with diabetes and/or coronary heart disease. *Trials*. 2013; 14:136
- 303 Coventry P, Lovell K, Dickens C, Bower P, Chew-Graham C, McElvenny D et al. Integrated primary care for patients with mental and physical multimorbidity: cluster randomised controlled trial of collaborative care for patients with depression comorbid with diabetes or cardiovascular disease. *BMJ*. 2015; 350
- 304 Cowie L, Morgan M, White P, Gulliford M. Experience of continuity of care of patients with multiple long-term conditions in England. *Journal of Health Services Research and Policy*. 2009; 14(2):82-87
- 305 Cramm JM, Nieboer AP. High-quality chronic care delivery improves experiences of chronically ill patients receiving care. *International Journal for Quality in Health Care*. 2013; 25(6):689-695
- 306 Croft CH, Rude RE, Gustafson N, Stone PH, Poole WK, Roberts R et al. Abrupt withdrawal of beta-blockade therapy in patients with myocardial infarction: effects on infarct size, left ventricular function, and hospital course. *Circulation*. 1986; 73(6):1281-1290
- 307 Crooks CJ, West J, Card TR. A comparison of the recording of comorbidity in primary and secondary care by using the Charlson Index to predict short-term and long-term survival in a routine linked data cohort. *BMJ Open*. 2015; 5(6):e007974
- 308 Crotty MM, Henderson J, Ward PR, Fuller J, Rogers A, Kralik D et al. Analysis of social networks supporting the self-management of type 2 diabetes for people with mental illness. *BMC Health Services Research*. 2015; 15:257
- 309 Cubeddu LX, Seamon MJ. Statin withdrawal: clinical implications and molecular mechanisms. *Pharmacotherapy*. 2006; 26(9):1288-1296
- 310 Cudney S, Weinert C. An online approach to providing chronic illness self-management information. *Computers, Informatics, Nursing*. 2012; 30(2):110-117
- 311 Cui Y, Metge C, Ye X, Moffatt M, Oppenheimer L, Forget EL. Development and validation of a predictive model for all-cause hospital readmissions in Winnipeg, Canada. *Journal of Health Services Research and Policy*. 2015; 20(2):83-91
- 312 Cully JA, Breland JY, Robertson S, Utech AE, Hundt N, Kunik ME et al. Behavioral health coaching for rural veterans with diabetes and depression: a patient randomized effectiveness implementation trial. *BMC Health Services Research*. 2014; 14:191
- 313 Cummings DM, Letter AJ, Howard G, Howard VJ, Safford MM, Prince V et al. Medication adherence and stroke/TIA risk in treated hypertensives: results from the REGARDS study. *Journal of the American Society of Hypertension*. 2013; 7(5):363-369

- 314 Cunliffe AL, Gladman JR, Husbands SL, Miller P, Dewey ME, Harwood RH. Sooner and healthier: a randomised controlled trial and interview study of an early discharge rehabilitation service for older people. *Age and Ageing*. 2004; 33(3):246-252
- 315 Curtis L. Unit costs of health and social care 2010. Canterbury: Personal Social Services Research Unit, University of Kent; 2010. Available from: <http://www.pssru.ac.uk/project-pages/unit-costs/2010/>
- 316 Curtis L. Unit costs of health and social care 2014. Canterbury: Personal Social Services Research Unit, University of Kent; 2014. Available from: <http://www.pssru.ac.uk/project-pages/unit-costs/2014/>
- 317 D'Arcy C, Holman JE, Preen DB, Baynham NJ, Finn JC, Semmens JB. A multipurpose comorbidity scoring system performed better than the Charlson index. *Journal of Clinical Epidemiology*. 2005; 58(10):1006-1014
- 318 D'Hoore W, Bouckaert A, Tilquin C. Practical considerations on the use of the Charlson comorbidity index with administrative data bases. *Journal of Clinical Epidemiology*. 1996; 49(12):1429-1433
- 319 D'Hoore W, Sicotte C, Tilquin C. Risk adjustment in outcome assessment: the Charlson comorbidity index. *Methods of Information in Medicine*. 1993; 32(5):382-387
- 320 Daker-White G, Hays R, Esmail A, Minor B, Barlow W, Brown B et al. MAXimising Involvement in MULtiMorbidity (MAXIMUM) in primary care: protocol for an observation and interview study of patients, GPs and other care providers to identify ways of reducing patient safety failures. *BMJ Open*. 2014; 4(8):e005493
- 321 Dale MC, Burns A, Panter L, Morris J. Factors affecting survival of elderly nursing home residents. *International Journal of Geriatric Psychiatry*. 2001; 16(1):70-76
- 322 Daniels R, van Rossum E, Beurskens A, van den Heuvel W, de Witte L. The predictive validity of three self-report screening instruments for identifying frail older people in the community. *BMC Public Health*. 2012; 12:69
- 323 Dar O, Riley J, Chapman C, Dubrey SW, Morris S, Rosen SD et al. A randomized trial of home telemonitoring in a typical elderly heart failure population in North West London: results of the Home-HF study. *European Journal of Heart Failure*. 2009; 11(3):319-325
- 324 Darkins A, Ryan P, Kobb R, Foster L, Edmonson E, Wakefield B et al. Care Coordination/Home Telehealth: the systematic implementation of health informatics, home telehealth, and disease management to support the care of veteran patients with chronic conditions. *Telemedicine Journal and E-Health*. 2008; 14(10):1118-1126
- 325 Daskalopoulou SS, Delaney JAC, Filion KB, Brophy JM, Mayo NE, Suissa S. Discontinuation of statin therapy following an acute myocardial infarction: a population-based study. *European Heart Journal*. 2008; 29(17):2083-2091
- 326 Daskalopoulou SS, Doonan RJ, Delaney JA, Pilote L. Different patterns of statin use in patients with acute myocardial infarction. *Current Vascular Pharmacology*. 2014; 12(6):885-892
- 327 Daugherty SL, Powers JD, Magid DJ, Masoudi FA, Margolis KL, O'Connor PJ et al. The association between medication adherence and treatment intensification with blood pressure control in resistant hypertension. *Hypertension*. 2012; 60(2):303-309

- 328 Davies SJ, Phillips L, Naish PF, Russell GI. Quantifying comorbidity in peritoneal dialysis patients and its relationship to other predictors of survival. *Nephrology, Dialysis, Transplantation*. 2002; 17(6):1085-1092
- 329 Davis MM, Devoe M, Kansagara D, Nicolaidis C, Englander H. "Did I do as best as the system would let me?" Healthcare professional views on hospital to home care transitions. *Journal of General Internal Medicine*. 2012; 27(12):1649-1656
- 330 Davis P, Lay-Yee R, Fitzjohn J, Hider P, Schug S, Briant R et al. Co-morbidity and health outcomes in three Auckland hospitals. *New Zealand Medical Journal*. 2002; 115(1153):211-215
- 331 Dayhoff NE, Suhrheinrich J, Wigglesworth J, Topp R, Moore S. Balance and muscle strength as predictors of frailty among older adults. *Journal of Gerontological Nursing*. 1998; 24(7):18-27
- 332 De Buyser SL, Petrovic M, Taes YE, Vetrano DL, Onder G. A multicomponent approach to identify predictors of hospital outcomes in older in-patients: a multicentre, observational study. *PLoS ONE*. 2014; 9(12):e115413
- 333 de Heer EW, Dekker J, van Eck van der Sluijs, Beekman AT, van Marwijk HW, Holwerda TJ et al. Effectiveness and cost-effectiveness of transmural collaborative care with consultation letter (TCCCL) and duloxetine for major depressive disorder (MDD) and (sub)chronic pain in collaboration with primary care: design of a randomized placebo-controlled multi-Centre trial: TCC:PAINDIP. *BMC Psychiatry*. 2013; 13:147
- 334 de Torres JP, Casanova C, Marin JM, Pinto-Plata V, Divo M, Zulueta JJ et al. Prognostic evaluation of COPD patients: GOLD 2011 versus BODE and the COPD comorbidity index COTE. *Thorax*. 2014; 69(9):799-804
- 335 De Vera MA, Bhole V, Burns LC, Lacaille D. Impact of statin adherence on cardiovascular disease and mortality outcomes: a systematic review. *British Journal of Clinical Pharmacology*. 2014; 78(4):684-698
- 336 De Vera MA, Choi H, Abrahamowicz M, Kopec J, Goycochea-Robles MV, Lacaille D. Statin discontinuation and risk of acute myocardial infarction in patients with rheumatoid arthritis: a population-based cohort study. *Annals of the Rheumatic Diseases*. 2011; 70(6):1020-1024
- 337 De Vera MA, Choi H, Abrahamowicz M, Kopec J, Lacaille D. Impact of statin discontinuation on mortality in patients with rheumatoid arthritis: a population-based study. *Arthritis Care and Research*. 2012; 64(6):809-816
- 338 de Vries NM, Staal JB, Olde Rikkert MG, Nijhuis-van der Sanden MW. Evaluative frailty index for physical activity (EFIP): a reliable and valid instrument to measure changes in level of frailty. *Physical Therapy*. 2013; 93(4):551-561
- 339 de Vries OJ, Peeters GMEE, Elders PJM, Muller M, Knol DL, Danner SA et al. Multifactorial intervention to reduce falls in older people at high risk of recurrent falls: a randomized controlled trial. *Archives of Internal Medicine*. 2010; 170(13):1110-1117
- 340 De Witte N, Gobbens R, De Donder L, Dury S, Buffel T, Schols J et al. The comprehensive frailty assessment instrument: development, validity and reliability. *Geriatric Nursing*. 2013; 34(4):274-281

- 341 Degli Esposti L, Saragoni S, Batacchi P, Benemei S, Geppetti P, Sturani A et al. Adherence to statin treatment and health outcomes in an Italian cohort of newly treated patients: results from an administrative database analysis. *Clinical Therapeutics*. 2012; 34(1):190-199
- 342 DeKoekkoek T, Given B, Given CW, Ridenour K, Schueller M, Spoelstra SL. mHealth SMS text messaging interventions and to promote medication adherence: an integrative review. *Journal of Clinical Nursing*. Malden, Massachusetts: Wiley-Blackwell. 2015; 24(19/20):2722-2735
- 343 Demain S, Goncalves AC, Areia C, Oliveira R, Marcos AJ, Marques A et al. Living with, managing and minimising treatment burden in long term conditions: a systematic review of qualitative research. *PLoS ONE*. 2015; 10(5):e0125457
- 344 Dennis SM, Harris M, Lloyd J, Powell DG, Faruqi N, Zwar N. Do people with existing chronic conditions benefit from telephone coaching? A rapid review. *Australian Health Review*. 2013; 37(3):381-388
- 345 Dent E, Perez-Zepeda M. Comparison of five indices for prediction of adverse outcomes in hospitalised Mexican older adults: a cohort study. *Archives of Gerontology and Geriatrics*. 2015; 60(1):89-95
- 346 Dequito AB, Mol PGM, van Doormaal JE, Zaal RJ, van den Bemt PMLA, Haaijer-Ruskamp FM et al. Preventable and non-preventable adverse drug events in hospitalized patients: a prospective chart review in the Netherlands. *Drug Safety*. 2011; 34(11):1089-1100
- 347 Deschodt M, Claes V, Grootven B, Milisen K, Boland B, Flamaing J et al. Comprehensive geriatric care in hospitals: the role of inpatient geriatric consultation teams. Belgian Health Care Knowledge Centre (KCE), 2015. Available from: http://kce.fgov.be/sites/default/files/page_documents/KCE_245_geriatric_care_in_hospitals_Report.pdf
- 348 Deschodt M, Braes T, Broos P, Sermon A, Boonen S, Flamaing J et al. Effect of an inpatient geriatric consultation team on functional outcome, mortality, institutionalization, and readmission rate in older adults with hip fracture: a controlled trial. *Journal of the American Geriatrics Society*. 2011; 59(7):1299-1308
- 349 Devi P, Kamath DY, Anthony N, Santosh S, Dias B. Patterns, predictors and preventability of adverse drug reactions in the coronary care unit of a tertiary care hospital. *European Journal of Clinical Pharmacology*. 2012; 68(4):427-433
- 350 Di Bari M, Balzi D, Roberts AT, Barchielli A, Fumagalli S, Ungar A et al. Prognostic stratification of older persons based on simple administrative data: development and validation of the "Silver Code," to be used in emergency department triage. *Journals of Gerontology Series A, Biological Sciences and Medical Sciences*. 2010; 65(2):159-164
- 351 Di Bari M, Salvi F, Roberts AT, Balzi D, Lorenzetti B, Morichi V et al. Prognostic stratification of elderly patients in the emergency department: a comparison between the "Identification of Seniors at Risk" and the "Silver Code". *Journals of Gerontology Series A, Biological Sciences and Medical Sciences*. 2012; 67(5):544-550
- 352 Di Bari M, Virgillo A, Matteuzzi D, Inzitari M, Mazzaglia G, Pozzi C et al. Predictive validity of measures of comorbidity in older community dwellers: the Insufficienza Cardiaca negli Anziani Residenti a Dicomano Study. *Journal of the American Geriatrics Society*. 2006; 54(2):210-216

- 353 Di Iorio A, Longo AL, Mitidieri Costanza A, Bandinelli S, Capasso S, Gigante M et al. Characteristics of geriatric patients related to early and late readmissions to hospital. *Aging Clinical and Experimental Research*. 1998; 10(4):339-346
- 354 Di Iorio B, Cillo N, Cirillo M, De Santo NG. Charlson Comorbidity Index is a predictor of outcomes in incident hemodialysis patients and correlates with phase angle and hospitalization. *International Journal of Artificial Organs*. 2004; 27(4):330-336
- 355 Dias A, Teixeira-Lopes F, Miranda A, Alves M, Narciso M, Mieiro L et al. Comorbidity burden assessment in older people admitted to a Portuguese University Hospital. *Aging Clinical and Experimental Research*. 2015; 27(3):323-328
- 356 Dickinson WP, Dickinson LM, Nutting PA, Emsermann CB, Tutt B, Crabtree BF et al. Practice facilitation to improve diabetes care in primary care: a report from the EPIC randomized clinical trial. *Annals of Family Medicine*. 2014; 12(1):8-16
- 357 Diez-Manglano J, Cabrerizo Garcia JL, Garcia-Arilla Calvo E, Jimeno Sainz A, Calvo Begueria E, Martinez-Alvarez RM et al. External validation of the PROFUND index in polypathological patients from internal medicine and acute geriatrics departments in Aragon. *Internal and Emergency Medicine*. 2015; 10(8):915-926
- 358 Diez-Manglano J, Gimenez-Lopez M, Garces-Horna V, Sevil-Puras M, Castellar-Otin E, Gonzalez-Garcia P et al. Excessive polypharmacy and survival in polypathological patients. *European Journal of Clinical Pharmacology*. 2015; 71(6):733-739
- 359 Divo M, Cote C, de Torres JP, Casanova C, Marin JM, Pinto-Plata V et al. Comorbidities and risk of mortality in patients with chronic obstructive pulmonary disease. *American Journal of Respiratory and Critical Care Medicine*. 2012; 186(2):155-161
- 360 Dobscha SK, Corson K, Leibowitz RQ, Sullivan MD, Gerrity MS. Rationale, design, and baseline findings from a randomized trial of collaborative care for chronic musculoskeletal pain in primary care. *Pain Medicine*. 2008; 9:1050-1064
- 361 Dobscha SK, Corson K, Perrin NA, Hanson GC, Leibowitz RQ, Doak MN et al. Collaborative care for chronic pain in primary care: a cluster randomized trial. *JAMA*. 2009; 301:1242-1252
- 362 Dominick KL, Dudley TK, Coffman CJ, Bosworth HB. Comparison of three comorbidity measures for predicting health service use in patients with osteoarthritis. *Arthritis and Rheumatism*. 2005; 53(5):666-672
- 363 Donate-Martinez A, Garces FJ, Rodenas RF. Application of screening tools to detect risk of hospital readmission in elderly patients in Valencian Healthcare System (VHS) (Spain). *Archives of Gerontology and Geriatrics*. 2014; 59(2):408-414
- 364 Dong YH, Chang CH, Shau WY, Kuo RN, Lai MS, Chan KA. Development and validation of a pharmacy-based comorbidity measure in a population-based automated health care database. *Pharmacotherapy*. 2013; 33(2):126-136
- 365 Donnan PT. PEONY data, 2016
- 366 Donnan PT, Dorward DW, Mutch B, Morris AD. Development and validation of a model for predicting emergency admissions over the next year (PEONY): a UK historical cohort study. *Archives of Internal Medicine*. 2008; 168(13):1416-1422

- 367 Doos L, Bradley E, Rushton CA, Satchithananda D, Davies SJ, Kadam UT. Heart failure and chronic obstructive pulmonary disease multimorbidity at hospital discharge transition: A study of patient and carer experience. *Health Expectations*.: Wiley-Blackwell Publishing Ltd. Blackwell Publishing. 2014;
- 368 Doran DM, Hirdes J, Poss J, Jantzi M, Blais R, Baker GR et al. Identification of safety outcomes for Canadian home care clients: evidence from the resident assessment instrument--home care reporting system concerning emergency room visits. *Healthcare Quarterly*. 2009; 12(Sp):40-48
- 369 Dorr DA, Jones SS, Burns L, Donnelly SM, Brunner CP, Wilcox A et al. Use of health-related, quality-of-life metrics to predict mortality and hospitalizations in community-dwelling seniors. *Journal of the American Geriatrics Society*. 2006; 54(4):667-673
- 370 Dorresteyn TAC, Zijlstra GAR, Delbaere K, van Rossum E, Vlaeyen JWS, Kempen GIJM. Evaluating an in-home multicomponent cognitive behavioural programme to manage concerns about falls and associated activity avoidance in frail community-dwelling older people: Design of a randomised control trial [NCT01358032]. *BMC Health Services Research*. 2011; 11:228
- 371 Dougados M, Soubrier M, Perrodeau E, Gossec L, Fayet F, Gilson M et al. Impact of a nurse-led programme on comorbidity management and impact of a patient self-assessment of disease activity on the management of rheumatoid arthritis: results of a prospective, multicentre, randomised, controlled trial (COMEDRA). *Annals of the Rheumatic Diseases*. 2015; 74(9):1725-1733
- 372 Dowlathshahi D, Demchuk AM, Fang J, Kapral MK, Sharma M, Smith EE et al. Association of statins and statin discontinuation with poor outcome and survival after intracerebral hemorrhage. *Stroke; a Journal of Cerebral Circulation*. 2012; 43(6):1518-1523
- 373 Dragomir A, Cote R, Roy L, Blais L, Lalonde L, Berard A et al. Impact of adherence to antihypertensive agents on clinical outcomes and hospitalization costs. *Medical Care*. 2010; 48(5):418-425
- 374 Drame M, Novella JL, Lang PO, Somme D, Jovenin N, Laniece I et al. Derivation and validation of a mortality-risk index from a cohort of frail elderly patients hospitalised in medical wards via emergencies: the SAFES study. *European Journal of Epidemiology*. 2008; 23(12):783-791
- 375 Drennan IR, Dainty KN, Hoogveen P, Atzema CL, Barrette N, Hawker G et al. Expanding Paramedicine in the Community (EPIC): study protocol for a randomized controlled trial. *Trials*. 2014; 15:473
- 376 Drubbel I, Bleijenberg N, Kranenburg G, Eijkemans RJ, Schuurmans MJ, de Wit NJ et al. Identifying frailty: do the Frailty Index and Groningen Frailty Indicator cover different clinical perspectives? a cross-sectional study. *BMC Family Practice*. 2013; 14:64
- 377 Druss BG, Zhao L, von Esenwein SA, Bona JR, Fricks L, Jenkins-Tucker S et al. The Health and Recovery Peer (HARP) Program: a peer-led intervention to improve medical self-management for persons with serious mental illness. *Schizophrenia Research*. 2010; 118:264-270
- 378 Due TD, Thorsen T, Kousgaard MB, Siersma VD, Waldorff FB. The effectiveness of a semi-tailored facilitator-based intervention to optimise chronic care management in general practice: a stepped-wedge randomised controlled trial. *BMC Family Practice*. 2014; 15:65
- 379 DuGoff EH, Canudas-Romo V, Buttorff C, Leff B, Anderson GF. Multiple chronic conditions and life expectancy: a life table analysis. *Medical Care*. 2014; 52(8):688-694

- 380 Dunbar SB, Butts B, Reilly CM, Gary RA, Higgins MK, Ferranti EP et al. A pilot test of an integrated self-care intervention for persons with heart failure and concomitant diabetes. *Nursing Outlook*. 2014; 62:97-111
- 381 Dunbar SB, Reilly CM, Gary R, Higgins MK, Culler S, Butts B et al. Randomized clinical trial of an integrated self-care intervention for persons with heart failure and diabetes: quality of life and physical functioning outcomes. *Journal of Cardiac Failure*. 2015; 21(9):719-729
- 382 Eakin EG, Bull SS, Riley KM, Reeves MM, McLaughlin P, Gutierrez S. Resources for health: a primary-care-based diet and physical activity intervention targeting urban Latinos with multiple chronic conditions. *Health Psychology : Official Journal of the Division of Health Psychology, American Psychological Association*. 2007; 26(4):392-400
- 383 Edelman D, Fredrickson SK, Melnyk SD, Coffman CJ, Jeffreys AS, Datta S et al. Medical clinics versus usual care for patients with both diabetes and hypertension: a randomized trial. *Annals of Internal Medicine*. 2010; 152:689-696
- 384 Edelstein EL, Cesta TG. Nursing case management: an innovative model of care for hospitalized patients with diabetes. *Diabetes Educator*. 1993; 19:517-521
- 385 Edmans J, Bradshaw L, Franklin M, Gladman J, Conroy S. Specialist geriatric medical assessment for patients discharged from hospital acute assessment units: randomised controlled trial. *BMJ*. 2013; 347:f5874
- 386 Egstrup K. Transient myocardial ischemia after abrupt withdrawal of antianginal therapy in chronic stable angina. *American Journal of Cardiology*. 1988; 61(15):1219-1222
- 387 Ehrlich C, Kendall E, Frey N, Denton M, Kisely S. Consensus building to improve the physical health of people with severe mental illness: a qualitative outcome mapping study. *BMC Health Services Research*. 2015; 15:83
- 388 Eikelenboom N, van Lieshout J, Wensing M, Smeele I, Jacobs AE. Implementation of personalized self-management support using the self-management screening questionnaire SeMaS; a study protocol for a cluster randomized trial. *Trials*. 2013; 14:336
- 389 Ekblom T, Lindholm LH, Oden A, Dahlof B, Hansson L, Wester PO et al. A 5-year prospective, observational study of the withdrawal of antihypertensive treatment in elderly people. *Journal of Internal Medicine*. 1994; 235(6):581-588
- 390 Ekdahl AW, Andersson L, Wirehn AB, Friedrichsen M. Are elderly people with co-morbidities involved adequately in medical decision making when hospitalised? A cross-sectional survey. *BMC Geriatrics*. 2011; 11:46
- 391 Ekdahl AW, Wirehn AB, Alwin J, Jaarsma T, Unosson M, Husberg M et al. Costs and effects of an ambulatory geriatric unit (the AGE-FIT Study): a randomized controlled trial. *Journal of the American Medical Directors Association*. 2015; 16(6):497-503
- 392 Ekdahl AW, Hellstrom I, Andersson L, Friedrichsen M. Too complex and time-consuming to fit in! Physicians' experiences of elderly patients and their participation in medical decision making: a grounded theory study. *BMJ Open*. 2012; 2(3)
- 393 Ekerstad N, Lofmark R, Carlsson P. Elderly people with multi-morbidity and acute coronary syndrome: doctors' views on decision-making. *Scandinavian Journal of Public Health*. 2010; 38(3):325-331

- 394 Eklund K, Wilhelmson K, Gustafsson H, Landahl S, Dahlin-Ivanoff S. One-year outcome of frailty indicators and activities of daily living following the randomised controlled trial: "Continuum of care for frail older people". *BMC Geriatrics*. 2013; 13:76
- 395 El Hajji FWD, Scullin C, Scott MG, McElnay JC. Enhanced clinical pharmacy service targeting tools: risk-predictive algorithms. *Journal of Evaluation in Clinical Practice*. 2015; 21(2):187-197
- 396 Elissen AM, Duimel-Peeters IG, Spreeuwenberg C, Spreeuwenberg M, Vrijhoef HJ. Toward tailored disease management for type 2 diabetes. *American Journal of Managed Care*. 2012; 18:619-630
- 397 Ell K, Katon W, Xie B, Lee PJ, Kapetanovic S, Guterman J et al. Collaborative care management of major depression among low-income, predominantly Hispanic subjects with diabetes: a randomized controlled trial. *Diabetes Care*. 2010; 33(4):706-713
- 398 Ellis G, Whitehead MA, O'Neill D, Langhorne P, Robinson D. Comprehensive geriatric assessment for older adults admitted to hospital. *Cochrane Database of Systematic Reviews*. 2011; Issue 7:CD006211. DOI:10.1002/14651858.CD006211.pub2
- 399 Elzen H, Slaets JP, Snijders TA, Steverink N. Evaluation of the chronic disease self-management program (CDSMP) among chronically ill older people in the Netherlands. *Social Science and Medicine*. 2007; 64(9):1832-1841
- 400 Emmons KM, Puleo E, Greaney ML, Gillman MW, Bennett GG, Haines J et al. A randomized comparative effectiveness study of Healthy Directions 2-A multiple risk behavior intervention for primary care. *Preventive Medicine*. 2014; 64:96-102
- 401 Endres M, Laufs U. Discontinuation of statin treatment in stroke patients. *Stroke; a Journal of Cerebral Circulation*. 2006; 37(10):2640-2643
- 402 Ensrud KE, Ewing SK, Cawthon PM, Fink HA, Taylor BC, Cauley JA et al. A comparison of frailty indexes for the prediction of falls, disability, fractures, and mortality in older men. *Journal of the American Geriatrics Society*. 2009; 57(3):492-498
- 403 Ensrud KE, Barrett-Connor EL, Schwartz A, Santora AC, Bauer DC, Suryawanshi S et al. Randomized trial of effect of alendronate continuation versus discontinuation in women with low BMD: results from the Fracture Intervention Trial long-term extension. *Journal of Bone and Mineral Research*. 2004; 19(8):1259-1269
- 404 Epstein AM, Hall JA, Fretwell M, Feldstein M, DeCiantis ML, Tognetti J et al. Consultative geriatric assessment for ambulatory patients. A randomized trial in a health maintenance organization. *JAMA*. 1990; 263(4):538-544
- 405 Erceg P, Despotovic N, Milosevic DP, Soldatovic I, Zdravkovic S, Tomic S et al. Health-related quality of life in elderly patients hospitalized with chronic heart failure. *Clinical Interventions In Aging*. 2013; 8:1539-1546
- 406 Ersek M, Turner JA, McCurry SM, Gibbons L, Kraybill BM. Efficacy of a self-management group intervention for elderly persons with chronic pain. *Clinical Journal of Pain*. 2003; 19(3):156-167
- 407 Espauella J, Arnau A, Cubi D, Amblas J, Yanez A. Time-dependent prognostic factors of 6-month mortality in frail elderly patients admitted to post-acute care. *Age and Ageing*. 2007; 36(4):407-413

- 408 Espino DV, Bazaldua OV, Palmer RF, Mouton CP, Parchman ML, Miles TP et al. Suboptimal medication use and mortality in an older adult community-based cohort: results from the Hispanic EPESE Study. *Journals of Gerontology Series A, Biological Sciences and Medical Sciences*. 2006; 61(2):170-175
- 409 Eton DT, Elraiyah TA, Yost KJ, Ridgeway JL, Johnson A, Egginton JS et al. A systematic review of patient-reported measures of burden of treatment in three chronic diseases. *Patient Related Outcome Measures*. 2013; 4:7-20
- 410 Eton DT, Ramalho de Oliveira D, Egginton JS, Ridgeway JL, Odell L, May CR et al. Building a measurement framework of burden of treatment in complex patients with chronic conditions: a qualitative study. *Patient Related Outcome Measures*. 2012; 3:39-49
- 411 Eton DT, Ridgeway JL, Egginton JS, Tiedje K, Linzer M, Boehm DH et al. Finalizing a measurement framework for the burden of treatment in complex patients with chronic conditions. *Patient Related Outcome Measures*. 2015; 6:117-126
- 412 Evangelista LS, Lee JA, Moore AA, Motie M, Ghasemzadeh H, Sarrafzadeh M et al. Examining the effects of remote monitoring systems on activation, self-care, and quality of life in older patients with chronic heart failure. *Journal of Cardiovascular Nursing*. 2015; 30(1):51-57
- 413 Evans DC, Cook CH, Christy JM, Murphy CV, Gerlach AT, Eiferman D et al. Comorbidity-polypharmacy scoring facilitates outcome prediction in older trauma patients. *Journal of the American Geriatrics Society*. 2012; 60(8):1465-1470
- 414 Evans DC, Gerlach AT, Christy JM, Jarvis AM, Lindsey DE, Whitmill ML et al. Pre-injury polypharmacy as a predictor of outcomes in trauma patients. *International Journal of Critical Illness and Injury Science*. 2011; 1(2):104-109
- 415 Fabbian F, Pala M, De Giorgi A, Manfredini F, Mallozzi Menegatti A, Salmi R et al. In-hospital mortality in patients with renal dysfunction admitted for myocardial infarction: the Emilia-Romagna region of Italy database of hospital admissions. *International Urology and Nephrology*. 2013; 45(3):769-775
- 416 Fagerberg B, Wikstrand J, Berglund G, Hartford M, Ljungman S, Wendelhag I. Withdrawal of antihypertensive drug treatment: Time-course for redevelopment of hypertension and effects upon left ventricular mass. *Journal of Hypertension*. 1992; 10(6):587-593
- 417 Fairhall N, Sherrington C, Kurrle SE, Lord SR, Lockwood K, Cameron ID. Effect of a multifactorial interdisciplinary intervention on mobility-related disability in frail older people: randomised controlled trial. *BMC Medicine*. 2012; 10:120
- 418 Falasca P, Berardo A, Di Tommaso F. Development and validation of predictive MoSaiCo (Modello Statistico Combinato) on emergency admissions: can it also identify patients at high risk of frailty? *Annali Dell'Istituto Superiore Di Sanita*. 2011; 47(2):220-228
- 419 Fallouh N, Chopra V. Statin withdrawal after major noncardiac surgery: risks, consequences, and preventative strategies. *Journal of Hospital Medicine*. 2012; 7(7):573-579
- 420 Farmer C, K H. Q-BAST: a new checklist for evaluating risk of bias in questionnaires with no gold standard. G-I-N Conference 2015, Amsterdam, The Netherlands 2015;
- 421 Feltz-Cornelis C. Comorbid diabetes and depression: Do E-health treatments achieve better diabetes control? *Diabetes Management*. 2013; 3(5):379-388

- 422 Ferrer A, Formiga F, Sanz H, de Vries OJ, Badia T, Pujol R et al. Multifactorial assessment and targeted intervention to reduce falls among the oldest-old: a randomized controlled trial. *Clinical Interventions In Aging*. 2014; 9:383-393
- 423 Field TS, Gurwitz JH, Avorn J, McCormick D, Jain S, Eckler M et al. Risk factors for adverse drug events among nursing home residents. *Archives of Internal Medicine*. 2001; 161(13):1629-1634
- 424 Field TS, Gurwitz JH, Harrold LR, Rothschild J, Debellis KR, Seger AC et al. Risk factors for adverse drug events among older adults in the ambulatory setting. *Journal of the American Geriatrics Society*. 2004; 52(8):1349-1354
- 425 Fischer SM, Gozansky WS, Sauaia A, Min SJ, Kutner JS, Kramer A. A practical tool to identify patients who may benefit from a palliative approach: the CARING criteria. *Journal of Pain and Symptom Management*. 2006; 31(4):285-292
- 426 Fitzner K, Moss G. Telehealth--an effective delivery method for diabetes self-management education? *Population Health Management*. 2013; 16:169-177
- 427 Fitzpatrick LA, Wooddell M, Dabrowski CE, Cicconetti G, Gordon DN. Bone mineral density changes following discontinuation of ronacaleret treatment: off-treatment extension of a randomized, dose-finding phase II trial. *Bone*. 2014; 67:104-108
- 428 Flacker JM, Kiely DK. Mortality-related factors and 1-year survival in nursing home residents. *Journal of the American Geriatrics Society*. 2003; 51(2):213-221
- 429 Fletcher AE, Franks PJ, Bulpitt CJ. The effect of withdrawing antihypertensive therapy: a review. *Journal of Hypertension*. 1988; 6(6):431-436
- 430 Floege J, Gillespie IA, Kronenberg F, Anker SD, Gioni I, Richards S et al. Development and validation of a predictive mortality risk score from a European hemodialysis cohort. *Kidney International*. 2015; 87(5):996-1008
- 431 Formiga F, Ferrer A, Chivite D, Montero A, Sanz H, Pujol R et al. Utility of geriatric assessment to predict mortality in the oldest old: the Octabaix study 3-year follow-up. *Rejuvenation Research*. 2013; 16(4):279-284
- 432 Formiga F, Ferrer A, Chivite D, Rubio-Rivas M, Cuerpo S, Pujol R. Predictors of long-term survival in nonagenarians: the NonaSantfeliu study. *Age and Ageing*. 2011; 40(1):111-116
- 433 Forster AJ, Murff HJ, Peterson JF, Gandhi TK, Bates DW. Adverse drug events occurring following hospital discharge. *Journal of General Internal Medicine*. 2005; 20(4):317-323
- 434 Fortin M, Hudon C, Dubois MF, Almirall J, Lapointe L, Soubhi H. Comparative assessment of three different indices of multimorbidity for studies on health-related quality of life. *Health and Quality of Life Outcomes*. 2005; 3:74
- 435 Fortin M, Hudon C, Gallagher F, Ntetu AL, Maltais D, Soubhi H. Nurses joining family doctors in primary care practices: perceptions of patients with multimorbidity. *BMC Family Practice*. 2010; 11:84
- 436 Fortin M, Steenbakkers K, Hudon C, Poitras ME, Almirall J, van den Akker M. The electronic Cumulative Illness Rating Scale: a reliable and valid tool to assess multi-morbidity in primary care. *Journal of Evaluation in Clinical Practice*. 2011; 17(6):1089-1093

- 437 Fortin M, Bravo G, Hudon C, Lapointe L, Almirall J, Dubois MF et al. Relationship between multimorbidity and health-related quality of life of patients in primary care. *Quality of Life Research*. 2006; 15(1):83-91
- 438 Fotherby MD, Potter JF. Orthostatic hypotension and anti-hypertensive therapy in the elderly. *Postgraduate Medical Journal*. 1994; 70(830):878-881
- 439 Fotherby MD, Potter JF. Possibilities for antihypertensive drug therapy withdrawal in the elderly. *Journal of Human Hypertension*. 1994; 8(11):857-863
- 440 Fox PJ, Vazquez L, Tonner C, Stevens JA, Fineman N, Ross LK. A randomized trial of a multifaceted intervention to reduce falls among community-dwelling adults. *Health Education and Behavior*. 2010; 37(6):831-848
- 441 Fraccaro P, Arguello Casteleiro M, Ainsworth J, Buchan I. Adoption of clinical decision support in multimorbidity: a systematic review. *JMIR Medical Informatics*. 2015; 3(1):e4
- 442 Franchi C, Nobili A, Mari D, Tettamanti M, Djade CD, Pasina L et al. Risk factors for hospital readmission of elderly patients. *European Journal of Internal Medicine*. 2013; 24(1):45-51
- 443 Franek J. Self-management support interventions for persons with chronic disease: an evidence-based analysis. *Ontario Health Technology Assessment Series*. 2013; 13(9):1-60
- 444 Franic DM, Jiang JZ. Potentially inappropriate drug use and health-related quality of life in the elderly. *Pharmacotherapy*. 2006; 26(6):768-778
- 445 Franz CE, Barker JC, Kim K, Flores Y, Jenkins C, Kravitz RL et al. When help becomes a hindrance: mental health referral systems as barriers to care for primary care physicians treating patients with Alzheimer's disease. *American Journal of Geriatric Psychiatry*. 2010; 18(7):576-585
- 446 Fraser LA, Vogt KN, Adachi JD, Thabane L. Fracture risk associated with continuation versus discontinuation of bisphosphonates after 5 years of therapy in patients with primary osteoporosis: a systematic review and meta-analysis. *Therapeutics and Clinical Risk Management*. 2011; 7:157-166
- 447 Freedland KE, Carney RM, Rich MW, Steinmeyer BC, Rubin EH. Cognitive behavior therapy for depression and self-care in heart failure patients: a randomized clinical trial. *JAMA Internal Medicine*. 2015; 175(11):1773-1782
- 448 Freis ED. Return of elevated blood pressure after withdrawal of antihypertensive drugs. *Circulation*. 1975; 51(6):1107-1113
- 449 Freis ED, Thomas JR, Fisher SG, Hamburger R, Borreson RE, Mezey KC et al. Effects of reduction in drugs or dosage after long-term control of systemic hypertension. *American Journal of Cardiology*. 1989; 63(11):702-708
- 450 Frese T, Deutsch T, Keyser M, Sandholzer H. In-home preventive comprehensive geriatric assessment (CGA) reduces mortality--a randomized controlled trial. *Archives of Gerontology and Geriatrics*. 2012; 55(3):639-644
- 451 Freund T, Campbell SM, Geissler S, Kunz CU, Mahler C, Peters-Klimm F et al. Strategies for reducing potentially avoidable hospitalizations for ambulatory care-sensitive conditions. *Annals of Family Medicine*. 2013; 11(4):363-370

- 452 Fried L, Bernardini J, Piraino B. Charlson comorbidity index as a predictor of outcomes in incident peritoneal dialysis patients. *American Journal of Kidney Diseases*. 2001; 37(2):337-342
- 453 Fried L, Bernardini J, Piraino B. Comparison of the Charlson Comorbidity Index and the Davies score as a predictor of outcomes in PD patients. *Peritoneal Dialysis International*. 2003; 23(6):568-573
- 454 Fried TR, McGraw S, Agostini JV, Tinetti ME. Views of older persons with multiple morbidities on competing outcomes and clinical decision-making. *Journal of the American Geriatrics Society*. 2008; 56(10):1839-1844
- 455 Fried TR, O'Leary J, Towle V, Goldstein MK, Trentalange M, Martin DK. Health outcomes associated with polypharmacy in community-dwelling older adults: a systematic review. *Journal of the American Geriatrics Society*. 2014; 62(12):2261-2272
- 456 Fried TR, Tinetti ME, Iannone L. Primary care clinicians' experiences with treatment decision making for older persons with multiple conditions. *Archives of Internal Medicine*. 2011; 171(1):75-80
- 457 Friedman B, Li Y, Liebel DV, Powers BA. Effects of a home visiting nurse intervention versus care as usual on individual activities of daily living: a secondary analysis of a randomized controlled trial. *BMC Geriatrics*. 2014; 14:24
- 458 Friedman RH, Kazis LE, Jette A, Smith MB, Stollerman J, Torgerson J et al. A telecommunications system for monitoring and counseling patients with hypertension. Impact on medication adherence and blood pressure control. *American Journal of Hypertension*. 1996; 9:285-292
- 459 Frishman WH, Klein N, Strom J, Cohen MN, Shamooh H, Willens H et al. Comparative effects of abrupt withdrawal of propranolol and verapamil in angina pectoris. *American Journal of Cardiology*. 1982; 50(5):1191-1195
- 460 Frisoli AJ, Ingham SJM, Paes AT, Tinoco E, Greco A, Zanata N et al. Frailty predictors and outcomes among older patients with cardiovascular disease: Data from Fragicor. *Archives of Gerontology and Geriatrics*. 2015; 61(1):1-7
- 461 Fu D, Fu H, McGowan P, Shen YE, Zhu L, Yang H et al. Implementation and quantitative evaluation of chronic disease self-management programme in Shanghai, China: randomized controlled trial. *Bulletin of the World Health Organization*. 2003; 81(3):174-182
- 462 Fuji KT, Abbott AA, Norris JF. Exploring care transitions from patient, caregiver, and health-care provider perspectives. *Clinical Nursing Research*. 2013; 22(3):258-274
- 463 Gabriel SE, Crowson CS, O'Fallon WM. A comparison of two comorbidity instruments in arthritis. *Journal of Clinical Epidemiology*. 1999; 52(12):1137-1142
- 464 Gage H, Ting S, Williams P, Drennan V, Goodman C, Iliffe S et al. Nurse-led case management for community dwelling older people: an explorative study of models and costs. *Journal of Nursing Management*. United Kingdom 2013; 21(1):191-201
- 465 Gagne JJ, Glynn RJ, Avorn J, Levin R, Schneeweiss S. A combined comorbidity score predicted mortality in elderly patients better than existing scores. *Journal of Clinical Epidemiology*. 2011; 64(7):749-759

- 466 Gallacher K, May CR, Montori VM, Mair FS. Understanding patients' experiences of treatment burden in chronic heart failure using normalization process theory. *Annals of Family Medicine*. 2011; 9(3):235-243
- 467 Gallucci M, Battistella G, Bergamelli C, Spagnolo P, Mazzuco S, Carlini A et al. Multidimensional prognostic index in a cognitive impairment outpatient setting: mortality and hospitalizations. The Treviso Dementia (TREDDEM) study. *Journal of Alzheimer's Disease*. 2014; 42(4):1461-1468
- 468 Gandhi TK, Burstin HR, Cook EF, Puopolo AL, Haas JS, Brennan TA et al. Drug complications in outpatients. *Journal of General Internal Medicine*. 2000; 15(3):149-154
- 469 Ganna A, Ingelsson E. 5 year mortality predictors in 498,103 UK Biobank participants: a prospective population-based study. *The Lancet*. 2015; 386(9993):533-540
- 470 Garcia-Ptacek S, Farahmand B, Kareholt I, Religa D, Cuadrado ML, Eriksdotter M. Mortality risk after dementia diagnosis by dementia type and underlying factors: a cohort of 15,209 patients based on the Swedish Dementia Registry. *Journal of Alzheimer's Disease*. 2014; 41(2):467-477
- 471 Gardner R, Li Q, Baier RR, Butterfield K, Coleman EA, Gravenstein S. Is implementation of the care transitions intervention associated with cost avoidance after hospital discharge? *Journal of General Internal Medicine*. 2014; 29(6):878-884
- 472 Garfinkel D, Mangin D. Feasibility study of a systematic approach for discontinuation of multiple medications in older adults: addressing polypharmacy. *Archives of Internal Medicine*. 2010; 170(18):1648-1654
- 473 Garfinkel D, Zur-Gil S, Ben-Israel J. The war against polypharmacy: a new cost-effective geriatric-palliative approach for improving drug therapy in disabled elderly people. *Israel Medical Association Journal*. 2007; 9(6):430-434
- 474 Garvey J, Connolly D, Boland F, Smith SM. OPTIMAL, an occupational therapy led self-management support programme for people with multimorbidity in primary care: a randomized controlled trial. *BMC Family Practice*. 2015; 16:59
- 475 Gellis ZD, Kenaley BL, Ten Have T. Integrated telehealth care for chronic illness and depression in geriatric home care patients: the Integrated Telehealth Education and Activation of Mood (I-TEAM) study. *Journal of the American Geriatrics Society*. 2014; 62(5):889-895
- 476 Gensichen J, Torge M, Peitz M, Wendt-Hermainski H, Beyer M, Rosemann T et al. Case management for the treatment of patients with major depression in general practices--rationale, design and conduct of a cluster randomized controlled trial--PRoMPT (PRimary care Monitoring for depressive Patient's Trial) [ISRCTN66386086]--study protocol. *BMC Public Health*. 2005; 5:101
- 477 George J, Vuong T, Bailey MJ, Kong DC, Marriott JL, Stewart K. Development and validation of the medication-based disease burden index. *Annals of Pharmacotherapy*. 2006; 40(4):645-650
- 478 Ghali WA, Hall RE, Rosen AK, Ash AS, Moskowitz MA. Searching for an improved clinical comorbidity index for use with ICD-9-CM administrative data. *Journal of Clinical Epidemiology*. 1996; 49(3):273-278
- 479 Gharacholou SM, Sloane R, Cohen HJ, Schmader KE. Geriatric inpatient units in the care of hospitalized frail adults with a history of heart failure. *International Journal of Gerontology*. 2012; 6(2):112-116

- 480 Giandinoto JA, Edward KL. Challenges in acute care of people with co-morbid mental illness. *British Journal of Nursing*. 2014; 23(13):728-732
- 481 Gibbons CJ, Kenning C, Coventry PA, Bee P, Bundy C, Fisher L et al. Development of a multimorbidity illness perceptions scale (MULTIPLEs). *PLoS ONE*. 2013; 8(12):e81852
- 482 Gibson DAJ, Moorin RE, Preen D, Emery J, D'Arcy JH. Enhanced Primary Care improves GP service regularity in older patients without impacting on service frequency. *Australian Journal of Primary Health*. 2012; 18(4):295-303
- 483 Gill A, Kuluski K, Jaakkimainen L, Naganathan G, Upshur R, Wodchis WP. "Where do we go from here?" health system frustrations expressed by patients with multimorbidity, their caregivers and family physicians. *Healthcare Policy*. 2014; 9(4):73-89
- 484 Gill TM, Baker DI, Gottschalk M, Gahbauer EA, Charpentier PA, de Regt PT et al. A prehabilitation program for physically frail community-living older persons. *Archives of Physical Medicine & Rehabilitation*. 2003; 84(3):394-404
- 485 Gill TM, McGloin JM, Gahbauer EA, Shepard DM, Bianco LM. Two recruitment strategies for a clinical trial of physically frail community-living older persons. *Journal of the American Geriatrics Society*. 2001; 49(8):1039-1045
- 486 Giordano A, Scalvini S, Paganoni AM, Baraldo S, Frigerio M, Vittori C et al. Home-based telesurveillance program in chronic heart failure: effects on clinical status and implications for 1-year prognosis. *Telemedicine Journal and E-Health*. 2013; 19:605-612
- 487 Giovannetti ER, Wolff JL, Xue Q-L, Weiss CO, Leff B, Boulton C. Difficulty assisting with health care tasks among caregivers of multimorbid older adults. *Journal of General Internal Medicine*. 2012; 27(1):37-44
- 488 Gislason GH, Rasmussen JN, Abildstrom SZ, Schramm TK, Hansen ML, Buch P et al. Persistent use of evidence-based pharmacotherapy in heart failure is associated with improved outcomes. *Circulation*. 2007; 116(7):737-744
- 489 Gitlin LN, Hauck WW, Dennis MP, Winter L, Hodgson N, Schinfeld S. Long-term effect on mortality of a home intervention that reduces functional difficulties in older adults: results from a randomized trial. *Journal of the American Geriatrics Society*. 2009; 57(3):476-481
- 490 Gitlin LN, Hauck WW, Winter L, Dennis MP, Schulz R. Effect of an in-home occupational and physical therapy intervention on reducing mortality in functionally vulnerable older people: preliminary findings. *Journal of the American Geriatrics Society*. 2006; 54(6):950-955
- 491 Gitlin LN, Winter L, Dennis MP, Corcoran M, Schinfeld S, Hauck WW. A randomized trial of a multicomponent home intervention to reduce functional difficulties in older adults. *Journal of the American Geriatrics Society*. 2006; 54(5):809-816
- 492 Giuli C, Papa R, Bevilacqua R, Felici E, Gagliardi C, Marcellini F et al. Correlates of perceived health related quality of life in obese, overweight and normal weight older adults: an observational study. *BMC Public Health*. 2014; 14:35
- 493 Glynn RJ, Knight EL, Levin R, Avorn J. Paradoxical relations of drug treatment with mortality in older persons. *Epidemiology*. 2001; 12(6):682-689

- 494 Gnjjidic D, Hilmer SN, Blyth FM, Naganathan V, Waite L, Seibel MJ et al. Polypharmacy cutoff and outcomes: five or more medicines were used to identify community-dwelling older men at risk of different adverse outcomes. *Journal of Clinical Epidemiology*. 2012; 65(9):989-995
- 495 Gnjjidic D, Pearson SA, Hilmer S. Optimizing the impact of drugs on symptom burden in older people with multimorbidity at the end of life... *JAMA Intern Med*. 2013 Sep 9;173(16):1534-40. *JAMA Internal Medicine*. 2014; 174(4):636-637
- 496 Goepfing J, Armstrong B, Schwartz T, Ensley D, Brady TJ. Self-management education for persons with arthritis: Managing comorbidity and eliminating health disparities. *Arthritis and Rheumatism*. 2007; 57:1081-1088
- 497 Goldberg RW, Dickerson F, Lucksted A, Brown CH, Weber E, Tenhula WN et al. Living well: an intervention to improve self-management of medical illness for individuals with serious mental illness. *Psychiatric Services*. 2013; 64:51-57
- 498 Goldman DP, Joyce GF, Karaca-Mandic P. Varying pharmacy benefits with clinical status: the case of cholesterol-lowering therapy. *American Journal of Managed Care*. 2006; 12(1):21-28
- 499 Gomez Sandoval YH, Braganza MV, Daskalopoulou SS. Statin discontinuation in high-risk patients: a systematic review of the evidence. *Current Pharmaceutical Design*. 2011; 17(33):3669-3689
- 500 Gomez C, Vega-Quiroga S, Bermejo-Pareja F, Medrano MJ, Louis ED, Benito-Leon J. Polypharmacy in the elderly: a marker of increased risk of mortality in a population-based prospective study (NEDICES). *Gerontology*. 2015; 61(4):301-309
- 501 Goncalves AR, Khwaja A, Ahmed AK, El Kossi M, El Nahas M. Stopping renin-angiotensin system inhibitors in chronic kidney disease: predictors of response. *Nephron Clinical Practice*. 2011; 119(4):c348-c354
- 502 Goodrich DE, Kilbourne AM, Lai Z, Post EP, Bowersox NW, Mezuk B et al. Design and rationale of a randomized controlled trial to reduce cardiovascular disease risk for patients with bipolar disorder. *Contemporary Clinical Trials*. 2012; 33:666-678
- 503 Gorwit J, Haidet GC, Russell DC, Tonkon M, Deedwania.P.C., Borer JS. Randomized placebo-controlled withdrawal study of amlodipine in angina pectoris. *American Journal of Therapeutics*. 1995; 2(1):34-42
- 504 Gottlieb SO, Gerstenblith G. Safety of acute calcium antagonist withdrawal: studies in patients with unstable angina withdrawn from nifedipine. *American Journal of Cardiology*. 1985; 55(12):27E-30E
- 505 Gottlieb SO, Ouyang P, Achuff SC, Baughman KL, Traill TA, Mellits ED et al. Acute nifedipine withdrawal: consequences of preoperative and late cessation of therapy in patients with prior unstable angina. *Journal of the American College of Cardiology*. 1984; 4(2):382-388
- 506 Graf CE, Karsegard VL, Spoerri A, Makhlof AM, Ho S, Herrmann FR et al. Body composition and all-cause mortality in subjects older than 65 y. *American Journal of Clinical Nutrition*. 2015; 101(4):760-767
- 507 Gray D, Armstrong CD, Dahrouge S, Hogg W, Zhang W. Cost-effectiveness of anticipatory and preventive multidisciplinary team care for complex patients: evidence from a randomized controlled trial. *Canadian Family Physician*. 2010; 56(1):e20-e29

- 508 Green JL, Hawley JN, Rask KJ. Is the number of prescribing physicians an independent risk factor for adverse drug events in an elderly outpatient population? *American Journal of Geriatric Pharmacotherapy*. 2007; 5(1):31-39
- 509 Greenberg G. Course of blood pressure in mild hypertensives after withdrawal of long term antihypertensive treatment. *BMJ*. 1986; 293(6553):988-992
- 510 Greene BR, Doheny EP, O'Halloran A, Anne Kenny R. Frailty status can be accurately assessed using inertial sensors and the TUG test. *Age and Ageing*. 2014; 43(3):406-411
- 511 Greene ME, Rolfson O, Gordon M, Garellick G, Nemes S. Standard comorbidity measures do not predict patient-reported outcomes 1 year after total hip arthroplasty. *Clinical Orthopaedics and Related Research*. 2015; 473(11):3370-3379
- 512 Greene VL, Ondrich JI. Risk factors for nursing home admissions and exits: a discrete-time hazard function approach. *Journal of Gerontology*. 1990; 45(6):S250-S258
- 513 Greenspan SL, Emkey RD, Bone HG, Weiss SR, Bell NH, Downs RW et al. Significant differential effects of alendronate, estrogen, or combination therapy on the rate of bone loss after discontinuation of treatment of postmenopausal osteoporosis. A randomized, double-blind, placebo-controlled trial. *Annals of Internal Medicine*. 2002; 137(11):875-883
- 514 Greenspan SL, Nelson JB, Trump DL, Wagner JM, Miller ME, Perera S et al. Skeletal health after continuation, withdrawal, or delay of alendronate in men with prostate cancer undergoing androgen-deprivation therapy. *Journal of Clinical Oncology*. 2008; 26(27):4426-4434
- 515 Griffiths C, Motlib J, Azad A, Ramsay J, Eldridge S, Feder G et al. Randomised controlled trial of a lay-led self-management programme for Bangladeshi patients with chronic disease. *British Journal of General Practice*. 2005; 55(520):831-837
- 516 Grimmer K, Milanese S, Beaton K, Atlas A. Additional measures do not improve the diagnostic accuracy of the Hospital Admission Risk Profile for detecting downstream quality of life in community-dwelling older people presenting to a hospital emergency department. *Clinical Interventions In Aging*. 2014; 9:233-242
- 517 Groll DL, Heyland DK, Caeser M, Wright JG. Assessment of long-term physical function in acute respiratory distress syndrome (ARDS) patients: comparison of the Charlson Comorbidity Index and the Functional Comorbidity Index. *American Journal of Physical Medicine and Rehabilitation*. 2006; 85(7):574-581
- 518 Groll DL, To T, Bombardier C, Wright JG. The development of a comorbidity index with physical function as the outcome. *Journal of Clinical Epidemiology*. 2005; 58(6):595-602
- 519 Grunau GL, Sheps S, Goldner EM, Ratner PA. Specific comorbidity risk adjustment was a better predictor of 5-year acute myocardial infarction mortality than general methods. *Journal of Clinical Epidemiology*. 2006; 59(3):274-280
- 520 Guaraldi G, Brothers TD, Zona S, Stentarelli C, Carli F, Malagoli A et al. A frailty index predicts survival and incident multimorbidity independent of markers of HIV disease severity. *AIDS*. 2015; 29(13):1633-1641
- 521 Guex J, Rahhali N, Taieb C. Development of a questionnaire to evaluate the burden of chronic venous disease in daily life. *Journal of Vascular Surgery*. 2010; 51(3):796

- 522 Gulliford M, Cowie L, Morgan M. Relational and management continuity survey in patients with multiple long-term conditions. *Journal of Health Services Research and Policy*. 2011; 16(2):67-74
- 523 Gusdal AK, Beckman C, Wahlstrom R, Tornkvist L. District nurses' use for an assessment tool in their daily work with elderly patients' medication management. *Scandinavian Journal of Public Health*. 2011; 39(4):354-360
- 524 Gustafsson M, Kristensson J, Holst G, Willman A, Bohman D. Case managers for older persons with multi-morbidity and their everyday work - a focused ethnography. *BMC Health Services Research*. 2013; 13:496
- 525 Gustafsson S, Eklund K, Wilhelmson K, Edberg AK, Johansson B, Kronlof GH et al. Long-term outcome for ADL following the health-promoting RCT--elderly persons in the risk zone. *Gerontologist*. 2013; 53(4):654-663
- 526 Gustafsson S, Wilhelmson K, Eklund K, Gosman-Hedstrom G, Ziden L, Kronlof GH et al. Health-promoting interventions for persons aged 80 and older are successful in the short term--results from the randomized and three-armed Elderly Persons in the Risk Zone study. *Journal of the American Geriatrics Society*. 2012; 60(3):447-454
- 527 Gustavsson C, Denison E, von Koch L. Self-management of persistent neck pain: a randomized controlled trial of a multi-component group intervention in primary health care. *European Journal of Pain*. 2010; 14(6):630
- 528 Gutierrez Vilaplana JM, Zampieron A, Craver L, Buja A. Evaluation of psychological outcomes following the intervention 'teaching group': study on predialysis patients. *Journal of Renal Care*. 2009; 35:159-164
- 529 Haapamaki J, Turunen U, Roine RP, Farkkila MA, Arkkila PET. Finnish patients with inflammatory bowel disease have fewer symptoms and are more satisfied with their treatment than patients in the previous European survey. *Scandinavian Journal of Gastroenterology*. 2008; 43(7):821-830
- 530 Hafner JWJ, Belknap SM, Squillante MD, Bucheit KA. Adverse drug events in emergency department patients. *Annals of Emergency Medicine*. 2002; 39(3):258-267
- 531 Haile DB, Ayen WY, Tiwari P. Prevalence and assessment of factors contributing to adverse drug reactions in wards of a tertiary care hospital, India. *Ethiopian Journal of Health Sciences*. 2013; 23(1):39-48
- 532 Hajjar ER, Cafiero AC, Hanlon JT. Polypharmacy in elderly patients. *American Journal of Geriatric Pharmacotherapy*. 2007; 5(4):345-351
- 533 Hajjar I, Hart M, Wan SH, Novak V. Safety and blood pressure trajectory of short-term withdrawal of antihypertensive medications in older adults: experience from a clinical trial sample. *Journal of the American Society of Hypertension*. 2013; 7(4):289-293
- 534 Hak E, Verheij TJ, van Essen GA, Lafeber AB, Grobbee DE, Hoes AW. Prognostic factors for influenza-associated hospitalization and death during an epidemic. *Epidemiology and Infection*. 2001; 126(2):261-268
- 535 Halava H, Korhonen MJ, Huupponen R, Setoguchi S, Pentti J, Kivimaki M et al. Lifestyle factors as predictors of nonadherence to statin therapy among patients with and without

- cardiovascular comorbidities. *CMAJ Canadian Medical Association Journal*. 2014; 186(12):E449-E456
- 536 Halm EA, Atlas SJ, Borowsky LH, Benzer TI, Metlay JP, Chang YC et al. Understanding physician adherence with a pneumonia practice guideline: effects of patient, system, and physician factors. *Archives of Internal Medicine*. 2000; 160(1):98-104
- 537 Halvorsen K, Slettebo A, Nortvedt P, Pedersen R, Kirkevold M, Nordhaug M et al. Priority dilemmas in dialysis: the impact of old age. *Journal of Medical Ethics*. 2008; 34(8):585-589
- 538 Hamaker ME, Jonker JM, de Rooij SE, Vos AG, Smorenburg CH, van Munster BC. Frailty screening methods for predicting outcome of a comprehensive geriatric assessment in elderly patients with cancer: a systematic review. *Lancet Oncology*. 2012; 13(10):e437-e444
- 539 Hamilton H, Gallagher P, Ryan C, Byrne S, O'Mahony D. Potentially inappropriate medications defined by STOPP criteria and the risk of adverse drug events in older hospitalized patients. *Archives of Internal Medicine*. 2011; 171(11):1013-1019
- 540 Hanlon JT, Pieper CF, Hajjar ER, Sloane RJ, Lindblad CI, Ruby CM et al. Incidence and predictors of all and preventable adverse drug reactions in frail elderly persons after hospital stay. *Journals of Gerontology Series A, Biological Sciences and Medical Sciences*. 2006; 61(5):511-515
- 541 Hansel NN, Merriman B, Haponik EF, Diette GB. Hospitalizations for tuberculosis in the United States in 2000: predictors of in-hospital mortality. *Chest*. 2004; 126(4):1079-1086
- 542 Hansen AG, Jensen H, Laugesen LP, Petersen A. Withdrawal of antihypertensive drugs in the elderly. *Acta Medica Scandinavica Supplementum*. 1983; 676:178-185
- 543 Hansen H, Schafer I, Schon G, Riedel-Heller S, Gensichen J, Weyerer S et al. Agreement between self-reported and general practitioner-reported chronic conditions among multimorbid patients in primary care - results of the MultiCare Cohort Study. *BMC Family Practice*. 2014; 15:39
- 544 Hansen LO, Young RS, Hinami K, Leung A, Williams MV. Interventions to reduce 30-day rehospitalization: a systematic review. *Annals of Internal Medicine*. 2011; 155(8):520-528
- 545 Harel Z, Bell CM, Dixon SN, McArthur E, James MT, Garg AX et al. Predictors of progression to chronic dialysis in survivors of severe acute kidney injury: a competing risk study. *BMC Nephrology*. 2014; 15:114
- 546 Harries C, Forrest D, Harvey N, McClelland A, Bowling A. Which doctors are influenced by a patient's age? A multi-method study of angina treatment in general practice, cardiology and gerontology. *Quality and Safety in Health Care*. 2007; 16(1):23-27
- 547 Harris M, Rhodes T. Hepatitis C treatment access and uptake for people who inject drugs: A review mapping the role of social factors. *Harm Reduction Journal*.: BioMed Central Limited. 2013; 10
- 548 Harris MF, Jayasinghe UW, Taggart JR, Christl B, Proudfoot JG, Crookes PA et al. Multidisciplinary team care arrangements in the management of patients with chronic disease in Australian general practice. *Medical Journal of Australia*. 2011; 194(5):236-239

- 549 Harrison M, Reeves D, Harkness E, Valderas J, Kennedy A, Rogers A et al. A secondary analysis of the moderating effects of depression and multimorbidity on the effectiveness of a chronic disease self-management programme. *Patient Education and Counseling*. 2012; 87:67-73
- 550 Harrold LR, Briesacher BA, Peterson D, Beard A, Madden J, Zhang F et al. Cost-related medication nonadherence in older patients with rheumatoid arthritis. *Journal of Rheumatology*. 2013; 40(2):137-143
- 551 Harvey P, Storer M, Berlowitz DJ, Jackson B, Hutchinson A, Lim WK. Feasibility and impact of a post-discharge geriatric evaluation and management service for patients from residential care: the Residential Care Intervention Program in the Elderly (RECIPE). *BMC Geriatrics*. 2014; 14:48
- 552 Haugli L, Steen E, Laerum E, Nygard R, Finset A. Psychological distress and employment status. Effects of a group learning programme for patients with chronic musculoskeletal pain. *Psychology, Health & Medicine*.: Routledge. 2003; 8(2):135-148
- 553 Haverhals LM, Lee C, Siek KA, Darr CA, Linnebur SA, Ruscin JM et al. Older adults with multimorbidity: medication management processes and design implications for personal health applications. *Journal of Medical Internet Research*. 2011; 13(2):e44
- 554 Health Quality Ontario. Continuity of care to optimize chronic disease management in the community setting: an evidence-based analysis. *Ontario Health Technology Assessment Series*. 2013; 13(6):1-41
- 555 Health Quality Ontario. In-home care for optimizing chronic disease management in the community: an evidence-based analysis. *Ontario Health Technology Assessment Series*. 2013; 13(5):1-65
- 556 Health Quality Ontario. Specialized nursing practice for chronic disease management in the primary care setting: an evidence-based analysis. *Ontario Health Technology Assessment Series*. 2013; 13(10):1-66
- 557 Heatley SA. Optimal referral is early referral. *Peritoneal Dialysis International*. 2009; 29 Suppl 2:S128-S131
- 558 Hebert R, Raiche M, Dubois MF, Gueye NR, Dubuc N, Tousignant M. Impact of PRISMA, a coordination-type integrated service delivery system for frail older people in Quebec (Canada): A quasi-experimental study. *Journals of Gerontology Series B, Psychological Sciences and Social Sciences*. 2010; 65 B(1):107-118
- 559 Heeschen C, Hamm CW, Laufs U, Bohm M, Snapinn S, White HD. Withdrawal of statins in patients with acute coronary syndromes. *Circulation*. 2003; 107(3):e27
- 560 Heeschen C, Hamm CW, Laufs U, Snapinn S, Bohm M, White HD et al. Withdrawal of statins increases event rates in patients with acute coronary syndromes. *Circulation*. 2002; 105(12):1446-1452
- 561 Heijmans M, Waverijn G, Rademakers J, van der Vaart R, Rijken M. Functional, communicative and critical health literacy of chronic disease patients and their importance for self-management. *Patient Education and Counseling*. 2015; 98(1):41-48
- 562 Heining-Rothbucher D, Bischinger S, Ulmer H, Pechlaner C, Speer G, Wiedermann CJ. Incidence and risk of potential adverse drug interactions in the emergency room. *Resuscitation*. 2001; 49(3):283-288

- 563 Heisler M, Cole I, Weir D, Kerr EA, Hayward RA. Does physician communication influence older patients' diabetes self-management and glycemic control? Results from the Health and Retirement Study (HRS). *Journals of Gerontology Series A, Biological Sciences and Medical Sciences*. 2007; 62(12):1435-1442
- 564 Helfrich CD, Dolan ED, Simonetti J, Reid RJ, Joos S, Wakefield BJ et al. Elements of team-based care in a patient-centered medical home are associated with lower burnout among VA primary care employees. *Journal of General Internal Medicine*. 2014; 29 Suppl 2:S659-S666
- 565 Helminen EE, Mantyselka P, Nykanen I, Kumpusalo E. Far from easy and accurate - detection of metabolic syndrome by general practitioners. *BMC Family Practice*. 2009; 10:76
- 566 Helstad CP, Wiegmann SM, Camponeschi J, Udalis S, Meredith M. The Wisconsin Medical Society diabetes study. *WMJ*. 2004; 103(3):71-78
- 567 Helvik AS, Engedal K, Selbaek G. Three-year mortality in previously hospitalized older patients from rural areas--the importance of co-morbidity and self-reported poor health. *BMC Geriatrics*. 2013; 13:17
- 568 Helvik AS, Engedal K, Selbaek G. The quality of life and factors associated with it in the medically hospitalised elderly. *Aging and Mental Health*. 2010; 14(7):861-869
- 569 Hemmelgarn BR, Manns BJ, Quan H, Ghali WA. Adapting the Charlson Comorbidity Index for use in patients with ESRD. *American Journal of Kidney Diseases*. 2003; 42(1):125-132
- 570 Henning-Smith C, McAlpine D, Shippee T, Priebe M. Delayed and unmet need for medical care among publicly insured adults with disabilities. *Medical Care*. 2013; 51(11):1015-1019
- 571 Henry R, Richardson JL, Stoyanoff S, Garcia GP, Dorey F, Iverson E et al. HIV/AIDS health service utilization by people who have been homeless. *AIDS and Behavior*. 2008; 12(5):815-821
- 572 Hernandez C, Alonso A, Garcia-Aymerich J, Serra I, Marti D, Rodriguez-Roisin R et al. Effectiveness of community-based integrated care in frail COPD patients: A randomised controlled trial. *Npj Primary Care Respiratory Medicine*. 2015; 25
- 573 Hershkovitz A, Rothschild BM, Rose JH, Hornick T, O'Toole EE. Medical care perceptions in elderly patients with musculoskeletal complaints. *Israel Medical Association Journal*. 2001; 3(11):822-827
- 574 Hewitson P, Skew A, Graham C, Jenkinson C, Coulter A. People with limiting long-term conditions report poorer experiences and more problems with hospital care. *BMC Health Services Research*. 2014; 14:33
- 575 Heyrani N, Picinic Norheim E, Elaine Ku Y, Nick Shamie A. Interspinous process implantation for the treatment of neurogenic intermittent claudication. *Anesthesiology and Pain Medicine*. 2012; 2(1):36-41
- 576 Heyworth ITM, Hazell ML, Linehan MF, Frank TL. How do common chronic conditions affect health-related quality of life? *British Journal of General Practice*. 2009; 59(568):e353-e358
- 577 Hickman RLJ, Clochesy JM, Pinto MD, Burant C, Pignatiello G. Impact of a serious game for health on chronic disease self-management: preliminary efficacy among community dwelling adults with hypertension. *Journal of Health and Human Services Administration*. 2015; 38(2):253-275

- 578 Hill-Briggs F, Gary TL, Hill MN, Bone LR, Brancati FL. Health-related quality of life in urban African Americans with type 2 diabetes. *Journal of General Internal Medicine*. 2002; 17(6):412-419
- 579 Hilmer SN, Perera V, Mitchell S, Murnion BP, Dent J, Bajorek B et al. The assessment of frailty in older people in acute care. *Australasian Journal on Ageing*. 2009; 28(4):182-188
- 580 Hinder S, Greenhalgh T. "This does my head in". Ethnographic study of self-management by people with diabetes. *BMC Health Services Research*. 2012; 12:83
- 581 Hindmarsh D, Loh M, Finch CF, Hayen A, Close JC. Effect of comorbidity on relative survival following hospitalisation for fall-related hip fracture in older people. *Australasian Journal on Ageing*. 2014; 33(3):E1-E7
- 582 Hiorth YH, Larsen JP, Lode K, Pedersen KF. Natural history of falls in a population-based cohort of patients with Parkinson's disease: an 8-year prospective study. *Parkinsonism and Related Disorders*. 2014; 20(10):1059-1064
- 583 Hippisley-Cox J, Coupland C. Predicting risk of emergency admission to hospital using primary care data: Derivation and validation of QAdmissions score. *BMJ Open*. 2013; 3(8)
- 584 Hirani SP, Beynon M, Cartwright M, Rixon L, Doll H, Henderson C et al. The effect of telecare on the quality of life and psychological well-being of elderly recipients of social care over a 12-month period: the Whole Systems Demonstrator cluster randomised trial. *Age and Ageing*. 2014; 43(3):334-341
- 585 Ho J, Kuluski K, Gill A. A patient-centered transitions framework for persons with complex chronic conditions. *Care Management Journals*. 2015; 16(3):159-169
- 586 Ho KM, Finn J, Knuiman M, Webb SA. Combining multiple comorbidities with Acute Physiology Score to predict hospital mortality of critically ill patients: a linked data cohort study. *Anaesthesia*. 2007; 62(11):1095-1100
- 587 Ho PM, Magid DJ, Shetterly SM, Olson KL, Maddox TM, Peterson PN et al. Medication nonadherence is associated with a broad range of adverse outcomes in patients with coronary artery disease. *American Heart Journal*. 2008; 155(4):772-779
- 588 Ho PM, Spertus JA, Masoudi FA, Reid KJ, Peterson ED, Magid DJ et al. Impact of medication therapy discontinuation on mortality after myocardial infarction. *Archives of Internal Medicine*. 2006; 166(17):1842-1847
- 589 Ho TW, Tsai YJ, Ruan SY, Huang CT, Lai F, Yu CJ et al. In-hospital and one-year mortality and their predictors in patients hospitalized for first-ever chronic obstructive pulmonary disease exacerbations: a nationwide population-based study. *PLoS ONE*. 2014; 9(12):e114866
- 590 Ho YL, Yu JY, Lin YH, Chen YH, Huang CC, Hsu TP et al. Assessment of the cost-effectiveness and clinical outcomes of a fourth-generation synchronous telehealth program for the management of chronic cardiovascular disease. *Journal of Medical Internet Research*. 2014; 16(6):e145
- 591 Hoang T, Goetz MB, Yano EM, Rossman B, Anaya HD, Knapp H et al. The impact of integrated HIV care on patient health outcomes. *Medical Care*. 2009; 47(5):560-567

- 592 Hochhalter AK, Song J, Rush J, Sklar L, Stevens A. Making the most of your healthcare intervention for older adults with multiple chronic illnesses. *Patient Education and Counseling*. 2010; 81(2):207-213
- 593 Hoer A, Gothe H, Khan ZM, Schiffhorst G, Vincze G, Haussler B. Persistence and adherence with antihypertensive drug therapy in a German sickness fund population. *Journal of Human Hypertension*. 2007; 21(9):744-746
- 594 Hofmann R, Voller H, Nagels K, Bindl D, Vettorazzi E, Dittmar R et al. First outline and baseline data of a randomized, controlled multicenter trial to evaluate the health economic impact of home telemonitoring in chronic heart failure - CardioBBEAT. *Trials*. 2015; 16(1)
- 595 Hogg W, Lemelin J, Dahrouge S, Liddy C, Armstrong CD, Legault F et al. Randomized controlled trial of anticipatory and preventive multidisciplinary team care: for complex patients in a community-based primary care setting. *Canadian Family Physician*. 2009; 55(12):e76-e85
- 596 Holland DC, Lam M. Predictors of hospitalization and death among pre-dialysis patients: a retrospective cohort study. *Nephrology, Dialysis, Transplantation*. 2000; 15(5):650-658
- 597 Holmboe ES, Wang Y, Meehan TP, Tate JP, Ho SY, Starkey KS et al. Association between maintenance of certification examination scores and quality of care for medicare beneficiaries. *Archives of Internal Medicine*. 2008; 168(13):1396-1403
- 598 Holmes H, Min L, Yee M, Varadhan R, Basran J, Dale W et al. Rationalizing prescribing for older patients with multimorbidity: considering time to benefit. *Drugs and Aging*. 2013; 30(9):655-666
- 599 Hong TB, Oddone EZ, Dudley TK, Bosworth HB. Subjective and objective evaluations of health among middle-aged and older veterans with hypertension. *Journal of Aging and Health*.: Sage Publications. 2005; 17(5):592-608
- 600 Hoogerduijn JG, Schuurmans MJ, Korevaar JC, Buurman BM, de Rooij SE. Identification of older hospitalised patients at risk for functional decline, a study to compare the predictive values of three screening instruments. *Journal of Clinical Nursing*. 2010; 19(9-10):1219-1225
- 601 Hopp F, Woodbridge P, Subramanian U, Copeland L, Smith D, Lowery J. Outcomes associated with a home care telehealth intervention. *Telemedicine Journal and E-Health*. 2006; 12:297-307
- 602 Hopper I, Samuel R, Hayward C, Tonkin A, Krum H. Can medications be safely withdrawn in patients with stable chronic heart failure? Systematic review and meta-analysis. *Journal of Cardiac Failure*. 2014; 20(7):522-532
- 603 Horrocks S, Somerset M, Stoddart H, Peters TJ. What prevents older people from seeking treatment for urinary incontinence? A qualitative exploration of barriers to the use of community continence services. *Family Practice*. 2004; 21(6):689-696
- 604 Houle J, Beaulieu MD, Lussier MT, Del Grande C, Pellerin JP, Authier M et al. Patients' experience of chronic illness care in a network of teaching settings. *Canadian Family Physician*. 2012; 58(12):1366-1373
- 605 Howes F, Hansen E, Williams D, Nelson M. Barriers to diagnosing and managing hypertension - a qualitative study in Australian general practice. *Australian Family Physician*. 2010; 39(7):511-516

- 606 Howes FS, Hansen EC, Nelson MR. Using qualitative means to get quantitative evidence into practice. *Translational research for primary healthcare*, Nova Science Publishers, Hauppauge, NY, 2012: 203-213
- 607 Hoyt KS. *Healthcare encounters of formerly incarcerated women: a grounded theory study* University of San Diego; 2006.
- 608 Hsiao PC, Chen TJ, Li CY, Chu CM, Su TP, Wang SH et al. Risk factors and incidence of repeat osteoporotic fractures among the elderly in Taiwan: a population-based cohort study. *Medicine*. 2015; 94(7):e532
- 609 Huan Loh P, Windram JD, Tin L, Reddy P, Velavan P, Rigby AS et al. The effects of initiation or continuation of statin therapy on cholesterol level and all-cause mortality after the diagnosis of left ventricular systolic dysfunction. *American Heart Journal*. 2007; 153(4):537-544
- 610 Huang YQ, Gou R, Diao YS, Yin QH, Fan WX, Liang YP et al. Charlson comorbidity index helps predict the risk of mortality for patients with type 2 diabetic nephropathy. *Journal of Zhejiang University SCIENCE B*. 2014; 15(1):58-66
- 611 Huang Y, Wei X, Wu T, Chen R, Guo A. Collaborative care for patients with depression and diabetes mellitus: a systematic review and meta-analysis. *BMC Psychiatry*. 2013; 13:260
- 612 Huber C, Huber J, Shaha M. Diabetes care of dependent older adults: an exploratory study of nurses' perspectives. *European Diabetes Nursing*. 2011; 8(3):88-92a
- 613 Hung SLL, Fu SN, Lau PS, Wong SYS. A qualitative study on why did the poorly educated Chinese elderly fail to attend nurse-led case manager clinic and how to facilitate their attendance. *International Journal for Equity in Health*. 2015; 14(1)
- 614 Huntley AL, Johnson R, Purdy S, Valderas JM, Salisbury C. Measures of multimorbidity and morbidity burden for use in primary care and community settings: a systematic review and guide. *Annals of Family Medicine*. 2012; 10(2):134-141
- 615 Hutchings HA, Evans BA, Fitzsimmons D, Harrison J, Heaven M, Huxley P et al. Predictive risk stratification model: a progressive cluster-randomised trial in chronic conditions management (PRISMATIC) research protocol. *Trials*. 2013; 14:301
- 616 Hutchinson A, Rasekaba TM, Graco M, Berlowitz DJ, Hawthorne G, Lim WK. Relationship between health-related quality of life, and acute care re-admissions and survival in older adults with chronic illness. *Health and Quality of Life Outcomes*. 2013; 11:136
- 617 Hutchinson AF, Graco M, Rasekaba TM, Parikh S, Berlowitz DJ, Lim WK. Relationship between health-related quality of life, comorbidities and acute health care utilisation, in adults with chronic conditions. *Health and Quality of Life Outcomes*. 2015; 13(1)
- 618 Hwang SW, Wilkins E, Chambers C, Estrabillo E, Berends J, MacDonald A. Chronic pain among homeless persons: characteristics, treatment, and barriers to management. *BMC Family Practice*. 2011; 12:73
- 619 Ijff MA, Huijbregts KM, van Marwijk HW, Beekman AT, Hakkaart-Van Roijen L, Rutten FF et al. Cost-effectiveness of collaborative care including PST and an antidepressant treatment algorithm for the treatment of major depressive disorder in primary care; a randomised clinical trial. *BMC Health Services Research*. 2007; 7:34

- 620 Imai H, Furukawa TA, Okumiya K, Wada T, Fukutomi E, Sakamoto R et al. The postcard intervention against depression among community-dwelling older adults: study protocol for a randomized controlled trial. *Trials*. 2013; 14:202
- 621 Imhof L, Naef R, Wallhagen MI, Schwarz J, Mahrer-Imhof R. Effects of an advanced practice nurse in-home health consultation program for community-dwelling persons aged 80 and older. *Journal of the American Geriatrics Society*. 2012; 60(12):2223-2231
- 622 Incalzi RA, Capparella O, Gemma A, Landi F, Bruno E, Di Meo F et al. The interaction between age and comorbidity contributes to predicting the mortality of geriatric patients in the acute-care hospital. *Journal of Internal Medicine*. 1997; 242(4):291-298
- 623 Incalzi RA, Corsonello A, Pedone C, Masotti G, Rengo F, Grassi V et al. Use of antibiotics in elderly patients with exacerbated COPD: the OLD-chronic obstructive pulmonary disease study. *Journal of the American Geriatrics Society*. 2006; 54(4):642-647
- 624 Inouye SK, Bogardus ST, Jr., Vitagliano G, Desai MM, Williams CS, Grady JN et al. Burden of illness score for elderly persons: risk adjustment incorporating the cumulative impact of diseases, physiologic abnormalities, and functional impairments. *Medical Care*. 2003; 41(1):70-83
- 625 Ionescu-Ittu R, McCusker J, Ciampi A, Vadeboncoeur AM, Roberge D, Larouche D et al. Continuity of primary care and emergency department utilization among elderly people. *CMAJ Canadian Medical Association Journal*. 2007; 177(11):1362-1368
- 626 ISD Scotland. GP consultations: practice team information (PTI) statistics, 2013. Available from: <http://www.isdscotland.org/Health-Topics/General-Practice/GP-consultations/>
- 627 Ito H. What should we do to improve patients' adherence? *Journal of Experimental and Clinical Medicine*. 2013; 5(4):127-130
- 628 Iwata M, Kuzuya M, Kitagawa Y, Suzuki Y, Iguchi A. Underappreciated predictors for postdischarge mortality in acute hospitalized oldest-old patients. *Gerontology*. 2006; 52(2):92-98
- 629 Iyer S, Naganathan V, McLachlan AJ, Le Couteur DG. Medication withdrawal trials in people aged 65 years and older: a systematic review. *Drugs and Aging*. 2008; 25(12):1021-1031
- 630 Jager C, Szecsenyi J, Steinhauser J. Design and delivery of a tailored intervention to implement recommendations for multimorbid patients receiving polypharmacy into primary care practices. *BioMed Research International*. 2015; 2015:938069
- 631 Jang SH, Chea JW, Lee KB. Charlson comorbidity index using administrative database in incident PD patients. *Clinical Nephrology*. 2010; 73(3):204-209
- 632 Jani B, Blane D, Browne S, Montori V, May C, Shippee N et al. Identifying treatment burden as an important concept for end of life care in those with advanced heart failure. *Current Opinion in Supportive and Palliative Care*. 2013; 7(1):3-7
- 633 Janig H, Muller W. Outpatient geriatric remobilisation. *Journal Fur Mineralstoffwechsel*. 2014; 21(3):89-95

- 634 Janke EA, Ramirez ML, Haltzman B, Fritz M, Kozak AT. Patient's experience with comorbidity management in primary care: a qualitative study of comorbid pain and obesity. *Primary Health Care Research and Development*. 2016; 17(1):33-41
- 635 Janke EA, Fritz M, Hopkins C, Haltzman B, Sautter JM, Ramirez ML. A randomized clinical trial of an integrated behavioral self-management intervention Simultaneously Targeting Obesity and Pain: the STOP trial. *BMC Public Health*. 2014; 14:621
- 636 Jansa M, Hernandez C, Vidal M, Nunez M, Bertran MJ, Sanz S et al. Multidimensional analysis of treatment adherence in patients with multiple chronic conditions. A cross-sectional study in a tertiary hospital. *Patient Education and Counseling*. 2010; 81(2):161-168
- 637 Janzen W, Turpin KVL, Warren SA, Marrie RA, Warren KG. Change in the health-related quality of life of multiple sclerosis patients over 5 years. *International Journal of MS Care*. 2013; 15(1):46-53
- 638 Jatrana S, Crampton P. Primary health care in New Zealand: who has access? *Health Policy*. 2009; 93(1):1-10
- 639 Jatrana S, Crampton P, Norris P. Ethnic differences in access to prescription medication because of cost in New Zealand. *Journal of Epidemiology and Community Health*. 2011; 65(5):454-460
- 640 Jensen GL, Friedmann JM, Coleman CD, Smiciklas-Wright H. Screening for hospitalization and nutritional risks among community-dwelling older persons. *American Journal of Clinical Nutrition*. 2001; 74(2):201-205
- 641 Jeon YH, Essue B, Jan S, Wells R, Whitworth JA. Economic hardship associated with managing chronic illness: a qualitative inquiry. *BMC Health Services Research*. 2009; 9:182
- 642 Jeon YH, Jowsey T, Yen L, Glasgow NJ, Essue B, Kljakovic M et al. Achieving a balanced life in the face of chronic illness. *Australian Journal of Primary Health*. 2010; 16(1):66-74
- 643 Jeon YH, Kraus SG, Jowsey T, Glasgow NJ. The experience of living with chronic heart failure: a narrative review of qualitative studies. *BMC Health Services Research*. 2010; 10:77
- 644 Jepsen P, Vilstrup H, Andersen PK, Lash TL, Sorensen HT. Comorbidity and survival of Danish cirrhosis patients: a nationwide population-based cohort study. *Hepatology*. 2008; 48(1):214-220
- 645 Jepsen P, Vilstrup H, Lash TL. Development and validation of a comorbidity scoring system for patients with cirrhosis. *Gastroenterology*. 2014; 146(1):147-156
- 646 Jerant A, Moore-Hill M, Franks P. Home-based, peer-led chronic illness self-management training: findings from a 1-year randomized controlled trial. *Annals of Family Medicine*. 2009; 7(4):319-327
- 647 Jerant AF, von Friederichs-Fitzwater MM, Moore M. Patients' perceived barriers to active self-management of chronic conditions. *Patient Education and Counseling*. 2005; 57(3):300-307
- 648 Jia H, Chuang HC, Wu SS, Wang X, Chumbler NR. Long-term effect of home telehealth services on preventable hospitalization use. *Journal of Rehabilitation Research and Development*. 2009; 46(5):557-566

- 649 Jiang HX, Majumdar SR, Dick DA, Moreau M, Raso J, Otto DD et al. Development and initial validation of a risk score for predicting in-hospital and 1-year mortality in patients with hip fractures. *Journal of Bone and Mineral Research*. 2005; 20(3):494-500
- 650 Johansson R, Sjoberg E, Sjogren M, Johnsson E, Carlbring P, Andersson T et al. Tailored vs. standardized internet-based cognitive behavior therapy for depression and comorbid symptoms: a randomized controlled trial. *PLoS ONE*. 2012; 7:e36905
- 651 Johnson TL, Toliver JC, Mao L, Oramasionwu CU. Differences in outpatient care and treatment utilization for patients with HIV/HCV coinfection, HIV, and HCV mono-infection, a cross-sectional study. *BMC Infectious Diseases*. 2014; 14:217
- 652 Johnston K, Grimmer-Somers K, Young M, Antic R, Frith P. Which chronic obstructive pulmonary disease care recommendations have low implementation and why? A pilot study. *BMC Research Notes*. 2012; 5:652
- 653 Johnston SE, Liddy CE, Ives SM. Self-management support: a new approach still anchored in an old model of health care. *Canadian Journal of Public Health*. 2011; 102(1):68-72
- 654 Jones D, Song X, Mitnitski A, Rockwood K. Evaluation of a frailty index based on a comprehensive geriatric assessment in a population based study of elderly Canadians. *Aging Clinical and Experimental Research*. 2005; 17(6):465-471
- 655 Jong P, Vowinckel E, Liu PP, Gong Y, Tu JV. Prognosis and determinants of survival in patients newly hospitalized for heart failure: a population-based study. *Archives of Internal Medicine*. 2002; 162(15):1689-1694
- 656 Jonker AAGC, Comijs HC, Knipscheer KCPM, Deeg DJH. Benefits for elders with vulnerable health from the Chronic Disease Self-management Program (CDSMP) at short and longer term. *BMC Geriatrics*. 2015; 15:101
- 657 Jonkers CCM, Lamers F, Bosma H, Metsemakers JFM, van Eijk JT. The effectiveness of a minimal psychological intervention on self-management beliefs and behaviors in depressed chronically ill elderly persons: a randomized trial. *International Psychogeriatrics*. 2012; 24(2):288-297
- 658 Jonsen A, Clarke AE, Joseph L, Belisle P, Bernatsky S, Nived O et al. Association of the Charlson comorbidity index with mortality in systemic lupus erythematosus. *Arthritis Care and Research*. 2011; 63(9):1233-1237
- 659 Joo MJ, Sharp LK, Au DH, Lee TA, Fitzgibbon ML. Use of spirometry in the diagnosis of COPD: a qualitative study in primary care. *COPD*. 2013; 10(4):444-449
- 660 Jorgensen T, Johansson S, Kennerfalk A, Wallander MA, Svardsudd K. Prescription drug use, diagnoses, and healthcare utilization among the elderly. *Annals of Pharmacotherapy*. 2001; 35(9):1004-1009
- 661 Jotheeswaran AT, Bryce R, Prina M, Acosta D, Ferri CP, Guerra M et al. Frailty and the prediction of dependence and mortality in low- and middle-income countries: A 10/66 population-based cohort study. *BMC Medicine*. 2015; 13(1)
- 662 Joubert A, Kidd-Taylor A, Christopher G, Nanda J, Warren R, Lindong I et al. Complementary and alternative medical practice: self-care preferred vs. practitioner-based care among patients with asthma. *Journal of the National Medical Association*. 2010; 102(7):562-569

- 663 Jowsey T, Jeon YH, Dugdale P, Glasgow NJ, Kljakovic M, Usherwood T. Challenges for co-morbid chronic illness care and policy in Australia: a qualitative study. *Australia and New Zealand Health Policy*. 2009; 6:22
- 664 Jung HW, Kim SW, Ahn S, Lim JY, Han JW, Kim TH et al. Prevalence and outcomes of frailty in Korean elderly population: comparisons of a multidimensional frailty index with two phenotype models. *PLoS ONE*. 2014; 9(2):e87958
- 665 Junius-Walker U, Wrede J, Voigt I, Hofmann W, Wiese B, Hummers-Pradier E et al. Impact of a priority-setting consultation on doctor-patient agreement after a geriatric assessment: cluster randomised controlled trial in German general practices. *Quality in Primary Care*. 2012; 20:321-334
- 666 Justice AC, Braithwaite RS. Lessons learned from the first wave of aging with HIV. *AIDS*. 2012; 26 Suppl 1:S11-S18
- 667 Jyrkka J, Enlund H, Korhonen MJ, Sulkava R, Hartikainen S. Polypharmacy status as an indicator of mortality in an elderly population. *Drugs and Aging*. 2009; 26(12):1039-1048
- 668 Kan WC, Wang JJ, Wang SY, Sun YM, Hung CY, Chu CC et al. The new comorbidity index for predicting survival in elderly dialysis patients: a long-term population-based study. *PLoS ONE*. 2013; 8(8):e68748
- 669 Kanis J, Johnell O, Gullberg B, Allander E, Elffors L, Ranstam J et al. Risk factors for hip fracture in men from southern Europe: the MEDOS study. *Mediterranean Osteoporosis Study*. *Osteoporosis International*. 1999; 9(1):45-54
- 670 Kannegaard PN, van der Mark S, Eiken P, Abrahamsen B. Excess mortality in men compared with women following a hip fracture. National analysis of comedication, comorbidity and survival. *Age and Ageing*. 2010; 39(2):203-209
- 671 Kaplan MH, Feinstein AR. The importance of classifying initial co-morbidity in evaluating the outcome of diabetes mellitus. *Journal of Chronic Diseases*. 1974; 27(7-8):387-404
- 672 Kaplan RC, Heckbert SR, Koepsell TD, Furberg CD, Polak JF, Schoen RE et al. Risk factors for hospitalized gastrointestinal bleeding among older persons. *Cardiovascular Health Study Investigators*. *Journal of the American Geriatrics Society*. 2001; 49(2):126-133
- 673 Karampampa K, Gustavsson A, Miltenburger C, Tyas D. Treatment experience, burden and unmet needs (TRIBUNE) in MS study: results from the United Kingdom. *Multiple Sclerosis*. 2012; 18(2 Suppl):41-45
- 674 Karhula T, Vuorinen AL, Raapysjarvi K, Pakanen M, Itkonen P, Tepponen M et al. Telemonitoring and mobile phone-based health coaching among Finnish diabetic and heart disease patients: randomized controlled trial. *Journal of Medical Internet Research*. 2015; 17(6):e153
- 675 Karppi P. Effects of a geriatric inpatient unit on elderly home care patients: a controlled trial. *Aging (Milan, Italy)*. 1995; 7(3):207-211
- 676 Karppi P, Tilvis R. Effectiveness of a Finnish geriatric inpatient assessment. Two-year follow up of a randomized clinical trial on community-dwelling patients. *Scandinavian Journal of Primary Health Care*. 1995; 13(2):93-98

- 677 Katon WJ, Lin EH, Von Korff M, Ciechanowski P, Ludman EJ, Young B et al. Collaborative care for patients with depression and chronic illnesses. *New England Journal of Medicine*. 2010; 363(27):2611-2620
- 678 Katon WJ, Russo JE, Von Korff M, Lin EH, Ludman E, Ciechanowski PS. Long-term effects on medical costs of improving depression outcomes in patients with depression and diabetes. *Diabetes Care*. 2008; 31:1155-1159
- 679 Katon WJ, Von Korff M, Lin EH, Simon G, Ludman E, Russo J et al. The Pathways Study: a randomized trial of collaborative care in patients with diabetes and depression. *Archives of General Psychiatry*. 2004; 61(10):1042-1049
- 680 Katon W, Russo J, Lin EHB, Schmittdiel J, Ciechanowski P, Ludman E et al. Cost-effectiveness of a multicondition collaborative care intervention: a randomized controlled trial. *Archives of General Psychiatry*. 2012; 69(5):506-514
- 681 Kellen E, Bulens P, Deckx L, Schouten H, Van Dijk M, Verdonck I et al. Identifying an accurate pre-screening tool in geriatric oncology. *Critical Reviews in Oncology-Hematology*. 2010; 75(3):243-248
- 682 Kenealy TW, Parsons MJG, Rouse AP, Doughty RN, Sheridan NF, Hindmarsh JKH et al. Telecare for diabetes, CHF or COPD: effect on quality of life, hospital use and costs. A randomised controlled trial and qualitative evaluation. *PLoS ONE*. 2015; 10(3):e0116188
- 683 Kenig J, Richter P, Zychiewicz B, Olszewska U. Vulnerable Elderly Survey 13 as a screening method for frailty in Polish elderly surgical patient--prospective study. *Polski Przegląd Chirurgiczny*. 2014; 86(3):126-131
- 684 Kenig J, Zychiewicz B, Olszewska U, Richter P. Screening for frailty among older patients with cancer that qualify for abdominal surgery. *Journal of Geriatric Oncology*. 2015; 6(1):52-59
- 685 Kennedy A, Reeves D, Bower P, Lee V, Middleton E, Richardson G et al. The effectiveness and cost effectiveness of a national lay-led self care support programme for patients with long-term conditions: a pragmatic randomised controlled trial. *Journal of Epidemiology and Community Health*. 2007; 61(3):254-261
- 686 Kenning C, Coventry PA, Gibbons C, Bee P, Fisher L, Bower P. Does patient experience of multimorbidity predict self-management and health outcomes in a prospective study in primary care? *Family Practice*. 2015;
- 687 Kenning C, Fisher L, Bee P, Bower P, Coventry P. Primary care practitioner and patient understanding of the concepts of multimorbidity and self-management: A qualitative study. *SAGE Open Medicine*. 2013; 1
- 688 Kenning C, Protheroe J, Gray N, Ashcroft D, Bower P. The potential for using a Universal Medication Schedule (UMS) to improve adherence in patients taking multiple medications in the UK: a qualitative evaluation. *BMC Health Services Research*. 2015; 15:94
- 689 Kerr EA, Heisler M, Krein SL, Kabeto M, Langa KM, Weir D et al. Beyond comorbidity counts: how do comorbidity type and severity influence diabetes patients' treatment priorities and self-management? *Journal of General Internal Medicine*. 2007; 22(12):1635-1640
- 690 Khan NF, Perera R, Harper S, Rose PW. Adaptation and validation of the Charlson Index for Read/OXMIS coded databases. *BMC Family Practice*. 2010; 11:1

- 691 Kiely DK, Cupples LA, Lipsitz LA. Validation and comparison of two frailty indexes: The MOBILIZE Boston Study. *Journal of the American Geriatrics Society*. 2009; 57(9):1532-1539
- 692 Kieszak SM, Flanders WD, Kosinski AS, Shipp CC, Karp H. A comparison of the Charlson comorbidity index derived from medical record data and administrative billing data. *Journal of Clinical Epidemiology*. 1999; 52(2):137-142
- 693 Kil SR, Lee SI, Khang YH, Lee MS, Kim HJ, Kim SO et al. Development and validation of comorbidity index in South Korea. *International Journal for Quality in Health Care*. 2012; 24(4):391-402
- 694 Kilbourne AM, Biswas K, Pirraglia PA, Sajatovic M, Williford WO, Bauer MS. Is the collaborative chronic care model effective for patients with bipolar disorder and co-occurring conditions? *Journal of Affective Disorders*. 2009; 112:256-261
- 695 Kim MC, Cho JY, Jeong HC, Lee KH, Park KH, Sim DS et al. Impact of postdischarge statin withdrawal on long-term outcomes in patients with acute myocardial infarction. *American Journal of Cardiology*. 2015; 115(1):1-7
- 696 Kim SW, Han HS, Jung HW, Kim KI, Hwang DW, Kang SB et al. Multidimensional frailty score for the prediction of postoperative mortality risk. *JAMA Surgery*. 2014; 149(7):633-640
- 697 Kinder LS, Katon WJ, Ludman E, Russo J, Simon G, Lin EH et al. Improving depression care in patients with diabetes and multiple complications. *Journal of General Internal Medicine*. 2006; 21(10):1036-1041
- 698 Kirchnerberger I, Hunger M, Stollenwerk B, Seidl H, Burkhardt K, Kuch B et al. Effects of a 3-year nurse-based case management in aged patients with acute myocardial infarction on rehospitalisation, mortality, risk factors, physical functioning and mental health. A secondary analysis of the randomized controlled KORINNA study. *PLoS ONE*. 2015; 10(3)
- 699 Kivipelto M, Solomon A, Ahtiluoto S, Ngandu T, Lehtisalo J, Antikainen R et al. The Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER): study design and progress. *Alzheimer's and Dementia*. 2013; 9(6):657-665
- 700 Klungel OH, Heckbert SR, de Boer A, Leufkens HGM, Sullivan SD, Fishman PA et al. Lipid-lowering drug use and cardiovascular events after myocardial infarction. *Annals of Pharmacotherapy*. 2002; 36(5):751-757
- 701 Knight E, Stuckey MI, Petrella RJ. Health promotion through primary care: enhancing self-management with activity prescription and mHealth. *Physician and Sportsmedicine*. 2014; 42(3):90-99
- 702 Knowles SE, Chew-Graham C, Adeyemi I, Coupe N, Coventry PA. Managing depression in people with multimorbidity: a qualitative evaluation of an integrated collaborative care model. *BMC Family Practice*. 2015; 16:32
- 703 Knowles SE, Chew-Graham C, Coupe N, Adeyemi I, Keyworth C, Thampy H et al. Better together? a naturalistic qualitative study of inter-professional working in collaborative care for co-morbid depression and physical health problems. *Implementation Science*. 2013; 8:110
- 704 Koberich S, Lohrmann C, Mittag O, Dassen T. Effects of a hospital-based education programme on self-care behaviour, care dependency and quality of life in patients with heart failure--a randomised controlled trial. *Journal of Clinical Nursing*. 2015; 24(11-12):1643-1655

- 705 Koch G, Wakefield BJ, Wakefield DS. Barriers and facilitators to managing multiple chronic conditions: A systematic literature review. *Western Journal of Nursing Research*. 2015; 37(4):498-516
- 706 Kochar MS, Landry KM, Ristow SM. Effects of reduction in dose and discontinuation of hydrochlorothiazide in patients with controlled essential hypertension. *Archives of Internal Medicine*. 1990; 150(5):1009-1011
- 707 Kogan AC, Gonzalez J, Hart B, Halloran S, Thomason B, Levine M et al. Be Well: results of a nutrition, exercise, and weight management intervention among at-risk older adults. *Journal of Applied Gerontology*. 2013; 32(7):889-901
- 708 Kohler S, Unger T, Hoffmann S, Mackert A, Ross B, Fydrich T. The relationship of health-related quality of life and treatment outcome during inpatient treatment of depression. *Quality of Life Research*. 2015; 24(3):641-649
- 709 Kongkaew C, Hann M, Mandal J, Williams SD, Metcalfe D, Noyce PR et al. Risk factors for hospital admissions associated with adverse drug events. *Pharmacotherapy*. 2013; 33(8):827-837
- 710 Kostis JB, Espeland MA, Appel L, Johnson KC, Pierce J, Wofford JL. Does withdrawal of antihypertensive medication increase the risk of cardiovascular events? Trial of Nonpharmacologic Interventions in the Elderly (TONE) Cooperative Research Group. *American Journal of Cardiology*. 1998; 82(12):1501-1508
- 711 Krahn DD, Bartels SJ, Coakley E, Oslin DW, Chen H, McIntyre J et al. PRISM-E: comparison of integrated care and enhanced specialty referral models in depression outcomes. *Psychiatric Services*. 2006; 57(7):946-953
- 712 Krause KJ. Mortality and prescription drug use: an analysis using the CHS limited access data. *Journal of Insurance Medicine*. 2007; 39(1):24-27
- 713 Krein SL, Heisler M, Piette JD, Butchart A, Kerr EA. Overcoming the influence of chronic pain on older patients' difficulty with recommended self-management activities. *Gerontologist*. 2007; 47(1):61-68
- 714 Kristjansson SR, Ronning B, Hurria A, Skovlund E, Jordhoy MS, Nesbakken A et al. A comparison of two pre-operative frailty measures in older surgical cancer patients. *Journal of Geriatric Oncology*. 2012; 3(1):1-7
- 715 Kroenke K, Krebs E, Wu J, Bair MJ, Damush T, Chumbler N et al. Stepped Care to Optimize Pain care Effectiveness (SCOPE) trial study design and sample characteristics. *Contemporary Clinical Trials*. 2013; 34:270-281
- 716 Kronish IM, Diefenbach MA, Edmondson DE, Phillips LA, Fei K, Horowitz CR. Key barriers to medication adherence in survivors of strokes and transient ischemic attacks. *Journal of General Internal Medicine*. 2013; 28(5):675-682
- 717 Krska J, Cromarty JA, Arris F, Jamieson D, Hansford D, Duffus PR et al. Pharmacist-led medication review in patients over 65: a randomized, controlled trial in primary care. *Age and Ageing*. 2001; 30(3):205-211

- 718 Kuluski K, Tracy CS, Upshur RE. Perceived risk factors of health decline: a qualitative study of hospitalized patients with multimorbidity. *Risk Management and Healthcare Policy*. 2015; 8:63-72
- 719 Kumar S, Grimmer-Somers K. A synthesis of the secondary literature on effectiveness of hospital avoidance and discharge programs. *Australian Health Review*. 2007; 31(1):34-48
- 720 Kumbhani DJ, Steg PG, Cannon CP, Eagle KA, Smith SCJ, Hoffman E et al. Adherence to secondary prevention medications and four-year outcomes in outpatients with atherosclerosis. *American Journal of Medicine*. 2013; 126(8):693-700
- 721 Kushner DS, Peters KM, Johnson-Greene D. Evaluating Siebens Domain Management Model for inpatient rehabilitation to increase functional independence and discharge rate to home in geriatric patients. *Archives of Physical Medicine & Rehabilitation*. Philadelphia, Pennsylvania: W B Saunders. 2015; 96(7):1310-1318
- 722 Kutner JS, Blatchford PJ, Taylor DH, Jr., Ritchie CS, Bull JH, Fairclough DL et al. Safety and benefit of discontinuing statin therapy in the setting of advanced, life-limiting illness: a randomized clinical trial. *JAMA Internal Medicine*. 2015; 175(5):691-700
- 723 Kwok T, Lee J, Woo J, Lee DT, Griffith S. A randomized controlled trial of a community nurse-supported hospital discharge programme in older patients with chronic heart failure. *Journal of Clinical Nursing*. 2008; 17(1):109-117
- 724 Laakkonen ML, Holttä EH, Savikko N, Strandberg TE, Suominen M, Pitkälä KH. Psychosocial group intervention to enhance self-management skills of people with dementia and their caregivers: study protocol for a randomized controlled trial. *Trials*. 2012; 13:133
- 725 Lachs MS, Williams CS, O'Brien S, Pillemer KA. Adult protective service use and nursing home placement. *Gerontologist*. 2002; 42(6):734-739
- 726 Lai AY, Ishikawa H, Kiuchi T, Mooppil N, Griva K. Communicative and critical health literacy, and self-management behaviors in end-stage renal disease patients with diabetes on hemodialysis. *Patient Education and Counseling*. 2013; 91(2):221-227
- 727 Lalic J, Radovanovic RV, Mitic B, Nikolic V, Spasic A, Koracevic G. Medication adherence in outpatients with arterial hypertension. *Acta Facultatis Medicae Naissensis*. 2013; 30(4):209-218
- 728 Lam A. Practice innovations: delivering medication therapy management services via Videoconference interviews. *Consultant Pharmacist*. 2011; 26(10):764-774
- 729 Lam LCW, Lee JSW, Chung JCC, Lau A, Woo J, Kwok TCY. A randomized controlled trial to examine the effectiveness of case management model for community dwelling older persons with mild dementia in Hong Kong. *International Journal of Geriatric Psychiatry*. 2010; 25(4):395-402
- 730 Lamba S, Nagurka R, Desai KK, Chun SJ, Holland B, Koneru B. Self-reported non-adherence to immune-suppressant therapy in liver transplant recipients: Demographic, interpersonal, and intrapersonal factors. *Clinical Transplantation*. 2012; 26(2):328-335
- 731 Lambie M, Rayner HC, Bragg-Gresham JL, Pisoni RL, Andreucci VE, Canaud B et al. Starting and withdrawing haemodialysis--associations between nephrologists' opinions, patient

- characteristics and practice patterns (data from the Dialysis Outcomes and Practice Patterns Study). *Nephrology, Dialysis, Transplantation*. 2006; 21(10):2814-2820
- 732 Lamers F, Jonkers CCM, Bosma H, Kempen GIJM, Meijer JAMJ, Penninx BWJH et al. A minimal psychological intervention in chronically ill elderly patients with depression: a randomized trial. *Psychotherapy and Psychosomatics*. 2010; 79(4):217-226
- 733 Lampela P, Hartikainen S, Lavikainen P, Sulkava R, Huupponen R. Effects of medication assessment as part of a comprehensive geriatric assessment on drug use over a 1-year period: a population-based intervention study. *Drugs and Aging*. 2010; 27(6):507-521
- 734 Lampela P, Lavikainen P, Huupponen R, Leskinen E, Hartikainen S. Comprehensive geriatric assessment decreases prevalence of orthostatic hypotension in older persons. *Scandinavian Journal of Public Health*. 2013; 41(4):351-358
- 735 Lang P, Vogt-Ferrier N, Hasso Y, Le Saint L, Drame M, Zekry D et al. Interdisciplinary geriatric and psychiatric care reduces potentially inappropriate prescribing in the hospital: interventional study in 150 acutely ill elderly patients with mental and somatic comorbid conditions. *Journal of the American Medical Directors Association*. 2012; 13(4):406-407
- 736 Langer S, Chew-Graham C, Hunter C, Guthrie EA, Salmon P. Why do patients with long-term conditions use unscheduled care? A qualitative literature review. *Health and Social Care in the Community*. 2013; 21(4):339-351
- 737 Langford HG, Blaurock MD, Oberman A, Hawkins CM, Curb JD, Cutter GR et al. Return of hypertension after withdrawal of prolonged antihypertensive therapy, effect of weight loss, sodium reduction, and baseline factors. *Transactions of the Association of American Physicians*. 1984; 97:190-196
- 738 Lapane KL, Hughes CM, Daiello LA, Cameron KA, Feinberg J. Effect of a pharmacist-led multicomponent intervention focusing on the medication monitoring phase to prevent potential adverse drug events in nursing homes. *Journal of the American Geriatrics Society*. 2011; 59(7):1238-1245
- 739 Lasser KE, Ayanian JZ, Fletcher RH, Good MJD. Barriers to colorectal cancer screening in community health centers: a qualitative study. *BMC Family Practice*. 2008; 9:15
- 740 Lassere MN, Baker S, Parle A, Sara A, Johnson KR. Improving quality of care and long-term health outcomes through continuity of care with the use of an electronic or paper patient-held portable health file (COMMUNICATE): study protocol for a randomized controlled trial. *Trials*. 2015; 16:253
- 741 Lattanzio F, Laino I, Pedone C, Corica F, Maltese G, Salerno G et al. Geriatric conditions and adverse drug reactions in elderly hospitalized patients. *Journal of the American Medical Directors Association*. 2012; 13(2):96-99
- 742 Le Manach Y, Godet G, Coriat P, Martinon C, Bertrand M, Fleron MH et al. The impact of postoperative discontinuation or continuation of chronic statin therapy on cardiac outcome after major vascular surgery. *Anesthesia and Analgesia*. 2007; 104(6):1326-contents
- 743 Lee BW, Murakami Y, Duncan MT, Kao AA, Huang JY, Lin S et al. Patient-related and system-related barriers to glaucoma follow-up in a county hospital population. *Investigative Ophthalmology and Visual Science*. 2013; 54(10):6542-6548

- 744 Lee H, Yoon JY, Lim Y, Jung H, Kim S, Yoo Y et al. The effect of nurse-led problem-solving therapy on coping, self-efficacy and depressive symptoms for patients with chronic obstructive pulmonary disease: a randomised controlled trial. *Age and Ageing*. 2015; 44(3):397-403
- 745 Lee KS, Lee Y, Back JH, Son SJ, Choi SH, Chung YK et al. Effects of a multidomain lifestyle modification on cognitive function in older adults: an eighteen-month community-based cluster randomized controlled trial. *Psychotherapy and Psychosomatics*. 2014; 83(5):270-278
- 746 Lee L, Heckman G, Molnar FJ. Frailty: Identifying elderly patients at high risk of poor outcomes. *Canadian Family Physician*. 2015; 61(3):227-231
- 747 Lee SJ, Lindquist K, Segal MR, Covinsky KE. Development and validation of a prognostic index for 4-year mortality in older adults. *JAMA*. 2006; 295(7):801-808
- 748 Lee SH, Kwon HS, Park YM, Ko SH, Choi YH, Yoon KH et al. Statin discontinuation after achieving a target low density lipoprotein cholesterol level in type 2 diabetic patients without cardiovascular disease: a randomized controlled study. *Diabetes and Metabolism*. 2014; 38(1):64-73
- 749 Lee VW, Pang KK, Hui KC, Kwok JC, Leung SL, Yu DSF et al. Medication adherence: Is it a hidden drug-related problem in hidden elderly? *Geriatrics and Gerontology International*. 2013; 13(4):978-985
- 750 Leendertse AJ, de Koning GHP, Goudswaard AN, Belitser SV, Verhoef M, de Gier HJ et al. Preventing hospital admissions by reviewing medication (PHARM) in primary care: an open controlled study in an elderly population. *Journal of Clinical Pharmacy and Therapeutics*. 2013; 38(5):379-387
- 751 Leendertse AJ, Egberts ACG, Stoker LJ, van den Bemt PMLA, HARM Study Group. Frequency of and risk factors for preventable medication-related hospital admissions in the Netherlands. *Archives of Internal Medicine*. 2008; 168(17):1890-1896
- 752 Legrain S, Tubach F, Bonnet-Zamponi D, Lemaire A, Aquino JP, Paillaud E et al. A new multimodal geriatric discharge-planning intervention to prevent emergency visits and rehospitalizations of older adults: the optimization of medication in AGEd multicenter randomized controlled trial. *Journal of the American Geriatrics Society*. 2011; 59(11):2017-2028
- 753 Lekas HM, Siegel K, Leider J. Challenges facing providers caring for HIV/HCV-coinfected patients. *Qualitative Health Research*.: Sage Publications. 2012; 22(1):54-66
- 754 Lenferink A, Frith P, van der Valk P, Buckman J, Sladek R, Cafarella P et al. A self-management approach using self-initiated action plans for symptoms with ongoing nurse support in patients with Chronic Obstructive Pulmonary Disease (COPD) and comorbidities: the COPE-III study protocol. *Contemporary Clinical Trials*. 2013; 36:81-89
- 755 Lenihan CR, Hurley MP, Tan JC. Comorbidities and kidney transplant evaluation in the elderly. *American Journal of Nephrology*. 2013; 38(3):204-211
- 756 Lenzen MJ, Boersma E, Bertrand ME, Maier W, Moris C, Piscione F et al. Management and outcome of patients with established coronary artery disease: the Euro Heart Survey on coronary revascularization. *European Heart Journal*. 2005; 26(12):1169-1179

- 757 Lenzi J, Mongardi M, Rucci P, Di Ruscio E, Vizioli M, Randazzo C et al. Sociodemographic, clinical and organisational factors associated with delayed hospital discharges: a cross-sectional study. *BMC Health Services Research*. 2014; 14:128
- 758 Lesaffre E, Kocmanova D, Lemos PA, Disco CMC, Serruys PW. A retrospective analysis of the effect of noncompliance on time to first major adverse cardiac event in LIPS. *Clinical Therapeutics*. 2003; 25(9):2431-2447
- 759 Leung AYM, Kwan CW, Chi I. Residents with Alzheimer's disease in long-term care facilities in Hong Kong: patterns of hospitalization and emergency room use. *Aging and Mental Health*. 2013; 17(8):959-965
- 760 Levine SK, Sachs GA, Jin L, Meltzer D. A prognostic model for 1-year mortality in older adults after hospital discharge. *American Journal of Medicine*. 2007; 120(5):455-460
- 761 Levy C, Kheirbek R, Alemi F, Wojtusiak J, Sutton B, Williams AR et al. Predictors of six-month mortality among nursing home residents: diagnoses may be more predictive than functional disability. *Journal of Palliative Medicine*. 2015; 18(2):100-106
- 762 Lewin G, Allan J, Patterson C, Knuiiman M, Boldy D, Hendrie D. A comparison of the home-care and healthcare service use and costs of older Australians randomised to receive a restorative or a conventional home-care service. *Health and Social Care in the Community*. 2014; 22(3):328-336
- 763 Lewis KE, Annandale JA, Warm DL, Rees SE, Hurlin C, Blyth H et al. Does home telemonitoring after pulmonary rehabilitation reduce healthcare use in optimized COPD? A pilot randomized trial. *Journal of Chronic Obstructive Pulmonary Disease*. 2010; 7(1):44-50
- 764 Li CM, Chen CY, Li CY, Wang WD, Wu SC. The effectiveness of a comprehensive geriatric assessment intervention program for frailty in community-dwelling older people: a randomized, controlled trial. *Archives of Gerontology and Geriatrics*. 2010; 50 Suppl 1:S39-S42
- 765 Li TR, Li Y, Zhang L, Tan AJ. Effects of comprehensive geriatric assessment intervention on Chinese han older patients with multiple chronic comorbidities. *Journal of the American Geriatrics Society*. 2015; 63:S397-S398
- 766 Liao PJ, Shih CP, Mao CT, Deng ST, Hsieh MC, Hsu KH. The cutaneous adverse drug reactions: risk factors, prognosis and economic impacts. *International Journal of Clinical Practice*. 2013; 67(6):576-584
- 767 Liddy C, Dusseault JJ, Dahrouge S, Hogg W, Lemelin J, Humbert J. Telehomecare for patients with multiple chronic illnesses: Pilot study. *Canadian Family Physician*. 2008; 54(3):58-65
- 768 Lifshitz AE, Goldstein LH, Sharist M, Strugo R, Asulin E, Bar Haim S et al. Medication prescribing errors in the prehospital setting and in the ED. *American Journal of Emergency Medicine*. 2012; 30(5):726-731
- 769 Lihavainen K, Sipila S, Rantanen T, Seppanen J, Lavikainen P, Sulkava R et al. Effects of comprehensive geriatric intervention on physical performance among people aged 75 years and over. *Aging Clinical and Experimental Research*. 2012; 24(4):331-338
- 770 Lihavainen K, Sipila S, Rantanen T, Kauppinen M, Sulkava R, Hartikainen S. Effects of comprehensive geriatric assessment and targeted intervention on mobility in persons aged 75 years and over: a randomized controlled trial. *Clinical Rehabilitation*. 2012; 26(4):314-326

- 771 Lima-Costa MF, Peixoto SV, Matos DL, Firmo JOA, Uchoa E. Predictors of 10-year mortality in a population of community-dwelling Brazilian elderly: the Bambui Cohort Study of Aging. *Cadernos De Saude Publica*. 2011; 27 Suppl 3:S360-S369
- 772 Linden A, Butterworth S. A comprehensive hospital-based intervention to reduce readmissions for chronically ill patients: a randomized controlled trial. *American Journal of Managed Care*. 2014; 20(10):783-792
- 773 Lisby M, Thomsen A, Nielsen LP, Lyhne NM, Breum-Leer C, Fredberg U et al. The effect of systematic medication review in elderly patients admitted to an acute ward of internal medicine. *Basic and Clinical Pharmacology and Toxicology*. 2010; 106(5):422-427
- 774 Litaker D, Mion L, Planavsky L, Kippes C, Mehta N, Frolkis J. Physician - nurse practitioner teams in chronic disease management: the impact on costs, clinical effectiveness, and patients' perception of care. *Journal of Interprofessional Care*. 2003; 17(3):223-237
- 775 Loeb DF, Binswanger IA, Candrian C, Bayliss EA. Primary care physician insights into a typology of the complex patient in primary care. *Annals of Family Medicine*. 2015; 13(5):451-455
- 776 Loffler C, Drewelow E, Paschka SD, Frankenstein M, Eger J, Jatsch L et al. Optimizing polypharmacy among elderly hospital patients with chronic diseases--study protocol of the cluster randomized controlled POLITE-RCT trial. *Implementation Science*. 2014; 9:151
- 777 Lorig KR, Ritter P, Stewart AL, Sobel DS, Brown BW, Jr., Bandura A et al. Chronic disease self-management program: 2-year health status and health care utilization outcomes. *Medical Care*. 2001; 39(11):1217-1223
- 778 Lorig KR, Ritter PL, Gonzalez VM. Hispanic chronic disease self-management: a randomized community-based outcome trial. *Nursing Research*. 2003; 52(6):361-369
- 779 Lorig KR, Ritter PL, Laurent DD, Plant K. Internet-based chronic disease self-management: a randomized trial. *Medical Care*. 2006; 44(11):964-971
- 780 Lorig KR, Sobel DS, Stewart AL, Brown BW, Jr., Bandura A, Ritter P et al. Evidence suggesting that a chronic disease self-management program can improve health status while reducing hospitalization: a randomized trial. *Medical Care*. 1999; 37(1):5-14
- 781 Low LL, Lee KH, Hock Ong ME, Wang S, Tan SY, Thumboo J et al. Predicting 30-day readmissions: performance of the LACE index compared with a regression model among general medicine patients in Singapore. *BioMed Research International*. 2015; 2015:169870
- 782 Loza E, Lajas C, Andreu JL, Balsa A, Gonzalez-Alvaro I, Illera O et al. Consensus statement on a framework for the management of comorbidity and extra-articular manifestations in rheumatoid arthritis. *Rheumatology International*. 2015; 35(3):445-458
- 783 Lu CY, Barratt J, Vitry A, Roughead E. Charlson and Rx-Risk comorbidity indices were predictive of mortality in the Australian health care setting. *Journal of Clinical Epidemiology*. 2011; 64(2):223-228
- 784 Lu CY, Roughead E. Determinants of patient-reported medication errors: a comparison among seven countries. *International Journal of Clinical Practice*. 2011; 65(7):733-740
- 785 Lucas CP, Darga LL, Fox AA, Stimpel M. A study of the efficacy and safety of moexipril in mild to moderate hypertension. *American Journal of Therapeutics*. 1995; 2(11):886-892

- 786 Luce S, De Breucker S, Van Gossum A, Demols A, Mekinda Z, Ena G et al. How to identify older patients with cancer who should benefit from comprehensive geriatric assessment? *Journal of Geriatric Oncology*. 2012; 3(4):351-358
- 787 Luciani A, Ascione G, Bertuzzi C, Marussi D, Codeca C, Di Maria G et al. Detecting disabilities in older patients with cancer: comparison between comprehensive geriatric assessment and vulnerable elders survey-13. *Journal of Clinical Oncology*. 2010; 28(12):2046-2050
- 788 Luck T, Motzek T, Lupp M, Matschinger H, Fleischer S, Sesselmann Y et al. Effectiveness of preventive home visits in reducing the risk of falls in old age: a randomized controlled trial. *Clinical Interventions In Aging*. 2013; 8:697-702
- 789 Ludman EJ, Peterson D, Katon WJ, Lin EH, Von Korff M, Ciechanowski P et al. Improving confidence for self care in patients with depression and chronic illnesses. *Behavioral Medicine*. 2013; 39:1-6
- 790 Luijckx HD, Loeffen MJW, Lagro-Janssen AL, van Weel C, Lucassen PL, Schermer TR. GPs' considerations in multimorbidity management: a qualitative study. *British Journal of General Practice*. 2012; 62(600):e503-e510
- 791 Luo TYS, Wong GHY, Kwan JSK, Tang JYM, Chi I. Predicting adverse health outcomes in nursing homes: a 9-year longitudinal study and development of the FRAIL-Minimum Data Set (MDS) quick screening tool. *Journal of the American Medical Directors Association*. 2015; 16(12):1042-1047
- 792 Lupari M, Coates V, Adamson G, Crealey G. 'We're just not getting it right'- how should we provide care to the older person with multi-morbid chronic conditions? *Journal of Clinical Nursing*. 2011; 20(9/10):1225-1235
- 793 Lupp M, Luck T, Weyerer S, Konig HH, Braehler E, Riedel-Heller SG. Prediction of institutionalization in the elderly. A systematic review. *Age and Ageing*. 2010; 39(1):31-38
- 794 Lynch EB, Liebman R, Ventrelle J, Avery EF, Richardson D. A self-management intervention for African Americans with comorbid diabetes and hypertension: a pilot randomized controlled trial. *Preventing Chronic Disease*. 2014; 11:E90
- 795 MacDonald TM, Morant SV, Mozaffari E. Drug treatment discontinuation and achievement of target blood pressure and cholesterol in United Kingdom primary care. *Current Medical Research and Opinion*. 2007; 23(11):2765-2774
- 796 Macedo AF, Alves C, Craveiro N, Marques FB. Multiple drug exposure as a risk factor for the seriousness of adverse drug reactions. *Journal of Nursing Management*. 2011; 19(3):395-399
- 797 Maciejewski ML, Powers BJ, Sanders LL, Farley JF, Hansen RA, Sleath B et al. The intersection of patient complexity, prescriber continuity and acute care utilization. *Journal of General Internal Medicine*. 2014; 29(4):594-601
- 798 MacLaughlin EJ, Raehl CL, Treadway AK, Sterling TL, Zoller DP, Bond CA. Assessing medication adherence in the elderly: which tools to use in clinical practice? *Drugs and Aging*. 2005; 22(3):231-255
- 799 MacNeil Vroomen JL, Boorsma M, Bosmans JE, Frijters DH, Nijpels G, van Hout HP. Is it time for a change? A cost-effectiveness analysis comparing a Multidisciplinary Integrated Care model for residential homes to usual care. *PLoS ONE*. Netherlands 2012; 7(5):e37444

- 800 Maggiore RJ, Dale W, Gross CP, Feng T, Tew WP, Mohile SG et al. Polypharmacy and potentially inappropriate medication use in older adults with cancer undergoing chemotherapy: effect on chemotherapy-related toxicity and hospitalization during treatment. *Journal of the American Geriatrics Society*. 2014; 62(8):1505-1512
- 801 Maland LJ, Lutz LJ, Castle CH. Effects of withdrawing diuretic therapy on blood pressure in mild hypertension. *Hypertension*. 1983; 5(4):539-544
- 802 Malhotra S, Karan RS, Pandhi P, Jain S. Drug related medical emergencies in the elderly: role of adverse drug reactions and non-compliance. *Postgraduate Medical Journal*. 2001; 77(913):703-707
- 803 Mandavi, D'Cruz S, Sachdev A, Tiwari P. Adverse drug reactions & their risk factors among Indian ambulatory elderly patients. *Indian Journal of Medical Research*. 2012; 136(3):404-410
- 804 Manias E, Claydon-Platt K, McColl GJ, Bucknall TK, Brand CA. Managing complex medication regimens: perspectives of consumers with osteoarthritis and healthcare professionals. *Annals of Pharmacotherapy*. 2007; 41(5):764-771
- 805 Mann BS, Manns BJ, Dart A, Kappel J, Molzahn A, Naimark D et al. An assessment of dialysis provider's attitudes towards timing of dialysis initiation in Canada. *Canadian Journal of Kidney Health and Disease*. 2014; 1:3
- 806 Mannesse CK, Derkx FH, de Ridder MA, Man in 't Veld AJ, van der Cammen TJ. Contribution of adverse drug reactions to hospital admission of older patients. *Age and Ageing*. 2000; 29(1):35-39
- 807 Mansur N, Weiss A, Beloosesky Y. Relationship of in-hospital medication modifications of elderly patients to postdischarge medications, adherence, and mortality. *Annals of Pharmacotherapy*. 2008; 42(6):783-789
- 808 Manzano L, Babalis D, Roughton M, Shibata M, Anker SD, Ghio S et al. Predictors of clinical outcomes in elderly patients with heart failure. *European Journal of Heart Failure*. 2011; 13(5):528-536
- 809 Marcum ZA, Amuan ME, Hanlon JT, Aspinall SL, Handler SM, Ruby CM et al. Prevalence of unplanned hospitalizations caused by adverse drug reactions in older veterans. *Journal of the American Geriatrics Society*. 2012; 60(1):34-41
- 810 Marek KD, Stetzer F, Ryan PA, Bub LD, Adams SJ, Schlidt A et al. Nurse care coordination and technology effects on health status of frail older adults via enhanced self-management of medication: randomized clinical trial to test efficacy. *Nursing Research*. 2013; 62(4):269-278
- 811 Marinella MA, Jones N, Markert RJ. Acute care of patients aged 95 to 99 years: experience in a community teaching hospital. *Southern Medical Journal*. 2000; 93(7):677-680
- 812 Markenson JA, Gibofsky A, Palmer WR, Keystone EC, Schiff MH, Feng J et al. Persistence with anti-tumor necrosis factor therapies in patients with rheumatoid arthritis: observations from the RADIUS registry. *Journal of Rheumatology*. 2011; 38(7):1273-1281
- 813 Markle-Reid M, Browne G, Gafni A. Nurse-led health promotion interventions improve quality of life in frail older home care clients: lessons learned from three randomized trials in Ontario, Canada. *Journal of Evaluation in Clinical Practice*. 2013; 19(1):118-131

- 814 Marrett E, Zhang Q, Kanitscheider C, Davies MJ, Radican L, Feinglos MN. Physician reasons for nonpharmacologic treatment of hyperglycemia in older patients newly diagnosed with type 2 diabetes mellitus. *Diabetes Therapy*. 2012; 3(1):1-12
- 815 Marsteller JA, Hsu YJ, Reider L, Frey K, Wolff J, Boyd C et al. Physician satisfaction with chronic care processes: a cluster-randomized trial of guided care. *Annals of Family Medicine*. 2010; 8:308-315
- 816 Martin MY, Kohler C, Kim Y, Kratt P, Schoenberger Y, Litaker MS et al. Taking less than prescribed: Medication nonadherence and provider-patient relationships in lower-income, rural minority adults with hypertension. *Journal of Clinical Hypertension*. 2010; 12(9):706-713
- 817 Martin-Lesende I, Orruno E, Cairo C, Bilbao A, Asua J, Romo MI et al. Assessment of a primary care-based telemonitoring intervention for home care patients with heart failure and chronic lung disease. The TELBIL study. *BMC Health Services Research*. 2011; 11:56
- 818 Martinez-Garcia A, Moreno-Conde A, Jodar-Sanchez F, Leal S, Parra C. Sharing clinical decisions for multimorbidity case management using social network and open-source tools. *Journal of Biomedical Informatics*. 2013; 46(6):977-984
- 819 Martinez-Velilla N, Cambra-Contin K, Ibanez-Beroiz B. Comorbidity and prognostic indices do not improve the 5-year mortality prediction of components of comprehensive geriatric assessment in hospitalized older patients. *BMC Geriatrics*. 2014; 14:64
- 820 Marusic S, Sicaja M, Obreli Neto PR, Franic M, Marinovic I, Bacic-Vrca V. Adverse drug reactions in elderly patients following discharge from an internal medicine clinic. *International Journal of Clinical Pharmacology and Therapeutics*. 2014; 52(10):906-913
- 821 Marzolini S, Leung YM, Alter DA, Wu G, Grace SL. Outcomes associated with cardiac rehabilitation participation in patients with musculoskeletal comorbidities. *European Journal of Physical and Rehabilitation Medicine*. 2013; 49(6):775-783
- 822 Masters S, Oliver-Baxter J, Barton C, Summers M, Howard S, Roeger L et al. Programmes to support chronic disease self-management: Should we be concerned about the impact on spouses? *Health and Social Care in the Community*. 2013; 21(3):315-326
- 823 Mathew E, Rajiah K. Assessment of medication adherence in type-2 diabetes patients on poly pharmacy and the effect of patient counseling given to them in a multispecialty hospital. *Journal of Basic and Clinical Pharmacy*. 2014; 5(1):15-18
- 824 Mathew R, Young Y, Shrestha S. Factors associated with potentially preventable hospitalization among nursing home residents in New York State with chronic kidney disease. *Journal of the American Medical Directors Association*. 2012; 13(4):337-343
- 825 Matsumura K, Arima H, Tominaga M, Ohtsubo T, Sasaguri T, Fujii K et al. Impact of antihypertensive medication adherence on blood pressure control in hypertension: the COMFORT study. *QJM*. 2013; 106(10):909-914
- 826 Matsuzawa Y, Konishi M, Akiyama E, Suzuki H, Nakayama N, Kiyokuni M et al. Association between gait speed as a measure of frailty and risk of cardiovascular events after myocardial infarction. *Journal of the American College of Cardiology*. 2013; 61(19):1964-1972

- 827 Matthews M, Lucas A, Boland R, Hirth V, Odenheimer G, Wieland D et al. Use of a questionnaire to screen for frailty in the elderly: an exploratory study. *Aging Clinical and Experimental Research*. 2004; 16(1):34-40
- 828 Matzen LE, Jepsen DB, Ryg J, Masud T. Functional level at admission is a predictor of survival in older patients admitted to an acute geriatric unit. *BMC Geriatrics*. 2012; 12:32
- 829 Mazzaglia G, Roti L, Corsini G, Colombini A, Maciocco G, Marchionni N et al. Screening of older community-dwelling people at risk for death and hospitalization: the Assistenza Socio-Sanitaria in Italia project. *Journal of the American Geriatrics Society*. 2007; 55(12):1955-1960
- 830 McCall N, Cromwell J. Results of the Medicare Health Support disease-management pilot program. *New England Journal of Medicine*. 2011; 365(18):1704-1712
- 831 McCarthy L, Dolovich L, Haq M, Thabane L, Kaczorowski J. Frequency of risk factors that potentially increase harm from medications in older adults receiving primary care. *Canadian Journal of Clinical Pharmacology*. 2007; 14(3):e283-e290
- 832 McCusker J, Cole M, Yaffe M, Sussman T, Lavoie KL, Strumpf E et al. A feasibility study of a telephone-supported self-care intervention for depression among adults with a comorbid chronic physical illness in primary care. *Mental Health in Family Medicine*. 2012; 9:257-273
- 833 McCusker J, Cole MG, Yaffe M, Strumpf E, Sewitch M, Sussman T et al. A randomized trial of a depression self-care toolkit with or without lay telephone coaching for primary care patients with chronic physical conditions. *General Hospital Psychiatry*. 2015; 37(3):257-265
- 834 McDowell JE, McClean S, FitzGibbon F, Tate S. A randomised clinical trial of the effectiveness of home-based health care with telemonitoring in patients with COPD. *Journal of Telemedicine and Telecare*. 2015; 21(2):80-87
- 835 McEntee ML, Cuomo LR, Dennison CR. Patient-, provider-, and system-level barriers to heart failure care. *Journal of Cardiovascular Nursing*. 2009; 24(4):290-298
- 836 McGee HM, O'Hanlon A, Barker M, Hickey A, Montgomery A, Conroy R et al. Vulnerable older people in the community: relationship between the Vulnerable Elders Survey and health service use. *Journal of the American Geriatrics Society*. 2008; 56(1):8-15
- 837 McGinnis BD, Olson KL, Delate TMA, Stolcpart RS. Statin adherence and mortality in patients enrolled in a secondary prevention program. *American Journal of Managed Care*. 2009; 15(10):689-695
- 838 McGowan MP, Treating to New Target (TNT) Study Group. There is no evidence for an increase in acute coronary syndromes after short-term abrupt discontinuation of statins in stable cardiac patients. *Circulation*. 2004; 110(16):2333-2335
- 839 McGregor M, Lin EHB, Katon WJ. TEAMcare: an integrated multicondition collaborative care program for chronic illnesses and depression. *Journal of Ambulatory Care Management*. 2011; 34(2):152-162
- 840 McMartin K. Discharge planning in chronic conditions: an evidence-based analysis. *Ontario Health Technology Assessment Series*. 2013; 13(4):1-72

- 841 McVey LJ, Becker PM, Saltz CC, Feussner JR, Cohen HJ. Effect of a geriatric consultation team on functional status of elderly hospitalized patients. A randomized, controlled clinical trial. *Annals of Internal Medicine*. 1989; 110(1):79-84
- 842 Md Yusof MY, Horan MA, Jones M, McInnes L, Rabbitt PMA, Pendleton N. Developing a self-reported comorbidity index to predict mortality of community-dwelling older adults. *Archives of Gerontology and Geriatrics*. 2010; 50(3):e63-e67
- 843 Mehta SH, Genberg BL, Astemborski J, Kavasery R, Kirk GD, Vlahov D et al. Limited uptake of hepatitis C treatment among injection drug users. *Journal of Community Health*. 2008; 33(3):126-133
- 844 Melis RJ, van Eijken MI, Borm GF, Wensing M, Adang E, Van De Lisdonk EH et al. The design of the Dutch EASYcare study: a randomised controlled trial on the effectiveness of a problem-based community intervention model for frail elderly people [NCT00105378]. *BMC Health Services Research*. 2005; 5:65
- 845 Menendez ME, Ring D, Harris MB, Cha TD. Predicting in-hospital mortality in elderly patients with cervical spine fractures: a comparison of the Charlson and Elixhauser comorbidity measures. *Spine*. 2015; 40(11):809-815
- 846 Menon AS, Kondapavalru P, Krishna P, Chrismer JB, Raskin A, Hebel JR et al. Evaluation of a portable low cost videophone system in the assessment of depressive symptoms and cognitive function in elderly medically ill veterans. *Journal of Nervous and Mental Disease*. 2001; 189:399-401
- 847 Meranius MS, Hammar LM. How does the healthcare system affect medication self-management among older adults with multimorbidity? *Scandinavian Journal of Caring Sciences*.: Wiley-Blackwell Publishing Ltd. Blackwell Publishing. 2015;
- 848 Mercer SW, Jani BD, Maxwell M, Wong SYS, Watt GCM. Patient enablement requires physician empathy: a cross-sectional study of general practice consultations in areas of high and low socioeconomic deprivation in Scotland. *BMC Family Practice*. 2012; 13:6
- 849 Mercer SW, Watt GCM. The inverse care law: clinical primary care encounters in deprived and affluent areas of Scotland. *Annals of Family Medicine*. 2007; 5(6):503-510
- 850 Mercier E, Giraudeau B, Ginies G, Perrotin D, Dequin PF. Iatrogenic events contributing to ICU admission: a prospective study. *Intensive Care Medicine*. 2010; 36(6):1033-1037
- 851 Metcalfe A, Lix LM, Johnson JA, Currie G, Lyon AW, Bernier F et al. Validation of an obstetric comorbidity index in an external population. *BJOG*. 2015; 122(13):1748-1755
- 852 Metra M, Torp-Pedersen C, Cleland JGF, Di Lenarda A, Komajda M, Remme WJ et al. Should beta-blocker therapy be reduced or withdrawn after an episode of decompensated heart failure? Results from COMET. *European Journal of Heart Failure*. 2007; 9(9):901-909
- 853 Metzelthin SF, Daniels R, van Rossum E, de Witte L, van den Heuvel WJ, Kempen GI. The psychometric properties of three self-report screening instruments for identifying frail older people in the community. *BMC Public Health*. 2010; 10:176
- 854 Metzelthin SF, van Rossum E, de Witte LP, Ambergen AW, Hobma SO, Sipers W et al. Effectiveness of interdisciplinary primary care approach to reduce disability in community dwelling frail older people: cluster randomised controlled trial. *BMJ*. 2013; 347:f5264

- 855 Michalska D, Stepan JJ, Basson BR, Pavo I. The effect of raloxifene after discontinuation of long-term alendronate treatment of postmenopausal osteoporosis. *Journal of Clinical Endocrinology and Metabolism*. 2006; 91(3):870-877
- 856 Middeke M, Richter WO, Schwandt P, Beck B, Holzgreve H. Normalization of lipid metabolism after withdrawal from antihypertensive long-term therapy with beta blockers and diuretics. *Arteriosclerosis*. 1990; 10(1):145-147
- 857 Millard T, Elliott J, Girdler S. Self-management education programs for people living with HIV/AIDS: a systematic review. *AIDS Patient Care and Stds*. 2013; 27:103-113
- 858 Miller PD, Watts NB, Licata AA, Harris ST, Genant HK, Wasnich RD et al. Cyclical etidronate in the treatment of postmenopausal osteoporosis: efficacy and safety after seven years of treatment. *American Journal of Medicine*. 1997; 103(6):468-476
- 859 Min L, Yoon W, Mariano J, Wenger NS, Elliott MN, Kamberg C et al. The vulnerable elders-13 survey predicts 5-year functional decline and mortality outcomes in older ambulatory care patients. *Journal of the American Geriatrics Society*. 2009; 57(11):2070-2076
- 860 Min LC, Wenger NS, Fung C, Chang JT, Ganz DA, Higashi T et al. Multimorbidity is associated with better quality of care among vulnerable elders. *Medical Care*.: Lippincott Williams & Wilkins. 2007; 45(6):480-488
- 861 Mira JJ, Navarro I, Botella F, Borrás F, Nuno-Solinis R, Orozco D et al. A Spanish pillbox app for elderly patients taking multiple medications: randomized controlled trial. *Journal of Medical Internet Research*. 2014; 16(4):e99
- 862 Mira JJ, Orozco-Beltran D, Perez-Jover V, Martinez-Jimeno L, Gil-Guillen VF, Carratala-Munuera C et al. Physician patient communication failure facilitates medication errors in older polymedicated patients with multiple comorbidities. *Family Practice*. 2013; 30(1):56-63
- 863 Mishuris RG, Stewart M, Fix GM, Marcello T, McInnes DK, Hogan TP et al. Barriers to patient portal access among veterans receiving home-based primary care: A qualitative study. *Health Expectations*.: Wiley-Blackwell Publishing Ltd. Blackwell Publishing. 2014;
- 864 Mistiaen P, Francke AL, Poot E. Interventions aimed at reducing problems in adult patients discharged from hospital to home: a systematic meta-review. *BMC Health Services Research*. 2007; 7:47
- 865 Mitchell KE, Johnson-Warrington V, Apps LD, Bankart J, Sewell L, Williams JE et al. A self-management programme for COPD: a randomised controlled trial. *European Respiratory Journal*. 2014; 44(6):1538-1547
- 866 Mitchell RS, Padwal RS, Chuck AW, Klarenbach SW. Cancer screening among the overweight and obese in Canada. *American Journal of Preventive Medicine*.: Elsevier Science. 2008; 35(2):127-132
- 867 Mitnitski A, Fallah N, Rockwood MR, Rockwood K. Transitions in cognitive status in relation to frailty in older adults: a comparison of three frailty measures. *Journal of Nutrition, Health and Aging*. 2011; 15(10):863-867
- 868 Modi M, McMorris C, Palucka A, Raina P, Lunskey Y. Predictors of specialized inpatient admissions for adults with intellectual disability. *American Journal on Intellectual and Developmental Disabilities*. 2015; 120(1):46-57

- 869 Mohile SG, Bylow K, Dale W, Dignam J, Martin K, Petrylak DP et al. A pilot study of the vulnerable elders survey-13 compared with the comprehensive geriatric assessment for identifying disability in older patients with prostate cancer who receive androgen ablation. *Cancer*. 2007; 109(4):802-810
- 870 Molina-Garrido MJ, Guillen-Ponce C. Comparison of two frailty screening tools in older women with early breast cancer. *Critical Reviews in Oncology-Hematology*. 2011; 79(1):51-64
- 871 Molina-Garrido MJ, Guillen-Ponce C. Ability of the comprehensive geriatric assessment to predict frailty in older people diagnosed with cancer in a general hospital. *European Oncology and Haematology*. 2012; 8(2):85-88
- 872 Moller UO, Kristensson J, Midlov P, Ekdahl C, Jakobsson U. Effects of a one-year home-based case management intervention on falls in older people: a randomized controlled trial. *Journal of Aging and Physical Activity*. 2014; 22(4):457-464
- 873 Monane M, Monane S, Semla T. Optimal medication use in elders: Key to successful aging. *Western Journal of Medicine*. 1997; 167(4):233-237
- 874 Monroe AK, Rowe TL, Moore RD, Chander G. Medication adherence in HIV-positive patients with diabetes or hypertension: a focus group study. *BMC Health Services Research*. 2013; 13:488
- 875 Monteserin R, Brotons C, Moral I, Altimir S, San Jose A, Santauegenia S et al. Effectiveness of a geriatric intervention in primary care: a randomized clinical trial. *Family Practice*. 2010; 27(3):239-245
- 876 Morandi A, Bellelli G, Vasilevskis EE, Turco R, Guerini F, Torpilliesi T et al. Predictors of rehospitalization among elderly patients admitted to a rehabilitation hospital: the role of polypharmacy, functional status, and length of stay. *Journal of the American Medical Directors Association*. 2013; 14(10):761-767
- 877 Morgan M, Dunbar J, Reddy P, Coates M, Leahy R. The TrueBlue study: is practice nurse-led collaborative care effective in the management of depression for patients with heart disease or diabetes? *BMC Family Practice*. 2009; 10:46
- 878 Morgan MA, Coates MJ, Dunbar JA. Using care plans to better manage multimorbidity. *Australasian Medical Journal*. 2015; 8(6):208-215
- 879 Morgan MA, Coates MJ, Dunbar JA, Reddy P, Schlicht K, Fuller J. The TrueBlue model of collaborative care using practice nurses as case managers for depression alongside diabetes or heart disease: a randomised trial. *BMJ Open*. 2013; 3(1)
- 880 Morris RL, Sanders C, Kennedy AP, Rogers A. Shifting priorities in multimorbidity: a longitudinal qualitative study of patient's prioritization of multiple conditions. *Chronic Illness*. 2011; 7(2):147-161
- 881 Morrissey PE, Flynn ML, Lin S. Medication noncompliance and its implications in transplant recipients. *Drugs*. 2007; 67(10):1463-1481
- 882 Mosley DG, Peterson E, Martin DC. Do hierarchical condition category model scores predict hospitalization risk in newly enrolled Medicare advantage participants as well as probability of repeated admission scores? *Journal of the American Geriatrics Society*. 2009; 57(12):2306-2310

- 883 Mosquera RA, Avritscher EBC, Samuels CL, Harris TS, Pedroza C, Evans P et al. Effect of an enhanced medical home on serious illness and cost of care among high-risk children with chronic illness: a randomized clinical trial. *JAMA*. 2014; 312(24):2640-2648
- 884 Mueser K, Bartels S, Santos M, Pratt S, I, Riera E. Integrated illness management and recovery: a program for integrating physical and psychiatric illness self-management in older persons with severe mental illness. *American Journal of Psychiatric Rehabilitation*. 2012; 15(2):131-156
- 885 Munding MO, Kane RL, Lenz ER, Totten AM, Tsai WY, Cleary PD et al. Primary care outcomes in patients treated by nurse practitioners or physicians: a randomized trial. *JAMA*. 2000; 283(1):59-68
- 886 Muntner P, Levitan EB, Joyce C, Holt E, Mann D, Oparil S et al. Association between antihypertensive medication adherence and visit-to-visit variability of blood pressure. *Journal of Clinical Hypertension*. 2013; 15(2):112-117
- 887 Naik AD, White CD, Robertson SM, Armento ME, Lawrence B, Stelljes LA et al. Behavioral health coaching for rural-living older adults with diabetes and depression: an open pilot of the HOPE Study. *BMC Geriatrics*. 2012; 12:37
- 888 Nakamura K, Takano T, Akao C. The effectiveness of videophones in home healthcare for the elderly. *Medical Care*. 1999; 37(2):117-125
- 889 Nassar BS, Vaughan-Sarrazin MS, Jiang L, Reisinger HS, Bonello R, Cram P. Impact of an intensive care unit telemedicine program on patient outcomes in an integrated health care system. *JAMA Internal Medicine*. 2014; 174:1160-1167
- 890 National Institute for Health and Care Excellence. Developing NICE guidelines: the manual. London. National Institute for Health and Care Excellence, 2014. Available from: <http://www.nice.org.uk/article/PMG20/chapter/1%20Introduction%20and%20overview>
- 891 National Institute for Health and Care Excellence. Cost-consequence and cost-utility analysis of an outpatient geriatric multidisciplinary assessment and case management intervention: the 'GRACE' model of care. NG22 Older people with social care needs and multiple long term conditions: Appendix C3, 2015. Available from: <https://www.nice.org.uk/guidance/ng22/evidence/appendix-c3-economic-report-552742674>
- 892 National Institute for Health and Clinical Excellence. Social value judgements: principles for the development of NICE guidance. 2nd edition. London: National Institute for Health and Clinical Excellence; 2008. Available from: <http://www.nice.org.uk/media/C18/30/SVJ2PUBLICATION2008.pdf>
- 893 National Institute for Health and Clinical Excellence. The guidelines manual. London: National Institute for Health and Clinical Excellence; 2012. Available from: <http://publications.nice.org.uk/the-guidelines-manual-pmg6/>
- 894 National Institute for Health and Clinical Excellence. Guide to the methods of technology appraisal 2013. 2nd edition. London: National Institute for Health and Clinical Excellence; 2013. Available from: <http://publications.nice.org.uk/pmg9>
- 895 Naylor MD, Aiken LH, Kurtzman ET, Olds DM, Hirschman KB. The care span: the importance of transitional care in achieving health reform. *Health Affairs*. 2011; 30(4):746-754

- 896 Naylor MD, Brooten DA, Campbell RL, Maislin G, McCauley KM, Schwartz JS. Transitional care of older adults hospitalized with heart failure: a randomized, controlled trial. *Journal of the American Geriatrics Society*. 2004; 52(5):675-684
- 897 Neele SJM, Evertz R, De Valk-De Roo G, Roos JC, Netelenbos JC. Effect of 1 year of discontinuation of raloxifene or estrogen therapy on bone mineral density after 5 years of treatment in healthy postmenopausal women. *Bone*. 2002; 30(4):599-603
- 898 Nelson K, Drain N, Robinson J, Kapp J, Hebert P, Taylor L et al. Peer Support for Achieving Independence in Diabetes (Peer-AID): design, methods and baseline characteristics of a randomized controlled trial of community health worker assisted diabetes self-management support. *Contemporary Clinical Trials*. 2014; 38:361-369
- 899 Nelson M, Reid C, Krum H, McNeil J. A systematic review of predictors of maintenance of normotension after withdrawal of antihypertensive drugs. *American Journal of Hypertension*. 2001; 14(2):98-105
- 900 Nelson MR, Reid CM, Krum H, Muir T, Ryan P, McNeil JJ. Predictors of normotension on withdrawal of antihypertensive drugs in elderly patients: prospective study in second Australian national blood pressure study cohort. *BMJ*. 2002; 325(7368):815
- 901 Nelson MR, Reid CM, Krum H, Ryan P, Wing LMH, McNeil JJ et al. Short-term predictors of maintenance of normotension after withdrawal of antihypertensive drugs in the second Australian National Blood Pressure Study (ANBP2). *American Journal of Hypertension*. 2003; 16(1):39-45
- 902 Neuhaus V, King J, Hageman MG, Ring DC. Charlson comorbidity indices and in-hospital deaths in patients with hip fractures. *Clinical Orthopaedics and Related Research*. 2013; 471(5):1712-1719
- 903 Ng JH, Elliott MN, Scholle SH, Ahmed K, Collins RL, Bierman AS. Identifying older adults at high risk of mortality using the Medicare health outcomes survey. *Journal of Ambulatory Care Management*. 2012; 35(4):277-291
- 904 Nguyen JK, Fouts MM, Kotabe SE, Lo E. Polypharmacy as a risk factor for adverse drug reactions in geriatric nursing home residents. *American Journal of Geriatric Pharmacotherapy*. 2006; 4(1):36-41
- 905 Nicolaidis-Bouman A, van Rossum E, Kempen GI, Knipschild P. Effects of home visits by home nurses to elderly people with health problems: design of a randomised clinical trial in the Netherlands [ISRCTN92017183]. *BMC Health Services Research*. 2004; 4(1):35
- 906 Nikolaus T, Specht-Leible N, Bach M, Oster P, Schlierf G. A randomized trial of comprehensive geriatric assessment and home intervention in the care of hospitalized patients. *Age and Ageing*. Germany 1999; 28(6):543-550
- 907 Nishtala PS, Narayan SW, Wang T, Hilmer SN. Associations of drug burden index with falls, general practitioner visits, and mortality in older people. *Pharmacoepidemiology and Drug Safety*. 2014; 23(7):753-758
- 908 Nivya K, Sri Sai Kiran V, Rago N, Jayaprakash B, Sonal Sekhar M. Systemic review on drug related hospital admissions - A pubmed based search. *Saudi Pharmaceutical Journal*. 2015; 23(1):1-8

- 909 Nobili A, Licata G, Salerno F, Pasina L, Tettamanti M, Franchi C et al. Polypharmacy, length of hospital stay, and in-hospital mortality among elderly patients in internal medicine wards. The REPOSI study. *European Journal of Clinical Pharmacology*. 2011; 67(5):507-519
- 910 Nobis S, Lehr D, Ebert DD, Berking M, Heber E, Baumeister H et al. Efficacy and cost-effectiveness of a web-based intervention with mobile phone support to treat depressive symptoms in adults with diabetes mellitus type 1 and type 2: design of a randomised controlled trial. *BMC Psychiatry*. 2013; 13:306
- 911 Noel HC, Vogel DC, Erdos JJ, Cornwall D, Levin F. Home telehealth reduces healthcare costs. *Telemedicine Journal and E-Health*. 2004; 10(2):170-183
- 912 Nombela F, Blanco M, Lopez-Manzanares L, Rodriguez-Yanez M, Silva Y, Millan M. The effect of statins withdrawal on stroke outcome depends on stroke subtype. *Cerebrovascular Diseases*. 2006; 21(Suppl 4):148
- 913 Nykanen I, Rissanen TH, Sulkava R, Hartikainen S. Effects of individual dietary counseling as part of a comprehensive geriatric assessment (CGA) on nutritional status: a population-based intervention study. *Journal of Nutrition, Health and Aging*. 2014; 18(1):54-58
- 914 O'Brien R, Wyke S, Guthrie B, Watt G, Mercer S. An 'endless struggle': a qualitative study of general practitioners' and practice nurses' experiences of managing multimorbidity in socio-economically deprived areas of Scotland. *Chronic Illness*. 2011; 7(1):45-59
- 915 O'Caomh R, FitzGerald C, Cronin U, Svendrovski A, Gao Y, Healy E et al. Which part of a short, global risk assessment, the risk instrument for screening in the community, predicts adverse healthcare outcomes? *Journal of Aging Research*. 2015; 2015:256414
- 916 O'Caomh R, Gao Y, Svendrovski A, Healy E, O'Connell E, O'Keeffe G et al. The Risk Instrument for Screening in the Community (RISC): a new instrument for predicting risk of adverse outcomes in community dwelling older adults. *BMC Geriatrics*. 2015; 15:92
- 917 O'Connor MN, Gallagher P, Byrne S, O'Mahony D. Adverse drug reactions in older patients during hospitalisation: are they predictable? *Age and Ageing*. 2012; 41(6):771-776
- 918 O'Hara L, Cadbury H, De Souza L, Ide L. Evaluation of the effectiveness of professionally guided self-care for people with multiple sclerosis living in the community: a randomized controlled trial. *Clinical Rehabilitation*. 2002; 16(2):119-128
- 919 O'Keeffe J, Long SK, Liu K, Kerr M. How do they manage? Disabled elderly persons in the community who are not receiving Medicaid long-term care services. *Home Health Care Services Quarterly*. 2001; 20(4):73-90
- 920 O'Neil A, Hawkes AL, Chan B, Sanderson K, Forbes A, Hollingsworth B et al. A randomised, feasibility trial of a tele-health intervention for acute coronary syndrome patients with depression ('MoodCare'): study protocol. *BMC Cardiovascular Disorders*. 2011; 11:8
- 921 Obreli Neto PR, Nobili A, de Lyra DPJ, Pilger D, Guidoni CM, de Oliveira Baldoni A et al. Incidence and predictors of adverse drug reactions caused by drug-drug interactions in elderly outpatients: a prospective cohort study. *Journal of Pharmacy and Pharmaceutical Sciences*. 2012; 15(2):332-343

- 922 Office for National Statistics. Life tables. 2013. Available from: <http://www.ons.gov.uk/ons/publications/re-reference-tables.html?edition=tcm%3A77-365199> [Last accessed: 11 February 2016]
- 923 Olesen C, Harbig P, Buus KM, Barat I, Damsgaard EM. Impact of pharmaceutical care on adherence, hospitalisations and mortality in elderly patients. *International Journal of Clinical Pharmacy*. 2014; 36(1):163-171
- 924 Olsson G, Oden A, Johansson L, Sjogren A, Rehnqvist N. Prognosis after withdrawal of chronic postinfarction metoprolol treatment: a 2-7 year follow-up. *European Heart Journal*. 1988; 9(4):365-372
- 925 Onder G, Liperoti R, Foebel A, Fialova D, Topinkova E, van der Roest HG et al. Polypharmacy and mortality among nursing home residents with advanced cognitive impairment: results from the SHELTER study. *Journal of the American Medical Directors Association*. 2013; 14(6):450-12
- 926 Onder G, Pedone C, Landi F, Cesari M, Della Vedova C, Bernabei R et al. Adverse drug reactions as cause of hospital admissions: results from the Italian Group of Pharmacoepidemiology in the Elderly (GIFA). *Journal of the American Geriatrics Society*. 2002; 50(12):1962-1968
- 927 Oo MT, Tencheva A, Khalid N, Chan YP, Ho SF. Assessing frailty in the acute medical admission of elderly patients. *Journal of the Royal College of Physicians of Edinburgh*. 2013; 43(4):301-308
- 928 Oo M, Chan Y, Chamberlain H, Ho S. Developing a clinical screening tool for frailty in the acute care setting. *Clinical Medicine*. 2015; 15 Suppl 3:s8
- 929 Organisation for Economic Co-operation and Development (OECD). Purchasing power parities (PPP). 2008. Available from: <http://www.oecd.org/std/ppp> [Last accessed: 17 February 2016]
- 930 Orueta JF, Nuno-Solinis R, Mateos M, Vergara I, Grandes G, Esnaola S. Predictive risk modelling in the Spanish population: a cross-sectional study. *BMC Health Services Research*. 2013; 13:269
- 931 Ory M, Ahn S, Jiang L, Smith M, Ritter P, Whitelaw N et al. Successes of a national study of the chronic disease self-management program: meeting the triple aim of health care reform. *Medical Care*. 2013; 51(11):992-998
- 932 Overend K, Lewis H, Bailey D, Bosanquet K, Chew-Graham C, Ekers D et al. CASPER plus (Collaborative care in Screen-Positive ElDeRs with major depressive disorder): study protocol for a randomised controlled trial. *Trials*. 2014; 15:451
- 933 Overgaard K, Hansen MA, Nielsen VA, Riis BJ, Christiansen C. Discontinuous calcitonin treatment of established osteoporosis--effects of withdrawal of treatment. *American Journal of Medicine*. 1990; 89(1):1-6
- 934 Owusu C, Koroukian SM, Schluchter M, Bakaki P, Berger NA. Screening older cancer patients for a Comprehensive Geriatric Assessment: A comparison of three instruments. *Journal of Geriatric Oncology*. 2011; 2(2):121-129
- 935 Oza BB, Patel BM, Malhotra SD, Patel VJ. Health related quality of life in hypertensive patients in a tertiary care teaching hospital. *Journal of the Association of Physicians of India*. 2014; 62(10):22-29

- 936 Pacala JT, Boulton C, Reed RL, Aliberti E. Predictive validity of the Pra instrument among older recipients of managed care. *Journal of the American Geriatrics Society*. 1997; 45(5):614-617
- 937 Packer M, Gheorghide M, Young JB, Costantini PJ, Adams KF, Cody RJ et al. Withdrawal of digoxin from patients with chronic heart failure treated with angiotensin-converting-enzyme inhibitors. RADIANCE Study. *New England Journal of Medicine*. 1993; 329(1):1-7
- 938 Packer TL, Boldy D, Ghahari S, Melling L, Parsons R, Osborne RH. Self-management programs conducted within a practice setting: Who participates, who benefits and what can be learned? *Patient Education and Counseling*. 2012; 87(1):93-100
- 939 Paddison CAM, Saunders CL, Abel GA, Payne RA, Campbell JL, Roland M. Why do patients with multimorbidity in England report worse experiences in primary care? Evidence from the General Practice Patient Survey. *BMJ Open*. 2015; 5(3):e006172
- 940 Padwal RS, Sharma AM, Fradette M, Jelinski S, Klarenbach S, Edwards A et al. The evaluating self-management and educational support in severely obese patients awaiting multidisciplinary bariatric care (EVOLUTION) trial: rationale and design. *BMC Health Services Research*. 2013; 13:321
- 941 Palacios-Cena D, Hernandez-Barrera V, Jimenez-Garcia R, Valle-Martin B, Fernandez-de-las-Penas C, Carrasco-Garrido P. Has the prevalence of health care services use increased over the last decade (2001-2009) in elderly people? A Spanish population-based survey. *Maturitas*. 2013; 76(4):326-333
- 942 Pardo Cabello AJ, Gonzalez Contreras LG, Manzano Gamero MV, Gomez Jimenez FJ, Puche Canas E. Prevalence of fatal adverse drug reactions in hospitalized patients. *International Journal of Clinical Pharmacology and Therapeutics*. 2009; 47(10):596-602
- 943 Pare G, Poba-Nzaou P, Sicotte C. Home telemonitoring for chronic disease management: an economic assessment. *International Journal of Technology Assessment in Health Care*. 2013; 29(2):155-161
- 944 Park YH, Chang H. Effect of a health coaching self-management program for older adults with multimorbidity in nursing homes. *Patient Preference and Adherence*. 2014; 8:959-970
- 945 Parke B, Hunter KF, Strain LA, Marck PB, Waugh EH, McClelland AJ. Facilitators and barriers to safe emergency department transitions for community dwelling older people with dementia and their caregivers: a social ecological study. *International Journal of Nursing Studies*. 2013; 50(9):1206-1218
- 946 Parker L, Moran GM, Roberts LM, Calvert M, McCahon D. The burden of common chronic disease on health-related quality of life in an elderly community-dwelling population in the UK. *Family Practice*. 2014; 31(5):557-563
- 947 Parkerson GR, Jr., Harrell FE, Jr., Hammond WE, Wang XQ. Characteristics of adult primary care patients as predictors of future health services charges. *Medical Care*. 2001; 39(11):1170-1181
- 948 Passarelli MC, Jacob-Filho W, Figueras A. Adverse drug reactions in an elderly hospitalised population: inappropriate prescription is a leading cause. *Drugs and Aging*. 2005; 22(9):767-777
- 949 Patel AY, Shah P, Flaherty JH. Number of medications is associated with outcomes in the elderly patient with metabolic syndrome. *Journal of Geriatric Cardiology*. 2012; 9(3):213-219

- 950 Paterson C. Seeking the patient's perspective: a qualitative assessment of EuroQol, COOP-WONCA charts and MYMOP. *Quality of Life Research*. 2004; 13(5):871-881
- 951 Payne RA, Oliver JJ, Bain M, Elders A, Bateman DN. Patterns and predictors of re-admission to hospital with self-poisoning in Scotland. *Public Health*. 2009; 123(2):134-137
- 952 Payne RA, Abel GA, Avery AJ, Mercer SW, Roland MO. Is polypharmacy always hazardous? A retrospective cohort analysis using linked electronic health records from primary and secondary care. *British Journal of Clinical Pharmacology*. 2014; 77(6):1073-1082
- 953 Pecina JL, Hanson GJ, Van Houten H, Takahashi PY. Impact of telemonitoring on older adults health-related quality of life: the Tele-ERA study. *Quality of Life Research*. 2013; 22:2315-2321
- 954 Pedone C, Costanzo L, Cesari M, Bandinelli S, Ferrucci L, Antonelli Inc. Are performance measures necessary to predict loss of independence in elderly people? *Journals of Gerontology Series A, Biological Sciences and Medical Sciences*. 2016; 71(1):84-89
- 955 Pedone C, Rossi FF, Cecere A, Costanzo L, Antonelli Inc. Efficacy of a physician-led multiparametric telemonitoring system in very old adults with heart failure. *Journal of the American Geriatrics Society*. 2015; 63(6):1175-1180
- 956 Penning-van Beest FJA, Termorshuizen F, Goettsch WG, Klungel OH, Kastelein JJP, Herings RMC. Adherence to evidence-based statin guidelines reduces the risk of hospitalizations for acute myocardial infarction by 40%: a cohort study. *European Heart Journal*. 2007; 28(2):154-159
- 957 Perkins AJ, Kroenke K, Unutzer J, Katon W, Williams JWJ, Hope C et al. Common comorbidity scales were similar in their ability to predict health care costs and mortality. *Journal of Clinical Epidemiology*. 2004; 57(10):1040-1048
- 958 Perreault S, Ellia L, Dragomir A, Cote R, Blais L, Berard A et al. Effect of statin adherence on cerebrovascular disease in primary prevention. *American Journal of Medicine*. 2009; 122(7):647-655
- 959 Perreault S, Dragomir A, Blais L, Berard A, Lalonde L, White M. Impact of adherence to statins on chronic heart failure in primary prevention. *British Journal of Clinical Pharmacology*. 2008; 66(5):706-716
- 960 Perreault S, Dragomir A, Blais L, Berard A, Lalonde L, White M et al. Impact of better adherence to statin agents in the primary prevention of coronary artery disease. *European Journal of Clinical Pharmacology*. 2009; 65(10):1013-1024
- 961 Peters-Klimm F, Muller-Tasch T, Schellberg D, Gensichen J, Muth C, Herzog W et al. Rationale, design and conduct of a randomised controlled trial evaluating a primary care-based complex intervention to improve the quality of life of heart failure patients: HICMan (Heidelberg Integrated Case Management). *BMC Cardiovascular Disorders*. 2007; 7:25
- 962 Peters-Klimm F, Natanzon I, Muller-Tasch T, Ludt S, Nikendei C, Lossnitzer N et al. Barriers to guideline implementation and educational needs of general practitioners regarding heart failure: a qualitative study. *GMS Zeitschrift Fur Medizinische Ausbildung*. 2012; 29(3):Doc46
- 963 Petersen JJ, Konig J, Paulitsch MA, Mergenthal K, Rauck S, Pagitz M et al. Long-term effects of a collaborative care intervention on process of care in family practices in Germany: a 24-month

- follow-up study of a cluster randomized controlled trial. *General Hospital Psychiatry*. 2014; 36(6):570-574
- 964 Petersen LA, Burstin HR, O'Neil AC, Orav EJ, Brennan TA. Nonurgent emergency department visits: the effect of having a regular doctor. *Medical Care*. 1998; 36(8):1249-1255
- 965 Petkov J, Harvey P, Battersby M. The internal consistency and construct validity of the partners in health scale: validation of a patient rated chronic condition self-management measure. *Quality of Life Research*. 2010; 19(7):1079-1085
- 966 Phillips CO, Wright SM, Kern DE, Singa RM, Shepperd S, Rubin HR. Comprehensive discharge planning with postdischarge support for older patients with congestive heart failure: a meta-analysis. *JAMA*. 2004; 291(11):1358-1367
- 967 Phillips K, Wood F, Kinnersley P. Tackling obesity: the challenge of obesity management for practice nurses in primary care. *Family Practice*. 2014; 31(1):51-59
- 968 Pickett YR, Kennedy GJ, Freeman K, Cummings J, Woolis W. The effect of telephone-facilitated depression care on older, medically ill patients. *Journal of Behavioral Health Services and Research*. 2014; 41(1):90-96
- 969 Pijpers E, Ferreira I, Stehouwer CD, Nieuwenhuijzen Kruseman AC. The frailty dilemma. Review of the predictive accuracy of major frailty scores. *European Journal of Internal Medicine*. 2012; 23(2):118-123
- 970 Pilotto A, Addante F, Franceschi M, Leandro G, Rengo G, D'Ambrosio P et al. Multidimensional Prognostic Index based on a comprehensive geriatric assessment predicts short-term mortality in older patients with heart failure. *Circulation: Heart Failure*. 2010; 3(1):14-20
- 971 Pilotto A, Ferrucci L, Franceschi M, D'Ambrosio LP, Scarcelli C, Cascavilla L et al. Development and validation of a multidimensional prognostic index for one-year mortality from comprehensive geriatric assessment in hospitalized older patients. *Rejuvenation Research*. 2008; 11(1):151-161
- 972 Pilotto A, Gallina P, Fontana A, Sancarlo D, Bazzano S, Copetti M et al. Development and validation of a Multidimensional Prognostic Index for mortality based on a standardized Multidimensional Assessment Schedule (MPI-SVaMA) in community-dwelling older subjects. *Journal of the American Medical Directors Association*. 2013; 14(4):287-292
- 973 Pilotto A, Rengo F, Marchionni N, Sancarlo D, Fontana A, Panza F et al. Comparing the prognostic accuracy for all-cause mortality of frailty instruments: a multicentre 1-year follow-up in hospitalized older patients. *PLoS ONE*. 2012; 7(1):e29090
- 974 Pilotto A, Sancarlo D, Aucella F, Fontana A, Addante F, Copetti M et al. Addition of the multidimensional prognostic index to the estimated glomerular filtration rate improves prediction of long-term all-cause mortality in older patients with chronic kidney disease. *Rejuvenation Research*. 2012; 15(1):82-88
- 975 Pilotto A, Sancarlo D, Polidori MC, Cruz-Jentoft AJ, Mattace-Raso F, Paccalin M et al. The MPI-AGE European Project: Using Multidimensional Prognostic Indices (MPI) to improve cost-effectiveness of interventions in multimorbid frail older persons. Background, aim and design. *European Geriatric Medicine*. 2015; 6(2):184-188

- 976 Pilotto A, Panza F, Copetti M, Simonato M, Sancarolo D, Gallina P et al. Statin treatment and mortality in community-dwelling frail older patients with diabetes mellitus: a retrospective observational study. *PLoS ONE*. 2015; 10(6):e0130946
- 977 Pittman DG, Chen W, Bowlin SJ, Foody JM. Adherence to statins, subsequent healthcare costs, and cardiovascular hospitalizations. *American Journal of Cardiology*. 2011; 107(11):1662-1666
- 978 Pizzi LT, Jutkowitz E, Frick KD, Suh DC, Prioli KM, Gitlin LN. Cost-effectiveness of a community-integrated home-based depression intervention in older African Americans. *Journal of the American Geriatrics Society*. 2014; 62(12):2288-2295
- 979 Plant NA, Kelly PJ, Leeder SR, D'Souza M, Mallitt KA, Usherwood T et al. Coordinated care versus standard care in hospital admissions of people with chronic illness: a randomised controlled trial. *Medical Journal of Australia*. 2015; 203(1):33-38
- 980 Ploeg J, Brazil K, Hutchison B, Kaczorowski J, Dalby DM, Goldsmith CH et al. Effect of preventive primary care outreach on health related quality of life among older adults at risk of functional decline: randomised controlled trial. *BMJ*. 2010; 340:c1480
- 981 Plow M, Bethoux F, McDaniel C, McGlynn M, Marcus B. Randomized controlled pilot study of customized pamphlets to promote physical activity and symptom self-management in women with multiple sclerosis. *Clinical Rehabilitation*. 2014; 28:139-148
- 982 Poitras ME, Fortin M, Hudon C, Haggerty J, Almirall J. Validation of the disease burden morbidity assessment by self-report in a French-speaking population. *BMC Health Services Research*. 2012; 12:35
- 983 Polanczyk CA, Rohde LE, Philbin EA, Di Salvo TG. A new casemix adjustment index for hospital mortality among patients with congestive heart failure. *Medical Care*. 1998; 36(10):1489-1499
- 984 Popa-Velea O, Purcarea VL. Psychological intervention - a critical element of rehabilitation in chronic pulmonary diseases. *Journal of Medicine and Life*. 2014; 7:274-281
- 985 Pope G, Wall N, Peters CM, O'Connor M, Saunders J, O'Sullivan C et al. Specialist medication review does not benefit short-term outcomes and net costs in continuing-care patients. *Age and Ageing*. 2011; 40(3):307-312
- 986 Porock D, Oliver DP, Zweig S, Rantz M, Mehr D, Madsen R et al. Predicting death in the nursing home: development and validation of the 6-month Minimum Data Set mortality risk index. *Journals of Gerontology Series A, Biological Sciences and Medical Sciences*. 2005; 60(4):491-498
- 987 Poses RM, McClish DK, Smith WR, Bekes C, Scott WE. Prediction of survival of critically ill patients by admission comorbidity. *Journal of Clinical Epidemiology*. 1996; 49(7):743-747
- 988 Powell C, Montgomery P. The Age study: the admission of geriatric patients through emergency. *Age and Ageing*. 1990; 19(suppl 2):21-2d
- 989 Pozzi C, Lapi F, Mazzaglia G, Inzitari M, Boncinelli M, Geppetti P et al. Is suboptimal prescribing a risk factor for poor health outcomes in community-dwelling elders? The ICARE Dicomano study. *Pharmacoepidemiology and Drug Safety*. 2010; 19(9):954-960

- 990 Presseau J, Sniehotta FF, Francis JJ, Campbell NC. Multiple goals and time constraints: perceived impact on physicians' performance of evidence-based behaviours. *Implementation Science*. 2009; 4:77
- 991 Prestmo A, Hagen G, Sletvold O, Helbostad JL, Thingstad P, Taraldsen K et al. Comprehensive geriatric care for patients with hip fractures: A prospective, randomised, controlled trial. *The Lancet*. 2015; 385(9978):1623-1633
- 992 Preyde M, Brassard K. Evidence-based risk factors for adverse health outcomes in older patients after discharge home and assessment tools: a systematic review. *Journal of Evidence-Based Social Work*. 2011; 8(5):445-468
- 993 Putnam KG, Buist DS, Fishman P, Andrade SE, Boles M, Chase GA et al. Chronic disease score as a predictor of hospitalization. *Epidemiology*. 2002; 13(3):340-346
- 994 Putnam W, Twohig PL, Burge FI, Jackson LA, Cox JL. Evidence-based cardiovascular care. Family physicians' views of obstacles and opportunities. *Canadian Family Physician*. 2004; 50:1397-1405
- 995 Quach S, Hennessy DA, Faris P, Fong A, Quan H, Doig C. A comparison between the APACHE II and Charlson Index Score for predicting hospital mortality in critically ill patients. *BMC Health Services Research*. 2009; 9:129
- 996 Quail JM, Lix LM, Osman BA, Teare GF. Comparing comorbidity measures for predicting mortality and hospitalization in three population-based cohorts. *BMC Health Services Research*. 2011; 11:146
- 997 Quan H, Li B, Couris CM, Fushimi K, Graham P, Hider P et al. Updating and validating the Charlson comorbidity index and score for risk adjustment in hospital discharge abstracts using data from 6 countries. *American Journal of Epidemiology*. 2011; 173(6):676-682
- 998 Queneau P, Bannwarth B, Carpentier F, Guliana JM, Bouget J, Trombert B et al. Emergency department visits caused by adverse drug events: results of a French survey. *Drug Safety*. 2007; 30(1):81-88
- 999 Quinones AR, Richardson J, Freeman M, Fu R, O'Neil ME, Motu'apuaka M et al. Educational group visits for the management of chronic health conditions: a systematic review. *Patient Education and Counseling*. 2014; 95:3-29
- 1000 Rabow MW, Dibble SL, Pantilat SZ, McPhee SJ. The comprehensive care team: a controlled trial of outpatient palliative medicine consultation. *Archives of Internal Medicine*. 2004; 164:83-91
- 1001 Radhakrishnan K, Jacelon CS, Bigelow C, Roche J, Marquard J, Bowles KH. Use of a homecare electronic health record to find associations between patient characteristics and re-hospitalizations in patients with heart failure using telehealth. *Journal of Telemedicine and Telecare*. 2013; 19(2):107-112
- 1002 Radley DC, Gottlieb DJ, Fisher ES, Tosteson AN. Comorbidity risk-adjustment strategies are comparable among persons with hip fracture. *Journal of Clinical Epidemiology*. 2008; 61(6):580-587
- 1003 Radner H, Yoshida K, Mjaavatten MD, Aletaha D, Frits M, Lu B et al. Development of a multimorbidity index: Impact on quality of life using a rheumatoid arthritis cohort. *Seminars in Arthritis and Rheumatism*. 2015; 45(2):167-173

- 1004 Radovanovic D, Seifert B, Urban P, Eberli FR, Rickli H, Bertel O et al. Validity of Charlson Comorbidity Index in patients hospitalised with acute coronary syndrome. Insights from the nationwide AMIS Plus registry 2002-2012. *Heart*. 2014; 100(4):288-294
- 1005 Rae-Grant AD, Turner AP, Sloan A, Miller D, Hunziker J, Haselkorn JK. Self-management in neurological disorders: systematic review of the literature and potential interventions in multiple sclerosis care. *Journal of Rehabilitation Research and Development*. 2011; 48:1087-1100
- 1006 Rajgopal R, Rajan S, Sapru K, Paul J. Effect of pre-operative discontinuation of angiotensin-converting enzyme inhibitors or angiotensin II receptor antagonists on intra-operative arterial pressures after induction of general anesthesia. *Anesthesia, Essays and Researches*. 2014; 8(1):32-35
- 1007 Ramli A, Ahmad NS, Paraidathathu T. Medication adherence among hypertensive patients of primary health clinics in Malaysia. *Patient Preference and Adherence*. 2012; 6:613-622
- 1008 Ramli AS, Lakshmanan S, Haniff J, Selvarajah S, Tong SF, Bujang MA et al. Study protocol of EMPOWER participatory action research (EMPOWER-PAR): a pragmatic cluster randomised controlled trial of multifaceted chronic disease management strategies to improve diabetes and hypertension outcomes in primary care. *BMC Family Practice*. 2014; 15:151
- 1009 Rasmussen JN, Chong A, Alter DA. Relationship between adherence to evidence-based pharmacotherapy and long-term mortality after acute myocardial infarction. *JAMA*. 2007; 297(2):177-186
- 1010 Raven MC, Gillespie CC, DiBennardo R, Van Busum K, Elbel B. Vulnerable patients' perceptions of health care quality and quality data. *Medical Decision Making*. 2012; 32(2):311-326
- 1011 Ravindrarajah R, Lee DM, Pye SR, Gielen E, Boonen S, Vanderschueren D et al. The ability of three different models of frailty to predict all-cause mortality: results from the European Male Aging Study (EMAS). *Archives of Gerontology and Geriatrics*. 2013; 57(3):360-368
- 1012 Rector TS, Ringwala SN, Ringwala SN, Anand IS. Validation of a risk score for dying within 1 year of an admission for heart failure. *Journal of Cardiac Failure*. 2006; 12(4):276-280
- 1013 Reed RL, Battersby M, Osborne RH, Bond MJ, Howard SL, Roeger L. Protocol for a randomised controlled trial of chronic disease self-management support for older Australians with multiple chronic diseases. *Contemporary Clinical Trials*. 2011; 32:946-952
- 1014 Rees CE, Knight LV, Wilkinson CE. Doctors being up there and we being down here: a metaphorical analysis of talk about student/doctor-patient relationships. *Social Science and Medicine*. 2007; 65(4):725-737
- 1015 Reeve E, To J, Hendrix I, Shakib S, Roberts MS, Wiese MD. Patient barriers to and enablers of deprescribing: a systematic review. *Drugs and Aging*. 2013;(4):793-807
- 1016 Reeve E, Wiese MD. Benefits of deprescribing on patients' adherence to medications. *International Journal of Clinical Pharmacy*. 2014; 36(1):26-29
- 1017 Ricauda NA, Bo M, Molaschi M, Massaia M, Salerno D, Amati D et al. Home hospitalization service for acute uncomplicated first ischemic stroke in elderly patients: a randomized trial. *Journal of the American Geriatrics Society*. 2004; 52(2):278-283

- 1018 Richardson K, Ananou A, Lafortune L, Brayne C, Matthews FE. Variation over time in the association between polypharmacy and mortality in the older population. *Drugs and Aging*. 2011; 28(7):547-560
- 1019 Ridgeway JL, Egginton JS, Tiedje K, Linzer M, Boehm D, Poplau S et al. Factors that lessen the burden of treatment in complex patients with chronic conditions: a qualitative study. *Patient Preference and Adherence*. 2014; 8:339-351
- 1020 Ringbaek T, Green A, Laursen LC, Frausing E, Brondum E, Ulrik CS. Effect of tele health care on exacerbations and hospital admissions in patients with chronic obstructive pulmonary disease: A randomized clinical trial. *International Journal of COPD*. 2015; 10(1):1801-1808
- 1021 Risselada R, Straatman H, van Kooten F, Dippel DWJ, van der Lugt A, Niessen WJ et al. Withdrawal of statins and risk of subarachnoid hemorrhage. *Stroke; a Journal of Cerebral Circulation*. 2009; 40(8):2887-2892
- 1022 Ritholz MD, Beverly EA, Abrahamson MJ, Brooks KM, Hultgren BA, Weinger K. Physicians' perceptions of the type 2 diabetes multi-disciplinary treatment team: a qualitative study. *Diabetes Educator*. 2011; 37(6):794-800
- 1023 Ritt M, Schwarz C, Kronawitter V, Delinic A, Bollheimer LC, Gassmann KG et al. Analysis of Rockwood et al's clinical frailty scale and Fried et al's frailty phenotype as predictors of mortality and other clinical outcomes in older patients who were admitted to a geriatric ward. *Journal of Nutrition, Health and Aging*. 2015; 19(10):1043-1048
- 1024 Ritter PL, Lee J, Lorig K. Moderators of chronic disease self-management programs: who benefits? *Chronic Illness*. 2011; 7(2):162-172
- 1025 Rius C, Perez G, Rodriguez-Sanz M, Fernandez E, Cohesca Study Group. Comorbidity index was successfully validated among men but not in women. *Journal of Clinical Epidemiology*. 2008; 61(8):796-802
- 1026 Roberts D, Patrick W, Mojica J, Ostryzniuk P, Patrick M, MacKnight C et al. The ALERT scale: an observational study of early prediction of adverse hospital outcome for medical patients. *BMJ Open*. 2015; 5(4):e005501
- 1027 Roberts HC, Syddall HE, Cooper C, Aihie Sayer A. Is grip strength associated with length of stay in hospitalised older patients admitted for rehabilitation? Findings from the Southampton grip strength study. *Age and Ageing*. 2012; 41(5):641-646
- 1028 Robertson S, Witty K, Braybrook D, Lowcock D, South J, White A. 'It's coming at things from a very different standpoint': evaluating the 'Supporting Self-Care in General Practice Programme' in NHS East of England. *Primary Health Care Research and Development*. 2013; 14(2):113-125
- 1029 Robey-Williams C, Rush KL, Bendyk H, Patton LM, Chamberlain D, Sparks T. Spartanburg Fall Risk Assessment Tool: a simple three-step process. *Applied Nursing Research*. 2007; 20(2):86-93
- 1030 Rochette A, Korner-Bitensky N, Bishop D, Teasell R, White C, Bravo G et al. Study protocol of the YOU CALL--WE CALL TRIAL: impact of a multimodal support intervention after a "mild" stroke. *BMC Neurology*. 2010; 10:3

- 1031 Rochette A, Korner-Bitensky N, Bishop D, Teasell R, White CL, Bravo G et al. The YOU CALL-WE CALL randomized clinical trial: Impact of a multimodal support intervention after a mild stroke. *Circulation Cardiovascular Quality and Outcomes*. 2013; 6(6):674-679
- 1032 Rockwood K, Abeysondera MJ, Mitnitski A. How should we grade frailty in nursing home patients? *Journal of the American Medical Directors Association*. 2007; 8(9):595-603
- 1033 Rockwood K, Andrew M, Mitnitski A. A comparison of two approaches to measuring frailty in elderly people. *Journals of Gerontology Series A, Biological Sciences and Medical Sciences*. 2007; 62(7):738-743
- 1034 Rockwood K, Song X, MacKnight C, Bergman H, Hogan DB, McDowell I et al. A global clinical measure of fitness and frailty in elderly people. *CMAJ Canadian Medical Association Journal*. 2005; 173(5):489-495
- 1035 Rockwood K, McMillan M, Mitnitski A, Howlett SE. A frailty index based on common laboratory tests in comparison with a clinical frailty index for older adults in long-term care facilities. *Journal of the American Medical Directors Association*. 2015; 16(10):842-847
- 1036 Rockwood MR, MacDonald E, Sutton E, Rockwood K, Baron M, Canadian Scleroderma Research Group. Frailty index to measure health status in people with systemic sclerosis. *Journal of Rheumatology*. 2014; 41(4):698-705
- 1037 Rodriguez-Blazquez C, Forjaz MJ, Prieto-Flores ME, Rojo-Perez F, Fernandez-Mayoralas G, Martinez-Martin P et al. Health status and well-being of older adults living in the community and in residential care settings: are differences influenced by age? *Aging and Mental Health*. 2012; 16(7):884-891
- 1038 Rodriguez-Pascual C, Vilches-Moraga A, Paredes-Galan E, Ferrero-Marinez AI, Torrente-Carballido M, Rodriguez-Artalejo F. Comprehensive geriatric assessment and hospital mortality among older adults with decompensated heart failure. *American Heart Journal*. 2012; 164(5):756-762
- 1039 Roe B, Howell F, Riniotis K, Beech R, Crome P, Ong BN. Older people and falls: health status, quality of life, lifestyle, care networks, prevention and views on service use following a recent fall. *Journal of Clinical Nursing*. 2009; 18(16):2261-2272
- 1040 Roland K, Theou O, Jakobi J, Swan L, Jones G. Exploring frailty: community physical and occupational therapists' perspectives. *Physical & Occupational Therapy in Geriatrics*. 2011; 29(4):270-286
- 1041 Rolfe DE, Sutton EJ, Landry M, Sternberg L, Price JAD. Women's experiences accessing a women-centered cardiac rehabilitation program: a qualitative study. *Journal of Cardiovascular Nursing*. 2010; 25(4):332-341
- 1042 Rolfson DB, Majumdar SR, Tsuyuki RT, Tahir A, Rockwood K. Validity and reliability of the Edmonton Frail Scale. *Age and Ageing*. 2006; 35(5):526-529
- 1043 Romana A, Kamath L, Sarda A, Muraraiah S, Jayanthi CR. Polypharmacy leading to adverse drug reactions in elderly in a tertiary care hospital. *International Journal of Pharma and Bio Sciences*. 2012; 3(3):218-224
- 1044 Romano PS, Chan BK. Risk-adjusting acute myocardial infarction mortality: are APR-DRGs the right tool? *Health Services Research*. 2000; 34(7):1469-1489

- 1045 Romero-Ortuno R. The Frailty Instrument for primary care of the Survey of Health, Ageing and Retirement in Europe predicts mortality similarly to a frailty index based on comprehensive geriatric assessment. *Geriatrics and Gerontology International*. 2013; 13(2):497-504
- 1046 Romero-Ortuno R, Walsh CD, Lawlor BA, Kenny RA. A frailty instrument for primary care: findings from the Survey of Health, Ageing and Retirement in Europe (SHARE). *BMC Geriatrics*. 2010; 10:57
- 1047 Ross MM, McDonald B. Providing palliative care to older adults: context and challenges. *Journal of Palliative Care*. 1994; 10(4):5-10
- 1048 Royston P, Sauerbrei W. A new measure of prognostic separation in survival data. *Statistics in Medicine*. 2004; 23(5):723-748
- 1049 Rozzini R, Frisoni GB, Ferrucci L, Barbisoni P, Sabatini T, Ranieri P et al. Geriatric Index of Comorbidity: validation and comparison with other measures of comorbidity. *Age and Ageing*. 2002; 31(4):277-285
- 1050 Rubin CD, Sizemore MT, Loftis PA, Adams-Huet B, Anderson RJ. The effect of geriatric evaluation and management on Medicare reimbursement in a large public hospital: a randomized clinical trial. *Journal of the American Geriatrics Society*. 1992; 40(10):989-995
- 1051 Rubin CD, Sizemore MT, Loftis PA, de Mola NL. A randomized, controlled trial of outpatient geriatric evaluation and management in a large public hospital. *Journal of the American Geriatrics Society*. 1993; 41(10):1023-1028
- 1052 Ruiz B, Garcia M, Aguirre U, Aguirre C. Factors predicting hospital readmissions related to adverse drug reactions. *European Journal of Clinical Pharmacology*. 2008; 64(7):715-722
- 1053 Ruiz-Laiglesia FJ, Sanchez-Marteles M, Perez-Calvo JI, Formiga F, Bartolome-Satue JA, Armengou-Arxe A et al. Comorbidity in heart failure. Results of the Spanish RICA Registry. *QJM*. 2014; 107(12):989-994
- 1054 Rytter L, Jakobsen HN, Ronholt F, Hammer AV, Andreasen AH, Nissen A et al. Comprehensive discharge follow-up in patients' homes by GPs and district nurses of elderly patients. A randomized controlled trial. *Scandinavian Journal of Primary Health Care*. 2010; 28(3):146-153
- 1055 Sabin SL, Rosenfeld RM, Sundaram K, Har-El G, Lucente FE. The impact of comorbidity and age on survival with laryngeal cancer. *Ear, Nose, and Throat Journal*. 1999; 78(8):578, 581-578, 584
- 1056 Sada YH, Street RLJ, Singh H, Shada RE, Naik AD. Primary care and communication in shared cancer care: a qualitative study. *American Journal of Managed Care*. 2011; 17(4):259-265
- 1057 Sager MA, Rudberg MA, Jalaluddin M, Franke T, Inouye SK, Landefeld CS et al. Hospital admission risk profile (HARP): identifying older patients at risk for functional decline following acute medical illness and hospitalization. *Journal of the American Geriatrics Society*. 1996; 44(3):251-257
- 1058 Saheb Sharif-Askari N, Syed Sulaiman SA, Saheb Sharif-Askari F, Hussain AAS. Adverse drug reaction-related hospitalisations among patients with heart failure at two hospitals in the United Arab Emirates. *International Journal of Clinical Pharmacy*. 2015; 37(1):105-112
- 1059 Sahlen K-G, Dahlgren L, Hellner BM, Stenlund H, Lindholm L. Preventive home visits postpone mortality--a controlled trial with time-limited results. *BMC Public Health*. 2006; 6:220

- 1060 Saito Y, Shirai K, Sasaki N, Shinomiya M, Yoshida S, Committee of the Chiba Lipid Intervention Program Study. Prognosis of hypercholesterolemic patients taking pravastatin for five years: the Chiba Lipid Intervention Program (CLIP) Study. *Journal of Atherosclerosis and Thrombosis*. 2002; 9(2):99-108
- 1061 Sajatovic M, Dawson NV, Perzynski AT, Blixen CE, Bialko CS, McKibbin CL et al. Optimizing care for people with serious mental illness and comorbid diabetes. *Psychiatric Services*. 2011; 62(9):1001-1003
- 1062 Salisbury C. Multimorbidity: redesigning health care for people who use it. *The Lancet*. 2012; 380(9836):7-9
- 1063 Saltz CC, McVey LJ, Becker PM, Feussner JR, Cohen HJ. Impact of a geriatric consultation team on discharge placement and repeat hospitalization. *Gerontologist*. 1988; 28(3):344-350
- 1064 Salvi F, Miller MD, Grilli A, Giorgi R, Towers AL, Morichi V et al. A manual of guidelines to score the modified cumulative illness rating scale and its validation in acute hospitalized elderly patients. *Journal of the American Geriatrics Society*. 2008; 56(10):1926-1931
- 1065 Salvi F, Morichi V, Grilli A, Lancioni L, Spazzafumo L, Polonara S et al. Screening for frailty in elderly emergency department patients by using the Identification of Seniors At Risk (ISAR). *Journal of Nutrition, Health and Aging*. 2012; 16(4):313-318
- 1066 Salvi F, Marchetti A, D'Angelo F, Boemi M, Lattanzio F, Cherubini A. Adverse drug events as a cause of hospitalization in older adults. *Drug Safety*. 2012; 35 Suppl 1:29-45
- 1067 Sampalis JS, Nathanson R, Vaillancourt J, Nikolis A, Liberman M, Angelopoulos J et al. Assessment of mortality in older trauma patients sustaining injuries from falls or motor vehicle collisions treated in regional level I trauma centers. *Annals of Surgery*. 2009; 249(3):488-495
- 1068 Sampson EL, Leurent B, Blanchard MR, Jones L, King M. Survival of people with dementia after unplanned acute hospital admission: a prospective cohort study. *International Journal of Geriatric Psychiatry*. 2013; 28(10):1015-1022
- 1069 Sanabria A, Carvalho AL, Vartanian JG, Magrin J, Ikeda MK, Kowalski LP. Validation of the Washington University Head and Neck Comorbidity Index in a cohort of older patients. *Archives of Otolaryngology -- Head and Neck Surgery*. 2008; 134(6):603-607
- 1070 Sancarolo D, D'Onofrio G, Franceschi M, Scarcelli C, Niro V, Addante F et al. Validation of a Modified-Multidimensional Prognostic Index (m-MPI) including the Mini Nutritional Assessment Short-Form (MNA-SF) for the prediction of one-year mortality in hospitalized elderly patients. *Journal of Nutrition, Health and Aging*. 2011; 15(3):169-173
- 1071 Sancarolo D, Pilotto A, Panza F, Copetti M, Longo MG, D'Ambrosio P et al. A Multidimensional Prognostic Index (MPI) based on a comprehensive geriatric assessment predicts short- and long-term all-cause mortality in older hospitalized patients with transient ischemic attack. *Journal of Neurology*. 2012; 259(4):670-678
- 1072 Sanchez Munoz-Torrero JF, Barquilla P, Velasco R, Fernandez Capitan MdC, Pacheco N, Vicente L et al. Adverse drug reactions in internal medicine units and associated risk factors. *European Journal of Clinical Pharmacology*. 2010; 66(12):1257-1264

- 1073 Sanchez K, Watt TT. Collaborative care for the treatment of depression in primary care with a low-income, spanish-speaking population: Outcomes from a community-based program evaluation. *Primary Care Companion to the Journal of Clinical Psychiatry*. 2012; 14(6)
- 1074 Sanchis J, Bonanad C, Ruiz V, Fernandez J, Garcia-Blas S, Mainar L et al. Frailty and other geriatric conditions for risk stratification of older patients with acute coronary syndrome. *American Heart Journal*. 2014; 168(5):784
- 1075 Sanchis J, Nunez J, Bodi V, Nunez E, Garcia-Alvarez A, Bonanad C et al. Influence of comorbid conditions on one-year outcomes in non-ST-segment elevation acute coronary syndrome. *Mayo Clinic Proceedings*. 2011; 86(4):291-296
- 1076 Sandberg M, Kristensson J, Midlov P, Jakobsson U. Effects on healthcare utilization of case management for frail older people: a randomized controlled trial (RCT). *Archives of Gerontology and Geriatrics*. 2015; 60(1):71-81
- 1077 Santos Souza Ad, Calhau Andrade C, Reis Junior AP, Campos Meira E, do Rosario de Menezes M, Takase Goncalves LH. Service hospitalized elderly: perceptions of health professionals. *Ciencia, Cuidado e Saude*. 2013; 12(2):274-281
- 1078 Sato I, Akazawa M. Polypharmacy and adverse drug reactions in Japanese elderly taking antihypertensives: a retrospective database study. *Drug, Healthcare and Patient Safety*. 2013; 5:143-150
- 1079 Sav A, Kendall E, McMillan SS, Kelly F, Whitty JA, King MA et al. 'You say treatment, I say hard work': treatment burden among people with chronic illness and their carers in Australia. *Health and Social Care in the Community*. 2013; 21(6):665-674
- 1080 Sav A, King MA, Whitty JA, Kendall E, McMillan SS, Kelly F et al. Burden of treatment for chronic illness: a concept analysis and review of the literature. *Health Expectations*. 2015; 18(3):312-324
- 1081 Sav A, McMillan SS, Kelly F, Kendall E, Whitty JA, King MA et al. Treatment burden among people with chronic illness: what are consumer health organizations saying? *Chronic Illness*. 2013; 9(3):220-232
- 1082 Schafer I, Pawels M, Kuver C, Pohontsch NJ, Scherer M, van den Bussche H et al. Strategies for improving participation in diabetes education. A qualitative study. *PLoS ONE*. 2014; 9(4):e95035
- 1083 Scheitz JF, Nolte CH, Endres M. Should statins be paused or discontinued after thrombolysis or acute intracerebral hemorrhage? No! *Stroke; a Journal of Cerebral Circulation*. 2013; 44(5):1472-1476
- 1084 Schmieder RE, Rockstroh JK, Gatzka CD, Ruddel H, Schachinger H. Discontinuation of antihypertensive therapy: prevalence of relapses and predictors of successful withdrawal in a hypertensive community. *Cardiology*. 1997; 88(3):277-284
- 1085 Schmitt KE, Edie CF, Laflam P, Simbartl LA, Thakar CV. Adherence to antihypertensive agents and blood pressure control in chronic kidney disease. *American Journal of Nephrology*. 2010; 32(6):541-548
- 1086 Schneeweiss S, Maclure M. Use of comorbidity scores for control of confounding in studies using administrative databases. *International Journal of Epidemiology*. 2000; 29(5):891-898

- 1087 Schneeweiss S, Seeger JD, Maclure M, Wang PS, Avorn J, Glynn RJ. Performance of comorbidity scores to control for confounding in epidemiologic studies using claims data. *American Journal of Epidemiology*. 2001; 154(9):854-864
- 1088 Schneeweiss S, Wang PS, Avorn J, Glynn RJ. Improved comorbidity adjustment for predicting mortality in Medicare populations. *Health Services Research*. 2003; 38(4):1103-1120
- 1089 Schneeweiss S, Wang PS, Avorn J, Maclure M, Levin R, Glynn RJ. Consistency of performance ranking of comorbidity adjustment scores in Canadian and U.S. utilization data. *Journal of General Internal Medicine*. 2004; 19(5 Pt 1):444-450
- 1090 Schobel HP, Schmieder RE, Messerli FH. Risks versus benefits of withdrawing antihypertensive therapy. *Drug Safety*. 1992; 7(6):395-403
- 1091 Schoenberg NE, Bardach SH, Manchikanti KN, Goodenow AC. Appalachian residents' experiences with and management of multiple morbidity. *Qualitative Health Research*. 2011; 21(5):601-611
- 1092 Schonberg MA, Davis RB, McCarthy EP, Marcantonio ER. Index to predict 5-year mortality of community-dwelling adults aged 65 and older using data from the National Health Interview Survey. *Journal of General Internal Medicine*. 2009; 24(10):1115-1122
- 1093 Schonfeld TL, Stevens EA, Lampman MA, Lyons WL. Assessing challenges in end-of-life conversations with elderly patients with multiple morbidities. *American Journal of Hospice and Palliative Care*. 2012; 29(4):260-267
- 1094 Schoufour JD, Mitnitski A, Rockwood K, Evenhuis HM, Echteld MA. Predicting 3-year survival in older people with intellectual disabilities using a Frailty Index. *Journal of the American Geriatrics Society*. 2015; 63(3):531-536
- 1095 Schraeder C, Fraser CW, Clark I, Long B, Shelton P, Waldschmidt V et al. Evaluation of a primary care nurse case management intervention for chronically ill community dwelling older people. *Journal of Clinical Nursing*. 2008; 17(11c):407-417
- 1096 Schroeder K, Fahey T, Hay AD, Montgomery A, Peters TJ. Relationship between medication adherence and blood pressure in primary care: prospective study. *Journal of Human Hypertension*. 2006; 20(8):625-627
- 1097 Schuler J, Duckelmann C, Beindl W, Prinz E, Michalski T, Pichler M. Polypharmacy and inappropriate prescribing in elderly internal-medicine patients in Austria. *Wiener Klinische Wochenschrift*. 2008; 120(23-24):733-741
- 1098 Schuling J, Gebben H, Veehof LJG, Haaijer-Ruskamp FM. Deprescribing medication in very elderly patients with multimorbidity: the view of Dutch GPs. A qualitative study. *BMC Family Practice*. 2012; 13:56
- 1099 Schwarz KA, Mion LC, Hudock D, Litman G. Telemonitoring of heart failure patients and their caregivers: a pilot randomized controlled trial. *Progress in Cardiovascular Nursing*. 2008; 23(1):18-26
- 1100 Schwenk M, Mohler J, Wendel C, D'Huyvetter K, Fain M, Taylor-Piliae R et al. Wearable sensor-based in-home assessment of gait, balance, and physical activity for discrimination of frailty status: baseline results of the Arizona frailty cohort study. *Gerontology*. 2015; 61(3):258-267

- 1101 Scott IA. Preventing the rebound: improving care transition in hospital discharge processes. *Australian Health Review*. 2010; 34(4):445-451
- 1102 Sease JM, Franklin MA, Gerrald KR. Pharmacist management of patients with diabetes mellitus enrolled in a rural free clinic. *American Journal of Health-System Pharmacy*. 2013; 70:43-47
- 1103 Senior HEJ, Parsons M, Kerse N, Chen MH, Jacobs S, Hoorn SV et al. Promoting independence in frail older people: a randomised controlled trial of a restorative care service in New Zealand. *Age and Ageing*. 2014; 43(3):418-424
- 1104 Senni M, Parrella P, De Maria R, Cottini C, Bohm M, Ponikowski P et al. Predicting heart failure outcome from cardiac and comorbid conditions: the 3C-HF score. *International Journal of Cardiology*. 2013; 163(2):206-211
- 1105 Senni M, Santilli G, Parrella P, De Maria R, Alari G, Berzuini C et al. A novel prognostic index to determine the impact of cardiac conditions and co-morbidities on one-year outcome in patients with heart failure. *American Journal of Cardiology*. 2006; 98(8):1076-1082
- 1106 Sessler DI, Sigl JC, Manberg PJ, Kelley SD, Schubert A, Chamoun NG. Broadly applicable risk stratification system for predicting duration of hospitalization and mortality. *Anesthesiology*. 2010; 113(5):1026-1037
- 1107 Sewo Sampaio PY, Sampaio RA, Yamada M, Ogita M, Arai H. Validation and translation of the Kihon Checklist (frailty index) into Brazilian Portuguese. *Geriatrics and Gerontology International*. 2014; 14(3):561-569
- 1108 Shah SM, Carey IM, Harris T, DeWilde S, Cook DG. Mortality in older care home residents in England and Wales. *Age and Ageing*. 2013; 42(2):209-215
- 1109 Shalev V, Chodick G, Silber H, Kokia E, Jan J, Heymann AD. Continuation of statin treatment and all-cause mortality: a population-based cohort study. *Archives of Internal Medicine*. 2009; 169(3):260-268
- 1110 Shamliyan T, Talley KM, Ramakrishnan R, Kane RL. Association of frailty with survival: a systematic literature review. *Ageing Research Reviews*. 2013; 12(2):719-736
- 1111 Sharpe M, Walker J, Holm Hansen C, Martin P, Symeonides S, Gourley C et al. Integrated collaborative care for comorbid major depression in patients with cancer (SMaRT Oncology-2): a multicentre randomised controlled effectiveness trial. *The Lancet*. 2014; 384(9948):1099-1108
- 1112 Shelton P, Sager MA, Schraeder C. The community assessment risk screen (CARS): identifying elderly persons at risk for hospitalization or emergency department visit. *American Journal of Managed Care*. 2000; 6(8):925-933
- 1113 Sheperd J, Cobbe SM, Lorimer AR. Compliance and adverse event withdrawal: their impact on the West of Scotland Coronary Prevention Study. *European Heart Journal*. 1997; 18(11):1718-1724
- 1114 Shepherd J. Monotherapy vs combination therapy for dyslipidemia in the elderly. *American Journal of Geriatric Cardiology*. 2008; 17(2):108-113

- 1115 Shepperd S, McClaran J, Phillips CO, Lannin NA, Clemson LM, McCluskey A et al. Discharge planning from hospital to home. *Cochrane Database of Systematic Reviews*. 2010; Issue 1:CD000313. DOI:10.1002/14651858.CD000313.pub3
- 1116 Shigaki CL, Moore C, Wakefield B, Campbell J, LeMaster J. Nurse partners in chronic illness care: patients' perceptions and their implications for nursing leadership. *Nursing Administration Quarterly*. 2010; 34(2):130-140
- 1117 Shih SL, Gerrard P, Goldstein R, Mix J, Ryan CM, Niewczyk P et al. Functional status outperforms comorbidities in predicting acute care readmissions in medically complex patients. *Journal of General Internal Medicine*. 2015; 30(11):1688-1695
- 1118 Shin S, Jang S, Lee TJ, Kim H. Association between non-adherence to statin and hospitalization for cardiovascular disease and all-cause mortality in a national cohort. *International Journal of Clinical Pharmacology and Therapeutics*. 2014; 52(11):948-956
- 1119 Shively MJ, Gardetto NJ, Kodiath MF, Kelly A, Smith TL, Stepnowsky C et al. Effect of patient activation on self-management in patients with heart failure. *Journal of Cardiovascular Nursing*. 2013; 28:20-34
- 1120 Sidorov J, Shull R. "My patients are sicker:" using the Pra risk survey for case finding and examining primary care site utilization patterns in a medicare-risk MCO. *American Journal of Managed Care*. 2002; 8(6):569-575
- 1121 Silva TJA, Jerussalmy CS, Farfel JM, Curiati JAE, Jacob-Filho W. Predictors of in-hospital mortality among older patients. *Clinics*. 2009; 64(7):613-618
- 1122 Simmonds RL, Tylee A, Walters P, Rose D. Patients' perceptions of depression and coronary heart disease: a qualitative UPBEAT-UK study. *BMC Family Practice*. 2013; 14:38
- 1123 Simon TG, Beland MD, Machan JT, Dipetrillo T, Dupuy DE. Charlson Comorbidity Index predicts patient outcome, in cases of inoperable non-small cell lung cancer treated with radiofrequency ablation. *European Journal of Radiology*. 2012; 81(12):4167-4172
- 1124 Sinnott C, Hugh S, Browne J, Bradley C. GPs' perspectives on the management of patients with multimorbidity: systematic review and synthesis of qualitative research. *BMJ Open*. 2013; 3:e003610
- 1125 Sirola J, Pitkala KH, Tilvis RS, Miettinen TA, Strandberg TE. Definition of frailty in older men according to questionnaire data (RAND-36/SF-36): The Helsinki Businessmen study. *Journal of Nutrition, Health and Aging*. 2011; 15(9):783-787
- 1126 Slaets JP, Kauffmann RH, Duivenvoorden HJ, Pelemans W, Schudel WJ. A randomized trial of geriatric liaison intervention in elderly medical inpatients. *Psychosomatic Medicine*. 1997; 59:585-591
- 1127 Sledge WH, Wieland M, Sells D, Walden D, Holmberg C, Zhenqiu L et al. Qualitative study of high-cost patients in an urban primary care centre. *Chronic Illness*. 2011; 7(2):107-119
- 1128 Slejko JF, Ho M, Anderson HD, Nair KV, Sullivan PW, Campbell JD. Adherence to statins in primary prevention: yearly adherence changes and outcomes. *Journal of Managed Care Pharmacy*. 2014; 20(1):51-57

- 1129 Smith SM, O'Kelly S, O'Dowd T. GPs' and pharmacists' experiences of managing multimorbidity: A 'Pandora's box'. *British Journal of General Practice*. 2010; 60(576):e285-e294
- 1130 Smith SM, Soubhi H, Fortin M, Hudon C, O'Dowd T. Interventions for improving outcomes in patients with multimorbidity in primary care and community settings. *Cochrane Database of Systematic Reviews*. 2012; Issue 4:CD006560. DOI:10.1002/14651858.CD006560.pub2
- 1131 Snyder ME, Frail CK, Jaynes H, Pater KS, Zillich AJ. Predictors of medication-related problems among medicaid patients participating in a pharmacist-provided telephonic medication therapy management program. *Pharmacotherapy*. 2014; 34(10):1022-1032
- 1132 Soares I, Abecasis P, Ferro JM. Outcome of first-ever acute ischemic stroke in the elderly. *Archives of Gerontology and Geriatrics*. 2011; 53(2):e81-e87
- 1133 Solberg OG, Dahl M, Mowinckel P, Stavem K. Derivation and validation of a simple risk score for predicting 1-year mortality in stroke. *Journal of Neurology*. 2007; 254(10):1376-1383
- 1134 Solomon A, Dobranici L, Kareholt I, Tudose C, Lazarescu M. Comorbidity and the rate of cognitive decline in patients with Alzheimer dementia. *International Journal of Geriatric Psychiatry*. 2011; 26(12):1244-1251
- 1135 Sommers LS, Marton KI, Barbaccia JC, Randolph J. Physician, nurse, and social worker collaboration in primary care for chronically ill seniors. *Archives of Internal Medicine*. 2000; 160(12):1825-1833
- 1136 Sondergaard E, Willadsen TG, Guassora AD, Vestergaard M, Tomasdottir MO, Borgquist L et al. Problems and challenges in relation to the treatment of patients with multimorbidity: General practitioners' views and attitudes. *Scandinavian Journal of Primary Health Care*.: Taylor & Francis Informa Healthcare. 2015; 33(2):121-126
- 1137 Soong J, Poots AJ, Scott S, Donald K, Bell D. Developing and validating a risk prediction model for acute care based on frailty syndromes. *BMJ Open*. 2015; 5(10):e008457
- 1138 Soran OZ, Pina IL, Lamas GA, Kelsey SF, Selzer F, Pilotte J et al. A randomized clinical trial of the clinical effects of enhanced heart failure monitoring using a computer-based telephonic monitoring system in older minorities and women. *Journal of Cardiac Failure*. 2008; 14(9):711-717
- 1139 Soubeyran P, Fonck M, Blanc-Bisson C, Blanc JF, Ceccaldi J, Mertens C et al. Predictors of early death risk in older patients treated with first-line chemotherapy for cancer. *Journal of Clinical Oncology*. 2012; 30(15):1829-1834
- 1140 Southerland LT, Richardson DS, Caterino JM, Essenmacher AC, Swor RA. Emergency department recidivism in adults older than 65 years treated for fractures. *American Journal of Emergency Medicine*. 2014; 32(9):1089-1092
- 1141 Spector WD, Limcangco R, Williams C, Rhodes W, Hurd D. Potentially avoidable hospitalizations for elderly long-stay residents in nursing homes. *Medical Care*. 2013; 51(8):673-681
- 1142 Spencer FA, Allegrone J, Goldberg RJ, Gore JM, Fox KAA, Granger CB et al. Association of statin therapy with outcomes of acute coronary syndromes: the GRACE study. *Annals of Internal Medicine*. 2004; 140(11):857-866

- 1143 Spencer FA, Fonarow GC, Frederick PD, Wright RS, Every N, Goldberg RJ et al. Early withdrawal of statin therapy in patients with non-ST-segment elevation myocardial infarction: national registry of myocardial infarction. *Archives of Internal Medicine*. 2004; 164(19):2162-2168
- 1144 Stanhope V, Henwood BF. Activating people to address their health care needs: learning from people with lived experience of chronic illnesses. *Community Mental Health Journal*. 2014; 50(6):656-663
- 1145 Stanners MN, Barton CA, Shakib S, Winefield HR. A qualitative investigation of the impact of multimorbidity on GP diagnosis and treatment of depression in Australia. *Aging and Mental Health*. 2012; 16(8):1058-1064
- 1146 Stausberg J, Hagn S. New morbidity and comorbidity scores based on the structure of the ICD-10. *PLoS ONE*. 2015; 10(12):e0143365
- 1147 Steiner JF, Kramer AM, Eilertsen TB, Kowalsky JC. Development and validation of a clinical prediction rule for prolonged nursing home residence after hip fracture. *Journal of the American Geriatrics Society*. 1997; 45(12):1510-1514
- 1148 Steultjens Esther EMJ, Dekker JJ, Bouter LM, Cardol MM, Van den Ende ECHM, van de Nes J. Occupational therapy for multiple sclerosis. *Cochrane Database of Systematic Reviews*. 2003; Issue 3:CD003608. DOI:10.1002/14651858.CD003608
- 1149 Stewart S, Carrington MJ, Horowitz JD, Marwick TH, Newton PJ, Davidson PM et al. Prolonged impact of home versus clinic-based management of chronic heart failure: extended follow-up of a pragmatic, multicentre randomized trial cohort. *International Journal of Cardiology*. 2014; 174(3):600-610
- 1150 Stockl KM, Shin JS, Gong S, Harada AS, Solow BK, Lew HC. Improving patient self-management of multiple sclerosis through a disease therapy management program. *American Journal of Managed Care*. 2010; 16:139-144
- 1151 Stockler M. In palliative care, discontinuation of statins did not differ from continuation for mortality. *Annals of Internal Medicine*. 2015; 163(4):JC7
- 1152 Stokes J, Panagioti M, Alam R, Checkland K, Cheraghi-Sohi S, Bower P. Effectiveness of case management for 'at risk' patients in primary care: A systematic review and meta-analysis. *PLoS ONE*. 2015; 10(7)
- 1153 Stringer B, van Meijel B, Koekkoek B, Kerkhof A, Beekman A. Collaborative care for patients with severe borderline and NOS personality disorders: a comparative multiple case study on processes and outcomes. *BMC Psychiatry*. 2011; 11:102
- 1154 Stuck AE, Kharicha K, Dapp U, Anders J, von Renteln-Kruse W, Meier-Baumgartner HP et al. The PRO-AGE study: an international randomised controlled study of health risk appraisal for older persons based in general practice. *BMC Medical Research Methodology*. 2007; 7:2
- 1155 Stukenborg GJ, Wagner DP, Connors AF, Jr. Comparison of the performance of two comorbidity measures, with and without information from prior hospitalizations. *Medical Care*. 2001; 39(7):727-739
- 1156 Summer MM, Engstrom G. Experience of self-management of medications among older people with multimorbidity. *Journal of Clinical Nursing*. Malden, Massachusetts: Wiley-Blackwell. 2015; 24(19/20):2757-2764

- 1157 Summerfelt WT, Sulo S, Robinson A, Chess D, Catanzano K. Scalable hospital at home with virtual physician visits: pilot study. *American Journal of Managed Care*. 2015; 21(10):675-684
- 1158 Sundararajan V, Quan H, Halfon P, Fushimi K, Luthi JC, Burnand B et al. Cross-national comparative performance of three versions of the ICD-10 Charlson index. *Medical Care*. 2007; 45(12):1210-1215
- 1159 Susser SR, McCusker J, Belzile E. Comorbidity information in older patients at an emergency visit: self-report vs. administrative data had poor agreement but similar predictive validity. *Journal of Clinical Epidemiology*. 2008; 61(5):511-515
- 1160 Sweeney L, Halpert A, Waranoff J. Patient-centered management of complex patients can reduce costs without shortening life. *American Journal of Managed Care*. 2007; 13:84-92
- 1161 Swerissen H, Belfrage J, Weeks A, Jordan L, Walker C, Furler J et al. A randomised control trial of a self-management program for people with a chronic illness from Vietnamese, Chinese, Italian and Greek backgrounds. *Patient Education and Counseling*. 2006; 64(1-3):360-368
- 1162 Szeto CC, Chow KM, Kwan BCH, Leung CB, Chung KY, Law MC et al. Relation between number of prescribed medication and outcome in peritoneal dialysis patients. *Clinical Nephrology*. 2006; 66(4):256-262
- 1163 Taggart J, Schwartz A, Fanaian M, Taggart J, Davies P, Harris M et al. Facilitating teamwork in general practice: moving from theory to practice. *Australian Journal of Primary Health*. 2009; 15(1):24-28
- 1164 Takahashi PY, Hanson GJ, Pecina JL, Stroebel RJ, Chaudhry R, Shah ND et al. A randomized controlled trial of telemonitoring in older adults with multiple chronic conditions: the Tele-ERA study. *BMC Health Services Research*. 2010; 10:255
- 1165 Takahashi PY, Hanson GJ, Thorsteinsdottir B, Van Houten HK, Shah ND, Naessens JM et al. The impact of telemonitoring upon hospice referral in the community: a randomized controlled trial. *Clinical Interventions In Aging*. 2012; 7:445-451
- 1166 Takahashi PY, Pecina JL, Upatising B, Chaudhry R, Shah ND, Van Houten H et al. A randomized controlled trial of telemonitoring in older adults with multiple health issues to prevent hospitalizations and emergency department visits. *Archives of Internal Medicine*. 2012; 172:773-779
- 1167 Tal S, Guller V, Shavit Y, Stern F, Malnick S. Mortality predictors in hospitalized elderly patients. *QJM*. 2011; 104(11):933-938
- 1168 Tan SY, Low LL, Yang Y, Lee KH. Applicability of a previously validated readmission predictive index in medical patients in Singapore: a retrospective study. *BMC Health Services Research*. 2013; 13:366
- 1169 Tanajewski L, Franklin M, Gkoutouras G, Berdunov V, Edmans J, Conroy S et al. Cost-effectiveness of a specialist geriatric medical intervention for frail older people discharged from acute medical units: economic evaluation in a two-centre randomised controlled trial (AMIGOS). *PLoS ONE*. 2015; 10(5):e0121340
- 1170 Tang NK, Goodchild CE, Salkovskis PM. Hybrid cognitive-behaviour therapy for individuals with insomnia and chronic pain: a pilot randomised controlled trial. *Behaviour Research and Therapy*. 2012; 50:814-821

- 1171 Tang PF, Yang HJ, Peng YC, Chen HY. Motor dual-task Timed Up & Go test better identifies prefrailty individuals than single-task Timed Up & Go test. *Geriatrics and Gerontology International*. 2015; 15(2):204-210
- 1172 Tangherlini N, Pletcher MJ, Covec MA, Brown JF. Frequent use of emergency medical services by the elderly: a case-control study using paramedic records. *Prehospital and Disaster Medicine*. 2010; 25(3):258-264
- 1173 Tangiisuran B, Davies JG, Wright JE, Rajkumar C. Adverse drug reactions in a population of hospitalized very elderly patients. *Drugs and Aging*. 2012; 29(8):669-679
- 1174 Tanner JA, Black BS, Johnston D, Hess E, Leoutsakos J-M, Gitlin LN et al. A randomized controlled trial of a community-based dementia care coordination intervention: Effects of MIND at home on caregiver outcomes. *American Journal of Geriatric Psychiatry*. 2015; 23(4):391-402
- 1175 Tao P, Lin MH, Peng LN, Lee WC, Lin FY, Lee CH et al. Reducing the burden of morbidity and medical utilization of older patients by outpatient geriatric services: implications to primary health-care settings. *Geriatrics and Gerontology International*. 2012; 12(4):612-621
- 1176 Tapper EB, Finkelstein D, Mittleman MA, Piatkowski G, Lai M. Standard assessments of frailty are validated predictors of mortality in hospitalized patients with cirrhosis. *Hepatology*. 2015; 62(2):584-590
- 1177 Tarazona-Santabalbina FJ, Belenguer-Varea A, Rovira-Daudi E, Salcedo-Mahiques E, Cuesta-Peredo D, Domenech-Pascual JR et al. Early interdisciplinary hospital intervention for elderly patients with hip fractures : functional outcome and mortality. *Clinics*. 2012; 67(6):547-556
- 1178 Tate JP, Crothers K, Crystal S, Leaf DA, Womack J, Brown TT et al. An adapted frailty-related phenotype and the VACS index as predictors of hospitalization and mortality in HIV-infected and uninfected individuals. *Journal of Acquired Immune Deficiency Syndromes*. 2014; 67(4):397-404
- 1179 Taveira TH, Dooley AG, Cohen LB, Khatana SA, Wu WC. Pharmacist-led group medical appointments for the management of type 2 diabetes with comorbid depression in older adults. *Annals of Pharmacotherapy*. 2011; 45:1346-1355
- 1180 Teichert M, De Smet PAGM, Hofman A, Witteman JCM, Stricker BHC. Discontinuation of beta-blockers and the risk of myocardial infarction in the elderly. *Drug Safety*. 2007; 30(6):541-549
- 1181 Teno JM, Harrell FE, Jr., Knaus W, Phillips RS, Wu AW, Connors A, Jr. et al. Prediction of survival for older hospitalized patients: the HELP survival model. Hospitalized Elderly Longitudinal Project. *Journal of the American Geriatrics Society*. 2000; 48(5 Suppl):S16-S24
- 1182 Tessier A, Finch L, Daskalopoulou SS, Mayo NE. Validation of the Charlson Comorbidity Index for predicting functional outcome of stroke. *Archives of Physical Medicine & Rehabilitation*. 2008; 89(7):1276-1283
- 1183 Testa G, Cacciatore F, Galizia G, Della-Morte D, Mazzella F, Russo S et al. Charlson Comorbidity Index does not predict long-term mortality in elderly subjects with chronic heart failure. *Age and Ageing*. 2009; 38(6):734-740

- 1184 Tetsche MS, Norgaard M, Jacobsen J, Wogelius P, Sorensen HT. Comorbidity and ovarian cancer survival in Denmark, 1995-2005: a population-based cohort study. *International Journal of Gynecological Cancer*. 2008; 18(3):421-427
- 1185 Theou O, Brothers TD, Mitnitski A, Rockwood K. Operationalization of frailty using eight commonly used scales and comparison of their ability to predict all-cause mortality. *Journal of the American Geriatrics Society*. 2013; 61(9):1537-1551
- 1186 Thompson HJ, Rivara FP, Nathens A, Wang J, Jurkovich GJ, Mackenzie EJ. Development and validation of the mortality risk for trauma comorbidity index. *Annals of Surgery*. 2010; 252(2):370-375
- 1187 Thompson NR, Fan Y, Dalton JE, Jehi L, Rosenbaum BP, Vadera S et al. A new elixhauser-based comorbidity summary measure to predict in-hospital mortality. *Medical Care*. 2013; 53(4):374-379
- 1188 Thomsen K, Riis BJ, Johansen JS, Christiansen C, Rodbro P. Bone turnover in postmenopausal women after withdrawal of estrogen/gestagen replacement therapy. *Gynecological Endocrinology*. 1987; 1(2):169-175
- 1189 Thorpe CT, Bryson CL, Maciejewski ML, Bosworth HB. Medication acquisition and self-reported adherence in veterans with hypertension. *Medical Care*. 2009; 47(4):474-481
- 1190 Tibaldi V, Aimonino N, Ponzetto M, Stasi MF, Amati D, Raspo S et al. A randomized controlled trial of a home hospital intervention for frail elderly demented patients: behavioral disturbances and caregiver's stress. *Archives of Gerontology and Geriatrics Supplement*. 2004;(9):431-436
- 1191 Tierce-Hazard S, Sadarangani T. Optimizing the primary care management of chronic pain through telecare. *Journal of Clinical Outcomes Management*. 2014; 21(11):493-495
- 1192 Tierney MC, Charles J, Naglie G, Jaglal S, Kiss A, Fisher RH. Risk factors for harm in cognitively impaired seniors who live alone: a prospective study. *Journal of the American Geriatrics Society*. 2004; 52(9):1435-1441
- 1193 Tierney MC, Snow WG, Charles J, Moineddin R, Kiss A. Neuropsychological predictors of self-neglect in cognitively impaired older people who live alone. *American Journal of Geriatric Psychiatry*. 2007; 15(2):140-148
- 1194 Tilling K, Sterne JA, Rudd AG, Glass TA, Wityk RJ, Wolfe CD. A new method for predicting recovery after stroke. *Stroke; a Journal of Cerebral Circulation*. 2001; 32(12):2867-2873
- 1195 Timmer AJ, Unsworth CA, Taylor NF. Rehabilitation interventions with deconditioned older adults following an acute hospital admission: a systematic review. *Clinical Rehabilitation*. 2014; 28(11):1078-1086
- 1196 Ting B, Zurakowski D, Herder L, Wagner K, Appleton P, Rodriguez EK. Preinjury ambulatory status is associated with 1-year mortality following lateral compression Type I fractures in the geriatric population older than 80 years. *Journal of Trauma and Acute Care Surgery*. 2014; 76(5):1306-1309
- 1197 Tjia J, Givens JL, Karlawish JH, Okoli-Umeweni A, Barg FK. Beneath the surface: discovering the unvoiced concerns of older adults with type 2 diabetes mellitus. *Health Education Research*. 2008; 23(1):40-52

- 1198 Tjia J, Givens J. Ethical framework for medication discontinuation in nursing home residents with limited life expectancy. *Clinics in Geriatric Medicine*. 2012; 28(2):255-272
- 1199 Tobacman JK. Assessment of comorbidity: a review. *Clinical Performance and Quality Health Care*. 1994; 2(1):23-32
- 1200 Tocchi C, Dixon J, Naylor M, Jeon S, McCorkle R. Development of a frailty measure for older adults: the frailty index for elders. *Journal of Nursing Measurement*. 2014; 22(2):223-240
- 1201 Tong LS, Hu HT, Zhang S, Yan SQ, Lou M. Statin withdrawal beyond acute phase affected outcome of thrombolytic stroke patients: an observational retrospective study. *Medicine*. 2015; 94(17):e779
- 1202 Toobert DJ, Strycker LA, Barrera M, Jr., Osuna D, King DK, Glasgow RE. Outcomes from a multiple risk factor diabetes self-management trial for Latinas: Viva Bien! *Annals of Behavioral Medicine*. 2011; 41:310-323
- 1203 Torres OH, Francia E, Longobardi V, Gich I, Benito S, Ruiz D. Short- and long-term outcomes of older patients in intermediate care units. *Intensive Care Medicine*. 2006; 32(7):1052-1059
- 1204 Torres OH, Munoz J, Ruiz D, Ris J, Gich I, Coma E et al. Outcome predictors of pneumonia in elderly patients: importance of functional assessment. *Journal of the American Geriatrics Society*. 2004; 52(10):1603-1609
- 1205 Toson B, Harvey LA, Close JC. The ICD-10 Charlson Comorbidity Index predicted mortality but not resource utilization following hip fracture. *Journal of Clinical Epidemiology*. 2015; 68(1):44-51
- 1206 Townsend A, Leese J, Adam P, McDonald M, Li LC, Kerr S et al. eHealth, participatory medicine, and ethical care: a focus group study of patients' and health care providers' use of health-related internet information. *Journal of Medical Internet Research*. 2015; 17(6):e155
- 1207 Townsend A. Applying Bourdieu's theory to accounts of living with multimorbidity. *Chronic Illness*. 2012; 8(2):89-101
- 1208 Townsend A, Adam P, Li LC, McDonald M, Backman CL. Exploring eHealth ethics and multimorbidity: protocol for an interview and focus group study of patient and health care provider views and experiences of using digital media for health purposes. *JMIR Research Protocols*. 2013; 2(2):e38
- 1209 Townsend A, Hunt K, Wyke S. Managing multiple morbidity in mid-life: a qualitative study of attitudes to drug use. *BMJ*. 2003; 327(7419):837
- 1210 Townsend A, Wyke S, Hunt K. Self-managing and managing self: practical and moral dilemmas in accounts of living with chronic illness. *Chronic Illness*. 2006; 2(3):185-194
- 1211 Townsend A, Wyke S, Hunt K. Frequent consulting and multiple morbidity: a qualitative comparison of 'high' and 'low' consulters of GPs. *Family Practice*. 2008; 25(3):168-175
- 1212 Tran VT, Harrington M, Montori VM, Barnes C, Wicks P, Ravaud P. Adaptation and validation of the Treatment Burden Questionnaire (TBQ) in English using an internet platform. *BMC Medicine*. 2014; 12:109

- 1213 Tran VT, Montori VM, Eton DT, Baruch D, Falissard B, Ravaud P. Development and description of measurement properties of an instrument to assess treatment burden among patients with multiple chronic conditions. *BMC Medicine*. 2012; 10:68
- 1214 Trentini M, Semeraro S, Motta M. Effectiveness of geriatric evaluation and care. One-year results of a multicenter randomized clinical trial. *Aging (Milan, Italy)*. 2001; 13(5):395-405
- 1215 Trief PM, Morin PC, Izquierdo R, Teresi J, Eimicke JP, Goland R et al. Depression and glycemic control in elderly ethnically diverse patients with diabetes: the IDEATel project. *Diabetes Care*. 2006; 29:830-835
- 1216 Tsui E, Au SY, Wong CP, Cheung A, Lam P. Development of an automated model to predict the risk of elderly emergency medical admissions within a month following an index hospital visit: a Hong Kong experience. *Health Informatics Journal*. 2015; 21(1):46-56
- 1217 Tuppin P, Neumann A, Danchin N, de Peretti C, Weill A, Ricordeau P et al. Evidence-based pharmacotherapy after myocardial infarction in France: adherence-associated factors and relationship with 30-month mortality and rehospitalization. *Archives of Cardiovascular Diseases*. 2010; 103(6-7):363-375
- 1218 Turner J, Yates P, Kenny L, Gordon LG, Burmeister B, Thomson D et al. The ENHANCES study-- Enhancing Head and Neck Cancer patients' Experiences of Survivorship: study protocol for a randomized controlled trial. *Trials*. 2014; 15:191
- 1219 Uggerby P, Nielsen RE, Correll CU, Nielsen J. Characteristics and predictors of long-term institutionalization in patients with schizophrenia. *Schizophrenia Research*. 2011; 131(1-3):120-126
- 1220 Upatising B, Hanson GJ, Kim YL, Cha SS, Yih Y, Takahashi PY. Effects of home telemonitoring on transitions between frailty states and death for older adults: a randomized controlled trial. *International Journal of General Medicine*. 2013; 6:145-151
- 1221 Upshur C, Weinreb L, Bharel M, Reed G, Frisard C. A randomized control trial of a chronic care intervention for homeless women with alcohol use problems. *Journal of Substance Abuse Treatment*. 2015; 51:19-29
- 1222 Urbina O, Ferrandez O, Luque S, Grau S, Mojal S, Pellicer R et al. Patient risk factors for developing a drug-related problem in a cardiology ward. *Therapeutics and Clinical Risk Management*. 2015; 11:9-15
- 1223 Utriyaprasit K, Moore SM, Chaiseri P. Recovery after coronary artery bypass surgery: effect of an audiotape information programme. *Journal of Advanced Nursing*. 2010; 66:1747-1759
- 1224 Uusi-Rasi K, Sievanen H, Heinonen A, Kannus P, Vuori I. Effect of discontinuation of alendronate treatment and exercise on bone mass and physical fitness: 15-month follow-up of a randomized, controlled trial. *Bone*. 2004; 35(3):799-805
- 1225 Vaiciuniene R, Kuzminskis V, Ziginiskiene E, Petruliene K. Risk factors for cardiovascular hospitalization in hemodialysis patients. *Medicina*. 2010; 46(8):544-549
- 1226 van Bastelaar KM, Pouwer F, Cuijpers P, Twisk JW, Snoek FJ. Web-based cognitive behavioural therapy (W-CBT) for diabetes patients with co-morbid depression: design of a randomised controlled trial. *BMC Psychiatry*. 2008; 8:9

- 1227 van den Bemt PM, Egberts AC, Lenderink AW, Verzijl JM, Simons KA, van der Pol WS et al. Risk factors for the development of adverse drug events in hospitalized patients. *Pharmacy World and Science*. 2000; 22(2):62-66
- 1228 van der Kluit MJ, Goossens PJJ. Factors influencing attitudes of nurses in general health care toward patients with comorbid mental illness: An integrative literature review. *Issues in Mental Health Nursing*.: Informa Healthcare Taylor & Francis. 2011; 32(8):519-527
- 1229 van der Voort TY, van Meijel B, Goossens PJ, Renes J, Beekman AT, Kupka RW. Collaborative care for patients with bipolar disorder: a randomised controlled trial. *BMC Psychiatry*. 2011; 11:133
- 1230 van Doorn C, Bogardus ST, Williams CS, Concato J, Towle VR, Inouye SK. Risk adjustment for older hospitalized persons: a comparison of two methods of data collection for the Charlson index. *Journal of Clinical Epidemiology*. 2001; 54(7):694-701
- 1231 Van Durme T, Macq J, Anthierens S, Symons L, Schmitz O, Paulus D et al. Stakeholders' perception on the organization of chronic care: a SWOT analysis to draft avenues for health care reforms. *BMC Health Services Research*. 2014; 14:179
- 1232 van Hasselt FM, Oud MJT, Loonen AJM. Improvement of care for the physical health of patients with severe mental illness: a qualitative study assessing the view of patients and families. *BMC Health Services Research*. 2013; 13:426
- 1233 van Hout HP, Nijpels G, van Marwijk HW, Jansen AP, Van't Veer PJ, Tybout W et al. Design and pilot results of a single blind randomized controlled trial of systematic demand-led home visits by nurses to frail elderly persons in primary care [ISRCTN05358495]. *BMC Geriatrics*. 2005; 5:11
- 1234 van Kempen JAL, Schers HJ, Philp I, Olde Rikkert MGM, Melis RJF. Predictive validity of a two-step tool to map frailty in primary care. *BMC Medicine*. 2015; 13:287
- 1235 van Manen JG, Korevaar JC, Dekker FW, Boeschoten EW, Bossuyt PM, Krediet RT et al. How to adjust for comorbidity in survival studies in ESRD patients: a comparison of different indices. *American Journal of Kidney Diseases*. 2002; 40(1):82-89
- 1236 van Walraven C. The Hospital-patient One-year Mortality Risk score accurately predicted long-term death risk in hospitalized patients. *Journal of Clinical Epidemiology*. 2014; 67(9):1025-1034
- 1237 van Wijk BLG, Avorn J, Solomon DH, Klungel OH, Heerdink ER, de Boer A et al. Rates and determinants of reinitiating antihypertensive therapy after prolonged stoppage: a population-based study. *Journal of Hypertension*. 2007; 25(3):689-697
- 1238 Vanderlip ER. Depression and diabetes: improving outcomes through collaborative care. *Psychiatric Times*. Nowalk, California: UBM Medica. 2015; 35(2):1-5
- 1239 Velghe A, Petrovic M, De Buyser S, Demuyneck R, Noens L. Validation of the G8 screening tool in older patients with aggressive haematological malignancies. *European Journal of Oncology Nursing*. 2014; 18(6):645-648
- 1240 Vellas B, Balardy L, Gillette-Guyonnet S, Abellan van Kan G, Ghisolfi-Marque A, Subra J et al. Looking for frailty in community-dwelling older persons: the Gerontopole Frailty Screening Tool (GFST). *Journal of Nutrition, Health and Aging*. 2013; 17(7):629-631

- 1241 Venkat A, Pastin RB, Hegde GG, Shea JM, Cook JT, Culig C. An analysis of ED utilization by adults with intellectual disability. *American Journal of Emergency Medicine*. 2011; 29(4):401-411
- 1242 Vera M, Perez-Pedrogo C, Huertas SE, Reyes-Rabanillo ML, Juarbe D, Huertas A et al. Collaborative care for depressed patients with chronic medical conditions: a randomized trial in Puerto Rico. *Psychiatric Services*. 2010; 61:144-150
- 1243 Verdalles U, Abad S, Aragoncillo I, Villaverde M, Jofre R, Verde E et al. Factors predicting mortality in elderly patients on dialysis. *Nephron Clinical Practice*. 2010; 115(1):c28-c34
- 1244 Veronesi M, Cicero AFG, Prandin MG, Dormi A, Cosentino E, Strocchi E et al. A prospective evaluation of persistence on antihypertensive treatment with different antihypertensive drugs in clinical practice. *Vascular Health and Risk Management*. 2007; 3(6):999-1005
- 1245 Vetrano DL, Landi F, De Buyser SL, Carfi A, Zuccala G, Petrovic M et al. Predictors of length of hospital stay among older adults admitted to acute care wards: a multicentre observational study. *European Journal of Internal Medicine*. 2014; 25(1):56-62
- 1246 Vidan MT, Sanchez E, Fernandez-Aviles F, Serra-Rexach JA, Ortiz J, Bueno H. FRAIL-HF, a study to evaluate the clinical complexity of heart failure in nondependent older patients: rationale, methods and baseline characteristics. *Clinical Cardiology*. 2014; 37(12):725-732
- 1247 Vieira ER, Berean C, Paches D, Caveny P, Yuen D, Ballash L et al. Reducing falls among geriatric rehabilitation patients: a controlled clinical trial. *Clinical Rehabilitation*. 2013; 27:325-335
- 1248 Vik K, Nygard L, Lilja M. Encountering staff in the home: three older adults' experience during six months of home-based rehabilitation. *Disability and Rehabilitation*. 2009; 31(8):619-629
- 1249 Vind AB, Andersen HE, Pedersen KD, Joergensen T, Schwarz P. Effect of a program of multifactorial fall prevention on health-related quality of life, functional ability, fear of falling and psychological well-being. A randomized controlled trial. *Aging Clinical and Experimental Research*. 2010; 22(3):249-254
- 1250 Vinogradova Y, Coupland C, Brindle P, Hippisley-Cox J. Patients who discontinued statin treatment: a protocol for cohort study using primary care data. *BMJ Open*. 2015; 5(10):e008701
- 1251 Vischer UM, Frangos E, Graf C, Gold G, Weiss L, Herrmann FR et al. The prognostic significance of malnutrition as assessed by the Mini Nutritional Assessment (MNA) in older hospitalized patients with a heavy disease burden. *Clinical Nutrition*. 2012; 31(1):113-117
- 1252 Visser M, Marinus J, van Hilten JJ, Schipper RG, Stiggelbout AM. Assessing comorbidity in patients with Parkinson's disease. *Movement Disorders*. 2004; 19(7):824-828
- 1253 Vitry A, Wong SA, Roughead EE, Ramsay E, Barratt J. Validity of medication-based co-morbidity indices in the Australian elderly population. *Australian and New Zealand Journal of Public Health*. 2009; 33(2):126-130
- 1254 Vlaeyen JW, Teeken-Gruben NJ, Goossens ME, Rutten-van Molken MP, Pelt RA, van Eek H et al. Cognitive-educational treatment of fibromyalgia: a randomized clinical trial. I. Clinical effects. *Journal of Rheumatology*. 1996; 23(7):1237-1245
- 1255 Voeller H, Dovifat C, Wegscheider K. Experience with INR self-management: patient selection and complication rates. *Zeitschrift Fur Kardiologie*. 2005; 94:801-807

- 1256 Voisin T, Andrieu S, Cantet C, Vellas B, REAL.FR Group. Predictive factors of hospitalizations in Alzheimer's disease: a two-year prospective study in 686 patients of the REAL.FR study. *Journal of Nutrition, Health and Aging*. 2010; 14(4):288-291
- 1257 Vojta CL, Vojta DD, TenHave TR, Amaya M, Lavizzo-Mourey R, Asch DA. Risk screening in a medicare/medicaid population administrative data versus self report. *Journal of General Internal Medicine*. 2001; 16(8):525-530
- 1258 Volk ML, Tocco RS, Bazick J, Rakoski MO, Lok AS. Hospital readmissions among patients with decompensated cirrhosis. *American Journal of Gastroenterology*. 2012; 107(2):247-252
- 1259 Volpato S, Onder G, Cavalieri M, Guerra G, Sioulis F, Maraldi C et al. Characteristics of nondisabled older patients developing new disability associated with medical illnesses and hospitalization. *Journal of General Internal Medicine*. 2007; 22(5):668-674
- 1260 Von Korff M, Katon WJ, Lin EH, Ciechanowski P, Peterson D, Ludman EJ et al. Functional outcomes of multi-condition collaborative care and successful ageing: results of randomised trial. *BMJ*. 2011; 343:d6612
- 1261 Von Korff M, Vitiello MV, McCurry SM, Balderson BH, Moore AL, Baker LD et al. Group interventions for co-morbid insomnia and osteoarthritis pain in primary care: the lifestyles cluster randomized trial design. *Contemporary Clinical Trials*. 2012; 33:759-768
- 1262 Von Korff M, Wagner EH, Saunders K. A chronic disease score from automated pharmacy data. *Journal of Clinical Epidemiology*. 1992; 45(2):197-203
- 1263 Voskaridou E, Christoulas D, Konstantinidou M, Tsiftsakis E, Alexakos P, Terpos E. Continuous improvement of bone mineral density two years post zoledronic acid discontinuation in patients with thalassemia-induced osteoporosis: long-term follow-up of a randomized, placebo-controlled trial. *Haematologica*. 2008; 93(10):1588-1590
- 1264 Wade V, Cheek F, Schrader G, Hordacre AL, Marker J. Depression after cardiac hospitalisation--the Identifying Depression as a Comorbid Condition (IDACC) study. *Australian Family Physician*. 2005; 34(11):985-989
- 1265 Wagner JT, Bachmann LM, Boult C, Harari D, von Renteln-Kruse W, Egger M et al. Predicting the risk of hospital admission in older persons--validation of a brief self-administered questionnaire in three European countries. *Journal of the American Geriatrics Society*. 2006; 54(8):1271-1276
- 1266 Wagner M, Ansell D, Kent DM, Griffith JL, Naimark D, Wanner C et al. Predicting mortality in incident dialysis patients: an analysis of the United Kingdom Renal Registry. *American Journal of Kidney Diseases*. 2011; 57(6):894-902
- 1267 Wakabayashi R, Motegi T, Yamada K, Ishii T, Jones RC, Hyland ME et al. Efficient integrated education for older patients with chronic obstructive pulmonary disease using the Lung Information Needs Questionnaire. *Geriatrics and Gerontology International*. 2011; 11:422-430
- 1268 Wakefield BJ, Holman JE, Ray A, Scherubel M, Adams MR, Hillis SL et al. Effectiveness of home telehealth in comorbid diabetes and hypertension: a randomized, controlled trial. *Telemedicine Journal and E-Health*. 2011; 17:254-261

- 1269 Wakefield BJ, Holman JE, Ray A, Scherubel M, Adams MR, Hills SL et al. Outcomes of a home telehealth intervention for patients with diabetes and hypertension. *Telemedicine Journal and E-Health*. 2012; 18:575-579
- 1270 Walker L, Jamrozik K, Wingfield D. The Sherbrooke Questionnaire predicts use of emergency services. *Age and Ageing*. 2005; 34(3):233-237
- 1271 Wallace E, Hinchey T, Dimitrov BD, Bennett K, Fahey T, Smith SM. A systematic review of the probability of repeated admission score in community-dwelling adults. *Journal of the American Geriatrics Society*. 2013; 61(3):357-364
- 1272 Wallace E, Stuart E, Vaughan N, Bennett K, Fahey T, Smith SM. Risk prediction models to predict emergency hospital admission in community-dwelling adults: a systematic review. *Medical Care*. 2014; 52(8):751-765
- 1273 Wallis SJ, Wall J, Biram RWS, Romero-Ortuno R. Association of the clinical frailty scale with hospital outcomes. *QJM*. 2015; 108(12):943-949
- 1274 Walsh EK, Cussen K. "Take ten minutes": a dedicated ten minute medication review reduces polypharmacy in the elderly. *Irish Medical Journal*. 2010; 103(8):236-238
- 1275 Walter LC, Brand RJ, Counsell SR, Palmer RM, Landefeld CS, Fortinsky RH et al. Development and validation of a prognostic index for 1-year mortality in older adults after hospitalization. *JAMA*. 2001; 285(23):2987-2994
- 1276 Walter LC, Covinsky KE. Cancer screening in elderly patients: a framework for individualized decision making. *JAMA*. 2001; 285(21):2750-2756
- 1277 Wang H, Robinson RD, Johnson C, Zenarosa NR, Jayswal RD, Keithley J et al. Using the LACE index to predict hospital readmissions in congestive heart failure patients. *BMC Cardiovascular Disorders*. 2014; 14:97
- 1278 Wang L, Li J. Role of educational intervention in the management of comorbid depression and hypertension. *Blood Pressure*. 2003; 12:198-202
- 1279 Wang L, Porter B, Maynard C, Evans G, Bryson C, Sun H et al. Predicting risk of hospitalization or death among patients receiving primary care in the Veterans Health Administration. *Medical Care*. 2013; 51(4):368-373
- 1280 Wang R, Chen L, Fan L, Gao D, Liang Z, He J et al. Incidence and effects of polypharmacy on clinical outcome among patients aged 80+: a five-year follow-up study. *PLoS ONE*. 2015; 10(11):e0142123
- 1281 Warrington D, Cholowski K, Peters D. Effectiveness of home-based cardiac rehabilitation for special needs patients. *Journal of Advanced Nursing*. 2003; 41:121-129
- 1282 Warsi A, Wang PS, LaValley MP, Avorn J, Solomon DH. Self-management education programs in chronic disease: a systematic review and methodological critique of the literature. *Archives of Internal Medicine*. 2004; 164:1641-1649
- 1283 Wasnich RD, Bagger YZ, Hosking DJ, McClung MR, Wu M, Mantz AM et al. Changes in bone density and turnover after alendronate or estrogen withdrawal. *Menopause*. 2004; 11(6 Pt 1):622-630

- 1284 Wassertheil-Smoller S, Langford H, Blaufox MD. Rate of hypertension return after withdrawal of prolonged antihypertensive therapy. *Clinical Science*. 1982; 63(8):423s-425s
- 1285 Wasson JH, Sauvigne AE, Mogielnicki RP, Frey WG, Sox CH, Gaudette C et al. Continuity of outpatient medical care in elderly men. A randomized trial. *JAMA*. 1984; 252(17):2413-2417
- 1286 Waterworth S, Arroll B, Raphael D, Parsons J, Gott M. A qualitative study of nurses' clinical experience in recognising low mood and depression in older patients with multiple long-term conditions. *Journal of Clinical Nursing*. 2015; 24(17-18):2562-2570
- 1287 Waterworth S, Gott M, Raphael D, Parsons J, Arroll B. Working with older people with multiple long-term conditions: a qualitative exploration of nurses' experiences. *Journal of Advanced Nursing*. 2015; 71(1):90-99
- 1288 Watkin L, Blanchard MR, Tookman A, Sampson EL. Prospective cohort study of adverse events in older people admitted to the acute general hospital: risk factors and the impact of dementia. *International Journal of Geriatric Psychiatry*. 2012; 27(1):76-82
- 1289 Watson A, Charlesworth L, Jacob R, Kendrick D, Logan P, Marshall F et al. The Community In-Reach and Care Transition (CIRACT) clinical and cost-effectiveness study: Study protocol for a randomised controlled trial. *Trials*. 2015; 16(1)
- 1290 Watts NB, Chines A, Olszynski WP, McKeever CD, McClung MR, Zhou X et al. Fracture risk remains reduced one year after discontinuation of risedronate. *Osteoporosis International*. 2008; 19(3):365-372
- 1291 Webster J, Jeffers A, Galloway DB, Petrie JC. Withdrawal of antihypertensive therapy. *The Lancet*. 1974; 2(7893):1381-1382
- 1292 Wei L, Wang J, Thompson P, Wong S, Struthers AD, MacDonald TM. Adherence to statin treatment and readmission of patients after myocardial infarction: a six year follow up study. *Heart*. 2002; 88(3):229-233
- 1293 Wei L, Fahey T, MacDonald TM. Adherence to statin or aspirin or both in patients with established cardiovascular disease: exploring healthy behaviour vs. drug effects and 10-year follow-up of outcome. *British Journal of Clinical Pharmacology*. 2008; 66(1):110-116
- 1294 Weinerman B, den Duyf J, Hughes A, Robertson S. Can subspecialty cancer consultations be delivered to communities using modern technology?--A pilot study. *Telemedicine Journal and E-Health*. 2005; 11:608-615
- 1295 Weinstock RS, Brooks G, Palmas W, Morin PC, Teresi JA, Eimicke JP et al. Lessened decline in physical activity and impairment of older adults with diabetes with telemedicine and pedometer use: results from the IDEATel study. *Age and Ageing*. 2011; 40:98-105
- 1296 Weiss JW, Platt RW, Thorp ML, Yang X, Smith DH, Petrik A et al. Predicting mortality in older adults with kidney disease: a pragmatic prediction model. *Journal of the American Geriatrics Society*. 2015; 63(3):508-515
- 1297 Wensing M, Huntink E, van Lieshout J, Godycki-Cwirko M, Kowalczyk A, Jager C et al. Tailored implementation of evidence-based practice for patients with chronic diseases. *PLoS ONE*. 2014; 9(7)

- 1298 Wentzlaff DM, Carter BL, Ardery G, Franciscus CL, Doucette WR, Chrischilles EA et al. Sustained blood pressure control following discontinuation of a pharmacist intervention. *Journal of Clinical Hypertension*. 2011; 13(6):431-437
- 1299 West of Scotland Coronary Prevention Study Group. The effects of pravastatin on hospital admission in hypercholesterolemic middle-aged men: West of Scotland Coronary Prevention Study. *Journal of the American College of Cardiology*. 1999; 33(4):909-915
- 1300 White HD, Blair J, Pinkney J, Cuthbertson DJ, Day R, Weber A et al. Improvement in the care of multiple endocrine neoplasia type 1 through a regional multidisciplinary clinic. *QJM*. 2010; 103:337-345
- 1301 Whitford DL, Chan WS. A randomised controlled trial of a lengthened and multi-disciplinary consultation model in a socially deprived community: a study protocol. *BMC Family Practice*. 2007; 8:38
- 1302 Whitson HE, Steinhauser K, Ammarell N, Whitaker D, Cousins SW, Ansah D et al. Categorizing the effect of comorbidity: a qualitative study of individuals' experiences in a low-vision rehabilitation program. *Journal of the American Geriatrics Society*. 2011; 59(10):1802-1809
- 1303 Widagdo IS, Pratt N, Russell M, Roughead EE. Predictive performance of four frailty measures in an older Australian population. *Age and Ageing*. 2015; 44(6):967-972
- 1304 Williams AF, Manias E, Walker RG. The devil is in the detail - a multifactorial intervention to reduce blood pressure in co-existing diabetes and chronic kidney disease: a single blind, randomized controlled trial. *BMC Family Practice*. 2010; 11:3
- 1305 Williams A. Patients with comorbidities: perceptions of acute care services. *Journal of Advanced Nursing*. 2004; 46(1):13-22
- 1306 Williams A, Dunning T, Manias E. Continuity of care and general wellbeing of patients with comorbidities requiring joint replacement. *Journal of Advanced Nursing*. 2007; 57(3):244-256
- 1307 Williams A, Manias E. Exploring motivation and confidence in taking prescribed medicines in coexisting diseases: a qualitative study. *Journal of Clinical Nursing*. 2014; 23(3-4):471-481
- 1308 Williams B, Shaw A, Durrant R, Crinson I, Pagliari C, de Lusignan S. Patient perspectives on multiple medications versus combined pills: a qualitative study. *QJM*. 2005; 98(12):885-893
- 1309 Williams JW, Jr., Katon W, Lin EH, Noel PH, Worchel J, Cornell J et al. The effectiveness of depression care management on diabetes-related outcomes in older patients. *Annals of Internal Medicine*. 2004; 140(12):1015-1024
- 1310 Wilson PM, Kataria N, McNeilly E. Patient and carer experience of obtaining regular prescribed medication for chronic disease in the English National Health Service: a qualitative study. *BMC Health Services Research*. 2013; 13:192
- 1311 Wimmer BC, Dent E, Bell JSS, Wiese MD, Chapman I, Johnell K et al. Medication regimen complexity and unplanned hospital readmissions in older people. *Annals of Pharmacotherapy*. 2014; 48(9):1120-1128
- 1312 Wimmer BC, Dent E, Visvanathan R, Wiese MD, Johnell K, Chapman I et al. Polypharmacy and medication regimen complexity as factors associated with hospital discharge destination among older people: a prospective cohort study. *Drugs and Aging*. 2014; 31(8):623-630

- 1313 Wister AV, Levasseur M, Griffith LE, Fyffe I. Estimating multiple morbidity disease burden among older persons: a convergent construct validity study to discriminate among six chronic illness measures, CCHS 2008/09. *BMC Geriatrics*. 2015; 15:12
- 1314 Woltmann E, Grogan-Kaylor A, Perron B, Georges H, Kilbourne AM, Bauer MS. Comparative effectiveness of collaborative chronic care models for mental health conditions across primary, specialty, and behavioral health care settings: systematic review and meta-analysis. *American Journal of Psychiatry*. 2012; 169:790-804
- 1315 Wong CK, Wong WC, Lam CL, Wan YF, Wong WH, Chung KL et al. Effects of Patient Empowerment Programme (PEP) on clinical outcomes and health service utilization in type 2 diabetes mellitus in primary care: an observational matched cohort study. *PLoS ONE*. 2014; 9:e95328
- 1316 Wong J, Taljaard M, Forster AJ, Escobar GJ, van Walraven C. Derivation and validation of a model to predict daily risk of death in hospital. *Medical Care*. 2011; 49(8):734-743
- 1317 Woo J, Leung J, Morley JE. Comparison of frailty indicators based on clinical phenotype and the multiple deficit approach in predicting mortality and physical limitation. *Journal of the American Geriatrics Society*. 2012; 60(8):1478-1486
- 1318 Worrall G, Knight J. Continuity of care for older patients in family practice: how important is it? *Canadian Family Physician*. 2006; 52:754-755
- 1319 Wrede J, Voigt I, Bleidorn J, Hummers-Pradier E, Dierks ML, Junius-Walker U. Complex health care decisions with older patients in general practice: patient-centeredness and prioritization in consultations following a geriatric assessment. *Patient Education and Counseling*. 2013; 90:54-60
- 1320 Wu CJ, Chang AM, Courtney M, Kostner K. Peer supporters for cardiac patients with diabetes: a randomized controlled trial. *International Nursing Review*. 2012; 59:345-352
- 1321 Wu C, Bell CM, Wodchis WP. Incidence and economic burden of adverse drug reactions among elderly patients in Ontario emergency departments: a retrospective study. *Drug Safety*. 2012; 35(9):769-781
- 1322 Wu PH, Lin YT, Lee TC, Lin MY, Kuo MC, Chiu YW et al. Predicting mortality of incident dialysis patients in Taiwan--a longitudinal population-based study. *PLoS ONE*. 2013; 8(4):e61930
- 1323 Wuerzner K, Hassler C, Burnier M. Difficult blood pressure control: watch out for non-compliance! *Nephrology, Dialysis, Transplantation*. 2003; 18(10):1969-1973
- 1324 Yan Y, Birman-Deych E, Radford MJ, Nilasena DS, Gage BF. Comorbidity indices to predict mortality from Medicare data: results from the national registry of atrial fibrillation. *Medical Care*. 2005; 43(11):1073-1077
- 1325 Yang Y, Thumboo J, Earnest A, Yong SL, Fong KY. The effect of comorbidity on hospital mortality in patients with SLE from an Asian tertiary hospital. *Lupus*. 2014; 23(7):714-720
- 1326 Yen L, Gillespie J, Rn YHJ, Kljakovic M, Anne Brien J, Jan S et al. Health professionals, patients and chronic illness policy: a qualitative study. *Health Expectations*. 2011; 14(1):10-20
- 1327 Yohannes AM, Caton S. Management of depression in older people with osteoarthritis: A systematic review. *Aging and Mental Health*. 2010; 14:637-651

- 1328 Yount SE, Rothrock N, Bass M, Beaumont JL, Pach D, Lad T et al. A randomized trial of weekly symptom telemonitoring in advanced lung cancer. *Journal of Pain and Symptom Management*. 2014; 47(6):973-989
- 1329 Yourman LC, Lee SJ, Schonberg MA, Widera EW, Smith AK. Prognostic indices for older adults: a systematic review. *JAMA*. 2012; 307(2):182-192
- 1330 Yu CH, Stacey D, Sale J, Hall S, Kaplan DM, Ivers N et al. Designing and evaluating an interprofessional shared decision-making and goal-setting decision aid for patients with diabetes in clinical care--systematic decision aid development and study protocol. *Implementation Science*. 2014; 9:16
- 1331 Yu DSF, Lee DTF, Stewart S, Thompson DR, Choi KC, Yu CM. Effect of nurse-implemented transitional care for Chinese individuals with chronic heart failure in Hong Kong: a randomized controlled trial. *Journal of the American Geriatrics Society*. 2015; 63(8):1583-1593
- 1332 Yurkovich M, Avina-Zubieta JA, Thomas J, Gorenchtein M, Lacaille D. A systematic review identifies valid comorbidity indices derived from administrative health data. *Journal of Clinical Epidemiology*. 2015; 68(1):3-14
- 1333 Zampieri FG, Colombari F. The impact of performance status and comorbidities on the short-term prognosis of very elderly patients admitted to the ICU. *BMC Anesthesiology*. 2014; 14:59
- 1334 Zed PJ, Abu-Laban RB, Balen RM, Loewen PS, Hohl CM, Brubacher JR et al. Incidence, severity and preventability of medication-related visits to the emergency department: a prospective study. *CMAJ Canadian Medical Association Journal*. 2008; 178(12):1563-1569
- 1335 Zekry D, Frangos E, Graf C, Michel JP, Gold G, Krause KH et al. Diabetes, comorbidities and increased long-term mortality in older patients admitted for geriatric inpatient care. *Diabetes and Metabolism*. 2012; 38(2):149-155
- 1336 Zekry D, Herrmann FR, Grandjean R, Vitale AM, De Pinho MF, Michel JP et al. Does dementia predict adverse hospitalization outcomes? A prospective study in aged inpatients. *International Journal of Geriatric Psychiatry*. 2009; 24(3):283-291
- 1337 Zekry D, Herrmann FR, Vischer UM. The association between the body mass index and 4-year all-cause mortality in older hospitalized patients. *Journals of Gerontology Series A, Biological Sciences and Medical Sciences*. 2013; 68(6):705-711
- 1338 Zekry D, Krause KH, Irminger-Finger I, Graf CE, Genet C, Vitale AM et al. Telomere length, comorbidity, functional, nutritional and cognitive status as predictors of 5 years post hospital discharge survival in the oldest old. *Journal of Nutrition, Health and Aging*. 2012; 16(3):225-230
- 1339 Zekry D, Loures Valle BH, Graf C, Michel JP, Gold G, Krause KH et al. Prospective comparison of 6 comorbidity indices as predictors of 1-year post-hospital discharge institutionalization, readmission, and mortality in elderly individuals. *Journal of the American Medical Directors Association*. 2012; 13(3):272-278
- 1340 Zekry D, Loures Valle BH, Lardi C, Graf C, Michel JP, Gold G et al. Geriatrics index of comorbidity was the most accurate predictor of death in geriatric hospital among six comorbidity scores. *Journal of Clinical Epidemiology*. 2010; 63(9):1036-1044

- 1341 Zekry D, Valle BH, Michel JP, Esposito F, Gold G, Krause KH et al. Prospective comparison of six co-morbidity indices as predictors of 5 years post hospital discharge survival in the elderly. *Rejuvenation Research*. 2010; 13(6):675-682
- 1342 Zeltser D, Justo D, Halkin A, Rosso R, Ish-Shalom M, Hochenberg M et al. Drug-induced atrioventricular block: prognosis after discontinuation of the culprit drug. *Journal of the American College of Cardiology*. 2004; 44(1):105-108
- 1343 Zeng A, Song X, Dong J, Mitnitski A, Liu J, Guo Z et al. Mortality in relation to frailty in patients admitted to a specialized geriatric intensive care unit. *Journals of Gerontology Series A, Biological Sciences and Medical Sciences*. 2015; 70(12):1586-1594
- 1344 Zeng C, Ellis JL, Steiner JF, Shoup JA, McQuillan DB, Bayliss EA. Assessment of morbidity over time in predicting health outcomes. *Medical Care*. 2014; 52 Suppl 3:S52-S59
- 1345 Zhao Y, Wong FK. Effects of a postdischarge transitional care programme for patients with coronary heart disease in China: a randomised controlled trial. *Journal of Clinical Nursing*. 2009; 18(17):2444-2455
- 1346 Zhu H, Hill MD. Stroke: the Elixhauser Index for comorbidity adjustment of in-hospital case fatality. *Neurology*. 2008; 71(4):283-287
- 1347 Zoghbi GJ, Sanderson B, Breland J, Adams C, Schumann C, Bittner V. Optimizing risk stratification in cardiac rehabilitation with inclusion of a comorbidity index. *Journal of Cardiopulmonary Rehabilitation*. 2004; 24(1):8-13
- 1348 Zonneveld LN, van 't Spijker A, Passchier J, van Busschbach JJ, Duivenvoorden HJ. The effectiveness of a training for patients with unexplained physical symptoms: protocol of a cognitive behavioral group training and randomized controlled trial. *BMC Public Health*. 2009; 9:251
- 1349 Zonneveld LN, van Rood YR, Kooiman CG, Timman R, van 't Spijker A, Busschbach JJ. Predicting the outcome of a cognitive-behavioral group training for patients with unexplained physical symptoms: a one-year follow-up study. *BMC Public Health*. 2012; 12:848
- 1350 Zopf Y, Rabe C, Neubert A, Gassmann KG, Rascher W, Hahn EG et al. Women encounter ADRs more often than do men. *European Journal of Clinical Pharmacology*. 2008; 64(10):999-1004
- 1351 Zopf Y, Rabe C, Neubert A, Hahn EG, Dormann H. Risk factors associated with adverse drug reactions following hospital admission: a prospective analysis of 907 patients in two German university hospitals. *Drug Safety*. 2008; 31(9):789-798
- 1352 Zuckerman IH, Langenberg P, Baumgarten M, Orwig D, Byrns PJ, Simoni-Wastila L et al. Inappropriate drug use and risk of transition to nursing homes among community-dwelling older adults. *Medical Care*. 2006; 44(8):722-730
- 1353 Zuckerman JD, Sakales SR, Fabian DR, Frankel VH. Hip fractures in geriatric patients. Results of an interdisciplinary hospital care program. *Clinical Orthopaedics and Related Research*. 1992;213-225
- 1354 Zullig LL, Melnyk SD, Stechuchak KM, McCant F, Danus S, Oddone E et al. The Cardiovascular Intervention Improvement Telemedicine Study (CITIES): rationale for a tailored behavioral and educational pharmacist-administered intervention for achieving cardiovascular disease risk reduction. *Telemedicine Journal and E-Health*. 2014; 20:135-143

- 1355 Zulman DM, Jenchura EC, Cohen DM, Lewis ET, Houston TK, Asch SM. How can eHealth technology address challenges related to multimorbidity? Perspectives from patients with multiple chronic conditions. *Journal of General Internal Medicine*. 2015; 30(8):1063-1070
- 1356 Zwisler AD, Schou L, Soja AM, Bronnum-Hansen H, Gluud C, Iversen L et al. A randomized clinical trial of hospital-based, comprehensive cardiac rehabilitation versus usual care for patients with congestive heart failure, ischemic heart disease, or high risk of ischemic heart disease (the DANREHAB trial)--design, intervention, and population. *American Heart Journal*. 2005; 150:899