National Institute for Health and Care Excellence

1

Consultation

Chapter 38 Integrated care

Emergency and acute medical care in over 16s: service delivery and organisation

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1

Chapter 38 Integrated care

Contents

1

38 Integrated care

38.1 Introduction

Increasingly, patients treated by the NHS are complex with multiple morbidities and with needs that cross service boundaries – needs that are met with both physical and psychological healthcare, by several specialty departments at one or more hospitals, by health and social care provision and for the majority by both primary and secondary care. Given the complexity of delivering care to our contemporary patient population, it is often inconvenient and frustrating for patients to have multiple care providers with variable access to information about what each of the different providers have done and plan to do in the future to address need. Also, there are system inefficiencies due to duplication of work and time spent by clinicians trying to find out what other services have done. There are international examples where care has been 'integrated' across traditional service boundaries so that primary and secondary care can be delivered to patients with complex needs in a more efficient and convenient way.

There is currently no standard description of integrated care and so this is interpreted in a particular clinical context or for a particular patient group. In the setting of acute medical emergencies, integrated care can bring elements of care needed to assess, diagnose and treat AMEs from different services to improve patient experience and outcomes as well as reduce costs. However, whilst there have been policy statements to support and encourage integrated care, research evidence from UK settings has been sparse and there is uncertainty over how best to translate international evidence to the UK context.

Therefore there is current uncertainty over the most clinically and cost-effective models of integrated care for patients with acute medical emergencies.

38.2 Review question: Do integrated care models improve outcomes for patients with a suspected or confirmed acute medical emergency or at high risk of an acute medical emergency?

For full details see review protocol in Appendix A.

Table 1: PICO characteristics of review question

Population	Adults and young people (16 years and over) with a suspected or confirmed AME or at high risk of AME.
Interventions	Integration of care across teams within different levels of care. Stratified by features of the integrated health care model as defined by the following: • Coordinating and aligning of policies, rules and regulatory frameworks • Developing shared values, culture and vision across organisations, professional groups and individuals • Coordinating structures, governance systems and relationships across organisations • Aligning back-office functions, budgets and financial systems across integrating units • Coordinating information and services and integrating patient care within a single process.
Comparison	No integration of care.
Outcomes	• Mortality (CRITICAL) • Avoidable adverse events (Delayed or missed treatment) (Delayed, missed or duplicated investigations) (CRITICAL) • Quality of life (CRITICAL)

	• Patient satisfaction (CRITICAL) • Length of stay (CRITICAL) • Unplanned hospital admissions (IMPORTANT) • Readmission up to 30 days (IMPORTANT) • ED demand (reduction in number presenting to ED) (IMPORTANT) • Carer and family satisfaction (IMPORTANT)
Study design	Systematic reviews (SRs) of RCTs, RCTs, observational studies only to be included if no relevant SRs or RCTs are identified.

38.3 Clinical evidence

Fifteen randomised controlled studies were included in the review[10,16,22,28,32,40-43,61,64,67,79,103,108]; these are summarised in Table 2. Evidence from these studies is summarised in the clinical evidence summary below (Table 3). See also the study selection flow chart in Appendix B, forest plots in Appendix C, study evidence tables in Appendix D, GRADE tables in Appendix F and excluded studies list in Appendix G.

Table 2: Summary of studies included in the review

Study	Intervention and comparison	Population	Outcomes	Comments
Angermann 2012 [10] Conducted in Germany RCT	Intervention (n=352). Patients received HeartNetCare (HNC) as well as usual care. HNC included the following elements: (1) In-hospital face-to-face contact between specialist nurse, patient and relatives to explain the intervention, practice supervision of blood pressure, heart rate and symptoms and provide participants with teaching materials and self-monitoring schemes. (2) Telephone-based structured monitoring using a standardised 19-item questionnaire addressing indicators of worsening heart failure, other cardiac symptoms, medication, health care utilization, state of mood, and general health and well-being. (3) Uptitration of heart failure medication in cooperation with GPs, where possible, and teaching of patients regarding adjustment of diuretics. (4) Needs-adjusted specialist care, which nurses coordinated with patients' physician(s). (5) Measures for appropriate education and supervision of	People (n= 715) hospitalised with signs and symptoms of decompensated heart failure. Exclusion: past onset of structural heart disease, logistic or health reasons precluding participation in telephone-based interventions and lack of written consent.	Mortality at 180 days. Hospital admissions at 180 days. SF-36 – Physical Health Component at 180 days. SF-36- Physical Functioning Scale at 180 days. SF-36-Mental Health Component at 180 days.	

Study	Intervention and comparison	Population	Outcomes	Comments
	interveners to ensure high intervention quality. All nurses were trained in telephone skills, received supervision by a cardiologist (weekly) and a psychologist (bimonthly), and had unrestricted access to their supervisor for questions. Control (n=363) Usual care - patients underwent standard post-discharge planning, which typically included treatment plans, comprehensive discharge letters, and fixed appointments with GPs or cardiologists within 7–14 days.			
Bernabei 1998[16] Conducted in Italy RCT	Intervention (n=99): Assessment and care by the geriatric evaluation unit, which consisted of general practitioners, a geriatrician, a social worker and several nurses. Two case managers were selected among the trainees of a course on case management and comprehensive geriatric assessment. Case managers performed the initial assessment soon after randomisation and every 2 months thereafter. Also, they were constantly available to deal with problems, monitor the provision of services and to guarantee extra help as requested by patients and general practitioners. Duration: 12 months. Concurrent medication/care: not reported. Comments: "All the services considered necessary were provided in an integrated fashion after a formal agreement between the municipality and the local health agency". Control (n=100) Primary and community care "with the conventional and fragmented organisation of services".	Frail-elderly people (n=199) already receiving conventional community care services. Inclusion: Aged over 65 and recipients of home health services or home assistance programmes.	Admission to hospital at 12 months. Mortality at 12 months. ED presentation at 12 months.	
Boyd 2014[22] New Zealand	Intervention (n=1425): A secondary care Gerontology nurse specialist (GNS) intervention to improve the	Long-term care residents at facilities. Facilities included	Medical hospital admissions at 12 months.	Cluster randomised by facility. Informed

Study	Intervention and comparison	Population	Outcomes	Comments
Cluster-RCT	quality of care in aged care facilities through proactive GNS outreach. Components consisted of: regular, proactive bi-monthly GNS visits, collaborative relationship between GNS and facility staff, telephone consultation and site visits as needed, quality initiatives, RN care guides, wound care consultant, standardised bimonthly education sessions at the facility, Gerontology clinical coaching at the bedside as needed, clinical practice development, quarterly district-wide education sessions, comprehensive geriatric assessment, GNS liaison with secondary care Older Adult Specialists Services, GNS liaison across primary and secondary care services. Control (n=1128): No GNS on-site integration.	combined low and high level care, low level care only (rest home), high level care only (private hospital) and dementia care only. Inclusion: Facility participation was voluntary.		consent of residents was not required. Each GNS responsible for 14 or 15 facilities, had at least 1 year of postgraduate education or a Master's degree in nursing, 10 years of gerontology experience. Control facilities receive the intervention after a year. Hospital admissions were sub-grouped by medical and surgical. Intervention group had a greater number of hospitalisations per bed at baseline (0.43 versus 0.32).
Casas 2006[28] Conducted in Belgium and Spain RCT	Intervention (n=65): A comprehensive assessment of the patient at discharge, including severity of the respiratory disease, evaluation of comorbid conditions and analysis of requirements in terms of social support. Educational programme on self-management of the disease administered at discharge. Agreement on an individually tailored care plan following international guidelines was shared across the system via interaction between the	All patients (n=155) admitted because of a previous episode of exacerbation requiring hospitalisation for over 48 hours at 2 tertiary hospitals. Exclusion: Not living in the healthcare area (39%); severe	Hospital admissions at 12 months. Mortality at 12 months.	Intervention group had higher hospitalisations during previous year (1.0 versus 0.64) and lower influenza vaccination rate (56% versus 78%).

Study	Intervention and comparison	Population	Outcomes	Comments
	specialised nurse case manager and the primary care team. Accessibility of the specialised nurse to patients/carers and primary care professionals during the follow-up period was ensured through an ICT platform including a web-based call centre. Control (n=90): Patients included in the UC arm were discharged from hospital by the attending physician who decided on the outpatient control regime. Pharmacological prescriptions at discharge and in-hospital treatment followed the standard protocols of the centres involved in the study, which were similar in IC and UC. Patients in the UC arm of the study were visited by their own physician without additional support. Visits were usually scheduled every 6 months. The controls did not receive help from the specialised nurse, nor were they included in the educational programme or had access to the call-centre.	comorbid conditions, that is, lung cancer or other advanced malignancies, and extremely severe neurological or cardiovascular disorders (25%); logistical limitations due to extremely poor social conditions, such as illiteracy or no phone access at home (10%); and being admitted to a nursing home (7%).		
Doughty 2002[40] Cluster-RCT Conducted in New Zealand	Intervention (n=100): Outpatient clinical review with the study team within 2 weeks of hospital discharge. One-on-one education with the study nurse was initiated at the first clinic visit. A patient diary, for daily weights, medication record, clinical notes and appointments, and education booklet were provided. A follow-up plan was devised for each patient aiming for 6-weekly visits alternating between the GP and heart failure clinic, patients were free to see their GPs at any time they wished. A detailed letter was faxed to the GP on the same day as the patient visited the heart failure clinic. This letter included summary comments outlining the rationale for any changes in treatment, and was followed-up with a phone call to the patient's GP to discuss any relevant changes in the management plan. Subsequently, group education	All admitted patients undergoing heart failure management (n=197) within the general medical wards at an urban tertiary hospital. Inclusion: primary diagnosis of heart failure. Exclusion: surgically remediable cause for heart failure, such as severe aortic stenosis, consideration for heart transplantation, inability to provide informed	Hospital admissions at 12 months. Mortality at 12 months.	Cluster randomised by GP as unit of randomisation. The content of the one-on-one and group education included explanation of the symptoms and signs of heart failure, importance of monitoring of daily body weight and action plans should weight change, effects of medications and importance of

Study	Intervention and comparison	Population	Outcomes	Comments
	sessions (each lasting 1.5–2 h) were offered, 2 within 6 weeks of hospital discharge and a further after 6 months. These sessions were run by a cardiologist and the study nurse. The study team at the hospital heart failure clinic was available for consultation during normal working hours and received calls from both patients and their GPs. At times of worsening symptoms patients were initially advised to see their GP. No explicit criteria for readmission were pre-specified and the decision to request admission rested with the GP. If admission was not required then an earlier heart failure clinic visit could be arranged Control (n=97): Patients randomised to the control group continued under the care of their GP with additional follow-up measures as usually recommended by the medical team responsible for their in-patient care.	consent, terminal cancer and participation in any other clinical trial.		compliance and recommendations regarding exercise and diet. Intervention group had lower proportion of ischaemic HF patients (48% versus 59%), Less patients living alone (29% versus 41%), less patients treated for hypertension (46% versus 56%), and more diabetics (32% versus 25%).
Drummond 1994[41] Conducted in the UK RCT	Intervention (n=363): Chest physicians review patients annually. Interim reviews take place in general practice, typically every 3 months; however, the interval between reviews can be shortened if the patient's condition merits this. Patients are sent computer generated questionnaires at the appropriate time, inviting them to make an appointment with their general practitioner, and asking for information about symptoms, days of restricted activity, nights of disturbed sleep, courses of oral steroids, general practice consultations, and admissions for asthma. Patients are asked to give the completed questionnaire to their general practitioner at the consultation. Simultaneously, the patient's general practitioner is sent a separate computer generated questionnaire, mentioning that the patient is due to attend shortly for an	(n=712) adults attending hospital outpatient clinics with a diagnosis of asthma confirmed by a chest physician and pulmonary function reversibility of at least 20%. Exclusion: most severe asthma patients excluded (no further details given).	Hospital admissions for asthma at 12 months.	Did not report baseline of participants.

Study	Intervention and comparison	Population	Outcomes	Comments
	asthma review and enclosing a questionnaire about consultations, pulmonary function, β agonist bronchodilators and steroid courses prescribed, changes to the patient's medication, and hospital admissions. The general practitioner is asked to return all documentation to the consultant. The information from both questionnaires is then added to the patient's computerised record. Copies of the updated record are sent to the general practitioner, along with any suggestions from the consultant for changes in the management plan. Control n=349): Patients receiving conventional outpatient care are seen at their regular outpatient clinic, typically every 3 months. During the study year, they too were sent a clinical questionnaire before each visit, to be returned to the specialist. Additional clinic attendances were arranged by the consultant or general practitioner if necessary.			
Druss 2001[42] Conducted in the USA RCT	Intervention (n=59): The psychiatry service assumed clinical responsibility for the primary medical care of all patients randomised to the integrated care intervention and paid the salaries of all clinic staff through clinical funds. The clinic was located contiguous to the mental health clinics. The clinic was staffed by a nurse practitioner (1 full-time equivalent [FTE]), a part-time family practitioner (0.5 FTE), a nurse case manager (1 FTE), and an administrative assistant (0.5 FTE). The medical nurse practitioner was the main provider of basic medical care. The family practitioner supervised the nurse practitioner and acted as a liaison to physicians in the psychiatry and medical services. The registered	Patients with severe mental illness (n=120) who were recruited after mental health care providers were asked to refer any patients whom they thought would benefit from primary care to be assigned a medical 'treater'. Exclusion: Current primary care provider or an urgent or multiple serious chronic problems. Patients	Medical ED presentations at 12 months.	ED utilisation was stratified by medical service use and mental health service use. Differences in (%): race (76.3 versus 63.9), high school graduate (93.2 versus 82.0), and cardiac disease (13.0 versus 2.3).

Study	Intervention and comparison	Population	Outcomes	Comments
	nurse provided patient education, liaison with mental health care providers, and case management services. The administrative assistant scheduled appointments and took telephone messages for the clinic. Clinic staff emphasised patient education, preventive services, and close contact with mental health care providers, including e-mail, telephone, and face-to-face discussion about patients. Patients were prompted with telephone reminders the day before appointments, and whenever possible, clinic appointments were scheduled immediately following mental health visits. When appointments were missed, clinic staff made active efforts to reschedule visits through contacting patients, their family members, and/or mental health care providers. One provider from the integrated clinic served as a liaison to each of 3 mental health teams, attending weekly team meetings. Mental health care providers were notified about patients' medical status, were asked to keep the integrated care clinic abreast of changes in patients' psychiatric status, and were encouraged to coordinate efforts with the integrated care clinic to ensure that patients attended medical appointments and followed through with needed medical tests. Control (n=61): Veterans randomised to the usual care group in this study were referred to the VA general medicine clinic, located in a building adjacent to the mental health clinic. For each patient randomised to usual care, a referral form was sent and verbal contact was made with the clinic administrator. This process ensured that all veterans referred for care were provided a primary care provider, following the	determined by the family practitioner to have had a medical hospitalisation in the past 6 months or 4 or more serious chronic conditions were referred to the general medical clinics.		

Study	Intervention and comparison	Population	Outcomes	Comments
	referral pattern that was available before introduction of the integrated care clinic.			
Ducharme 2005 [43] Conducted in Canada RCT	Intervention (n=115): Patients in the intervention group were referred to a multidisciplinary specialised heart failure outpatient clinic at the Montreal Heart Institute, where they were evaluated by the study team within 2 weeks of hospital discharge. The heart failure clinic provided rapid access to expert health care professionals (cardiologists, clinician nurses, dieticians and pharmacists, with access to social workers and other medical specialists as required). At the clinic, the patient could be evaluated both clinically and para-clinically, receive intravenous diuretics if required and be observed for up to 5 hours. Additional to these services, a nurse telephoned all patients in the intervention group within 72 hours of hospital discharge and then monthly, unless a problem occurred that required more frequent contact. During the telephone consultation, the nurse pursued problems as clinically indicated. One-on-one education of the patient, family members or both with the study nurse was initiated at the first clinic visit. A follow-up plan was developed for each patient that included monthly visits with both a cardiologist and nurse at the clinic. Control (n=115): Usual care - had excellent access to medical, including specialist care. No further details reported.	People (n=230) seen at the emergency department of or admitted to the Montreal Heart Institute with a primary diagnosis of congestive heart failure between January 1998 and January 2000. Exclusion: A primary diagnosis of acute myocardial infarction, discharge to a chronic care facility, scheduled cardiac surgery, unwillingness to sign informed consent or to attend the outpatient clinic, participation in another research trial, or residence in an outlying area.	Mortality at 6 months. Hospital admissions at 6 months Total number of ED visits at 6 months.	
GRACE: Geriatric Resources for Assessment and Care of Elders trial:	Intervention (n=474) Initial and annual in-home comprehensive geriatric assessment by a GRACE support team consisting of an advanced practice nurse and social worker. Individualised care plan	Community dwelling low-income seniors (n=951) were recruited from 6 community-based health centres	Admissions at 2 years. Hospital readmission at 30 days.	

Study	Intervention and comparison	Population	Outcomes	Comments
Counsell 2007[32] (Bielaszka-duvernay 2011[17], Counsell 2009[31]) Conducted in the USA RCT	development annually by GRACE support team with assistance from the GRACE interdisciplinary team involving a geriatrician, pharmacist, physical therapist, mental health social worker, and community-based services liaison. Activation new each year of indicated GRACE protocols and corresponding team suggestions for care related to the 12 targeted geriatric conditions: advance care planning, health maintenance, medication management, difficulty walking/falls, chronic pain, urinary incontinence, depression, hearing loss, visual impairment, malnutrition or weight loss, dementia, and caregiver burden. GRACE support team meeting with patient's primary care physician to review, modify, and prioritise initial and annual care plan protocols and team suggestions. Implementation of care plan and team suggestions by GRACE support team in collaboration with the primary care physician and consistent with the patient's goals. Weekly GRACE interdisciplinary team meetings to review GRACE support team success in implementing care protocols and problem solve barriers to implementation. Ongoing GRACE support team home–based care management (including at least monthly patient contacts) supported by an electronic medical record and Web-based tracking system, and providing coordination and continuity of care among all health care professionals and sites of care. Control (n=477): Control patients had access to all primary and specialty care services available as part of usual care. Duration: 2 years. Concurrent medication/care: at the time of implementation of the GRACE intervention, the following geriatric clinical services	affiliated with a university-affiliated urban health care system serving medically indigent patients. Inclusion: 65 years old or older, annual income less than 200% of the federal poverty level, have had 1 or more primary care visits in the past 12 months and reside in the community (non-institutionalised) Exclusion: non-English speaking, no regular access to a telephone, currently undergoing kidney dialysis treatments or residing with a patient already participating in the GRACE clinical trial.	ED visits at 2 years.	

Study	Intervention and comparison	Population	Outcomes	Comments
	existed: outpatient geriatric assessment and multispecialty centre, inpatient ACE unit and consult service, skilled nursing facility, and physician house calls program. Psychiatric care was available through the health system's community mental health centre.			
Hernandez 2015 [61] Conducted in Spain RCT	Intervention (n=84): A comprehensive assessment of the patient at entry, A 2 hour educational programme was administered at entry by a respiratory nurse, followed by distribution of patient-specific support material covering knowledge of the disease, instructions on non-pharmacological treatment, administration techniques for proper pharmacological therapy and techniques for self-management of the disease and co-morbid conditions including strategies to adopt with future exacerbations. One joint visit of the specialised nurse and the primary care team (physician, nurse and social worker) at the patient home was completed within 72 hours after entry into the study. Therapeutic plan for each patient was customised and shared with the primary care team. Accessibility to the specialised nurse at the hospital was ensured for primary care professionals during the follow-up period through an ICT platform including a web-based call centre. The community care teams received training: a 2 hour face to face educational training and 1-day stay at the hospital ward, aiming at enhancing home-based management of frail COPD patients. Control (n=71): Usual care – managed by physician without any support from specialised nurses. Visits were usually scheduled every 6 months in the out-patient clinic.	Frail community-dwelling COPD patients (n=155). Inclusion: history of at least 2 hospital admissions owing to severe respiratory exacerbations during 2 consecutive years, 45 years and over living at home within the health care area of the hospital, diagnosed with a COPD-related diagnostic term including: emphysema, asthma, tuberculosis, chronic bronchitis and COPD. Exclusions: nursing home or not living in the area or participants in another clinical trial.	COPD-related hospital admissions at 6 years follow-up. COPD-related ED admission at 6 years follow-up. All-cause mortality at 6 years follow-up.	The educational programme covered knowledge of the disease, instructions on non-pharmacological treatment, administration techniques for proper pharmacological therapy and techniques for self-management of the disease and co-morbid conditions including strategies to adopt with future exacerbations. Hospital admissions and ED use was adjusted for differences in influenza and pneumococcal vaccination.

Study	Intervention and comparison	Population	Outcomes	Comments
Holm 2002[64] Conducted in Denmark Cluster-RCT	Intervention (n=453): Integration of care across teams or between different levels of care - Clinical Coordinating information and services and integrating patient care within a single process for example, developing extended clinical roles, guidelines and inter-professional education. The GPs responsibility - participation in a 3 hour intensive OAT course. Referral of patients to the OAT clinic for evaluation of the OAT. Maintaining routine OAT monitoring. The patient's responsibility - evaluation of the OAT once a year at the OAT clinic. Participation in patient education. OAT clinic responsibility - intensive OAT course for GPs, patient education, written patient information, OAT telephone hotline for GPs throughout the study period, evaluation of the OAT of all admitted patients once a year, and mailing anonymous OAT quality reports to GPs for self-evaluation. Control (n=422): Usual care - not defined.	All patients (n=875) identified from a laboratory information system as receiving oral anticoagulant therapy (OAT). Inclusion: 3 or more consecutive (no more than 4 months between tests) international normalised ration system tests, at least 1 INR test >1.9. Exclusion: INR determinations performed less than 3 times by their own GP.	Adverse events (Major bleeding or thrombosis during the study period) at 2 years. Mortality from major bleeding or thrombosis at 2 years.	Patients were cluster randomised by GP.
Johnson 2015[67] Conducted in New Zealand RCT	Intervention (n=51): Project coordinator to assist with patient care and information, and PCP educational resource ("upskilling") packages detailing anticipated adverse effects of each treatment regimen and actions to be taken. Patients were asked to see their Project coordinator after each chemotherapy treatment. Control (n=46): Usual care was provided by specialists and their associated primary care provider. Primary care provider received a letter from the specialist team after each visit, discharge summaries, and telephone communication,	Patients (n=100) receiving their first round of chemotherapy in participating outpatient clinics were invited to participate. Inclusion: eligible patients were > 16 years of age, able to understand and complete trial documentation, and had biopsy-proven malignancy.	Emergency Department Use/hospital admissions during the study period.	Unclear duration of study. Only statement was "Recruitment was open for 2 years, but stopped early as a result of slow accrual". Unclear how outcome is reported. Heading for section refers to "ED use" but other sentences describe ED

Study	Intervention and comparison	Population	Outcomes	Comments
	where appropriate. Communication frequency and content for standard care was not prescribed by the study.	Exclusion: individual PCPs could have only 1 patient on study.		use/hospital admissions. Concurrent chemotherapy .
Lanzeta 2016 [79] Conducted in Spain Cluster-RCT	Intervention (n=70) Integrated health care model - improving communication between primary care and hospital professionals. Patients were managed by the primary care team (general practitioner and nurse) with the support of a reference internist and a liaison nurse. Every time patients with multi-morbidity went to the hospital they were seen by their assigned internist. Control (n=70) In the control group (CG), patients received usual care corresponding to routine practice, with no strengthening of the coordination between primary and hospital-based care.	People with multimorbidity (n=140). Exclusion: living in a nursing home or being on haemodialysis.	Hospital admissions at 1 year. ED use at 1 year.	
Sahota 2016[103] Conducted in the UK RCT	Intervention (n=125): The CIRACT [Community In-reach Rehabilitation And Care Transition service] consisted of a senior occupational therapist (transition coach), senior physiotherapist and assistant practitioner, and linked directly to a social services practitioner and working more closely across multiple boundaries with patients and their carers. The service provided a comprehensive assessment of each participant's ability to perform certain tasks, which was completed within 24 hours of randomisation, enabling the formulation of a rehabilitation plan. While in hospital the participants were treated daily (7 days a week if appropriate). The CIRACT service utilised the team's expertise in community working to form links with the appropriate services to ensure a	n=250 Older people (age ≥ 70 years) admitted to the general medical wards as an acute medical emergency.	Length of stay. Re-admission at 28 days. Quality of life (Barthel ADL Score).	

Study	Intervention and comparison	Population	Outcomes	Comments
	smooth and effective discharge. Following discharge, the CIRACT team visited the participant at home within 48 hours to assess the level of rehabilitation required and further follow-up visits were provided as deemed necessary. Comparison (n=125): Standard care - the traditional hospital-based Rehabilitation (THB-Rehab) service was provided by the ward therapy teams (usually a band 6 occupational therapist and a band 6 physiotherapist) on weekdays only. The team jointly conducted an assessment of each participant's ability to perform certain tasks and provided recommendation for rehabilitation. The service referred the participants to the appropriate community-based services for provision of equipment at home, personal care and ongoing rehabilitation when appropriate at discharge. Once discharged from hospital, participants had no direct contact with the THB-Rehab service.			
Smith 2008[108] (Anon 2008[2]) Conducted in the USA Cluster-RCT	Intervention (n=358): Appointment of a diabetes educator in primary care, communicating on a regular basis with patients to support their self-management, the primary care team, and a supervising endocrinologist via a Diabetes Electronic Management System. Control (n=277) Control groups received periodic generic information via e-mail about cardiovascular risk reduction in diabetes.	Patients (n=635) under the care of participating family medicine practitioners. Inclusion: written consent. Exclusion: none stated.	Mortality at 30 months.	Patients were cluster randomised by family physician. Randomisation took place following first referral to the on-site diabetes educator. Concurrent treatment for diabetes.

1

Table 3: Clinical evidence summary: Integrated care versus no integrated care

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Integrated care versus no integrated care (95% CI)
Mortality	945 (2 studies) 6 months	⨁⨁⊖⊖ LOW[a,b] due to risk of bias, imprecision	RR 0.52 (0.32 to 0.84)	94 per 1000	45 fewer per 1000 (from 15 fewer to 64 fewer)
Mortality	551 (3 studies) 1 years	⨁⊖⊖⊖ VERY LOW[a,b] due to risk of bias, imprecision	RR 0.91 (0.63 to 1.31)	156 per 1000	14 fewer per 1000 (from 58 fewer to 48 more)
Mortality	2461 (3 studies) 2 years	⨁⊖⊖⊖ VERY LOW[a,b] due to risk of bias, imprecision	RR 1.01 (0.77 to 1.33)	78 per 1000	1 more per 1000 (from 18 fewer to 26 more)
Mortality	114 (1 study) 6 years	⨁⊖⊖⊖ VERY LOW[a] due to risk of bias, imprecision	RR 0.36 (0.16 to 0.8)	327 per 1000	209 fewer per 1000 (from 65 fewer to 275 fewer)
Readmission	618 (2 studies) 28-30 days	⨁⨁⨁⊖ MODERATE[b] due to imprecision	RR 0.90 (0.68 to 1.19)	255 per 1000	25 fewer per 1000 (from 82 fewer to 48 more)
Hospital admission rate	2750 (2 studies) 1 years	⨁⊖⊖⊖ VERY LOW[a] due to risk of bias, imprecision	Rate ratio 0.68 (0.58 to 0.8)	598 per 1000	191 fewer per 1000 (from 120 fewer to 251 fewer)
Admission	354 (2 studies) 1 years	⨁⨁⊖⊖ LOW[a] due to risk of bias	HR 0.69 (0.54 to 0.87)	532 per 1000	124 fewer per 1000 (from 49 fewer to 196 fewer)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Integrated care versus no integrated care (95% CI)
Hospital admissions	1288 (2 studies) 6 months - 1 year	⊕⊕⊕⊖ MODERATE[a] due to risk of bias		The mean hospital admissions in the control groups was 0.32 admissions per person	The mean hospital admissions in the intervention groups was 0.04 higher (0.01 lower to 0.10 higher)
Hospital admissions	155 (1 study) 6 years	⊕⊖⊖⊖ VERY LOW[a,b] due to risk of bias, imprecision	RR 2.17 (0.60 to 7.85)	36 per 1000	42 more per 1000 (from 14 fewer to 245 more)
Hospital admissions	370 (2 studies) 6 months-12 months	⊕⊖⊖⊖ VERY LOW[a,b,c] due to risk of bias, imprecision, inconsistency	RR 0.89 (0.72 to 1.09)	535 per 1000	59 fewer per 1000 (from 150 fewer to 48 more)
Length of stay	212 (1 study) 90 days	⊕⊕⊕⊕ HIGH		The mean length of stay in the control group was 8.7 days	The mean length of stay in the intervention group was 0.90 lower (2.38 lower to 0.58 higher)
Emergency department use/hospital admissions	97 (1 study) 2 years	⊕⊕⊖⊖ LOW[a] due to risk of bias		The mean emergency department use/hospital admissions in the control groups was 1.0 admissions per person	The mean emergency department use/hospital admissions in the intervention groups was 0.3 lower (1.34 lower to 0.74 higher)
ED use	199 (1 study) 1 years	⊕⊕⊖⊖ LOW[a] due to risk of bias, imprecision	HR 0.64 (0.48 to 0.85)	170 per 1000	58 fewer per 1000 (from 24 fewer to 84 fewer)
ED use	155 (1 study) 6 years	⊕⊕⊖⊖ LOW[a,b] due to risk of bias,	RR 0.33 (0.13 to 0.84)	214 per 1000	144 fewer per 1000 (from 34 fewer to 186 fewer)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Integrated care versus no integrated care (95% CI)
		imprecision			
ED use	490 (3 studies) 6 months - 1 year	⨁⨁⨁⊖ MODERATE[a] due to risk of bias	RR 0.89 (0.77 to 1.02)	589 per 1000	65 fewer per 1000 (from 136 fewer to 12 more)
Adverse effects	875 (1 study) 2 years	⨁⊖⊖⊖ VERY LOW[a,b] due to risk of bias, imprecision	RR 0.75 (0.5 to 1.13)	111 per 1000	28 fewer per 1000 (from 56 fewer to 14 more)
Quality of life (SF-36) – Physical Health Component Scale from: 0-100	418 (1 study) 6 months	⨁⨁⊖⊖ LOW[a] due to risk of bias		The mean quality of life – physical health component in the control groups was 1.3 higher	The mean quality of life – physical health component in the intervention groups was 1.50 higher (0.41 lower to 3.41 higher)
Quality of life (SF-36) – Physical Functioning Component Scale from: 0-100	418 (1 study) 6 months	⨁⨁⊖⊖ LOW[a] due to risk of bias		The mean quality of life – physical functioning component in the control groups was 1.8 higher	The mean quality of life – physical functioning component in the intervention groups was 4.10 higher (0.74 lower to 8.94 higher)
Quality of life (SF-36) – Mental Health Component Scale from: 0-100	418 (1 study) 6 months	⨁⨁⊖⊖ LOW[a] due to risk of bias		The mean quality of life –mental health component in the control groups was 2.3 higher	The mean quality of life –mental health component in the intervention groups was 0.00 higher (2.34 lower to 2.34 higher)
Barthel ADL Score Scale from: 0-20; higher values better	212 (1 study) 90 days	⨁⨁⨁⊖ MODERATE[b] due to imprecision		The mean Barthel ADL Score in the control group was 12.6	The mean Barthel ADL Score in the intervention group was 1.70 higher (0.19 to 3.21 higher)

(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 of heterogeneity, I2= >50%, unexplained by subgroup analysis.

38.4 Economic evidence

Published literature

Four health economic studies were identified with the relevant comparison and have been included in this review[65,79,90,103]. These are summarised in the economic evidence profile below (Table 4) and the economic evidence table in Appendix E.

Four economic studies relating to this review question were identified but were excluded due to a combination of limited applicability and methodological limitations or the availability of more applicable evidence. These are listed in Appendix H, with reasons for exclusion given.

The economic article selection protocol and flow chart for the whole guideline can found in the guideline's Appendix 41A and Appendix 41B.

Table 4: Economic evidence profile: Integrated care versus usual care

Study	Applicability	Limitations	Other comments	Incremental cost	Incremental effects	Cost-effectiveness	Uncertainty
Hunter 2013[65] (UK)	Directly applicable[(a)]	Potentially serious limitations[(b)]	**Population:** Patients who have had a stroke **Model design**: Markov **Time horizon**: 10 years **Intervention 1:** Standard care **Intervention 2:** Hub-and-spoke stroke model where integrated services treat suspected stroke patients in a hyper acute stroke unit before discharge	Saves £3,869	0.65 QALYs	Integrated care dominates usual care, producing better health outcomes at a lower cost.	All sensitivity analyses using a 10-year time horizon resulted in integrated care dominating usual care or a very small increase in cost.
Lanzeta 2016[79] (Spain)	Partially applicable[(c)]	Potentially serious limitations[(d)]	**Population:** Patients with multimorbidities **Study design**: alongside a cluster randomised controlled trial (RCT) **Follow-up**: 12 months **Intervention 1:** Standard care **Intervention 2:** Improving communication between primary and secondary care healthcare professionals through the support of a reference internist and a liaison nurse during the management in primary care.	£946	-0.0553 QALYs	Integrated care is dominated by usual care, producing lower health outcomes at a higher cost.	A subgroup analysis on individuals under 80 years of age was conducted and found that in 89% of the bootstrapping simulations integrated care was cost saving. Integrated care was only cost saving for 15% of simulations from the bootstrapping for the whole sample.
Neumann 2014[90] (Germany)	Partially applicable[(e)]	Potentially serious limitations[(f)]	**Population:** Patients with systolic heart failure **Study design**:	£395 £255 –	0.022 QALYs	Using mean costs and mean QALYs the estimated ICER is	Bootstrapping found that the probability of the intervention being

Study	Applicability	Limitations	Other comments	Incremental cost	Incremental effects	Cost-effectiveness	Uncertainty
			economic evaluation alongside a randomised controlled trial (RCT) **Follow-up**: 6 months **Intervention 1:** Usual care **Intervention 2:** Interdisciplinary Network for Heart Failure; a Nurse led heart failure management programme.	excluding societal costs		calculated to be £11,605 per QALY gained. However the study reports an ICER of £39,255 which is greater than the mean cost divided by the mean benefit, even when societal costs are included.	cost effective at a £40,000 per QALY threshold was 55% although this included societal costs.
Sahota 2016[103] (UK)	Directly applicable[(g)]	Potentially serious limitations[(h)]	**Population:** Older people (age ≥ 70 years) admitted to the general medical wards as an acute medical emergency. **Study design**: economic evaluation alongside a randomised controlled trial (RCT) **Follow-up**: 12 months **Intervention 1:** The CIRACT [Community In-reach Rehabilitation And Care Transition service] service. The CIRACT service utilised the team's expertise in community working to form links with the appropriate services to ensure a smooth and effective discharge.(i) **Intervention 2:** Standard care – The traditional hospital-based Rehabilitation (THB-	£141	0.04 QALYs	£2,022 per QALY gained (adjusted for baseline differences)	Using non-parametric bootstrapping with replacement the probability of CIRACT being cost effective was 91% at a £30,000 per QALY threshold.

Study	Applicability	Limitations	Other comments	Incremental cost	Incremental effects	Cost-effectiveness	Uncertainty
			Rehab) service. Once discharged from hospital, participants had no direct contact with the THB-Rehab service.				

Abbreviations: QALY: quality-adjusted life years.

(a) UK NHS perspective study over a long time horizon with all relevant cost and health outcomes measured in QALYs.

(b) All relevant costs and outcomes were included, although based on non-randomised evidence. No RCTs were identified comparing a hub-and-spoke model and no hub-and-spoke model so this is likely to be the best source of evidence.

(c) Spanish healthcare perspective and therefore applicability to a UK setting may be limited. Unclear what tariff EQ-5D scores were derived from.

(d) 12 month follow up may not capture impacts on mortality. Unclear how the QALY was calculated and whether time of death was included in the QALY estimate.

(e) German healthcare perspective and therefore applicability to a UK setting may be limited. German EQ-5D tariff was used to derive utility scores.

(f) 6 month follow up may not capture full benefit. Unclear how the calculation to derive the ICER was made as this is different from the result of dividing the mean costs by the mean QALYs.

(g) UK NHS perspective study using QALYS with EQ-5D values derived from the UK tariff.

(h) Only a 12 month time horizon was used and this may not capture the full nature of future costs and benefits.

(i) Following discharge, the CIRACT team visited the participant at home within 48 hours to assess the level of rehabilitation required and further follow-up visits were provided as deemed necessary.

38.5 Evidence statements

Clinical

Fifteen studies comprising 7987 people evaluated the role of integrated care models for improving outcomes in adults and young people at risk of an AME, or with a suspected or confirmed AME or at high risk of an AME. The evidence suggested that integrated care models may provide a benefit in reduced mortality at 6 months (2 studies, low quality), 1 year (3 studies, very low quality) and 6 years (1 study, very low quality), ED use (1 study reported as a hazard ratio, low quality; 3 studies at 6-12 months, moderate quality; and 1 study at 6 years, low quality), readmission (2 studies, moderate quality), adverse events (1 study, very low quality), length of stay (1 study, high quality) and quality of life scores including barthel ADL score (1 study, moderate quality), physical health component and physical functioning component (1 study, low quality). Evidence for hospital admissions (reported separately due to varying methodologies) suggested an increase (1 study, very low quality), no difference (2 studies, moderate quality) and reduction (2 studies reporting a relative risk, very low quality; 2 studies reporting hazard ratios, low quality and 2 studies reporting rate ratios, very low quality) of admissions with integrated care. There was no effect on quality of life mental health component (1 study, low quality), mortality at 2 years (3 studies, very low quality) and the combined outcome of ED use and hospital admission (1 study, low quality).

Economic

One cost utility analysis showed that a hub and spoke model dominated usual care for patients with an acute stroke. This analysis was assessed as directly applicable with potentially serious limitations.

One cost utility analysis showed that integrated care was dominated by usual care in individuals over 70 years old with multimorbidities. This analysis was assessed as partially applicable with potentially serious limitations.

One cost utility analysis found that integrated care was cost effective, at a £20,000 per QALY threshold, when compared to usual care (ICER: £2,022 per QALY) in individuals over 70 years old who had been admitted to the general medical ward for an acute medical emergency. This study was assessed as being directly applicable with potentially serious limitations.

One cost utility analyses found that integrated care was cost effective, at a £20,000 per QALY threshold, when compared to usual care (ICERs: £11,605 per QALY) in patients with systolic heart failure. This study was assessed as being partially applicable with potentially serious limitations.

38.6 Recommendations and link to evidence

Recommendations	**22. Health and social care systems should develop and evaluate integrated care pathways.**
Research recommendation	-
Relative values of different outcomes	Mortality, avoidable adverse events, length of stay, quality of life, patient and/or carer satisfaction and unplanned hospital admissions were considered by the guideline committee to be critical outcomes. Hospital readmissions, ED demand, and family satisfaction were considered important outcomes.
Trade-off between benefits and harms	The committee considered various frameworks for characterising integrated care and the diverse interventions that might be grouped under this term. They chose to use the framework described by the Nuffield Trust[107], and the analysis of evidence was therefore based on this approach, using 5 strata: • coordinating and aligning of policies, rules and regulatory frameworks; • developing shared values, culture and vision across organisations, professional groups and individuals; • coordinating structures, governance systems and relationships across organisations; • aligning back-office functions, budgets and financial systems across integrating units; • coordinating of information and services and integrating patient care within a single process. The committee recognised that several of these elements would be interdependent, and within each, several interventions might be included, some of which have already been considered independently in this guideline such as information systems, alternatives to hospital care and GP involvement in Emergency Departments. Fifteen randomised controlled trials were found; however, all belonged to the stratum on coordinating of information and services and integrating patient care within a single process. These trials evaluated the use of integrated care exclusively in populations with a chronic disease condition. The interventions and specific conditions evaluated were heterogeneous and included management of COPD, heart failure, asthma, severe mental illness, geriatrics, diabetes and of patients receiving oral anticoagulants or chemotherapy. The evidence suggested that integrated care models may provide a benefit in reduced mortality (at 6 months, 1 year and 6 years), ED use, readmission, adverse events, length of stay and quality of life (Barthel ADL score, physical health component and physical functioning component). There was evidence for hospital admissions (reported separately due to varying methodologies). One study suggested an increase, 2 studies suggested no difference and 6 studies suggested a reduction of admissions with integrated care. There was no effect on quality of life (mental health component), mortality at 2 years and the combined outcome of ED use and hospital admission. No evidence was identified for patient and/or carer satisfaction and family satisfaction. The committee elected to make a strong recommendation for the development of integrated care pathways in the management of long-term conditions, based on the broadness of the evidence, the consistency of benefit identified and clinical and policy consensus that integration was required to enhance patient care.

Recommendations	**22. Health and social care systems should develop and evaluate integrated care pathways.**
Research recommendation	-
	The committee discussed the lack of evidence identified within the other strata. They noted that an intervention focused on clinical coordination would require effective changes in practice in areas associated with the other strata in the review. These areas would benefit from evaluation during the process of integration. The committee also noted that although the papers do not describe the other types of integration, it was likely that some of these would be required to achieve coordination of information and services for example, the alignment of policies, the sharing of values and the aligning of back office functions, budgets and financial systems.
Trade-off between net effects and costs	Integrated care across health services has the potential to improve health outcomes by providing better communication and co-ordination of care. This enables better care pathways to be established and therefore more prompt and pre-emptive responses to the patient's condition. These potential health gains, along with cost savings are what make integrated care pathways a potentially cost effective intervention. One cost utility analysis that was included compared a hub-and-spoke model of integrated care for acute stroke patients to usual care. This showed that the integrated care intervention dominated usual care as it was cost saving and had an increase in QALYs. The committee highlighted that some of the benefits of the integration in this study are specific to stroke care and might not necessarily apply to integrated systems in other populations, for example greater access to thrombolysis, which can improve outcomes for stroke care. One cost-utility analysis that was included assessed the cost effectiveness of integrated care in individuals with multimorbidities. This study evaluated the cost effectiveness of having a liaison nurse to co-ordinate care between primary and secondary care. The analysis showed that the intervention reduced QALYs although this decrease was highly uncertain and likely demonstrated the lack of impact the intervention was having, rather than indicating harm. Given there were significant increases in costs, the study showed that integrated care in this cohort of individuals was unlikely to be cost effective. The analysis did show that the intervention had an 89% chance of being cost saving in a subgroup of individuals over 80 years old. The other 2 cost-utility analyses included in the review were in elderly individuals (>70 years old) post AME and in people with systolic heart failure. Both analyses found that although neither intervention was cost saving, they provided enough QALYs to be considered cost effective at a £20,000 per QALY threshold. However, there was considerable uncertainty in both analyses and neither study strongly advocated the intervention. The committee believed that the evidence showed that integrated care could provide cost savings in some instances, and improve health outcomes but careful consideration and evaluation should be undertaken to find the right model. The resource impact is contingent on what type of integrated care is being pursued. Sometimes integrated care may mean better communication across services, which might be achieved through better information systems or by hiring dedicated liaison staff. Both approaches have very different resources impacts. Likewise, integrated care can sometimes mean setting up specialist multi-disciplinary teams, which would again have a very different resource impact. The committee felt that the resource impact of this recommendation would be low because integrated care is already being introduced across the health service and because integration can potentially avoid duplication of tests and appointments and

Recommendations	22. Health and social care systems should develop and evaluate integrated care pathways.
Research recommendation	-
	improve patient outcomes. However, the evidence was heterogeous with regard to impact on hospitalisation and the economic evaluations did not generally show cost savings. Overall, given the lack of evidence supporting a particular type of integrated care, the committee felt that measuring the resource impact would be a key component of the service evaluation that should occur alongside the implementation of any integrated care services.
Quality of evidence	Most evidence was graded at very low quality or low quality due to a combination of risk of bias and imprecision. Readmission and quality of life (Barthel ADL score) was graded as moderate due to serious imprecision. Length of stay was graded high quality. Inconsistency between outcomes reported using different methodologies, as identified in the evidence on hospital admissions, was not able to be assessed. However, the committee discussed this apparent inconsistency when making their recommendation. The cost utility analysis of hub and spoke model was assessed as directly applicable with potentially serious limitations. Two of the economic evaluations of models of integration between hospital and the community were evaluated as partially applicable because they were not set in the UK and the third was directly applicable. Although all three were based on randomised evidence, they were assessed as having potentially serious limitations because of a lack of clarity in reporting and fairly short time horizons.
Other considerations	The committee noted that integrated care models appeared to be most effective in clinical scenarios where a team-based approach was used, for example, in frailty, airway disease and heart disease. The committee decided to make a general recommendation covering integrated care models because they felt they had a diverse body of literature. Generally, the economic evidence was supportive of integrated care. However, it showed that some models could increase health service costs without delivering health benefits. The committee noted that future evaluation of integration of care should incorporate health economic evaluation and wished to draw attention to guidance from the MRC on process evaluation of complex interventions(2015).[89] There are many examples of integrated care, some of which could be considered examples of best practice. NHS England strongly supports the idea of delivering integrated care. Indeed, integration is currently viewed as essential if the growing number of people living with long-term conditions are to receive effective care within a finite budget. Although there are examples of good practice of integration within the NHS, much of it is delivered in a piece-meal way. Coordinating services and information around single disease processes across primary, secondary and social care will not adequately take into account multimorbidity requiring input from different specialists and services. The development of shared information systems is fundamental to service integration; the failure of the national programme for IT suggests that large-scale top-down projects are not the right approach. Smaller scale local projects using common platforms may have greater promise. Health and social care systems will need to invest sufficient time and resource to develop effective working relationships and shared goals between health sectors. Of greatest importance is aligning clinical, administrative, commissioning, political and policy objectives to focus on the care continuum and the patient pathway instead of single episodes of care, institutions and isolated performance targets. The need for new ways of planning care has been highlighted by the regulator, the Care Quality

Recommendations	**22. Health and social care systems should develop and evaluate integrated care pathways.**
Research recommendation	-
	Commission[26] and NHS England, the NHS Five Year Forward View.[92] Experience from other healthcare systems may be of value. Kaiser Permanente is the largest non-profit-making health maintenance organisation in the United States, serving 8.7 million people in 8 regions. It is a virtually integrated system in which the health plans, hospitals and medical groups in each region are distinct organisations linked through contracts. Kaiser Permanente is recognised as one of the top-performing systems in the United States with high levels of member satisfaction and excellent ratings for clinical quality. It is also one of the lowest-cost providers in most of the regions in which it operates. Studies that have compared the NHS with Kaiser Permanente show that the NHS uses around 3 times as many bed days for older people with common conditions like hip fracture and stroke as Kaiser Permanente. Part of the explanation is that, compared with the NHS, Kaiser Permanente delivers more care out of hospital in large medical offices (analogous to polyclinics) and it also makes use of step-down facilities. One of the key features of the Kaiser Permanente model is the emphasis placed on keeping members healthy and achieving close co-ordination of care through the use of the electronic medical record and team working[48,49,56,106]. The Better Care Fund (BCF) is a programme spanning both the NHS and local government.[93] A report by the National Audit Office found no evidence of benefit for this initiative in the early stages, and makes recommendations for continued and future evaluation of this and similar programmes. NHS England has launched their New Care Models programme including the Vanguard Sites initiative which encompasses a diverse range of interventions focused on care integration.[94] Collaboration between regional integrated care groupings could provide a platform for health services research testing combinations of care pathways using a stepped approach. Full evaluation of these schemes will be useful to inform future updates of the guideline.

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Appendices

Appendix A: Review protocol

Table 5: Review protocol: Integrated care models

Review question	Do integrated care models improve outcomes for patients with a suspected or confirmed acute medical emergency or at high risk of an acute medical emergency?
Guideline condition and its definition	Acute medical emergencies. Definition: people with suspected or confirmed acute medical emergencies or at risk of an acute medical emergency or at high risk of AME.
Review population	Adults and young people (16 years and over) with a suspected or confirmed AME.
	Line of therapy not an inclusion criterion.
Interventions and comparators: generic/class; specific/drug (All interventions will be compared with each other, unless otherwise stated)	Integration of care across teams or between different levels of care: - Coordinating and aligning policies, rules and regulatory frameworks. - Developing shared values, culture and vision across organisations, professional groups and individuals. - Coordinating structures, governance systems and relationships across organisations. - Aligning back-office functions, budgets and financial systems across integrating units. - Coordinating information and services and integrating patient care within a single. - No integration of care; As defined by study.
Outcomes	- Unplanned hospital admissions during the study period (Continuous) IMPORTANT - Avoidable adverse effects (Delayed, missed or duplicated investigations and treatment) during the study period (Dichotomous) CRITICAL - Quality of life during the study period (Continuous) CRITICAL - Patient and/or carer satisfaction during the study period (Dichotomous) CRITICAL - Mortality during the study period (Dichotomous) CRITICAL - Readmission up to 30 days (Continuous) IMPORTANT - Length of stay during the study period (Continuous) CRITICAL - ED presentations during the study period (Dichotomous) IMPORTANT - Carer and family satisfaction during the study period (Continuous) IMPORTANT
Study design	Systematic reviews (SRs) of RCTs, RCTs, observational studies only to be included if no relevant SRs or RCTs are identified.
Unit of randomisation	Patient. Hospital. Physician. Ward.
Crossover study	Not permitted.
Minimum duration of study	Not defined.
Other exclusions	Non-OECD country.
Other stratifications	Strata by type of integration model - as defined by the classes of intervention. These integration models are not similar, nor mutually exclusive in their implementation, and therefore separate recommendation would be

	made.
Subgroup analyses if there is heterogeneity	- Frail elderly (frail elderly; not frail elderly); frail elderly are thought to have a greater benefit from integrated care. - People with serious mental illness (serious mental illness; no serious mental illness); people with serious mental illness are thought to have a greater benefit from integrated care.
Search criteria	Databases: Medline, Embase, the Cochrane Library. Date limits for search: None. Language: English.

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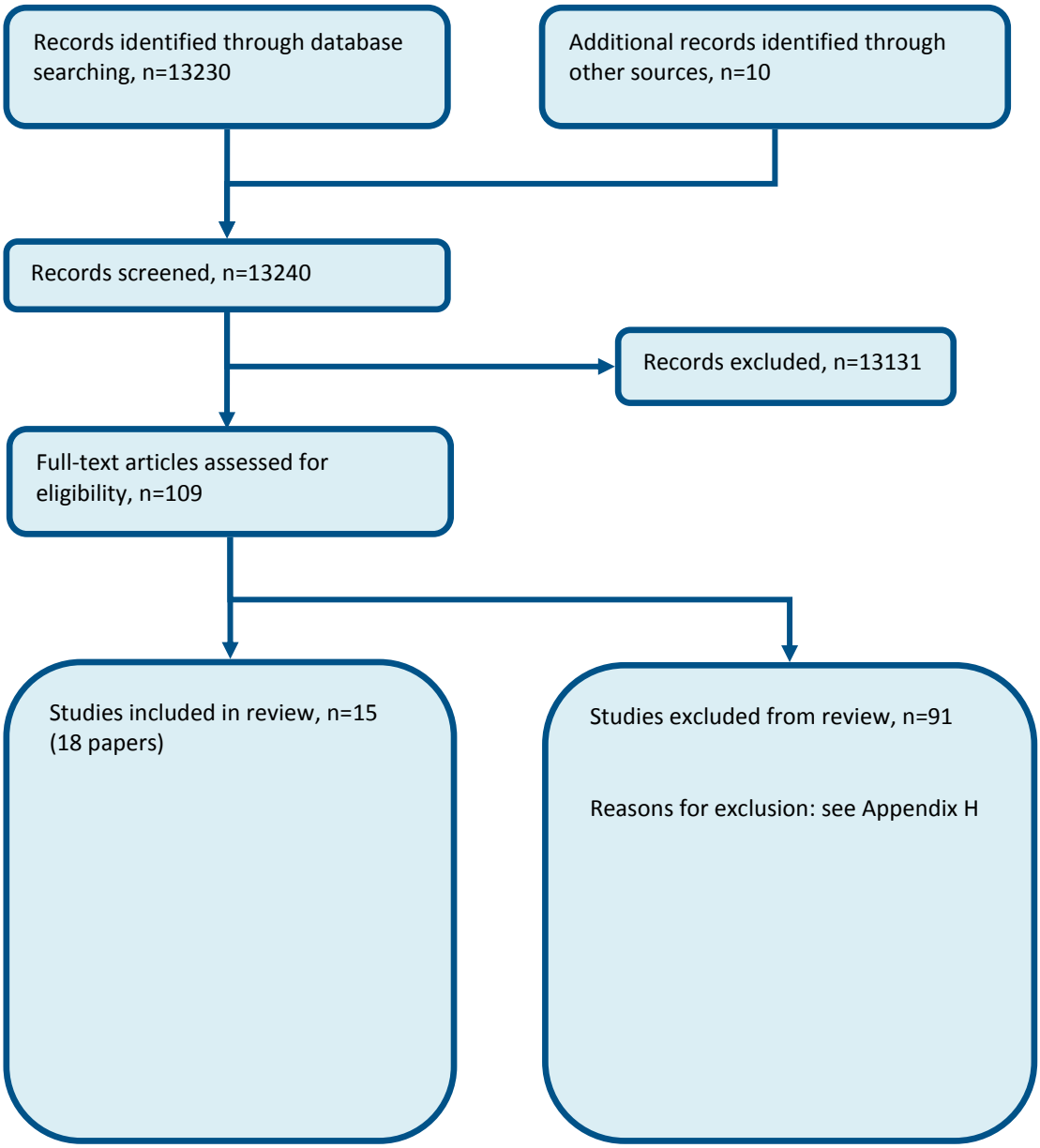
Appendix B: Clinical article selection

Figure 1: Flow chart of clinical article selection for the review of integrated care models



Appendix C: Forest plots

C.1 Integrated care versus no integrated care

Figure 2: Mortality

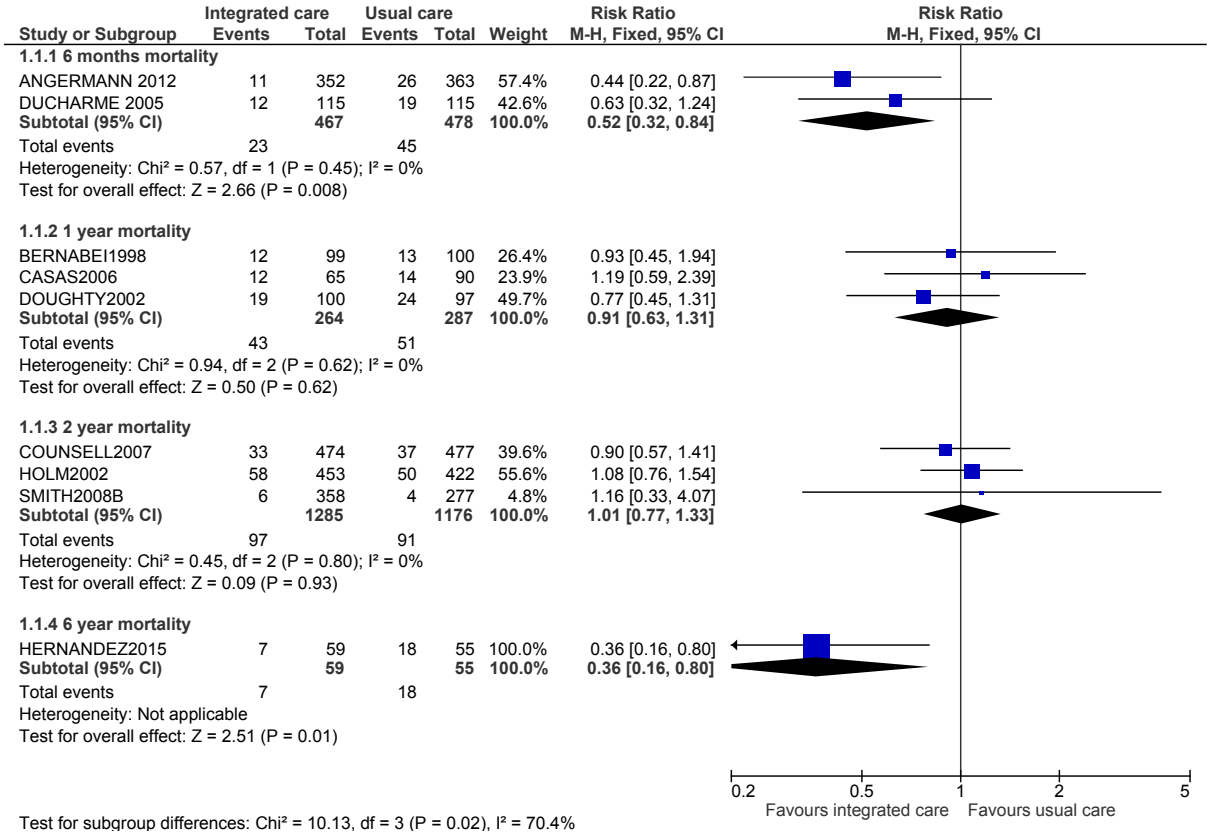


Figure 3: Readmission (28-30 days)

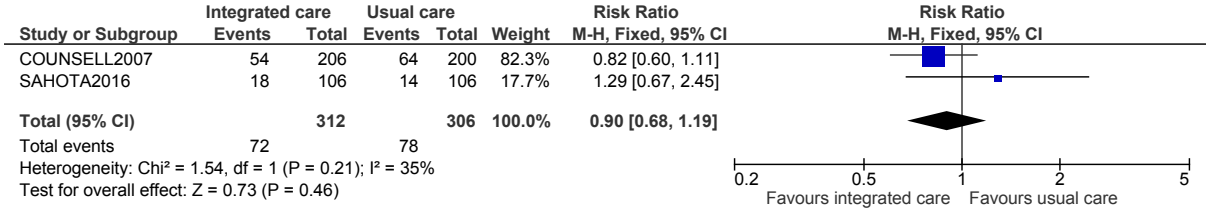


Figure 4: Hospital admission rate (1 year)

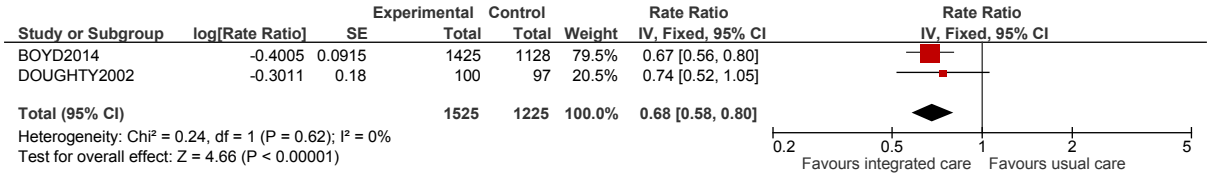


Figure 5: Hospital admission (1 year)

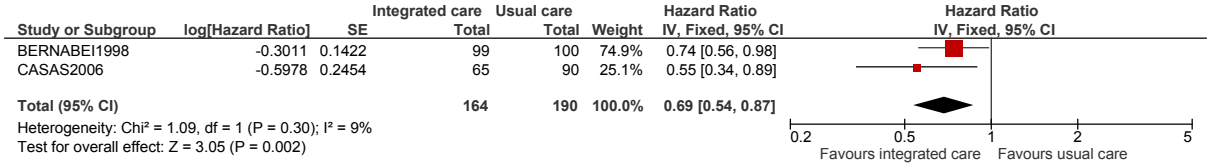


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Figure 6: Hospital admission (6 months – 1 year)

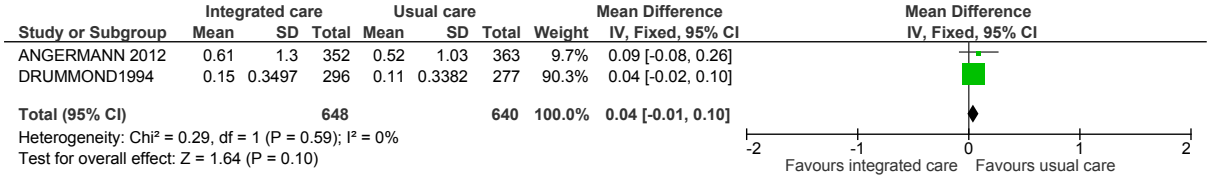

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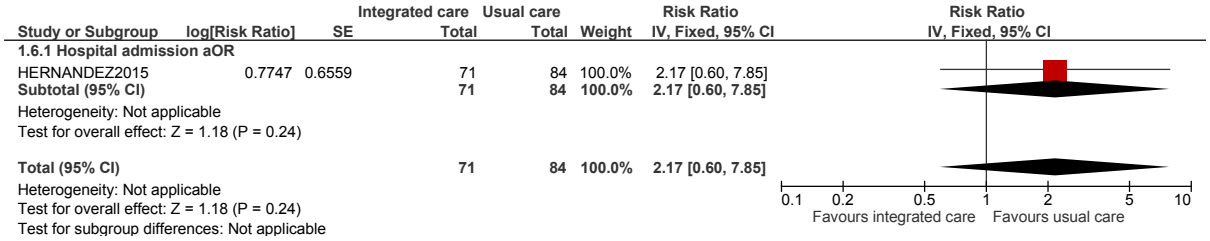
Figure 7: Hospital admission (6 years)



Note: Adjusted for differences in influenza and pneumococcal vaccination

3

Figure 8: Hospital admissions (6 months – 1 year)

4

Figure 9: Length of stay (follow-up at 90 days)

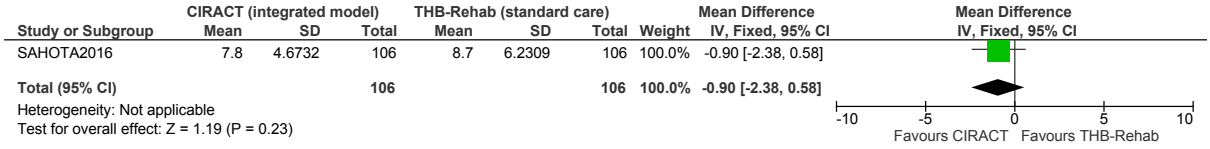


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Figure 10: Emergency Department use (2 years)

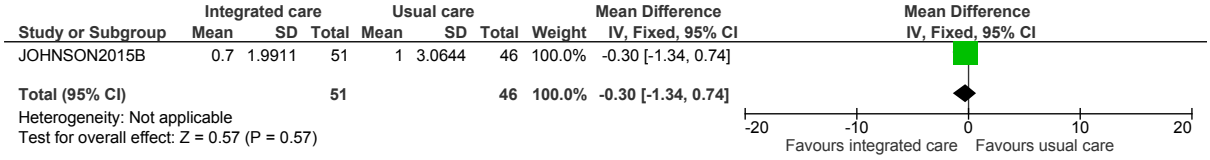

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Figure 11: Emergency Department use (1 year)

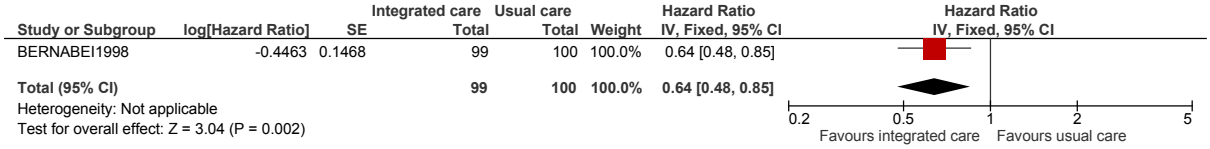

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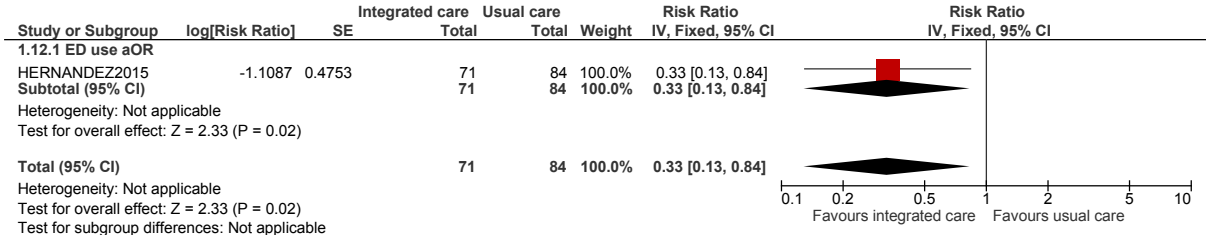
Figure 12: Emergency Department use (6 years)



Note: Adjusted for differences in influenza and pneumococcal vaccination

2

Figure 13: Emergency Department use (6 months – 1 year)

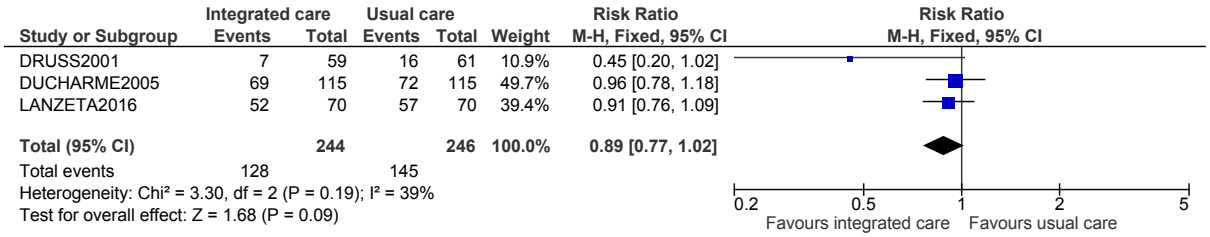


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Figure 14: Adverse effects (2 years)

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Figure 15: Quality of life (SF-36) (score: 0-100) (6 months)

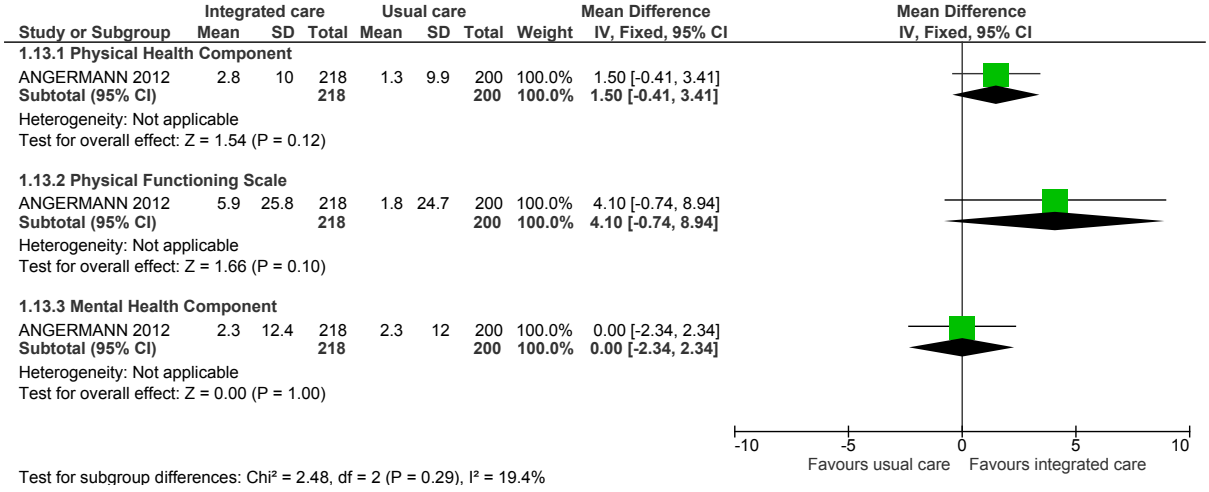

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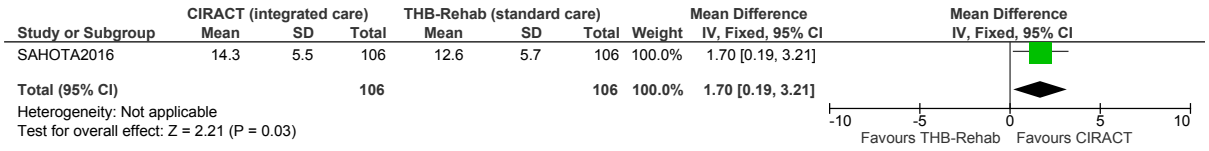
Figure 16: Barthel ADL Score (score: 0-20; higher values better) (90 days)



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Appendix D: Clinical evidence tables

Study	Angermann 2012[10]
Study type	RCT (Patient randomised; Parallel).
Number of studies (number of participants)	1 (n=715).
Countries and setting	Conducted in Germany; setting: 9 hospitals in Bavaria and Baden-Württemberg.
Line of therapy	Not applicable.
Duration of study	Follow up (post intervention): 180 days.
Method of assessment of guideline condition	Adequate method of assessment/diagnosis.
Stratum	Overall.
Subgroup analysis within study	Not applicable.
Inclusion criteria	Patients age ≥18 years were eligible when hospitalised with signs and symptoms of decompensated heart failure (dyspnea at rest/minimal exercise plus at least 1 of the following: raised jugular venous pressure, peripheral edema, third heart sound, or pulmonary congestion [clinical or chest radiography]) and had a left ventricular ejection fraction (LVEF) ≤40% (echocardiography).
Exclusion criteria	New-onset structural heart disease, logistic or health reasons precluding participation in telephone-based interventions, and lack of written consent.
Recruitment/selection of patients	Based on the inclusion criteria.
Age, gender and ethnicity	Age - Mean (SD): 69 (12) years. Gender (M:F): 2.45/1. Ethnicity: not reported.
Further population details	1. Frail elderly: Not applicable 2. People with serious mental illness: not applicable.
Indirectness of population	No indirectness.
Interventions	(n=352) Intervention 1: Integration of care across teams or between different levels of care - Systemic Coordinating and aligning policies, rules and regulatory frameworks for example, policy levers emphasising better coordinated care outside of hospitals. HNC included the following elements: (1) in-hospital face-to-face contact between specialist nurse, patient, and relatives to explain the intervention, practice supervision of blood pressure, heart rate and symptoms, and provide participants with teaching materials and self-monitoring schemes; (2) telephone-based structured monitoring using a standardised 19-item questionnaire addressing indicators of worsening heart failure, other cardiac symptoms, medication, health care utilisation, state of mood, and general health and well-being; (3) uptitration of heart failure medication in cooperation with GPs, where possible, and teaching of patients regarding adjustment of diuretics; (4) needs-adjusted specialist care, which nurses coordinated with patients' physician(s); (5)

Study	Angermann 2012[10]
	measures for appropriate education and supervision of interveners to ensure high intervention quality (see online-only Data Supplement Part I for details). All nurses were trained in telephone skills, received supervision by a cardiologist (weekly) and a psychologist (bimonthly), and had unrestricted access to their supervisor for questions Duration: 6 months (180 days). Concurrent medication/care: patients receiving the intervention underwent HNC on top of UC. (n=363) Intervention 2: No integration of care - As defined by study. Patients in UC underwent standard post-discharge planning, which typically included treatment plans, comprehensive discharge letters, and fixed appointments with GPs or cardiologists within 7–14 days. No restrictions were placed on outpatient care, and patients were urged to ensure that providers always documented type and extent of all health care utilisation in their INH patient pass. Duration: 6 months (180 days). Concurrent medication/care: n/a.
Funding	Academic or government funding (The main sponsor was the German Ministry of Education and Research ([BMBF, Berlin, Germany]). Additional support was provided by the German Competence Network Heart Failure [CNHF, Berlin, Germany, funded by the BMBF]).

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: HEARTNETCARE-HF versus USUAL CARE.

Protocol outcome 1: Quality of life.
- Actual outcome: SF-36 - Physical Health Component at 6 months; Group 1: mean 2.8 (SD 10); n=218, Group 2: mean 1.3 (SD 9.9); n=200; The Short Form (36) Scale 0-100 Top=High is good outcome; Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 134, Reason: Died, withdrew consent; Group 2 Number missing: 163, Reason: Died, withdrew consent
- Actual outcome: SF-36 - Physical Functioning Scale at 6 months; Group 1: mean 5.9 (SD 25.8); n=218, Group 2: mean 1.8 (SD 24.7); n=200; Short Form (36) Health Scale 0-100 Top=High is good outcome

- Actual outcome: SF-36 - Physical Functioning Scale at 6 months; Group 1: mean 5.9 (SD 25.8); n=218, Group 2: mean 1.8 (SD 24.7); n=200; Short Form (36) Health Scale 0-100 Top=High is good outcome; Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 134, Reason: Died, withdrew consent; Group 2 Number missing: 163, Reason: Died, withdrew consent
- Actual outcome: SF-36 - Mental Health Component at 6 months; Group 1: mean 2.3 (SD 12.4); n=218, Group 2: mean 2.3 (SD 12); n=200
- Actual outcome: SF-36 - Mental Health Component at 6 months; Group 1: mean 2.3 (SD 12.4); n=218, Group 2: mean 2.3 (SD 12); n=200; Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 134, Reason: Died, withdrew consent; Group 2 Number missing: 163, Reason: Died, withdrew consent

Protocol outcome 2: Mortality.

Study	Angermann 2012[10]
- Actual outcome: Mortality at 6 months; Group 1: 11/352, Group 2: 26/363; Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0 - Actual outcome: Re-hospitalisations at 6 months; Group 1: mean 0.61 (SD 1.3); n=352, Group 2: mean 0.52 (SD 1.03); n=363; Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0	
Protocol outcomes not reported by the study	Unplanned hospital admissions during study period; Avoidable adverse effects (Delayed, missed or duplicated investigations and treatment) during study period; Patient satisfaction during study period; Hospital readmissions during study period; Length of stay during study period; ED presentations during study period; Carer and family satisfaction during study period.

1

Study	Bernabei 1998[16]
Study type	RCT (Patient randomised; Parallel).
Number of studies (number of participants)	1 (n=199).
Countries and setting	Conducted in Italy; setting: Integration between primary and social care.
Line of therapy	Not applicable.
Duration of study	Follow up (post intervention): 12 months.
Method of assessment of guideline condition	Unclear method of assessment/diagnosis.
Stratum	Overall.
Subgroup analysis within study	Not applicable.
Inclusion criteria	Aged over 65 and recipients of home health services or home assistance programmes.
Exclusion criteria	Not reported.
Recruitment/selection of patients	Elderly already receiving conventional community care services
Age, gender and ethnicity	Age - Mean (SD): Group 1: 80.7 (7.7), Group 2: 81.3 (7.4). Gender (M:F): 58:141. Ethnicity: not reported.
Further population details	1. Frail elderly: Not applicable 2. People with serious mental illness: Not applicable
Indirectness of population	No indirectness.
Interventions	(n=99) Intervention 1: Integration of care across teams or between different levels of care - Clinical Coordinating information and services and integrating patient care within a single process for example, developing extended clinical

Study	Bernabei 1998[16]
	roles, guidelines and inter-professional education. Assessment and care by the geriatric evaluation unit, which consisted of general practitioners, a geriatrician, a social worker, and several nurses. Two case managers were selected among the trainees of a course on case management and comprehensive geriatric assessment. Case managers performed the initial assessment soon after randomisation and every 2 months thereafter. Also, they were constantly available to deal with problems, monitor the provision of services, and to guarantee extra help as requested by patients and general practitioners. Duration: 12 months. Concurrent medication/care: not reported. Comments: "All the services considered necessary were provided in an integrated fashion after a formal agreement between the municipality and the local health agency". (n=100) Intervention 2: No integration of care - As defined by study. Primary and community care "with the conventional and fragmented organisation of services". Duration: 12 months. Concurrent medication/care: not reported.
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: CLINICAL COORDINATING INFORMATION AND SERVICES AND INTEGRATING PATIENT CARE WITHIN A SINGLE PROCESS FOR EXAMPLE, DEVELOPING EXTENDED CLINICAL ROLES, GUIDELINES AND INTER-PROFESSIONAL EDUCATION versus CONTROL Protocol outcome 1: Unplanned hospital admissions during the study period. - Actual outcome: Admission to hospital at 12 months; HR 0.74 (95%CI 0.56 to 0.97) Reported; Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness--. Protocol outcome 2: Mortality during the study period. - Actual outcome: Mortality at 12 months; HR 0.99 (95%CI 0.89 to 1.09) Reported; Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectenss: Protocol outcome 3: ED presentations during the study period. - Actual outcome: ED presentation at 12 months; HR 0.64 (95%CI 0.48 to 0.85) Reported; Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Avoidable adverse effects (Delayed, missed or duplicated investigations and treatment) during the study period; Quality of life during the study period; Patient and/or carer satisfaction during the study period; Hospital readmissions during the study period; Length of stay during the study period; Carer and family satisfaction during the study period.

Study	Boyd 2014[22]

Study	Boyd 2014[22]
Study type	RCT (Hospital randomised; Parallel).
Number of studies (number of participants)	1 (n=2553).
Countries and setting	Conducted in New Zealand; setting: integration between secondary and social care.
Line of therapy	Not applicable.
Duration of study	Intervention time: 12 months.
Method of assessment of guideline condition	Partially adequate method of assessment/diagnosis.
Stratum	Overall.
Subgroup analysis within study	Not applicable.
Inclusion criteria	Facility participation was voluntary.
Exclusion criteria	None stated.
Recruitment/selection of patients	Long-term care residents at facilities. Facilities included combined low and high level care, low level care only (rest home), high level care only (private hospital) and dementia care only.
Age, gender and ethnicity	Age - Mean (SD): Group 1 pre-intervention: 85.0 (6.8), Group 1 post-intervention: 84.3 (7.7); Group 2 pre-intervention: 85.5 (6.9), Group 2 post-intervention: 84.7 (6.5). Gender (M:F): NR. Ethnicity: not reported.
Further population details	1. Frail elderly: Not applicable 2. People with serious mental illness: Not applicable.
Indirectness of population	No indirectness.
Interventions	(n=1425) Intervention 1: Integration of care across teams or between different levels of care - Clinical Coordinating information and services and integrating patient care within a single process for example, developing extended clinical roles, guidelines and inter-professional education. A secondary care Gerontology nurse specialist (GNS) intervention to improve the quality of care in aged care facilities through proactive GNS outreach. Components consisted of: Regular, proactive bi-monthly GNS visits, collaborative relationship between GNS and facility staff, telephone consultation and site visits as needed, quality initiatives, RN care guides, wound care consultant, standardised bimonthly education sessions at the facility, Gerontology clinical coaching at the bedside as needed, clinical practice development, quarterly district-wide education sessions, comprehensive geriatric assessment, GNS liaison with secondary care Older Adult Specialists Services, GNS liaison across primary and secondary care services. Duration: 12 months. Concurrent medication/care: residential care. (n=1128) Intervention 2: No integration of care - As defined by study. No GNS on-site integration. Duration: 12 months. Concurrent medication/care: residential care.
Funding	Academic or government funding (Waitemata District Health Board Program Based Margin Analysis innovations

Study	Boyd 2014[22]
	funding).
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: CLINICAL COORDINATING INFORMATION AND SERVICES AND INTEGRATING PATIENT CARE WITHIN A SINGLE PROCESS FOR EXAMPLE, DEVELOPING EXTENDED CLINICAL ROLES, GUIDELINES AND INTER-PROFESSIONAL EDUCATION versus CONTROL Protocol outcome 1: Unplanned hospital admissions during the study period. - Actual outcome: Hospital admissions at 12 months; Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - Very high, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness; Baseline details: Intervention group had a greater number of hospitalisations at baseline (615 vs 364); Group 1 Number missing: Reason: Three facilities were excluded - one ceased operation and two were under formal investigation. Group allocation and patient numbers not listed; Group 2 Number missing: Reason: Three facilities were excluded - one ceased operation and two were under formal investigation. Group allocation and patient numbers not listed	
Protocol outcomes not reported by the study	Avoidable adverse effects (Delayed, missed or duplicated investigations and treatment) during the study period; Quality of life during the study period; Patient and/or carer satisfaction during the study period; Mortality during the study period; Hospital readmissions during the study period; Length of stay during the study period; ED presentations during the study period; Carer and family satisfaction during the study period.

Study	Casas 2006[28]
Study type	RCT (Patient randomised; Parallel).
Number of studies (number of participants)	1 (n=155).
Countries and setting	Conducted in Belgium, Spain; setting: integration between secondary and community care.
Line of therapy	Not applicable.
Duration of study	Intervention time: 12 months.
Method of assessment of guideline condition	Partially adequate method of assessment/diagnosis: COPD hospitalisations.
Stratum	Overall: COPD.
Subgroup analysis within study	Not applicable.
Inclusion criteria	All patients admitted because of a previous episode of exacerbation requiring hospitalisation for over 48 hours.
Exclusion criteria	Not living in the healthcare area (39%); severe comorbid conditions, that is, lung cancer or other advanced malignancies, and extremely severe neurological or cardiovascular disorders (25%); logistical limitations due to extremely poor social conditions, such as illiteracy or no phone access at home (10%); and being admitted to a nursing home (7%).

Study	Casas 2006[28]
Recruitment/selection of patients	Two tertiary hospitals.
Age, gender and ethnicity	Age - Mean (SD): Group 1; 70 (9), Group 2: 72 (9). Gender (M:F): Define. Ethnicity: not reported.
Further population details	1. Frail elderly: Not applicable/Not stated/Unclear. 2. People with serious mental illness: Not applicable/Not stated/Unclear.
Extra comments	All patients admitted because of a previous episode of exacerbation requiring hospitalisation. At 1 site community care was provided by a primary care team (physician, nurse and social worker). Other site community care was provided by the patient's GP.
Indirectness of population	No indirectness.
Interventions	(n=65) Intervention 1: Integration of care across teams or between different levels of care - Clinical Coordinating information and services and integrating patient care within a single process for example, developing extended clinical roles, guidelines and inter-professional education. A comprehensive assessment of the patient at discharge, including severity of the respiratory disease, evaluation of comorbid conditions and analysis of requirements in terms of social support. Educational programme on self-management of the disease administered at discharge. Agreement on an individually tailored care plan following international guidelines was shared across the system via interaction between the specialised nurse case manager and the primary care team. Accessibility of the specialised nurse to patients/carers and primary care professionals during the follow-up period was ensured through an ICT platform including a web-based call centre. Duration: 12 months. Concurrent medication/care: none stated. (n=90) Intervention 2: No integration of care - As defined by study. Usual care: Patients included in the UC arm were discharged from hospital by the attending physician who decided on the outpatient control regime. Pharmacological prescriptions at discharge and in-hospital treatment followed the standard protocols of the centres involved in the study, which were similar in IC and UC. Patients in the UC arm of the study were visited by their own physician without additional support. Visits were usually scheduled every 6 months. The controls did not receive help from the specialised nurse, nor were they included in the educational programme or had access to the call-centre. Duration: 12 months. Concurrent medication/care: none stated.
Funding	-- (CHRONIC project (IST-1999/12158); Marato de TV3; Comissionat per a Universitats i Recerca de la Generalitat de Catalunya (SGR-00386); Red Respira Instituto de Salud Carlos III (ISCIII)-Redes Tema´ticas de Investigacio´n Cooperativa (RTIC)-03/11; and Red Telemedicina ISCIII-RTIC-03/117).
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: CLINICAL COORDINATING INFORMATION AND SERVICES AND INTEGRATING PATIENT CARE WITHIN A SINGLE PROCESS FOR EXAMPLE, DEVELOPING EXTENDED CLINICAL ROLES, GUIDELINES AND INTER-PROFESSIONAL EDUCATION versus CONTROL Protocol outcome 1: Unplanned hospital admissions during the study period.	

Study	Casas 2006[28]
- Actual outcome: readmission-free time during the study period; HR 0.55 (95%CI 0.34 to 0.87) Reported; Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Crossover - Low; Indirectness of outcome: -- ; Baseline details: Intervention group had higher hospitalisations during previous year (1.0 vs 0.64) and lower influenza vaccination rate (56% vs 78%); Group 1 Number missing: 5, Reason: Palliative care - 3, Change of address - 2; Group 2 Number missing: 4, Reason: Palliative care - 1, Change of address - 1, Neoplasm - 2 Protocol outcome 2: Mortality during the study period. - Actual outcome: Total deaths during the study period; Group 1: 12/65, Group 2: 14/90; Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Crossover - Low; Indirectness of outcome: -- ; Baseline details: Intervention group had higher hospitalisations during previous year (1.0 vs 0.64) and lower influenza vaccination rate (56% vs 78%); Group 1 Number missing: 5, Reason: Palliative care - 3, Change of address - 2; Group 2 Number missing: 4, Reason: Palliative care - 1, Change of address - 1, Neoplasm - 2	
Protocol outcomes not reported by the study	Avoidable adverse effects (Delayed, missed or duplicated investigations and treatment) during the study period; Quality of life during the study period; Patient and/or carer satisfaction during the study period; Hospital readmissions during the study period; Length of stay during the study period; ED presentations during the study period; Carer and family satisfaction during the study period.

1

Study	Doughty 2002[40]
Study type	RCT (Physician randomised; Parallel).
Number of studies (number of participants)	1 (n=197).
Countries and setting	Conducted in New Zealand; setting: integration between primary and secondary care.
Line of therapy	1st line.
Duration of study	Follow-up: 12 months.
Method of assessment of guideline condition	Adequate method of assessment/diagnosis.
Stratum	Overall: Heart failure management.
Subgroup analysis within study	Not applicable.
Inclusion criteria	Primary diagnosis of heart failure.
Exclusion criteria	Surgically remediable cause for heart failure, such as severe aortic stenosis, consideration for heart transplantation, inability to provide informed consent, terminal cancer and participation in any other clinical trial.
Recruitment/selection of patients	Admitted patients at general medical wards at an urban tertiary hospital.

Study	Doughty 2002[40]
Age, gender and ethnicity	Age - Mean (SD): Group 1: 72.5 (11.6), Group 2: 73.5 (10). Gender (M:F): 118:79. Ethnicity: NZ European: 78%, Maori: 8%, Pacific Islander: 12%, Other 2%.
Further population details	1. Frail elderly: Not applicable/Not stated/Unclear. 2. People with serious mental illness: Not applicable/Not stated/Unclear.
Indirectness of population	No indirectness.
Interventions	(n=100) Intervention 1: Integration of care across teams or between different levels of care - Clinical Coordinating information and services and integrating patient care within a single process for example, developing extended clinical roles, guidelines and inter-professional education. Outpatient clinical review with the study team within 2 weeks of hospital discharge. At this initial clinic visit the patient's clinical status was reviewed, with particular attention to possible remediable exacerbating factors. One-on-one education with the study nurse was initiated at the first clinic visit. A patient diary, for daily weights, medication record, clinical notes and appointments, and education booklet were provided. A follow-up plan was devised for each patient aiming for 6-weekly visits alternating between the GP and heart failure clinic, although the patients were free to see their GPs at any time they wished. A detailed letter was faxed to the GP on the same day as the patient visited the heart failure clinic. This letter included summary comments outlining the rationale for any changes in treatment, and was followed-up with a phone call to the patient's GP to discuss any relevant changes in the management plan. The aim was for a close liaison between the patient and family, the GP and the hospital heart failure clinic. GPs made changes to the patient's management as they saw fit but were encouraged to discuss aspects of the patient's management with the clinic team at any stage. Subsequently, group education sessions (each lasting 1•5–2 h) were offered, 2 within 6 weeks of hospital discharge and a further after 6 months. These sessions were run by a cardiologist and the study nurse. The content of the one-on-one and group education included explanation of the symptoms and signs of heart failure, importance of monitoring of daily body weight and action plans should weight change, effects of medications and importance of compliance and recommendations regarding exercise and diet. The advice given was individualised and reinforced at each subsequent clinic visit by the study nurse. Monitoring of daily weights, with documentation in the diary and knowing what action to take should weight change, was reinforced at every available opportunity, either in the clinic or during phone calls with the patient. No assistance with travel costs or other incentives were provided for the patients in the intervention group. The study team at the hospital heart failure clinic was available for consultation during normal working hours and received calls from both patients and their GPs. At times of worsening symptoms patients were initially advised to see their GP. No explicit criteria for readmission were pre-specified and the decision to request admission rested with the GP. If admission was not required then an earlier heart failure clinic visit could be arranged. Duration: 12 months. Concurrent medication/care: none stated. (n=97) Intervention 2: No integration of care - As defined by study. Patients randomised to the control group continued under the care of their GP with additional follow-up measures as usually recommended by the medical

Study	Doughty 2002[40]
	team responsible for their in-patient care. Duration: 12 months. Concurrent medication/care: none stated.
Funding	Academic or government funding (National Heart of New Zealand and an unrestricted educational grant from Merck Sharp Dohme (NZ) Ltd).
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: CLINICAL COORDINATING INFORMATION AND SERVICES AND INTEGRATING PATIENT CARE WITHIN A SINGLE PROCESS FOR EXAMPLE, DEVELOPING EXTENDED CLINICAL ROLES, GUIDELINES AND INTER-PROFESSIONAL EDUCATION versus CONTROL Protocol outcome 1: Unplanned hospital admissions during the study period. - Actual outcome: Hospital admission rate during the study period; Proportion 0.74 (95%CI 0.52 to 0.96); Risk of bias: All domain - Very high, Selection - Very high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness; Baseline details: Intervention group had lower proportion of ischaemic HF patients (48% vs 59%), Less patients living alone (29% vs 41%), less patients treated for hypertension (46% vs 56%), more diabetics (32% vs 25%); Group 1 Number missing: , Reason: 1 patient lost to follow-up (no group allocation); Group 2 Number missing: , Reason: 1 patient lost to follow-up (no group allocation) Protocol outcome 2: Mortality during the study period. - Actual outcome: Mortality during the study period; Group 1: 19/100, Group 2: 24/97; Risk of bias: All domain - Very high, Selection - Very high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Intervention group had lower proportion of ischaemic HF patients (48% vs 59%), Less patients living alone (29% vs 41%), less patients treated for hypertension (46% vs 56%), more diabetics (32% vs 25%); Group 1 Number missing: , Reason: 1 patient lost to follow-up (no group allocation); Group 2 Number missing: Reason: 1 patient lost to follow-up (no group allocation)	
Protocol outcomes not reported by the study	Avoidable adverse effects (Delayed, missed or duplicated investigations and treatment) during the study period; Quality of life during the study period; Patient and/or carer satisfaction during the study period; Hospital readmissions during the study period; Length of stay during the study period; ED presentations during the study period; Carer and family satisfaction during the study period.

Study	Drummond 1994[41]
Study type	RCT (Patient randomised; Parallel).
Number of studies (number of participants)	1 (n=712).
Countries and setting	Conducted in United Kingdom; setting: integration between primary and secondary care.
Line of therapy	Not applicable.

Study	Drummond 1994[41]
Duration of study	Intervention time: 12 months.
Method of assessment of guideline condition	Partially adequate method of assessment/diagnosis: Asthma suffers with AME outcomes, most severe asthma patients excluded (no further details given).
Stratum	Overall: Asthma.
Subgroup analysis within study	Not applicable.
Inclusion criteria	Diagnosis of asthma confirmed by a chest physician and pulmonary function reversibility of at least 20% on treatment, 16 years or over.
Exclusion criteria	Most severe asthma patients excluded (no further details given).
Recruitment/selection of patients	During attendance of outpatient clinics for review.
Age, gender and ethnicity	Age - Other: NR. Gender (M:F): NR. Ethnicity: not reported.
Further population details	1. Frail elderly: Not applicable/Not stated/Unclear. 2. People with serious mental illness: Not applicable/Not stated/Unclear.
Indirectness of population	No indirectness.
Interventions	(n=363) Intervention 1: Integration of care across teams or between different levels of care - Clinical Coordinating information and services and integrating patient care within a single process for example, developing extended clinical roles, guidelines and inter-professional education. Chest physicians review patients annually. Interim reviews take place in general practice, typically every 3 months; however, the interval between reviews can be shortened if the patient's condition merits this. Patients are sent computer generated questionnaires at the appropriate time, inviting them to make an appointment with their general practitioner, and asking for information about symptoms, days of restricted activity, nights of disturbed sleep, courses of oral steroids, general practice consultations, and admissions for asthma. Patients are asked to give the completed questionnaire to their general practitioner at the consultation. Simultaneously, the patient's general practitioner is sent a separate computer generated questionnaire, mentioning that the patient is due to attend shortly for an asthma review and enclosing a questionnaire about consultations, pulmonary function, β agonist bronchodilators and steroid courses prescribed, changes to the patient's medication, and hospital admissions. The general practitioner is asked to return all documentation to the consultant. The information from both questionnaires is then added to the patient's computerised record. Copies of the updated record are sent to the general practitioner, along with any suggestions from the consultant for changes in the management plan. Duration: 12 months. Concurrent medication/care: none stated. (n=349) Intervention 2: No integration of care - As defined by study. Patients receiving conventional outpatient care are seen at their regular outpatient clinic, typically every 3 months. During the study year, they too were sent a clinical

Study	Drummond 1994[41]
	questionnaire before each visit, to be returned to the specialist. Additional clinic attendances were arranged by the consultant or general practitioner if necessary. Duration: 12 months. Concurrent medication/care: none stated.
Funding	Funding not stated.
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: CLINICAL COORDINATING INFORMATION AND SERVICES AND INTEGRATING PATIENT CARE WITHIN A SINGLE PROCESS FOR EXAMPLE, DEVELOPING EXTENDED CLINICAL ROLES, GUIDELINES AND INTER-PROFESSIONAL EDUCATION versus CONTROL Protocol outcome 1: Unplanned hospital admissions during the study period. - Actual outcome: Number of hospital admissions for asthma at 12 months; Group 1: mean 0.15 (SD 0.3497); n=296, Group 2: mean 0.11 (SD 0.3382); n=277; Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Avoidable adverse effects (Delayed, missed or duplicated investigations and treatment) during the study period; Quality of life during the study period; Patient and/or carer satisfaction during the study period; Mortality during the study period; Hospital readmissions during the study period; Length of stay during the study period; ED presentations during the study period; Carer and family satisfaction during the study period.

Study	Druss 2001[42]
Study type	RCT (Patient randomised; Parallel).
Number of studies (number of participants)	1 (n=120).
Countries and setting	Conducted in USA; setting: integration between mental health clinic and primary care.
Line of therapy	1st line.
Duration of study	Intervention time: 12 months.
Method of assessment of guideline condition	Partially adequate method of assessment/diagnosis.
Stratum	Overall: Severe mental illnesses.
Subgroup analysis within study	Not applicable.
Inclusion criteria	All patients.
Exclusion criteria	Current primary care provider or an urgent or multiple serious chronic problems. Patients determined by the family practitioner to have had a medical hospitalisation in the past 6 months or 4 or more serious chronic conditions were referred to the general medical clinics.
Recruitment/selection of patients	Mental health care providers were asked to refer any patients whom they thought would benefit from primary care to

Study	Druss 2001[42]
	be assigned a medical treater.
Age, gender and ethnicity	Age - Mean (SD): Group 1: 45.7 (8.4), Group 2: 44.8 (8.0). Gender (M:F): 119:1. Ethnicity: 70% White.
Further population details	1. Frail elderly: Not applicable/Not stated/Unclear. 2. People with serious mental illness: Serious mental illness.
Indirectness of population	No indirectness.
Interventions	(n=59) Intervention 1: Integration of care across teams or between different levels of care - Clinical Coordinating information and services and integrating patient care within a single process for example, developing extended clinical roles, guidelines and inter-professional education. The psychiatry service assumed clinical responsibility for the primary medical care of all patients randomised to the integrated care intervention and paid the salaries of all clinic staff through clinical funds. The clinic was located contiguous to the mental health clinics. The clinic was staffed by a nurse practitioner (1 full-time equivalent [FTE]), a part-time family practitioner (0.5 FTE), a nurse case manager (1 FTE), and an administrative assistant (0.5 FTE). The medical nurse practitioner was the main provider of basic medical care. The family practitioner supervised the nurse practitioner and acted as a liaison to physicians in the psychiatry and medical services. The registered nurse provided patient education, liaison with mental health care providers, and case management services. The administrative assistant scheduled appointments and took telephone messages for the clinic. Clinic staff emphasised patient education, preventive services, and close contact with mental health care providers, including e-mail, telephone, and face-to-face discussion about patients. Patients were prompted with telephone reminders the day before appointments, and whenever possible, clinic appointments were scheduled immediately following mental health visits to minimise barriers to attendance. When appointments were missed, clinic staff made active efforts to reschedule visits through contacting patients, their family members, and/or mental health care providers. One provider from the integrated clinic served as a liaison to each of 3 mental health teams, attending weekly team meetings. Mental health care providers were notified about patients' medical status, were asked to keep the integrated care clinic abreast of changes in patients' psychiatric status, and were encouraged to coordinate efforts with the integrated care clinic to ensure that patients attended medical appointments and followed through with needed medical tests. Duration: 12 months. Concurrent medication/care: none stated. (n=61) Intervention 2: No integration of care - As defined by study. Veterans randomised to the usual care group in this study were referred to the VA general medicine clinic, located in a building adjacent to the mental health clinic. For each patient randomised to usual care, a referral form was sent and verbal contact was made with the clinic administrator. This process ensured that all veterans referred for care were provided a primary care provider, following the referral pattern that was available before introduction of the integrated care clinic. Duration: 12 months. Concurrent medication/care: none stated.
Funding	Academic or government funding (VA Connecticut Mental Illness Research, Education, and Clinical Centre and by grant K08 MH01556 from the National Institute of Mental Health, Rockville, Md).

Study	Druss 2001[42]
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: CLINICAL COORDINATING INFORMATION AND SERVICES AND INTEGRATING PATIENT CARE WITHIN A SINGLE PROCESS FOR EXAMPLE, DEVELOPING EXTENDED CLINICAL ROLES, GUIDELINES AND INTER-PROFESSIONAL EDUCATION versus CONTROL Protocol outcome 1: ED presentations during the study period. - Actual outcome: Any ED presentation during the study period; Group 1: 7/59, Group 2: 16/61; Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness; Baseline details: Differences in (%): race (76.3 vs 63.9), high school graduate (93.2 vs 82.0), and cardiac disease (13.0 vs 2.3)	
Protocol outcomes not reported by the study	Unplanned hospital admissions during the study period; Avoidable adverse effects (Delayed, missed or duplicated investigations and treatment) during the study period; Quality of life during the study period; Patient and/or carer satisfaction during the study period; Mortality during the study period; Hospital readmissions during the study period; Length of stay during the study period; Carer and family satisfaction during the study period.

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Study	Ducharme 2005[43]
Study type	RCT (Patient randomised; Parallel).
Number of studies (number of participants)	1 (n=230).
Countries and setting	Conducted in Canada; setting: Montreal Heart Institute.
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	Patients seen at the emergency department of or admitted to the Montreal Heart Institute with a primary diagnosis of congestive heart failure.
Exclusion criteria	Exclusion criteria were kept to a minimum: a primary diagnosis of acute myocardial infarction, discharge to a chronic care facility, scheduled cardiac surgery, unwillingness to sign informed consent or to attend the outpatient clinic, participation in another research trial, or residence in an outlying area.
Recruitment/selection of patients	Between January 1998 and January 2000, we recruited patients seen at the emergency department of or admitted to the Montreal Heart Institute with a primary diagnosis of congestive heart failure. The diagnosis required the presence of both signs (at least 1 of tachycardia, gallop rhythm, increased jugular venous pressure [> 10 cm] or pulmonary crackles) and symptoms (at least 1 of dyspnea at rest or minimal effort, paroxysmal nocturnal dyspnea or orthopnea).

Study	Ducharme 2005[43]
Age, gender and ethnicity	Age - Mean (range): 68-70 years. Gender (M:F): 2.6/1. Ethnicity: not reported.
Further population details	1. Frail elderly: Not applicable/Not stated/Unclear. 2. People with serious mental illness: Not applicable/Not stated/Unclear.
Indirectness of population	No indirectness.
Interventions	(n=115) Intervention 1: Integration of care across teams or between different levels of care - Normative Developing shared values, culture and vision across organisations, professional groups and individuals for example, developing common integration goals, identifying and addressing communication gaps, building clinical relationships and trust. Patients in the intervention group were referred to a multidisciplinary specialised heart failure outpatient clinic at the Montreal Heart Institute, where they were evaluated by the study team within 2 weeks of hospital discharge. The heart failure clinic provided rapid access to expert health care professionals (cardiologists, clinician nurses, dieticians and pharmacists, with access to social workers and other medical specialists as required). At the clinic, the patient could be evaluated both clinically and para-clinically, receive intravenous diuretics if required and be observed for up to 5 hours. Additional to these services, a nurse telephoned all patients in the intervention group within 72 hours of hospital discharge and then monthly, unless a problem occurred that required more frequent contact. During the telephone consultation, the nurse pursued problems as clinically indicated. After the baseline evaluation, the clinic cardiologists individualised a treatment plan for each patient in the intervention group. Pharmacologic treatment was designed using clinical experience and evidence-based guidelines current at the time of the study. One-on-one education of the patient, family members or both with the study nurse was initiated at the first clinic visit. Patient education included an explanation of the disease process, the symptoms and signs of heart failure (including changes in symptoms indicative of worsening heart failure), fluid and sodium intake restrictions, the importance of daily monitoring of body weight and action plans to remedy changes in weight, effects of medications and the importance of compliance, and recommendations regarding exercise and diet. The advice given was individualised and complimented with a patient diary for daily weight measurement, medication record, clinical notes and appointments, physical activity recommendations, an education booklet produced in house (“Living with Heart Failure”) and a telephone number to contact the clinic during business hours. This individualised program of patient education was reinforced at each subsequent clinic visit. A follow-up plan was developed for each patient that included monthly visits with both a cardiologist and nurse at the clinic. The study team was available for ad hoc consultation during normal working hours. Duration: 6 months. Concurrent medication/care: n/a. (n=115) Intervention 2: No integration of care - As defined by study. Well-defined treatment plan including planned follow-up with a primary care physician and often involving outpatient visits at the university hospital with a cardiologist not involved in the study. No further details provided. Duration: 6 months. Concurrent medication/care: n/a.

Study	Ducharme 2005[43]
Funding	Academic or government funding (Educational grants from Merck Frosst and GlaxoSmithKline).
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: MULTIDISCIPLINARY SPECIALISED HEART FAILURE OUTPATIENT CLINIC versus CONTROL/STANDARD GROUP. Protocol outcome 1: Mortality. - Actual outcome: Mortality at 6 months; Group 1: 12/115, Group 2: 19/115; Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness Protocol outcome 2: Hospital readmissions. - Actual outcome: Patients admitted to hospital at 6 months; Group 1: 45/115, Group 2: 66/115; Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0 Protocol outcome 3: ED presentations. - Actual outcome: Patients seen in ED at 6 months; Group 1: 69/115, Group 2: 72/115; Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0	
Protocol outcomes not reported by the study	Unplanned hospital admissions as defined by study; Avoidable adverse effects (Delayed, missed or duplicated investigations and treatment) as defined by study; Quality of life as defined by study; Patient and/or carer satisfaction as defined by study; Length of stay as defined by study; Carer and family satisfaction as defined by study.

Study (subsidiary papers)	GRACE: Geriatric Resources for Assessment and Care of Elders trial: Counsell 200732 (Bielaszka-duvernay 201117, Counsell 2009[31])
Study type	RCT (Ward randomised; Parallel).
Number of studies (number of participants)	1 (n=951).
Countries and setting	Conducted in USA.
Line of therapy	Adjunctive to current care.
Duration of study	Intervention time: 4 years.
Method of assessment of guideline condition	Partially adequate method of assessment/diagnosis: Includes a population which is at risk of an AME (community dwelling low-income seniors), and with reported AME outcomes.

Study (subsidiary papers)	GRACE: Geriatric Resources for Assessment and Care of Elders trial: Counsell 200732 (Bielaszka-duvernay 201117, Counsell 2009[31])
Stratum	Overall: geriatrics.
Subgroup analysis within study	Not applicable.
Inclusion criteria	65 years old or older, Annual income less than 200% of the federal poverty level, Have had 1 or more primary care visits in the past 12 months, Reside in the community (non-institutionalised).
Exclusion criteria	Non-English speaking, No regular access to a telephone, Currently undergoing kidney dialysis treatments, Residing with a patient already participating in the GRACE clinical trial.
Recruitment/selection of patients	Recruitment from 6 community-based health centres affiliated with a university-affiliated urban health care system serving medically indigent patients.
Age, gender and ethnicity	Age - Mean (SD): Group 1: 71.8 (5.6), Group 2: 71.6 (5.8). Gender (M:F): 1:3. Ethnicity: Black: 59%.
Further population details	1. Frail elderly: Frail elderly 2. People with serious mental illness: Not applicable/Not stated/Unclear.
Indirectness of population	No indirectness.
Interventions	(n=474) Intervention 1: Integration of care across teams or between different levels of care - Clinical Coordinating information and services and integrating patient care within a single process for example, developing extended clinical roles, guidelines and inter-professional education. Initial and annual in-home comprehensive geriatric assessment by a GRACE support team consisting of an advanced practice nurse and social worker. Individualised care plan development annually by GRACE support team with assistance from the GRACE interdisciplinary team involving a geriatrician, pharmacist, physical therapist, mental health social worker, and community-based services liaison. Activation new each year of indicated GRACE protocols and corresponding team suggestions for care related to the 12 targeted geriatric conditions: advance care planning, health maintenance, medication management, difficulty walking/falls, chronic pain, urinary incontinence, depression, hearing loss, visual impairment, malnutrition or weight loss, dementia, and caregiver burden. GRACE support team meeting with patient's primary care physician to review, modify, and prioritise initial and annual care plan protocols and team suggestions. Implementation of care plan and team suggestions by GRACE support team in collaboration with the primary care physician and consistent with the patient's goals. Weekly GRACE interdisciplinary team meetings to review GRACE support team success in implementing care protocols and problem solve barriers to implementation. On-going GRACE support team home–based care management (including at least monthly patient contacts) supported by an electronic medical record and Web-based tracking system, and providing coordination and continuity of care among all health care professionals and sites of care. Duration: 2 years. Concurrent medication/care: not stated. (n=477) Intervention 2: No integration of care - As defined by study. Control patients had access to all primary and specialty care services available as part of usual care. Duration: 2 years. Concurrent medication/care: at the time of

Study (subsidiary papers)	GRACE: Geriatric Resources for Assessment and Care of Elders trial: Counsell 200732 (Bielaszka-duvernay 201117, Counsell 2009[31])
	implementation of the GRACE intervention, the following geriatric clinical services existed: outpatient geriatric assessment and multispecialty centre, inpatient ACE unit and consult service, skilled nursing facility, and physician house calls program. Psychiatric care was available through the health system's community mental health centre.
Funding	Academic or government funding (National Institute on Aging [NIA]).
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: CLINICAL COORDINATING INFORMATION AND SERVICES AND INTEGRATING PATIENT CARE WITHIN A SINGLE PROCESS FOR EXAMPLE, DEVELOPING EXTENDED CLINICAL ROLES, GUIDELINES AND INTER-PROFESSIONAL EDUCATION versus CONTROL Protocol outcome 1: Unplanned hospital admissions during the study period. - Actual outcome: Cumulative 2-year Hospital admission rate per 1000 patients; Group 1: 700, Group 2: 740, (p=0.66); Risk of bias: All domain - Very high, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - High, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 17, Reason: 16 unable to contact, 11 moved out of area; Group 2 Number missing: 58, Reason: 51 unable to contact, 7 moved out of area Protocol outcome 2: Mortality during the study period. - Actual outcome: Mortality during the study period; Group 1: 33/474, Group 2: 37/477; Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 62, Reason: 16 unable to contact, 35 dropped out, 11 moved out of area; Group 2 Number missing: 78, Reason: 51 unable to contact, 20 dropped out, 7 moved out of area Protocol outcome 3: Hospital readmissions during the study period. - Actual outcome: Hospital readmission after first hospitalisation at 30 days; Group 1: 54/206, Group 2: 64/200; Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness; Group 1 Number missing: , Reason: 16 unable to contact, 35 dropped out, 11 moved out of area. No details on any missing data after hospitalisation; Group 2 Number missing: Reason: 51 unable to contact, 20 dropped out, 7 moved out of area. No details on any missing data after hospitalisation Protocol outcome 4: ED presentations during the study period. - Actual outcome: Cumulative 2-year ED visit rate per 1000 patients; Group 1: 1445, Group 2: 1748, (p=0.03); Risk of bias: Very high; Indirectness of outcome: No indirectness.	
Protocol outcomes not reported by the study	Avoidable adverse effects (Delayed, missed or duplicated investigations and treatment) during the study period; Quality of life during the study period; Patient and/or carer satisfaction during the study period; Length of stay during the study period; Carer and family satisfaction during the study period.

Study	Hernandez 2015[61]
Study type	RCT (Patient randomised; Parallel).
Number of studies (number of participants)	1 (n=155).
Countries and setting	Conducted in Spain; setting: integration between secondary and community care.
Line of therapy	Not applicable.
Duration of study	Intervention + follow up: 12 months + 6 years.
Method of assessment of guideline condition	Partially adequate method of assessment/diagnosis.
Stratum	Overall: COPD patients.
Subgroup analysis within study	Not applicable.
Inclusion criteria	History of at least 2 hospital admissions owing to severe respiratory exacerbations during 2 consecutive years, 45 years and over living at home within the health care area of the hospital, diagnosed with a COPD-related diagnostic term including: emphysema, asthma, tuberculosis, chronic bronchitis and COPD.
Exclusion criteria	Nursing home or not living in the area, participants in another clinical trial.
Recruitment/selection of patients	Records of hospital.
Age, gender and ethnicity	Age - Mean (SD): Group 1: 75 (9), Group 2: 73 (8). Gender (M:F): 131:24. Ethnicity: not reported.
Further population details	1. Frail elderly: Frail elderly. 2. People with serious mental illness.
Extra comments	Community care was carried out at community clinics with care delivered from a primary care team (physicians, nurses and social workers).
Indirectness of population	No indirectness.
Interventions	(n=71) Intervention 1: Integration of care across teams or between different levels of care - Clinical Coordinating information and services and integrating patient care within a single process for example, developing extended clinical roles, guidelines and inter-professional education. A comprehensive assessment of the patient at entry, A 2-h educational programme was administered at entry by a respiratory nurse, followed by distribution of patient-specific support material covering knowledge of the disease, instructions on non-pharmacological treatment, administration techniques for proper pharmacological therapy and techniques for self-management of the disease and co-morbid conditions including strategies to adopt with future exacerbations. One joint visit of the specialised nurse and the primary care team (physician, nurse and social worker) at the patient home was completed within 72 h after entry into the study. Therapeutic plan for each patient was customised and shared with the primary care team. Accessibility to the specialised nurse at the hospital was ensured for primary care professionals during the follow-up period through an ICT platform including a web-based call centre. The community care teams received training: a 2-h face to face educational training and 1-day stay at the hospital ward, aiming at enhancing home-based management of frail

Study	Hernandez 2015[61]
	COPD patients. Duration: 12 months. Concurrent medication/care: not stated. (n=84) Intervention 2: No integration of care - As defined by study. Usual care. Duration: 12 months. Concurrent medication/care: managed by their physician without any support from specialised nurses. Visits were usually scheduled every 6 months in the out-patient clinic.
Funding	Principal author funded by industry (NEXES (Supporting Healthier and Independent Living for Chronic Patients and Elderly (UE Grant CIP-ICT-PSP-2007-225025), PITES (FIS-PI09/90634), Pites PI12/01241, PII-EPOC (SEPAR), Fundació Marató TV3 042010; Comissionat per a Universitats i Recerca de la Generalitat de Catalunya (2009SGR1308, 2009SGR911 and 2009-SGR-393) and Vitalaire).
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: CLINICAL COORDINATING INFORMATION AND SERVICES AND INTEGRATING PATIENT CARE WITHIN A SINGLE PROCESS FOR EXAMPLE, DEVELOPING EXTENDED CLINICAL ROLES, GUIDELINES AND INTER-PROFESSIONAL EDUCATION versus CONTROL Protocol outcome 1: Unplanned hospital admissions during the study period. - Actual outcome: Hospital admissions owing to COPD exacerbations at 6 years; OR 2.17 (95%CI 0.67 to 7.87); Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness; Baseline details: Differences in infulenza and pneumococcal vaccination (adjusted for in analysis); Group 1 Number missing: 5, Reason: 5 Lost; Group 2 Number missing: 18, Reason: 18 Lost Protocol outcome 2: Mortality during the study period. - Actual outcome: All-cause mortality at 6 years; HR 0.36 (95%CI 0.14 to 0.93) Reported; Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness; Baseline details: Greater infulenza and pneumococcal vaccination in intervention group; Group 1 Number missing: 5, Reason: 5 Lost; Group 2 Number missing: 18, Reason: 18 Lost Protocol outcome 3: ED presentations during the study period. - Actual outcome: ED visits owing to COPD exacerbations at 6 years; OR 0.33 (95%CI 0.13 to 0.84); Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness; Baseline details: Differences in infulenza and pneumococcal vaccination (adjusted for in analysis); Group 1 Number missing: 5, Reason: 5 Lost; Group 2 Number missing: 18, Reason: 18 Lost	
Protocol outcomes not reported by the study	Avoidable adverse effects (Delayed, missed or duplicated investigations and treatment) during the study period; Quality of life during the study period; Patient and/or carer satisfaction during the study period; Hospital readmissions during the study period; Length of stay during the study period; Carer and family satisfaction during the study period.

Study	Holm 2002[64]

Study	Holm 2002[64]
Study type	RCT (Physician randomised; Parallel).
Number of studies (number of participants)	1 (n=875).
Countries and setting	Conducted in Denmark; setting: integration between primary care and secondary care clinics.
Line of therapy	Adjunctive to current care.
Duration of study	Intervention time: 2 years.
Method of assessment of guideline condition	Partially adequate method of assessment/diagnosis.
Stratum	Overall: Oral anticoagulant therapy (OAT)
Subgroup analysis within study	Not applicable.
Inclusion criteria	Three or more consecutive (no more than 4 months between tests) International normalised ration system tests, at least 1 INR test >1.9.
Exclusion criteria	INR determinations performed less than 3 times by their own GP.
Recruitment/selection of patients	Patients identified from laboratory information system.
Age, gender and ethnicity	Age - Median (IQR): Group 1: 70 (60.0-77.0), Group 2: 70 (60.0-77.0). Gender (M:F): 494:381. Ethnicity: not reported.
Further population details	1. Frail elderly: Not applicable/Not stated/Unclear. 2. People with serious mental illness: Not applicable/Not stated/Unclear.
Indirectness of population	No indirectness.
Interventions	(n=453) Intervention 1: Integration of care across teams or between different levels of care - Clinical Coordinating information and services and integrating patient care within a single process for example, developing extended clinical roles, guidelines and inter-professional education. The GPs responsibility - Participation in a three-hour intensive OAT course, Referral of patients to the OAT clinic for evaluation of the OAT, Maintaining routine OAT monitoring; The patients responsibility - Evaluation of the OAT once a year at the OAT clinic, Participation in patient education; OAT clinic responsibility - Intensive OAT course for GPs, Patient education, Written patient information, OAT telephone hotline for GPs, throughout the study period, Evaluation of the OAT of all admitted patients once a year, Mailing anonymous OAT quality reports to GPs for self-evaluation. Duration: 2 years. Concurrent medication/care: OAT therapy. (n=422) Intervention 2: No integration of care - As defined by study. Usual care - not defined. Duration: 2 years. Concurrent medication/care: OAT therapy.
Funding	Other (‘Apotekerfonden af 1991’, ‘Sundhedsstyrelsens Sundhedspuljen’ and ‘Kvalitetsudviklingsfonden i Århus Amt’).
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: CLINICAL COORDINATING INFORMATION AND SERVICES AND INTEGRATING PATIENT CARE	

Study	Holm 2002[64]
WITHIN A SINGLE PROCESS FOR EXAMPLE, DEVELOPING EXTENDED CLINICAL ROLES, GUIDELINES AND INTER-PROFESSIONAL EDUCATION versus CONTROL Protocol outcome 1: Avoidable adverse effects (Delayed, missed or duplicated investigations and treatment) during the study period. - Actual outcome: Major bleeding or thrombosis during the study period; Group 1: 36/453, Group 2: 47/422; Risk of bias: All domain - Very high, Selection - Very high, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness; Blinding details: Different care 159 patients in intervention started in 1998/1999 compared with 91 in control; Group 1 Number missing: , Reason: 150 ceased OAT; Group 2 Number missing: , Reason: 132 ceased OAT Protocol outcome 2: Mortality during the study period. - Actual outcome: All-cause mortality during the study period; Group 1: 58/453, Group 2: 50/422; Risk of bias: All domain - Very high, Selection - Very high, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness; Blinding details: Different care 159 patients in intervention started in 1998/1999 compared with 91 in control; Group 1 Number missing: , Reason: 150 ceased OAT; Group 2 Number missing: , Reason: 132 ceased	
Protocol outcomes not reported by the study	Unplanned hospital admissions during the study period; Quality of life during the study period; Patient and/or carer satisfaction during the study period; Hospital readmissions during the study period; Length of stay during the study period; ED presentations during the study period; Carer and family satisfaction during the study period.

Study	Johnson 2015[67]
Study type	RCT (Physician randomised; Parallel).
Number of studies (number of participants)	1 (n=100).
Countries and setting	Conducted in New Zealand; setting: primary and tertiary care.
Line of therapy	Adjunctive to current care.
Duration of study	Not clear: "Recruitment was open for 2 years, but stopped early as a result of slow accrual".
Method of assessment of guideline condition	Partially adequate method of assessment/diagnosis.
Stratum	Overall: Cancer.
Subgroup analysis within study	Not applicable.
Inclusion criteria	Eligible patients were > 16 years of age, able to understand and complete trial documentation, and had biopsy-proven malignancy.
Exclusion criteria	Individual PCPs could have only 1 patient on study.

Study	Johnson 2015[67]
Recruitment/selection of patients	Patients receiving their first round of chemotherapy in participating outpatient clinics were invited to participate.
Age, gender and ethnicity	Age - Mean (range): Overall: 54.7 (28-77). Gender (M:F): 83:17. Ethnicity.
Further population details	1. Frail elderly: Not applicable/Not stated/Unclear. 2. People with serious mental illness: Not applicable/Not stated/Unclear.
Indirectness of population	No Indirectness.
Interventions	(n=52) Intervention 1: Integration of care across teams or between different levels of care - Clinical Coordinating information and services and integrating patient care within a single process for example, developing extended clinical roles, guidelines and inter-professional education. Project coordinator to assist with patient care and information, and PCP educational resource ("upskilling") packages detailing anticipated adverse effects of each treatment regimen and actions to be taken. Patients were asked to see their Project coordinator after each chemotherapy treatment. Duration: unclear. Concurrent medication/care: chemotherapy. (n=48) Intervention 2: No integration of care - As defined by study. Usual care was provided by specialists and their associated primary care provider. Primary care provider received a letter from the specialist team after each visit, discharge summaries, and telephone communication, where appropriate. Communication frequency and content for standard care was not prescribed by the study. Duration: unclear. Concurrent medication/care: chemotherapy.
Funding	Academic or government funding (Supported by the National Health and Medical Research Council, Australia Grant No. 353678).
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: CLINICAL COORDINATING INFORMATION AND SERVICES AND INTEGRATING PATIENT CARE WITHIN A SINGLE PROCESS FOR EXAMPLE, DEVELOPING EXTENDED CLINICAL ROLES, GUIDELINES AND INTER-PROFESSIONAL EDUCATION versus CONTROL Protocol outcome 1: Unplanned hospital admissions during the study period. - Actual outcome: Emergency Department Use/hospital admissions during the study period; Group 1: mean 0.7 (SD 1.9911); n=51, Group 2: mean 1 (SD 3.0644); n=46; Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - Very high, Outcome reporting - High, Measurement - Very high, Crossover - Low; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Avoidable adverse effects (Delayed, missed or duplicated investigations and treatment) during the study period; Quality of life during the study period; Patient and/or carer satisfaction during the study period; Mortality during the study period; Hospital readmissions during the study period; Length of stay during the study period; ED presentations during the study period; Carer and family satisfaction during the study period.

Study	Lanzeta 2016[79]
Study type	RCT (Hospital randomised; Parallel).
Number of studies (number of participants)	1 (n=140).
Countries and setting	Conducted in Spain; setting: 7 primary healthcare centres of the Goierri-Alto Urola health district, together with the referral hospital, Zumarraga hospital.
Line of therapy	Not applicable.
Duration of study	Follow up (post intervention): 12 months.
Method of assessment of guideline condition	Adequate method of assessment/diagnosis.
Stratum	Overall.
Subgroup analysis within study	Not applicable.
Inclusion criteria	To have at least 1 hospitalisation episode during the past year, to be classified as multimorbid patients according the criteria of the Junta de Andalucía2 and to have given written informed consent.
Exclusion criteria	Exclusion criteria included patient refusal to participate in the study, living in a nursing home or being on hemodialysis.
Recruitment/selection of patients	Patients' randomisation was based on the primary care clinicians' randomisation carried out before this study started
Age, gender and ethnicity	Age - Other: <80 years = 53%; ≥80 years = 47%. Gender (M:F): 2.1/1. Ethnicity: not reported.
Further population details	1. Frail elderly: Not applicable/Not stated/Unclear. 2. People with serious mental illness: Not applicable/Not stated/Unclear.
Indirectness of population	No indirectness.
Interventions	(n=70) Intervention 1: Integration of care across teams or between different levels of care - Systemic Coordinating and aligning policies, rules and regulatory frameworks for example, policy levers emphasising better coordinated care outside of hospitals. The intervention consisted on the implementation of an integrated health care model for multimorbid patients based on improving communication between primary care and hospital professionals. Specifically, intervention group (IG) multimorbid patients were managed by the primary care team (general practitioner and nurse) with the support of a reference internist and a liaison nurse. Reference internist gave direct support in the Health Centre and ensured smooth and flexible communication with primary care doctors. Moreover, every time patients with multimorbidity went to the hospital they were seen by their assigned internist, regardless of the required service. As soon as the patient was identified as being multimorbid the liaison nurse carried out a

Study	Lanzeta 2016[79]
	complete assessment (clinical, functional, psychosocial and quality of life). This information was aimed to enhance continuity of care after hospitalisation in coordination with primary care to avoid re-hospitalisations. Furthermore, the liaison nurse provided health education to improve self-management of each specific disease. Duration: 1 year. Concurrent medication/care: n/a. (n=70) Intervention 2: No integration of care - As defined by study. In the control group (CG), patients received usual care corresponding to routine practice, with no strengthening of the coordination between primary and hospital-based care. Duration: 1 year. Concurrent medication/care: n/a.
Funding	No funding
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: INTEGRATED HEALTH CARE MODEL versus CONTROL GROUP. Protocol outcome 1: Unplanned hospital admissions. - Actual outcome: Admissions at 1 year; Group 1: 43/70, Group 2: 33/70; Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness; Group 1 Number missing: 0; Group 2 Number missing: 0 Protocol outcome 2: ED presentations. - Actual outcome: ED use at 1 year; Group 1: 52/70, Group 2: 57/70; Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0	
Protocol outcomes not reported by the study	Avoidable adverse effects (Delayed, missed or duplicated investigations and treatment) during the study period; Quality of life during the study period; Patient and/or carer satisfaction during the study period; Mortality during the study period; Hospital readmissions during the study period; Length of stay during the study period; Carer and family satisfaction during the study period.

Study	Sahota 2016 [103]
Study type	RCT (Patient randomised; Parallel).
Number of studies (number of participants)	1 (n=250).
Countries and setting	Conducted in United Kingdom; setting: general medical elderly care wards at the Queen's Medical Centre, Nottingham (1800-bed hospital, serving a population of 680,000), with community follow-up.
Line of therapy	Not applicable.
Duration of study	Follow up (post intervention): 91 days.

Study	Sahota 2016 [103]
Method of assessment of guideline condition	Adequate method of assessment/diagnosis.
Stratum	Overall.
Subgroup analysis within study	Not applicable.
Inclusion criteria	Aged ≥ 70 years, GP registered within the Nottingham City CCG catchment area only.
Exclusion criteria	bed bound prior to admission or moribund on admission; receiving palliative care; previously included in the trial on an earlier admission; unable to be screened and recruited by the research team within 36 hours of admission to the study ward (a 36-hour deadline ensured that there was not a delay in the participant receiving therapy and enabled the recruitment of a large proportion of patients admitted over a weekend when the research team was not available); nursing home residents.
Recruitment/selection of patients	Study recruitment commenced on the 23rd June 2013 and ended on 31st July 2014, participants were older people admitted to the general medical wards as an acute medical emergency.
Age, gender and ethnicity	Age - Mean (range): 84.1 years (range 67-99 years). Gender (M:F): Define. Ethnicity: not reported.
Further population details	1. Frail elderly: Not applicable. 2. People with serious mental illness: Not applicable.
Indirectness of population	No indirectness.
Interventions	(n=125) Intervention 1: Integration of care across teams or between different levels of care - Systemic Coordinating and aligning policies, rules and regulatory frameworks for example, policy levers emphasising better coordinated care outside of hospitals. The CIRACT service provided a comprehensive assessment of each participant's ability to perform certain tasks, which was completed within 24 hours of randomisation, enabling the formulation of a rehabilitation plan. While in hospital the participants were treated daily (7 days a week if appropriate). During the hospital stay the team liaised with each participant and his or her carer(s) to enable a visit to the participant's home to assess and provide recommendations for equipment and make adaptations and/or modifications as required. The CIRACT service utilised the team's expertise in community working to form links with the appropriate services to ensure a smooth and effective discharge. In more complex cases the CIRACT team took the participant out of the hospital for a home visit prior to discharge. Following discharge, the CIRACT team visited the participant at home within 48 hours to assess the level of rehabilitation required and further follow-up visits were provided as deemed necessary. Duration: 90 days. Concurrent medication/care: n/a. (n=125) Intervention 2: No integration of care - As defined by study. THB-Rehab service was provided by the ward therapy teams (usually a band 6 occupational therapist and a band 6 physiotherapist) on weekdays only. The team jointly conducted an assessment of each participant's ability to perform certain tasks and provided recommendation for rehabilitation. The service referred the participants to the appropriate community-based services for provision of

Study	Sahota 2016 [103]
	equipment at home, personal care and ongoing rehabilitation when appropriate at discharge. Once discharged from hospital, participants had no direct contact with the THB-Rehab service. Duration: 90 days. Concurrent medication/care: n/a.
Funding	Academic or government funding: The National Institute for Health Research Health Services and Delivery Research programme.
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: COMMUNITY IN-REACH REHABILITATION AND CARE TRANSITION (CIRACT) versus STANDARD CARE: THB-REHAB SERVICE. Protocol outcome 1: Quality of life. - Actual outcome: Barthel ADL Score at 91 days post-discharge; Group 1: mean 14.3 (SD 5.5); n=106, Group 2: mean 12.6 (SD 5.7); n=106; Barthel ADL score 0-20 Top=High is good outcome; Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 19; Group 2 Number missing: 19 Protocol outcome 2: Hospital readmissions. - Actual outcome: Readmission at 28 days post-discharge; Group 1: 18/106, Group 2: 14/106; Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 19, Reason: Death post-discharge, withdrew consent, loss to follow-up; Group 2 Number missing: 19, Reason: Death post-discharge, withdrew consent, loss to follow-up Protocol outcome 3: Length of stay. - Actual outcome: Length of stay at 91 days post-discharge; Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 19, Reason: Death post-discharge, withdrew consent, loss to follow-up; Group 2 Number missing: 19, Reason: Death post-discharge, withdrew consent, loss to follow-up	
Protocol outcomes not reported by the study	Unplanned hospital admissions; Avoidable adverse effects (Delayed, missed or duplicated investigations and treatment); Patient and/or carer satisfaction; Mortality at Define; ED presentations; Carer and family satisfaction

Study (subsidiary papers)	Smith 2008[108] (Anon 2008[2])
Study type	RCT (Physician randomised; Parallel).
Number of studies (number of participants)	1 (n=635).
Countries and setting	Conducted in USA; setting: integration between primary and tertiary care.

Study (subsidiary papers)	Smith 2008[108] (Anon 2008[2])
Line of therapy	1st line.
Duration of study	Follow up (post intervention): 30 months.
Method of assessment of guideline condition	Partially adequate method of assessment/diagnosis.
Stratum	Overall: Diabetes (93% Type 2).
Subgroup analysis within study	Not applicable.
Inclusion criteria	Written consent.
Exclusion criteria	None stated.
Recruitment/selection of patients	Patients under the care of participating family medicine practitioners. Practitioners were recruited when they referred their first patient to the on-site diabetes educator.
Age, gender and ethnicity	Age - Median (range): Group 1: 62 (22-92), Group 2 (60 (27-90). Gender (M:F): 60:67. Ethnicity: not reported.
Further population details	1. Frail elderly: Not applicable/Not stated/Unclear. 2. People with serious mental illness: Not applicable/Not stated/Unclear.
Indirectness of population	No indirectness.
Interventions	(n=358) Intervention 1: Integration of care across teams or between different levels of care - Clinical Coordinating information and services and integrating patient care within a single process for example, developing extended clinical roles, guidelines and inter-professional education. Appointment of a diabetes educator in primary care, communicating on a regular basis with patients to support their self-management, the primary care team, and a supervising endocrinologist via a Diabetes Electronic Management System. Duration: 30 months. Concurrent medication/care: treatment for diabetes. (n=277) Intervention 2: No integration of care - As defined by study. Control groups received periodic generic information via e-mail about cardiovascular risk reduction in diabetes. Duration: 30 months. Concurrent medication/care: treatment for diabetes.
Funding	Funding not stated.
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: CLINICAL COORDINATING INFORMATION AND SERVICES AND INTEGRATING PATIENT CARE WITHIN A SINGLE PROCESS FOR EXAMPLE, DEVELOPING EXTENDED CLINICAL ROLES, GUIDELINES AND INTER-PROFESSIONAL EDUCATION versus CONTROL Protocol outcome 1: Mortality during the study period. - Actual outcome: Mortality during the study period; Group 1: 6/358, Group 2: 4/277; Risk of bias: All domain - Very high, Selection - Low, Blinding - Low, Incomplete outcome data - Very high, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 12, Reason: 2 refused, 10 lost to follow-up or moved; Group 2 Number missing: 4, Reason: 2 refused, 2 lost to follow-up or moved	

Study (subsidiary papers)	Smith 2008[108] (Anon 2008[2])
Protocol outcomes not reported by the study	Unplanned hospital admissions during the study period; Avoidable adverse effects (Delayed, missed or duplicated investigations and treatment) during the study period; Quality of life during the study period; Patient and/or carer satisfaction during the study period; Hospital readmissions during the study period; Length of stay during the study period; ED presentations during the study period; Carer and family satisfaction during the study period.

Appendix E: Economic evidence tables

Study	Hunter 2013 [65]			
Study details	**Population & interventions**	**Costs**	**Health outcomes**	**Cost-effectiveness**
Economic analysis: CUA (health outcome: QALY) **Study design:** Probabilistic decision analytic model. **Approach to analysis:** Two time dependent Markov models: The first from admission to 90 days with day cycles and the second from 90 days to 10 years with 90 day cycles. 'Health states' were based on ward type and discharge location. **Perspective:** UK NHS **Time horizon:** 10 years. **Treatment effect duration:** 10 years. **Discounting:** Costs: 3.5%; Outcomes: 3.5%	**Population:** Patients who have an ischaemic or haemorrhagic stroke. **Cohort settings:** Mean age: 71.3 Male: 52% **Intervention 1:** Usual care: Local stroke units. **Intervention 2:** Integrated care: Continuous specialist care during the first 72 hours at a hyper acute stroke unit followed by treatment at a stroke unit if necessary.	**Total costs (mean per patient):** Intervention 1: £39,614 Intervention 2: £35,745 Incremental (2−1): Saves £3,869 (95% CI: NR; p=NR) **Currency & cost year:** 2011 UK pounds **Cost components incorporated:** Transport, acute hospitalisation, imaging and surgical interventions, staff contacts, medications during acute hospitalisation and post-discharge care.	**QALYs (mean per patient):** Intervention 1: NR Intervention 2: NR Incremental (2−1): 0.65 (95% CI: NR; p=NR)	**ICER (Intervention 2 versus Intervention 1):** Intervention 2 dominates intervention 1. Probability Intervention 2 cost-effective (£20K/30K threshold): 100%/100% **Analysis of uncertainty:** Various additional analyses with a 10 year time horizon were performed including adjusting for national trends in mortality and/or length of stay; increasing HASU cost per day by 25%; restricting the analysis to only 2 datasets (as only 2 were available for the 'before' group); NHS costs only. All analyses were dominant except for the NHS costs only analysis which resulted in a very small ICER of £47 per QALY. The same analyses were performed with only a 90 day time horizon and only 1 analysis resulted in a large ICER above £20,000 per QALY – the analysis restricting the datasets to those available in the 'before' group. The ICER was £56,940 per QALY.
Data sources				
Health outcomes: Mortality, quality of life scores and transition probabilities were obtained by analysing various datasets: South London Stroke Register (SLSR), Stroke Improvement National Audit Programme (SINAP), London Minimum Dataset (LMDS), Sentinel Stroke Audit (SSA) and an audit of 2 North London hospitals. **Quality-of-life weights:** EQ-5D UK tariff mapped from Barthel Index. **Cost sources:** Transport costs were obtained from PSSRU 2008 and NHS Reference Costs 2009-2010. Acute hospitalisation costs were obtained from the National Audit Office, PSSRU 2008 and various publications.				
Comments				

Source of funding: The study was funded by NHS London. This study uses data obtained via independent research commissioned by the National Institute for Health Research (NIHR) under its Programme Grants for Applied Research funding scheme (RP-PG-0407-10184). The views expressed are not necessarily those of the NHS, the NIHR or the Department of Health. This work was undertaken at UCLH/UCL who received a proportion of funding from the Department of Health's NIHR Biomedical Research Centres funding scheme. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript. **Applicability and limitations** – Based on observational evidence.

Overall applicability: Directly applicable. [c] **Overall quality:** Potentially serious limitations. [d]

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); HASU: hyper acute stroke unit; ICER: incremental cost-effectiveness ratio; NR: not reported; QALYs: quality-adjusted life years.

(a) Directly applicable/Partially applicable/Not applicable.

(b) Minor limitations/Potentially serious limitations/Very serious limitations.

Study	Lanzeta 2016 [79]			
Study details	**Population & interventions**	**Costs**	**Health outcomes**	**Cost-effectiveness**
Economic analysis: CUA (health outcome: QALY) **Study design:** within trial RCT **Approach to analysis:** multivariate analysis was used to estimate costs and EQ-5D **Perspective:** Spanish healthcare **Time horizon/Follow-up** 12 months **Discounting:** NA	**Population:** Patients with multimorbidities classified by the criteria of Junta de Andalucia and having 1 hospitalisation in the past year. **Cohort settings:** Start age: 78.2, Male: 68% **Intervention 1:** Usual care corresponding to usual practice with no strengthening of the coordination between primary and hospital based care. **Intervention 2:** Integrated care achieved by improving communication between primary and secondary care. The primary care team was supported by a reference internist who gave direct support and ensured smooth and flexible communication between different sectors. A liaison nurse also completed a full assessment when an individual was classed as being multimorbid and passed this information onto primary care.	**Total costs (mean per patient):** Incremental (2−1): £946 (95% CI: NR; p=NR) **Currency & cost year:** 2012 Euros (presented here as 2012 UK pounds[(a)]) **Cost components incorporated:** Hospital stay, emergency department consultation, 24-hour health clinic consultation, specialised consultation, home care visit, CT scan, ultrasound scan, cost of liaison nurse.	**QALYs (mean per patient):** Incremental (2−1): -0.0553 (95% CI: NR; p=NR)	**ICER (Intervention 2 versus Intervention 1):** Intervention 1 dominates intervention 2. **Analysis of uncertainty:** used bootstrapping methods to explore uncertainty. In the simulations run they found that integrated care was cost saving in only 15% of the 1,000 simulations. They found that it was cost saving in 89% of the simulations conducted on individuals under 80 years of age.
Data sources				
Health outcomes: QALYs were estimated using EQ-5D as the preference based utility measure. **Quality-of-life weights:** Unclear what tariff was used to apply weights to EQ-5D. **Cost sources:** taken from accountancy department within the trial.				
Comments				
Source of funding: none. **Applicability and limitations:** Spanish healthcare perspective and therefore applicability to a UK setting may be limited. Unclear what tariff EQ-5D scores were derived from. 12 month follow up may not capture impacts on mortality. Unclear how the QALY was calculated and whether time of death was included in the QALY estimate.				
Overall applicability: potentially applicable[(b)] **Overall quality: potentially serious limitations**[(c)]				

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; NR: not reported; QALYs: quality-adjusted life years.

(a) Converted using 2012 purchasing power parities[96].

(b) Directly applicable/Partially applicable/Not applicable.

(c) Minor limitations/Potentially serious limitations/Very serious limitations.

Study	Neumann 2014[90]			
Study details	**Population & interventions**	**Costs**	**Health outcomes**	**Cost-effectiveness**
Economic analysis: CUA (health outcome: QALY) **Study design:** within trial RCT **Approach to analysis:** costs and EQ-5D were collected and analysed throughout the trial. **Perspective:** German healthcare perspective **Time horizon/Follow-up** 6 months **Discounting:** NA	**Population:** Patients with systolic heart failure **Cohort settings**: Start age: 68 Male: 70.6% **Follow-up**: 6 months **Intervention 1:** Usual care **Intervention 2:** Interdisciplinary Network for Heart Failure; a Nurse led heart failure management programme.	**Total costs (mean per patient):** Intervention 1: £1,671 Intervention 2: £1,926 Incremental (2−1): £255 (95% CI: NR; p=NR) **Currency & cost year:** 2007 Euros (presented here as 2007 UK pounds[(a)]) **Cost components incorporated:** Hospitalisation, rehabilitation costs, GP visits, emergency visits, cardiology visits and programme costs	**QALYs (mean per patient):** Intervention 1: 0.363 Intervention 2: 0.385 Incremental (2−1): 0.022 (95% CI: NR; p=NR)	**ICER (Intervention 2 versus Intervention 1):** Using mean costs and mean QALYs the estimated ICER is calculated to be £11,605 per QALY gained. However the study reports an ICER of £39,255 which is greater than the mean cost divided by the mean benefit, even when societal costs are included. **Analysis of uncertainty:** Bootstrapping found that the probability of the intervention being cost effective at a £40,000 per QALY threshold was 55% although this included societal costs.
Data sources				
Health outcomes: QALYs were estimated using EQ-5D as the preference based utility measure. **Quality-of-life weights:** German tariff was used to apply weights to EQ-5D. **Cost sources:** German Institute for the Hospital Remuneration System (InEK)				
Comments				
Source of funding: Federal Ministry of Education and Research. **Applicability and limitations:** German healthcare perspective and therefore applicability to a UK setting may be limited. German tariff was used to derive EQ-utilities. 6 month follow up may not capture impacts on mortality. Unclear how the calculation to derive the ICER was made as this is different from the result of dividing the mean costs by the mean QALYs.				
Overall applicability: potentially applicable[(b)] **Overall quality: potentially serious limitations**[(c)]				

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; NR: not reported; QALYs: quality-adjusted life years.

(a) Converted using 2012 purchasing power parities[96].

(b) Directly applicable/Partially applicable/Not applicable.

(c) Minor limitations/Potentially serious limitations/Very serious limitations.

Study	Sahota 2016			
Study details	**Population & interventions**	**Costs**	**Health outcomes**	**Cost-effectiveness**
Economic analysis: CUA (health outcome: QALY) **Study design:** within trial RCT **Approach to analysis:** costs and EQ-5D were collected and analysed throughout the trial. **Perspective:** UK NHS **Time horizon/Follow-up** 12 months **Discounting:** NA	**Population:** Older people (age ≥ 70 years) admitted to the general medical wards as an acute medical emergency. **Cohort settings:** Start age: 84.1 years **Intervention 1:** Standard care – The traditional hospital-based Rehabilitation (THB-Rehab) service. Once discharged from hospital, participants had no direct contact with the THB-Rehab service. **Intervention 2:** The CIRACT [Community In-reach Rehabilitation And Care Transition service] service. The CIRACT service utilised the team's expertise in community working to form links with the appropriate services to ensure a smooth and effective discharge. Following discharge, the CIRACT team visited the participant at home within 48 hours to assess the level of rehabilitation required and further follow-up visits were provided as deemed necessary.	**Total costs (mean per patient):** Intervention 1: £3,603 Intervention 2: £3,744 Incremental (2−1): £141 (95% CI: -£1,645 to £1,934; p=NR) **Currency & cost year:** 2014 UK pounds **Cost components incorporated:** GP home visits, GP surgery visit, practice nurse, district nurse, dietitian, social worker, rehabilitation team, CIRACT team, pharmacist, paramedic, care home, day centre, home care, meals on wheels, outpatient appointment, NHS walk-in centre, accident and emergency	**QALYs (mean per patient):** Intervention 1: 0.806 Intervention 2: 0.846 Incremental (2−1): 0.04 (95% CI: –0.0566 to 0.1375; p=NR)	**ICER (Intervention 2 versus intervention1)** £2022 per QALY **Net monetary benefit, using a £30k per QALY threshold:** £1932 (95% CI: –£2,134 to £5,863) **Analysis of uncertainty:** used bootstrapping methods to explore uncertainty. In the simulations run they found that integrated care was cost effective in 91% of the 1,000 simulations at a £30,000 per QALY threshold.

Data sources
Health outcomes: QALYs were estimated using EQ-5D as the preference based utility measure. **Quality-of-life weights:** UK EQ-5D tariff used. **Cost sources:** taken from PSSRU and NHS reference costs.
Comments
Source of funding: The National Institute for Health Research Health Services and Delivery Research programme. **Applicability and limitations:** Only a 12 month time horizon was used and this may not capture the full nature of future costs and benefits.
Overall applicability: potentially applicable[(a)] **Overall quality: potentially serious limitations**[(b)]

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; NR: not reported; QALYs: quality-adjusted life years.

(c) Directly applicable/Partially applicable/Not applicable.

(d) Minor limitations/Potentially serious limitations/Very serious limitations.

Appendix F: GRADE tables

Table 6: Clinical evidence profile: Integrated care versus no integrated care

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Integrated care versus no integrated care	Control	Relative (95% CI)	Absolute		
Mortality (follow-up 6 months)												
2	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	23/467 (4.9%)	45/478 (9.4%)	RR 0.52 (0.32 to 0.84)	45 fewer per 1000 (from 15 fewer to 64 fewer)	⊕⊕OO LOW	CRITICAL
Mortality (follow-up 1 years)												
3	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	43/264 (16.3%)	15.6%	RR 0.91 (0.63 to 1.31)	14 fewer per 1000 (from 58 fewer to 48 more)	⊕OOO VERY LOW	CRITICAL
Mortality (follow-up 2 years)												
3	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	97/1285 (7.5%)	7.8%	RR 1.01 (0.77 to 1.33)	1 more per 1000 (from 18 fewer to 26 more)	⊕OOO VERY LOW	CRITICAL
Mortality (follow-up 6 years)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[1]	none	7/59 (11.9%)	32.7%	RR 0.36 (0.16 to 0.8)	209 fewer per 1000 (from 65 fewer to 275 fewer)	⊕OOO VERY LOW	CRITICAL
Readmission (follow-up 28-30 days)												

2	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	72/312 (23.1%)	78/306 (25.5%)	RR 0.90 (0.68 to 1.11)	25 fewer per 1000 (from 82 fewer to 48 more)	⊕⊕⊕O MODERATE	IMPORTANT
Hospital admission rate (follow-up 1 years)												
2	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	0/1525 (0%)	59.8%	Rate ratio 0.68 (0.58 to 0.8)	191 fewer per 1000 (from 120 fewer to 251 fewer)	⊕OOO VERY LOW	IMPORTANT
Admission (follow-up 1 years)												
2	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	0/164 (0%)	53.25%	HR 0.69 (0.54 to 0.87)	124 fewer per 1000 (from 49 fewer to 196 fewer)	⊕⊕OO LOW	IMPORTANT
Hospital admissions (follow-up 6 months - 1 years; Better indicated by lower values)												
2	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	648	640	-	MD 0.04 higher (0.01 lower to 0.1 higher)	⊕⊕⊕O MODERATE	IMPORTANT
Hospital admission (follow-up 6 years)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	0/71 (0%)	0%	OR 2.17 (0.6 to 7.85)	-	⊕OOO VERY LOW	IMPORTANT
Hospital admission (follow-up 6-12 months)												
2	randomised trials	serious[1]	serious[3]	no serious indirectness	serious[2]	none	88/185 (47.6%)	99/185 (53.5%)	RR 0.89 (0.72 to 1.09)	59 fewer per 1000 (from 150 fewer to 48 more)	⊕OOO VERY LOW	IMPORTANT
Length of stay (follow-up 90 days; Better indicated by lower values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	106	106	-	MD 0.90 lower (2.38 lower to 0.58 higher)	⊕⊕⊕⊕ HIGH	IMPORTANT

Emergency department use/hospital admissions (follow-up mean 2 years; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	51	46	-	MD 0.3 lower (1.34 lower to 0.74 higher)	⊕⊕OO LOW	IMPORTANT
ED use (follow-up 1 years)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[1]	none	0/99 (0%)	17%	HR 0.64 (0.48 to 0.85)	58 fewer per 1000 (from 24 fewer to 84 fewer)	⊕⊕OO LOW	IMPORTANT
ED use (follow-up 6 years)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	0/71 (0%)	0%	OR 0.33 (0.13 to 0.84)	-	⊕⊕OO LOW	IMPORTANT
ED use (follow-up 6 months - 1 years)												
3	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	128/244 (52.5%)	145/246 (58.9%)	RR 0.89 (0.77 to 1.02)	65 fewer per 1000 (from 136 fewer to 12 more)	⊕⊕⊕O MODERATE	IMPORTANT
Adverse effects (follow-up 2 years)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	38/453 (8.4%)	11.1%	RR 0.75 (0.5 to 1.13)	28 fewer per 1000 (from 56 fewer to 14 more)	⊕OOO VERY LOW	IMPORTANT
Quality of life - Physical Health Component (follow-up 6 months; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	218	200	-	MD 1.50 higher (0.41 lower to 3.41 higher)	⊕⊕OO LOW	CRITICAL
Quality of life - Physical Functioning Scale (follow-up 6 months; range of scores: 0-100; Better indicated by higher values)												
1	randomised	very	no serious	no serious	no serious	none	218	200	-	MD 4.10 higher (0.74 lower to 8.94	⊕⊕OO	CRITICAL

	trials	serious[1]	inconsistency	indirectness	imprecision					higher)	LOW	
Quality of life - Mental Health Component (follow-up 6 months; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	218	200	-	MD 0.00 higher (2.34 lower to 2.34 higher)	⊕⊕OO LOW	CRITICAL
Barthel ADL Score (follow-up 90 days; range of scores: 0-20; Better indicated by higher values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	106	106	-	MD 1.70 higher (0.19 to 3.21 higher)	⊕⊕⊕O MODERATE	CRITICAL

[1] 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.

[2] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.

[3] Downgraded by 1 or 2 increments because of heterogeneity, I^2= >50%, unexplained by subgroup analysis.

Appendix G: Excluded clinical studies

Table 7: Studies excluded from the clinical review

Study	Exclusion reason
Aberg-Wistedt 1995 [6]	Incorrect population – patients with schizophrenia
Adams 2001[7]	Study design: literature review
Allen 2008[8]	Systematic review: all relevant papers ordered
Altman 2012 [9]	Incorrect intervention
Anon 1994A [1]	No relevant outcomes
Anon 2013 [3]	Incorrect study design
Anon 2014 [4]	Incorrect study design
Anon 2015[5]	Protocol only
Armitage 2009[11]	Systematic review: study designs inappropriate
Bambra 2014[13]	Study design: literature review
Barcelo 2010[14]	Multi-component intervention (majority not integrated care). No outcomes of interest
Bekelman 2014 [15]	No relevant outcomes
Borenstein 2016 [18]	Incorrect intervention – considered for inclusion in the ECAU evidence review
Borgermans 2009 [19]	No relevant outcomes
Boustani 2011 [20]	Incorrect study design – narrative
Boyd 2010[21]	Incorrect interventions. Addition of RN trained in chronic care
Briggs 2006[23]	Non-OECD country
Buckingham 1994[24]	Economic analysis
Callahan 2006A [25]	Incorrect population – older adults with Alzheimer Disease
Carter 2009[27]	Not guideline condition. Management of hypertension
Clark 2015[29]	Systematic review is not relevant to review question or unclear PICO
Coulter 2015[30]	Systematic review: no papers of interest
De stampa 2014[33]	Study design: before and after
Demaerschalk 2010[35]	Inappropriate comparison. Hub and spoke using telemedicine versus hub and spoke using telephone
Demaerschalk 2012[34]	Inappropriate comparison. Hub and spoke using telemedicine versus hub and spoke using telephone
Demaerschalk 2012[36]	Inappropriate comparison. Hub and spoke using telemedicine versus hub and spoke using telephone
Dey 2002[37]	Not guideline condition. Missed or delayed diagnosis of breast cancer
Dey 2002[38]	Not guideline condition. Opiate use
Dobscha 2009 [39]	Incorrect intervention
Dziedzic 2014 [44]	Study protocol
Eastwood 1996[45]	Systematic review: all papers ordered
Emery 2014[46]	Protocol only
Fagerberg 2000[47]	Incorrect interventions. MDT versus no MDT
Finley 2003 [50]	No relevant outcomes
Foster 2012 [51]	Study protocol

Study	Exclusion reason
Frank 2015[52]	Study design: literature review
Gellis 2014[53]	Incorrect interventions. Hospital at home
Glassman 2002 [54]	Incorrect comparison and interventions
Goldzweig 2015[55]	Systematic review: no papers of interest
Hanks 2002 [57]	Incorrect population – palliative care patients
Health 2013[58]	Systematic review: Incorrect study designs
Hendriks 2015[59]	Study design: literature review
Hernandez 2003[60]	Incorrect interventions. Hospital at home/early discharge follow-up
Hillman 2005 [62]	Incorrect intervention; abstract only
Holm 2006[63]	Non-English article
Jansink 2013[66]	Incorrect interventions. Nurse-led structured care
Johri 2003[68]	Systematic review: study designs inappropriate
Joubert 2006[69]	Not guideline condition. Post-stroke depression
Kasper 2002 [70]	Incorrect intervention
Katon 2004[72]	Incorrect population – patients with diabetes and depression
Katon 2008 [71]	Incorrect population – patients with diabetes and depression
Khan 2015[73]	Protocol only. Incorrect intervention. MDT
Kodner 2000[74]	Study design: literature review
Korczak 2010[75]	Systematic review: no papers of interest
Kruis 2014 [76]	Incorrect intervention
Ladapo 2012 [77]	No relevant extractable outcomes
Lambeek 2010[78]	Not guideline condition. Low back pain
Le may 2010[80]	Incorrect interventions. Paramedic referred pathway versus ED pathway
Liou 2014[81]	Not guideline condition. Glycemic control of diabetes
Llewellyn-jones 1999[82]	Not guideline condition. Depression
Llwellyn-Jones 1999	Incorrect population – late-life depression; incorrect intervention
Martinez-gonzalez 2014[84]	Systematic review: study designs inappropriate
Mcdonald 2007[85]	Systematic review: study designs inappropriate
Mchugh 2001[86]	Not guideline condition. Coronary heart disease
Meyer 2007[87]	Inappropriate comparison. Hub and spoke using telemedicine versus hub and spoke using telephone
Meyer 2008[88]	Inappropriate comparison. Hub and spoke using telemedicine versus hub and spoke using telephone
Newman 2007[91]	Not guideline condition
Nielsen 2003[95]	Not guideline condition. Mortality of cancer patients
Ouwens 2009[97]	Systematic review: relevant papers ordered
Primdahl 2014[99]	Not guideline condition. Rheumatoid arthritis
Richards 2013 [100]	Incorrect intervention
Rollman 2009 [102]	Incorrect population; incorrect intervention
Scherpbier-de haan 2013[104]	Not guideline condition. Chronic Kidney disease
Schned 1995 [105]	Incorrect intervention
Smith 2008[109]	Systematic review: no papers of interest
Solomon 2011[110]	Study design: descriptive
Sorensen 2015[111]	Not review population. Rheumatoid arthritis

Study	Exclusion reason
Spencer 1995[112]	Not guideline condition. Glaucoma
Stiefel 2008 [113]	No relevant outcomes
Sulch 2000 [114]	Incorrect intervention
Sulch 2000[114]	Poster abstract
Sulch 2002[115]	Incorrect interventions. Unclear intervention. Nurse-led care
Sulch 2002[116]	Incorrect interventions. Not integrated care as defined in the protocol
Switzer 2013[117]	Economic model
Townsend 2015[118]	Study design: qualitative
Tully 2014[119]	Protocol only
Unutzer 2002 [120]	Incorrect population – late-life depression
Wensing 2006[121]	Systematic review: study designs inappropriate
Zhang 2007[122]	Systematic review is not relevant to review question or unclear PICO
Zwar 2008[124]	Community nurse-led intervention
Zwar 2012[123]	Community nurse-led intervention

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Appendix H: Excluded health economic studies

Table 8: Studies excluded from the health economic review

Study	Exclusion reason
Baeten 2010[12]	This was a non-UK study assessing non-randomised evidence. Given the inclusion of more applicable evidence this study was excluded from this review.
Looman 2016[83]	This was a non-UK study assessing non-randomised evidence. Given the inclusion of more applicable evidence this study was excluded from this review.
Pisano 2015[98]	This was a non-UK study assessing non-randomised evidence. Given the inclusion of more applicable evidence this study was excluded from this review.
Roberts 2010[101]	This study was assessed as partially applicable with very serious limitations. The study was a before and after study with no control group therefore differences attributed to the intervention could be due to regression to the mean or temporal changes in disease management in general. This was also a partial cost evaluation and did not consider all costs that the health service will incur such as the cost of setting up and running the intervention as well as primary care costs and drug costs.