National Institute for Health and Care Excellence

Final

Chapter 10 Community-based pharmacists

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

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Chapter 10 Community-based pharmacists

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10 Community-based pharmacists

10.1 Introduction

Pharmacists are highly trained medical professionals, qualified to give advice on health issues and medicines, and ensure the safe supply and use of medicines by the public. Medicines prevent, treat or manage many illnesses or conditions and are the most common intervention in healthcare.

The traditionally role of pharmacists in the community has involved dispensing and supply of prescriptions that have been issued by doctors. However in recent years the role and locations from which pharmacists in the community (primary care) work from has evolved and pharmacists have been undertaking more clinical roles in addition to the traditional dispensing services.

Overall it would be of interest to see if there is evidence to support the clinical and cost-effective development of services by community based pharmacists.

10.2 Review question: Do enhanced roles of pharmacists in the community have clinical and cost-effectiveness benefits for patients at risk of an acute medical emergency or have a suspected or confirmed acute medical emergency?

For full details see review protocol in Appendix A.

Table 1: PICO characteristics of review question

Population	Adults or young people (>16 years of age) at risk of an AME or have a suspected or confirmed AME.

Interventions	Intervention to be stratified by type of pharmacist (Community/Clinical) and location of intervention.
	
	• Community pharmacists with enhanced roles in disease management:
	  ○ Delivered at patient's home
	  ○ Delivered at community pharmacy
	  ○ Delivered at other community-based location
	  ○ Delivered at general practices
	  ○ Delivered at community clinics
	
	• Clinical pharmacists with enhanced roles in disease management:
	  ○ Delivered at patient's home
	  ○ Delivered at community pharmacy
	  ○ Delivered at other community-based location
	  ○ Delivered at general practices
	  ○ Delivered at community clinics

Comparisons	All interventions will be compared with usual care, or across 1 strata (that is, comparison with either the same type of pharmacist, or at the same location of intervention).
Outcomes	• Mortality (CRITICAL) • Avoidable adverse events (incorrect diagnosis and treatment) (CRITICAL) • Quality of life (CRITICAL) • Number of ED presentations (CRITICAL)

	• GP attendances (CRITICAL) • Hospital admissions (IMPORTANT) • Patient and/or carer satisfaction (CRITICAL)
Review strategy	Systematic reviews (SRs) of RCTs, RCTs, observational studies only to be included if no relevant SRs or RCTs are identified.

10.3 Clinical evidence

Thirty seven studies were included in the review;[5,6,8,17,27,29,30,39,53,53,54,63,79,91-93,103,115,116,120-123,129,130,135,141,146,151,162,172,173,176,182,188,189,191,192,198,199,201,202,205,207,227,229,230,232,233] these were split in 6 stratifications based on both type of pharmacist (community pharmacist or clinical pharmacist) and the location the intervention takes place. These stratifications are summarised in Table 2 to Table 7 below. Evidence from these studies is summarised in the clinical evidence summary below (Table 8 to Table 13). 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 for the strata: community pharmacist based within a community pharmacy

Study	Intervention and comparison	Population	Outcomes	Comments
Ali 2012[5] Conducted in the UK RCT	Intervention (n=25): Pharmaceutical care package designed for patients with Type 2 diabetes, with regular monitoring and consultations with the community pharmacist. Patients were seen every month for the first 2 months, and then every 3 months for the remainder of the 12 months, a total of 6 appointments. Pharmacists carried out a targeted medicine use review and lifestyle modification counselling with a referral to a general practitioner or healthcare professional where appropriate. Versus Control (n=23): Usual care - usual service received from general practice plus assessment by a pharmacist at the beginning of the study and then after 12 months for an assessment of study outcomes.	Solicited through posters and leaflets displayed in the pharmacies, and from computerised patient medication records held in the pharmacies, or by general practitioner referral. Patients were invited to take part by letter or at medication-dispensing opportunities. Inclusion - Type 2 diabetes mellitus on oral medication, not on insulin, over 18, HbA1c >53mmol/mol. Exclusion - Significant co-morbidity, Involved in any trial/study during last 3 months.	Hospital admissions. ED visits. Adverse events at 12 months.	Concurrent medication/care: treatment for type 2 diabetes. Adverse events: total hypoglycaemic and hyperglycaemic events per arm. No events in either arm for Hospital admissions or ED attendances.
Bouvy 2003[27] Conducted in the Netherlands	Intervention (n=74): Pharmacists received training for the intervention that consisted of a structured interview on the patient's first visit to the community pharmacy. A computerised	Inclusion - Admitted to hospital with heart failure or attended specialist heart failure clinic; diagnosis validated by hospital records including cardiac imaging. Treated	Mortality. Hospital admissions at 6 months.	

Study	Intervention and comparison	Population	Outcomes	Comments
RCT	medication history was used to discuss drug use, reasons for non-compliance (for example, possible adverse drug reactions and difficulties integrating medicine into daily life) to reinforce compliance. A short report of this interview was forwarded to the GP. Pharmacists contacted patients on a monthly basis for a maximum of 6 months. Versus Control (n=78): did not receive the structured interview or monthly follow up.	with loop diuretics. Exclusion - Severe psychiatric problems or dementia, planned admission to a nursing home, did not take care of their own medication (for example, filled or administered by relatives or district nurses), life expectancy <3 months.		
Bryant 2011[30] Cluster RCT Conducted in New Zealand	(n=269) The patients saw the study pharmacist for the Comprehensive Pharmaceutical Care (CPC) medication review consultation (at pharmacy or at home). It addressed patient concerns and expectations, adherence issues, provision of lifestyle and pharmacological advice and included a clinical assessment of medicine with recommendations if required to the GP in a pharmaceutical care plan. The pharmacist had access to the medical records from the GP and met with the GP after the patient consultation. The study pharmacist followed the patient at 3 and 6 months, updating the pharmaceutical care plan as needed (interim meetings could be agreed if necessary). Duration 6 months. Versus (n=229) Usual care. No further details.	All 76 pharmacists who had completed more than 5 care plans were invited to participate; those who agreed approached 2 GP practices and invited at least 1 GP (working 16 hours a week or more in general practice) from each practice. GPs invited eligible patients: starting on a different day each week, eligible patients were enrolled consecutively until 4 patients enrolled for that week. Each GP aimed to enrol 12 patients. Inclusion - age 65 or older; on 5 or more prescribed medicines; likely to be available for follow up for 1 year. Exclusion: Not stated.	Mortality at 6 months.	"Intervention occurred either in a private area of the pharmacy or at the patient's home" – no further details. Randomised by GP.
Community Pharmacy Medicines Management Project (MEDMAN) trial:	(n=980): Initial consultation informed by the extracted medical data supplied by the researchers. Further consultations were provided according to pharmacist-	Nine study sites were purposively selected (based on a range of population, general practice and community pharmacy characteristics)	Mortality at 12 months.	Community pharmacists received training designed and delivered by the Centre for

Study	Intervention and comparison	Population	Outcomes	Comments
Community pharmacy medicines management project evaluation team 2007[53]	determined patient need. Consultations included assessments of the following: therapy, medication compliance, lifestyle (for example, smoking cessation, exercise and diet) and social support (for example, difficulties in collecting prescriptions and opening bottles). Recommendations were recorded on a referral form which was sent to the GP, who returned annotated copies to the pharmacists. Duration: single visit or further consultations according to pharmacist-determined patient need (no further details). Versus Control (n=513): Usual care from their GP and community pharmacist (no further details).	from a list of 33 volunteer primary care organisations in England. Practices generated a list of all patients with CHD. GPs screened the list and sent invitation packs (invitation letter, trial information sheet and consent form) to eligible patients. Only pharmacies with private consultation areas were eligible to participate. Inclusion - 17 years and over and with CHD (previous myocardial infarction, angina, coronary artery bypass graft and/or angioplasty). Exclusion - illiterate/innumerate, history of alcohol/drug misuse, terminal/serious illness, severe mental illness and unable to provide informed consent or otherwise unsuitable for the trial.		Pharmacy Post-Graduate Education Concurrent medication/care: Treatment for CHD.
Elliott 2008[63] Conducted in the UK RCT	Intervention (n=255): Two weeks after the patient presented to the pharmacy for a prescription for a new medicine for a chronic condition, they received a telephone call from a community pharmacist based on a semi-structured interview; pharmacist listened to patient's problems and gave advice or reassurance if needed; asked the patient how they were getting on with their medicines, any medicine-related problems, adherence to the new medicine and whether they required any further information. Versus Control (n=237): Usual care - no further details.	Convenience sample: recruited opportunistically when patients presented a prescription in one of the 40 Moss pharmacies. Inclusion - Receiving the first prescription for a new medicine for a chronic condition; age 75 years or older; stroke, cardiovascular disease, asthma, diabetes or rheumatoid arthritis. Exclusion - Inability to understand written or spoken English or not having a telephone.	Number of ED presentations. Hospital admissions. GP attendances at 2 months.	Telephone based intervention, but pharmacist was based within the community pharmacy.
EMDADER-CV trial: Amariles	(n=356) The Dader method for pharmaceutical care: pharmacists obtained patient	Patients presenting at the pharmacy.	Mortality at 8 months.	Concurrent medication/care: treatment

Study	Intervention and comparison	Population	Outcomes	Comments
2012[6]	data related to CV medical problems and current drug therapy, obtained by interviewing the patient and reviewing the drug and clinical records. Used the collected data to complete the assessment form, which was interpreted and evaluated once all the necessary information was added. Evaluated the patient's drug therapy outcomes to assess whether the desired treatment goals for BP and TC were achieved. The pharmacist developed therapeutic plans that included interventions with the aim of achieving the desired clinical outcome. Conducted an intervention intended to directly prevent or resolve a Negative Outcomes associated with Medication (NOM). If the intervention was to modify drug therapy the recipient of the intervention was the physician. Completed a new assessment form to inform the physician of possible further modifications in the patient's care plan. Versus (n=358) Usual care. Usual care provided by the pharmacist.	Inclusion - 25 to 74 years; presented at the pharmacy with a prescription for at least 1 drug indicated for hypertension, hypercholesterolemia, CVD prophylaxis, or type 2 diabetes; high or moderate CV risk according to the Systematic Coronary Risk Evaluation (SCORE) system and/or Wilson-Grundy method. Exclusion - BP of 180/110 or higher, history of myocardial infarction in the previous 3 months, a terminal disease, an intellectual or physical disability that prevented them from participating in the study, currently included in a cardiac rehabilitation program.		for CVD. Verbal and written counselling regarding cardiovascular disease prevention (according to patient risk).
Gordois 2007[79] (Armour 2007[8]) Cluster-RCT Conducted in Australia	Intervention (n=191): Pharmacy Asthma Care Program which included targeted counselling and education on the condition, medication and lifestyle issues (such as trigger factors); review of inhaler technique; adherence assessment; detection of drug-related problems; goal setting and review and referral to a GP as appropriate (for example, for a change in medication or dose). Versus Control (n=205): Received no intervention other than the pharmacist's usual care.	Accredited pharmacies located within 300 km of any of the 4 participating institutions with inclusion criteria of: QCPP accreditation, availability of a computer system compatible with the spirometer software to be used in the study, ability to attend training sessions and a minimum of 2 pharmacists on duty at any one time. The exclusion criterion for pharmacies was current involvement in any other research project. Pharmacies were asked to recruit up to 10 subjects	ED visits. GP visits. Hospital admissions at 6 months.	Cluster randomised by pharmacy. Data extracted from a supplementary economic evaluation.

Study	Intervention and comparison	Population	Outcomes	Comments
		from their customers. Inclusion: age 18-75 years old, previous diagnosis of asthma, fulfilment of 1 or more of the following criteria: use of a reliever medication >3 times a week over the previous 4 weeks, waking at night or morning with cough/chest tightness on at least 1 occasion over the previous 4 weeks, time off work/study because of asthma over the previous 4 weeks, symptoms of asthma (cough, breathlessness or wheeze) at least once a week over the previous 4 weeks, and no visit to a doctor for asthma within the last 6 months. Exclusion: terminal illness, were currently enrolled in another clinical trial, did not self-administer their inhaler and/or did not speak English well enough to communicate.		
HOME study trial: Zillich 2005[233] Cluster-RCT Conducted in the USA	Intervention (n=64): Patients were scheduled to meet face-to-face with a pharmacist 4 times over 3 months. At each visit pharmacists provided patient-specific education about hypertension, including: disease process and complications, medication use and adherence, lifestyle modification and home SBP monitor (SBPM) technique. During the baseline and third visit the patients were provided with a validated, fully automated home SBPM. Patients were instructed to perform 2 home BP measurements, separated by 5 minutes of rest, at least once daily in the morning. Home BP readings were recorded by the patient in the log book. During the second and fourth visit, logs	Pharmacies were recruited based on commitment and willingness to participate (no further details). Patients receiving antihypertensive medications from participating pharmacies were informed of the study from a pharmacist or technician during medication refills. Inclusion - Over 20 years of age with a diagnosis of hypertension, taking 1-3 BP medications with no changes in the regimen or dose within the past 4 weeks, receiving BP medication from the same physician for at least 2 consecutive months, and	ED visits. GP visits. Hospital admissions. At 3 months.	Randomised by community pharmacy.

Study	Intervention and comparison	Population	Outcomes	Comments
	and monitors were returned to the pharmacist who calculated weekly BP averages and used the measurements to develop written treatment recommendations for the patient's physician. If home BP weekly averages exceeded 140/90 mmHg (130/80mmHg for patients with diabetes and/or kidney disease), the pharmacists' recommended intensification of the medication regimen. Recommendations and BP logs were sent via facsimile to the physician and followed by a telephone call. Versus Control: patients met face-to-face with a trained pharmacist 3 times over 3 months. At each visit, patients' BP was measure by the pharmacist. In most cases, patients were told that their BP was above normal and they should contact their physician. These patients did not receive any other pharmacist education or home BP monitors. The BP measurements were sent via facsimile to the patients' physician without treatment recommendations.	for non-diabetic patients SBP between 145 and 179 mmHg or DBO between 95 and 109 mmHg, for diabetic patients SBP between 135 and 179 mmHg or DBO between 90 and 109 mmHg. Exclusion - BP greater than 180/110 mmHg, a MI or Stroke within the last 6 months, serious renal or hepatic disease, pregnancy, dementia/cognitive impairment.		
Jodar-Sanchez 2015[103] Conducted in Spain Cluster-RCT	Intervention (n=688): Pharmacists allocated into the intervention group received a 3-day off-site training course and on-site visits by a facilitator during the 6 months follow up, to assist pharmacists in the provision of the service and ensuring quality and homogeneity of the interventions. Pharmacists and patients had follow-up visits every 1-2 months. Versus Control (n=715): Usual care - no further details.	Inclusion - Older adults aged 65 years or over with polypharmacy, that is, taking 5 or more officially registered (prescribed or over-the-counter) medicines per day. Exclusion - not stated.	Number of ED presentations. Hospital admissions at 6 months.	Randomised by practice.

Study	Intervention and comparison	Population	Outcomes	Comments
Murray 2007[146] RCT Conducted in the USA	Intervention (n=122): A pharmacist delivered the intervention using a protocol that included a baseline medication history of all prescriptions and over the counter drugs and dietary supplements taken by patients, and the results of an assessment of patient medication knowledge and skills. When medications were dispensed, the pharmacist provided patient-centred verbal instructions and written materials about the medications. We assigned each medication category an icon (for example, the icon for ACE inhibitors was a red ace of hearts). The same icon appeared on the container label and lid and on the written patient instructions. Written instructions were aimed at patients with low health literacy and contained an easy-to-follow timeline to remind patients when to take their medications. The pharmacist monitored patients' medication use, health care encounters, body weight and other relevant data by using a study database. Relevant information was communicated as needed to clinic nurses and primary care physicians by face-to-face visits, telephone, paging and email Versus Control (n=192): Patients received their prescription services from pharmacists who rotated through the study pharmacy. These pharmacists had not received the specialised training provided by the interdisciplinary team to the intervention pharmacist and did not have access to the patient-centred study materials.	Weekly list of eligible patients were created by using the Medical Record System. Clinically stable patients were invited to participate (no further details). Inclusion - Diagnosis of heart failure confirmed by their primary care physicians, 50 years or older, planned to receive all their care, including prescribed medications at within the study health service, regularly used at least 1 cardiovascular medication for heart failure and had access to a working telephone. Exclusion - Using or planning to use a medication aid (for example, a pill box) and dementia.	Mortality Number of ED presentation. Hospital admission at 12 months.	Treatment for congestive heart failure.
ProFiL trial: Santschi	Intervention (n=48): Community pharmacist	Community pharmacies were recruited if they	Mortality at 6	Clustered by pharmacy

Study	Intervention and comparison	Population	Outcomes	Comments
2011[182] Conducted in Canada Cluster-RCT	attended a 3 hour training workshop on clinical presentations of CKD, management of DRPs among CKD outpatients, presentations of the programme and clinical tools, and discussion of 2 real clinical cases. There was communication of clinical information (laboratory test results and medications documented by the nephrologist) between the predialysis clinic and community pharmacies and a pharmaceutical consultation service by hospital [clinical] pharmacists with expertise in nephrology was made available to the community pharmacists. Versus Control (n=42): Usual care. Pharmacists did not have access to the Profile programme and were asked to provide usual care.	attended the workshop if assigned to the ProFil group, and willing to give researchers copies of the written recommendations they sent to physicians and of the pharmacy's record. Patients were recruited consecutively from Laval predialysis clinics. Inclusion -Estimated CrCl over 60 ml/min, they were followed at a community pharmacy participating in the ProFil study and agreed to use the same pharmacy's services for the duration of the study, covered by the Quebec government drug plan 6 months prior to the study and throughout the duration and they spoke and wrote French.	months.	practice. Concurrent medication/care: Treatment for CKD.
RESPECT trial: Respect trial team 2010[173] (Respect trial team 2010[172]) Cluster randomised interrupted time-series Conducted in the UK	Intervention (n=563): Pharmaceutical care was undertaken by community pharmacists who interviewed patients, developed and implemented pharmaceutical care plans together with patients' GPs and thereafter undertook monthly medication reviews. Pharmacists and GPs attended training before the intervention. Duration: 12 months Versus Control (n=760): PCTs were randomised to receive usual care for 3, 5, 7, 9, or 11 months. Training for the intervention phase began 2 months prior to control period finishing. Duration: 3-11 months.	All general practices and all community pharmacies with a permanent pharmacist in the 5 PCTs were invited to participate. Eight practices from the largest PCT and 4 practices for the other PCTs were selected, all stratified by practice size. Practice records were search for patients meeting the inclusion criteria. Potential participants were interviewed in their home or at their GP's surgery. Inclusion - Aged 75 or over, taking 5 or more repeat drugs (excluding any taken 'when required'), living at home, scored 7 or over on the Abbreviated Mental Test, GP gave consent, community pharmacist	Emergency admission episodes per month at 2 years.	Randomised by healthcare. Results reported from a model of the interaction of the intervention component, and intervention – time component.

Study	Intervention and comparison	Population	Outcomes	Comments
		was taking part in the RESPECT trial and able to provide written consent. Exclusion - Living in in a residential or nursing home, their GP and community pharmacist were not in the same PCT or taken part in a local feasibility study.		
The BC Community Pharmacy Asthma Study trial: Mclean 2003[141] RCT Conducted in Canada	Intervention (n=235): EC patients received usual care plus pharmaceutical care, which included education on disease, identification of triggers and pharmacist-patient developed action plan, patient participation in decision making, patient monitoring of own therapy (PEFRs and using calendar/diary), pharmacist responsibility for outcomes, pharmacist promotion of evidence-based care, pharmacist-patient interaction at appointment in a private consultation area. The physician was informed or consulted regarding all results and interventions. Versus Control (n=214): initial interview with the patient to complete a symptom, drug utilisation and knowledge assessment. The patient was taught proper inhaler technique, and the pharmacist answered any questions the patient had about the project. Patients were asked to complete a monthly asthma calendar/diary. A second interview was conducted at the end of the study.	Recruited in the local community by each pharmacist. Methods included store notices, communication with local physicians and clinics, and information provided by BC. Inclusion - provided consent and diagnosis confirmed with their physician. No further details.	Number of ED presentations. GP attendances. Hospital admissions. At 9-12 months.	All results given as baseline and final value, no SDs given. ED Baseline - Group 1: 0.377; Group 2: 0.165.
Touchette 2012[205] Conducted in the USA	Intervention 1 (n=211): Basic Medication Therapy Management (MTM): 2 scheduled visits (0 and 3 months); MTM pharmacist performed a comprehensive medication review and drug-	Inclusion - Age 65 or older, primary use of English for written and oral communication, access to a telephone, 3 or more chronic comorbid conditions associated with	Number of ED presentations Adverse drug events	Adverse drug events not detailed

Study	Intervention and comparison	Population	Outcomes	Comments
RCT	related problem (DRP) assessment with no access to clinical information except from the patient. All medications were documented with directions for use and actual patient use; DRPs were classified using previously validated Pharmaceutical Care Network Europe (PCNE) classification. Unless DRPs required urgent attention, DRPs were sent to physician by fax. Study pharmacists underwent a 90-minute training session to ensure the MTM intervention was conducted in a similar manner among all sites. MTM pharmacists were not allowed to access patients' electronic medical records (like a typical community pharmacy). Versus Intervention 2 (n=218): Enhanced Medication Therapy Management (MTM): 2 scheduled visits (0 and 3 months); MTM pharmacist performed a comprehensive medication review and drug-related problem (DRP) assessment. All medications were documented with directions for use and actual patient use; DRPs were classified using previously validated Pharmaceutical Care Network Europe (PCNE) classification. Pharmacist attempted to resolve as many DRPS as possible through patient education and/or physician notification. Unless DRPs required urgent attention, DRPs were sent to physician by fax. Study pharmacists underwent a 90-minute training session to ensure the MTM intervention was conducted in a similar manner among all sites. MTM pharmacists were not allowed to access patients' electronic medical records (like a typical community pharmacy).	increased health care use (for example, congestive heart failure, diabetes, COPD or hypertension), 2 or more visits to a clinic provider during previous year, 6 or more chronic prescription medications in previous 6 months, 1 or more recent situations placing patient at high risk of drug-related problems (that is, 3 or more different healthcare providers visited in previous 12 months, any change in medication, new physician visit, ED visit, hospitalisation or invasive procedure requiring stopping medications in previous 30 days). Exclusion - Presence of a terminal condition with life expectancy 6 months or less or previous enrolment in a medication therapy management (MTM) programme involving comprehensive medication review in previous 12 months.	Hospital admissions GP attendances between 3 and 6 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	In the enhanced TM group, pharmacists were provided with a two-page clinical summary (extracted from electronic medical record by a research assistant within 10 minutes) containing basic data on the patient's medical history (including 2 most recent BP and heart rate measurements), laboratory values (electrolytes, liver tests, INR, complete blood count, lipid panel, thyroid panel, glycosylated haemoglobin, drug levels and dates) and current medication regimens including OTC and herbal medications where listed in the chart. Versus Control (n=208): Usual care - Patients received medication counselling according to their pharmacy's normal routine.			

Table 3: Summary of studies included in the review for the strata: community pharmacist at the patients' homes

Study	Intervention and comparison	Population	Outcomes	Comments
Holland 2007[93] Conducted in the UK RCT	Intervention (n=149): Community pharmacists with post-graduate qualification in pharmacy practice or recent CPD in therapeutics; not independent prescribers so could not directly modify drug regimen. Pharmacists provided with copy of discharge letter; arranged a home visit within 2 weeks of discharge; educated patient/carer about heart failure and drugs and gave basic exercise, dietary and smoking cessation advice; encouraged completion of simple sign and symptom monitoring diary cards (including weight); removed discontinued drugs; fed back recommendations to the GP; fed back to local pharmacist any need for drug adherence aid. Pharmacists were provided with detailed manual describing expected components of their visit and asked to deliver	Inclusion - Adults (over 18 years) admitted as an emergency in which heart failure was an important on-going clinical condition and prescribed 2 or more drugs (any class) on discharge. Exclusion - Living in residential or nursing home, awaiting surgery for ischaemic or valvular heart disease or heart transplant and terminal malignancy.	Mortality. Quality of life. Hospital admissions at 6 months.	

Study	Intervention and comparison	Population	Outcomes	Comments
	education in line with advice in the British Heart Foundation's booklet "Living with heart failure" which they left with the patients at the first visit. One follow-up visit occurred at 6-8 weeks after discharge to review progress and reinforce original advice. Versus Control (n=144): Usual care - no further details.			
Holland 2005[91] (Holland 2006[92]) RCT Conducted in the UK	Intervention (n=437): Initial referral to a review pharmacist included a copy of the patient's discharge letter. Pharmacists arranged home visits at times when they could meet patients and carers (mean was 7.2 days before visit). Pharmacists assessed patients' ability to self-medicate and drug adherence, and they completed a standardised visit form. Where appropriate, they educated the patient and carer, removed out of date drugs, reported possible drug reactions or interactions to the general practitioner, and reported the need for a compliance aid to the local pharmacist. One follow-up visit occurred at 6 to 8 weeks after recruitment to reinforce the original advice. Versus Control (n=435): Usual care. No further details.	Four general hospitals and 6 community hospitals. Inclusion - Over 80, admitted as an emergency, intended to be discharged to their own home or warden controlled accommodation, prescribed 2 or more drugs on discharge. Exclusion - Dialysis treatment and participation in an intensive discharge service on one site.	Hospital admissions. Mortality. Quality of life at 6 months. Hazard ratio adjusted for confusion and living alone.	67 did not receive intervention (46 visits not wanted, 11 pharmacist unavailable, 10 patients unavailable due to death or early readmission).
Lenaghan 2007[122] Conducted in the UK RCT	Intervention (n=69): One community pharmacist experienced in home-based medication reviews, with a post-graduate qualification in pharmacy practice, visited patients. The referral to the review pharmacist included a copy of the participant's current medication and medical history; this was used to highlight areas to be addressed including possible drug interactions,	Inclusion - Patients over 80 years, living in their own homes, prescribed at least 4 oral daily medicines plus at least 1 of the following criteria: living alone; record of confused mental state, vision or hearing impairment; prescribed medicines associated with medication-related morbidity; or prescribed	Mortality. Hospital admissions at 6 months.	

Study	Intervention and comparison	Population	Outcomes	Comments
	adverse effects or storage issues. Whenever possible, the home visit was arranged for a time when the pharmacist could meet any carers who helped with the patient's medications. The pharmacist educated the patient, removed out-of-date drugs and assessed the need for an adherence aid. The pharmacist and GP held regular meetings. Possible changes to the patient's prescribed medication were discussed and agreed amendments were put in place by the GP or delegated to the practice dispensing team. A follow up visit occurred 6-8 weeks later to reinforce the original advice and assess whether there were any further pharmaceutical care issues to address with the GP. Versus Control (n=67): Usual care - no further details.	>7 regular oral medicines. Exclusion - Residents in a care home or documented use of adherence aid.		

Table 4: Summary of studies included in the review for the strata: community pharmacist based within a GP practice

Study	Intervention and comparison	Population	Outcomes	Comments
Preventing hospital admissions by reviewing medication (PHARM) trial: Leendertse 2013[120] (Leendertse 2011[121]) Cluster-RCT Conducted in the Netherlands	Intervention (n=364): Patients receive a multi-step intervention consisting of pharmaceutical anamnesis (information gathering); a review of patients' pharmacotherapy, the formulation and execution of a pharmaceutical care plan combined with the monitoring and follow up evaluation of the care plan and pharmacotherapy. Interventions completed within 1 month with follow-up at 3 and 6 months. Versus Control (n=310): Usual care - dispensing of repeat prescriptions and automated medication surveillance according to current clinical guidelines. Patients do not	All Dutch GPs and community pharmacist working in primary care were eligible and invited to participate. Randomisation at a GP level takes place after informed consent of the participating GPs and pharmacists and before the selection of patients. Eligible patients were extracted from the pharmacy computer system and included in the order they appeared on this list. Inclusion - 65 years or older, had 5 or more chronically prescribed drugs of which at least 1	Survival. Hospital admissions related to medication. Adverse drug events at 12 months. Hazard ratio adjusted for number of diseases.	Randomised by GP. Concurrent medication/care: all patients on therapeutics that act on the alimentary tract, metabolism, blood, or blood-forming organs. Hospital admissions related to medication were determined by

Study	Intervention and comparison	Population	Outcomes	Comments
	routinely see a pharmacist when they go to their GP.	was filled with a refill rate of less than 80% or more than 120% as a measure of non-adherence, and were dispensed 1 or more drugs from the Anatomical Therapeutic Chemical (ATC) class A or class B (therapeutics that act on the alimentary tract, metabolism, blood or blood-forming organs). Exclusion - Residing in a nursing home, life expectancy less than 3 months, or refused informed consent.		2 blinded clinical pharmacists. No further details on adverse drug events.
Sellors 2001[188] RCT Conducted in Canada	Intervention (n=63): Specially trained community pharmacist who had received additional post-university training in the prevention, identification and resolution of drug-related problems completed structured drug therapy assessments with patients in the offices of their family physicians. The pharmacist wrote a consultation letter to the physician, which summarised the patient's medications, identified drug-related problems and recommended actions to resolve any such problems. The pharmacist and physician met to discuss the letter. Physicians used a data collection form to indicate which recommendations they intended to implement and when. The pharmacist and physician met again 3 months later to discuss progress in implementing the recommendations. Five months after the initial visit, they met again to determine which recommendations had been put in place. One and 3 months after meeting the physician, the pharmacist monitored the patient's drug therapy using a semi-structured patient interview.	Inclusion - Aged 65 years or more, taking 5 or more medications, seen by GP within past 12 months and no evidence of cognitive impairment and could understand English. Exclusion - Planned surgery, on nursing home waiting list or receiving palliative care.	Mortality at 6 months.	Pilot study for Sellors 2003.

Study	Intervention and comparison	Population	Outcomes	Comments
	Versus Control (n=63): Usual care - no further details.			
Sellors 2003[189] Cluster-RCT Conducted in Canada	Intervention (n=431): Specially trained community pharmacists who had received additional post-university training in the prevention, identification and resolution of drug-related problems completed structured drug therapy assessments with patients in the offices of their family physicians. The pharmacist wrote a consultation letter to the physician, which summarised the patient's medications, identified drug-related problems and recommended actions to resolve any such problems. The pharmacist and physician met to discuss the letter. Physicians used a data collection form to indicate which recommendations they intended to implement and when. The pharmacist and physician met again 3 months later to discuss progress in implementing the recommendations. Five months after the initial visit, they met again to determine which recommendations had been put in place. One and 3 months after meeting the physician, the pharmacist monitored the patient's drug therapy using a semi-structured patient interview. Versus Control (n=458): Usual care - no further details.	Inclusion - Aged 65 years or more, taking 5 or more medications, seen by GP within past 12 months, no evidence of cognitive impairment and could understand English. Exclusion - Planned surgery, on nursing home waiting list, receiving palliative care.	Mortality. Number of ED presentations. Hospital admissions. GP attendances at 5 months.	Randomisation by family practice.
Simpson 2011[192] RCT Conducted in Canada	(n=131): In-person visit to measure height weight, blood pressure, and to identify all prescription, non-prescription, complementary and alternative medications. Pharmacists then formulated guideline-concordant recommendations to optimise medication management of blood pressure and other	Patients who use the primary care network and who were identified from the clinic roster. Inclusion - Type 2 diabetes, regularly seen by the primary care team and did not qualify for an urgent referral and assessment (fasting	Mortality. ED visits. Hospital admissions at 12 months.	Concurrent medication/care: medication for hypertension and type 2 diabetes.

Study	Intervention and comparison	Population	Outcomes	Comments
	cardiovascular risk factors. Pharmacist then worked independently with the patient to implement these changes. Versus (n=129) Usual care. Control patients received usual care by the primary care team without contributions from study pharmacists, except for standardised blood pressure measurements at the end of the follow-up period.	blood glucose >17mmol/l, blood pressure >220/120 mmHg, or triglycerides >15mmol/l). Exclusion - Followed in speciality clinics for diabetes, hypertension, and dyslipidaemia; cognitively impaired; not responsible for their own medication or unable to communicate in English.		

Table 5: Summary of studies included in the review for the strata: clinical pharmacist based within a community clinic

Study	Intervention and comparison	Population	Outcomes	Comments
Cooney 2015[54] Cluster-RCT Conducted in the USA	Intervention (n=1070): The intervention included delivery system redesign which involved engaging pharmacists to interact with patients and collaborate electronically with primary care physicians; self-management support for patients in the form of an informational pamphlet regarding CKD (National Kidney Disease Education Program packet); and a CKD registry. The registry was used 1) to identify patients with CKD not receiving guideline adherent care; 2) by the pharmacist for decision support during the phone call with participants (phone script with branching logic); and 3) to facilitate documentation of the intervention (at the completion of the intervention phone call, the registry automatically generated a template note that was copied into the electronic medical record (EMR) as a progress note; only for study personnel, not used in daily practice). The registry was used to identify patients with an upcoming primary care appointment. Clinical pharmacists contacted subjects by phone prior to the appointment to discuss CKD and	Eligible patients in the primary care CBOCs. Inclusion: Moderate to severe chronic kidney disease (CKD) (calculated eGFR <45mL/min/1.73m2); GFR <60mL/min/1.73m2 between 90 days and 2 years prior to index GFR; at least 1 primary care visit in previous year. Exclusion: End-stage renal disease (ESRD); ever referred for hospice care; >85 years or <18 years.	Mortality at 1 year.	

Study	Intervention and comparison	Population	Outcomes	Comments
	hypertension; they reviewed medication and lifestyle modifications, ordered KDOQI recommended laboratory tests and arranged nephrology consults for patients with severe CKD (eGFR <30mL/min/1.73m2); once lab results were completed, the pharmacist called the patient again to review any abnormal results and initiated appropriate medication changes to treat acidosis, hypophosphatemia, hyperparathyroidism, vitamin D deficiency, hyperkalaemia and anaemia. BP medications were not adjusted by the pharmacists but recommendations to primary care providers regarding hypertension management were included in the progress note. Versus (n=1129) Usual care. No further details.			
Pai 2009 [162] Conducted in the USA RCT	Intervention (n=61): Patients had medication reviews conducted by a nephrology-trained clinical pharmacist or 1 of 2 pharmacists completing postdoctoral training in nephrology pharmacotherapy. These patients were asked to bring in their medications every 8 weeks. At each session the clinical pharmacist would conduct a 1:1 patient interview, generate a current medication profile, identify and address various DRPs through review of medication, chart, and laboratory data, and provide healthcare provider and patient education. Versus Control (n=46): Periodic medication profile updates by dialysis nursing staff as mandated by the dialysis clinic policy and procedure. These are typically brief interactions where patients are queried as to whether any medications have changed since	Set in a community-based haemodialysis clinic; no details on recruitment. Inclusion - over 18 years of age, stable haemodialysis regimen for at least 3 months. Exclusion - no informed consent, English not primary language.	Mortality. Hospital admissions at 2 years.	Mean per 1000 patient-days.

Study	Intervention and comparison	Population	Outcomes	Comments
	the last review.			
Taveira 2014[198] Conducted in the USA RCT	Intervention 1 (n=72): Attended 4 sessions, 3-monthly for 1 year, with 6-8 participants (plus family members/members of social support); sessions facilitated by clinical pharmacist: education for first hour (self-management for example, healthy eating or physical activity), then behavioural (individualised behavioural change goal for example exercise, diet, blood glucose or BP monitoring) and pharmacological interventions (initiating or titrating medications according to algorithm) for second hour for hyperglycaemia, hypertension and dyslipidaemia, based on individualised cardiovascular risk report card containing medical history, current medications, vitals and laboratory values, updated every 3 months. Demonstration and coaching were used to increase the frequency of self-care skills for example, blood glucose monitoring, logging dietary intake. Participants were contacted by phone as needed to follow up on pertinent laboratory values or to reinforce self-care monitoring or medication changes. Versus Intervention 2 (n=73): 30-minute visit with clinical pharmacist every 3 months to assess medication adherence, obtain vitals and laboratory parameters and titrate medications to address BP, hyperlipidaemia and diabetes. Participants were referred to nutritionist or physical therapist for an individual diet and exercise programmes needed. Versus Control (n=55): Usual care - Follow up in primary care, on	Inclusion - Actively enrolled in cardiovascular risk reduction clinic (CRRC); documented CVD or diabetes; meeting discharge criteria (HbA1c 7% or less; BP 140/80mmHg or less for those with diabetes and 140/90mmHg or less without diabetes; LDL cholesterol 2.59mmol/L or less) Exclusion - Had a condition that may limit long-term adherence to study visits (for example, severe dementia, acute psychiatric decompensating in previous 6 months, unstable psychiatric illness, metastatic cancer or terminal illness, or life expectancy <1 year.	Mortality. Number of ED presentations. Hospital admissions. GP attendances at 1 year.	Not explicit in the location of the intervention.

Study	Intervention and comparison	Population	Outcomes	Comments
	average 3-4 times a year; laboratory and vital signs obtained at the discretion and frequency of primary care provider, who had referral access to the nutrition and physical therapy and the same consultation services as the CRRC clinic provider (except patients were not referred to the CRRC for the study year).			
Xin 2016[227] RCT China	Pharmacy managed clinic (PMC). A structured education about COPD was provided by a clinical pharmacist. In order to help the patients easily understand the education plan, the pharmacists prepared many drug education materials. During telephone or network counselling, the pharmacist asked the patients about the effect of medication, explained the examination results, the possible ADR and reminded when the patients should visit their doctor. Versus Usual care delivered by the doctor, but no prescription services by the clinical pharmacist	n=244 Inclusion criteria: age >35 years, diagnosis of COPD, regular visit to pharmacist, no previous diagnosis of uncontrolled psychiatric disease, and no previous diagnosis of severe liver or kidney disease.	Hospitalisations.	Follow-up- 12 months.

Table 6: Summary of studies included in the review for the strata: clinical pharmacist at the patients' homes

Study	Intervention and comparison	Population	Outcomes	Comments
Begley 1997[17] Conducted in the UK RCT	Intervention (n=74): Patients were counselled on the correct use and storage of their drugs. The counselling included categorisation and a recall check at the end. Other practical strategies which have been validated to improve patient compliance were implemented. These included: emphasising the importance of compliance, giving clear instruction on the exact treatment regimen (in writing if necessary), arranging dosing times to fit into the patient's daily routine and recognising the	Recruited from 3 hospitals within the district. Identified when discharge prescriptions which met the study inclusion criteria were presented in the hospital pharmacy. Inclusion - Aged 75 years or older, prescribed 3 or more different drugs, at least a twice daily dosage for 1 or more of	GP between 3 and 12 months.	

Study	Intervention and comparison	Population	Outcomes	Comments
	patient's effort to comply at each visit, simplifying the regimen if necessary. Versus Control (n=75): Usual care. Received visits but no counselling.	the drugs, under the care of a participating consultant, consented to participate in the study, was returning to their own home following discharge. Exclusion - None stated.		
Krska 2001[115] (Krska 2007[116]) Conducted in the UK RCT	Intervention (n=168): Clinically-trained pharmacists completed a detailed profile for each patient using medical notes and practice computer records. All patients were then interviewed in their own home about their use of and responses to medication, and their use of health and social services. A pharmaceutical care plan was drawn up for each intervention group patient, copies of the plan were inserted in the patients' medical notes and given to their GP, who was asked to indicate their level of agreement with each Pharmaceutical Care Issues identified and with the suggested actions. The pharmacist then implemented all agreed actions, assisted by other practice staff where appropriate. Versus Control (n=164): Usual care. Control patients were similarly interviewed and PCIs identified, although no pharmaceutical care plan was implemented. Patients were advised to consult any with any usual carers or health-care professionals in response to direct queries during interview. When a pharmacist considered a PCI to potentially serious, an independent medical assessor decided on the need to withdraw the patient from the study on clinical grounds.	All medical practices within the area with at least 500 patients aged 65 years or over were stratified into 3 levels by the deprivation status (Jarman index) of their practice population and by fund-holder status (yes/no). Using random number tables, 1 practice from each of the 6 resultant categories was selected and invited to participate. One practice refused and a further practice was randomly selected. Inclusion - Aged at 65 years, regular request for at least 4 medicines via the computerised repeat prescribing system and at least 2 chronic conditions Exclusion - Dementia and being considered by the GP to be unable to cope with the study.	Emergency hospital admissions at 3 months.	Concurrent medication/care: treatment for at least 2 chronic conditions. Number of emergency admissions for the 3 months prior to study. – Intervention: 23; Control: 11.
Triller 2007[207]	Intervention (n=77): Usual home-based care plus 3 home visits from a clinical pharmacist. Role	Patients identified by discharge nurses from medical record or billing	Mortality. Hospital admission	Intervention was for 21 days.

Study	Intervention and comparison	Population	Outcomes	Comments
Conducted in the USA RCT	included initial comprehensive in-home medication assessment (concurrent with the initial usual care admission process). The follow-up visits were conducted at day 7-10 and 18-21 and were contingent on the patient's continue use of the home-based care service. During the initial visit, the pharmacist catalogued all medications and interviewed the patient regarding their medication use. The pharmacist sought to improve patient progress toward meeting pertinent pharmacotherapy goals related to heart failure and also endeavoured to reduce the use of inappropriate medications, encourage smoking cessations, suggest improvements in diet, and promote medication adherence. Throughout the 21 days the pharmacist accessed and reviewed all pertinent physician notes and laboratory test values via the NEH data system and interacted with prescribers on behalf of the patients. Individual physicians were not part of the trial and were not required to act on the pharmacist's recommendations. The physicians were contacted either by phone or by fax. Versus Control (n=77): Usual care. Received the home-based services typically provided by the visiting nurse association. These include basic nursing care, a brief physical assessment and medical history.	system before hospital discharge. Inclusion - Primary or secondary diagnosis of heart failure, aged 21 years or older and residence in the catchment area. Exclusion - residing outside the defined geographic area, without telephone service, disability or illness or lacked the mental capacity to provide informed consent.	at 180 days.	Study participants must receive at least 3 days of home care and 1 pharmacist visit if in the intervention arm to be included in the final analysis.
Zillich 2014[232] Conducted in the USA RCT	Intervention (n=415): Upon completion of the home health nurse's (who was bonded to the assignment of the patient) admission assessment on day 1 of the home health care episode, the patient's current medication information was faxed to the MTM intervention provider (HealthStat Rx). Following a pre-	Patients admitted into Medicare's defined 70-day home health care episode. Inclusion - All patients on plan, including those receiving physical/ occupational therapy services only.	Hospital admissions at 60 days. Hazard ratio adjusted for CMS risk score for	Downgraded for indirectness as this is a remote intervention, and it is unclear what type of pharmacist is conducting

Study	Intervention and comparison	Population	Outcomes	Comments
	MTM call by a pharmacy technician to verify medication information, there was an initial telephone call to the patient and/or caregiver from a trained pharmacist. During this telephone call, the pharmacist completed a comprehensive medication therapy review to identify any medication-related problems, constructed a written personal medication record for the patient and providers, and developed a medication-related action plan. The action plan served as a patient-centred document to assist the patient and pharmacist in the resolution of identified medication-related problems. The duration of the initial pharmacist telephone call with the patient was approximately 30 minutes. The pharmacist also spent 15 minutes reviewing patient information prior to the call and 15 minutes after the call to complete documentation pertaining to the encounter. For all patients, pharmacists provided a follow-up telephone call on day 7 to continue resolving medication-related problems according to the medication action plan and to identify any new medication-related problems. Additional telephone follow-up was provided as needed during the first 30 days of the 60-day home health care episode. The duration of each follow-up encounter was approximately 20 minutes. Versus Control (n=480): Usual care - no further details. Duration 60 days.	Exclusion - Reoccurring episode of care within the past 12 months were excluded.	hospitalisation, patient age, total number of medication, ability to use a telephone, and detection of medication-related problems during initial in-home assessment.	the intervention and where they are based.

Table 7: Summary of studies included in the review for the strata: clinical pharmacist based within a GP practice

Study	Intervention and comparison	Population	Outcomes	Comments
Bruhn 2013[29] (Neilson	Intervention (n=70): Pharmacists invited patients to a face-to-face consultation. Prior to the	Patients were identified by a computerised search and sent an	GP visits. Hospital admissions	Data taken from a supplementary economic

Study	Intervention and comparison	Population	Outcomes	Comments
2015[151]) RCT Conducted in the UK	consultation, pharmacists completed a paper-based medication review of each patient's medical record and patients were asked to complete a pain diary to inform the consultation. A pharmaceutical care plan was agreed between the pharmacist and the patient. The plan assessed and documented relevant medical history and current conditions; known allergies and adverse drug reactions; relevant laboratory results; pain-related medications prescribed in the previous10 years; current pain-related prescription medications; current symptoms; lifestyle issues, including units of alcohol consumed per week; recommendations for changes to medication (if any); whether non-pharmaceutical treatments had been considered; and any other relevant issue. At the end of the consultation any required prescriptions for medicines were issued by the pharmacist. Owing to Controlled Drug (CD) regulations in place at the time, prescribing for CDs was performed using a supplementary prescribing clinical management plan rather than independent prescribing. Patients were followed up either by phone or face-to-face, at each pharmacist's discretion. Versus Intervention 2 (n=63): The pharmacists conducted a paper-based medication review focussed on pain-related prescription medications, before creating a pharmaceutical care plan which detailed any recommendations for medication changes. The plan was passed to the patient's GP for implementation. The GPs were asked subsequently about actions taken as a result of the recommendations.	invitation pack contain a letter, information sheet and consent form. Inclusion: Over 18 years of age, living in their own houses and receiving 2 or more acute prescriptions, and/or 1 repeat prescription within the last 120 days for an analgesic and/or NSAID. Exclusion: Medications that can be used for analgesia but whose primary indication is not for chronic pain (for example, triptans, anti-epileptics or anti-depressants), concomitant severe mental health problem or terminal illness, suffered recent bereavement, had a known alcohol or drug addiction, suffered pain caused by cancer or other malignancy, were unable to give informed consent or other (unspecified) reasons.	at 6 months.	evaluation. Only reported results for patients who had filled out final QoL questionnaire. Unclear whether this is a community or clinical pharmacist, assumed clinical due to current practice within the UK.

Study	Intervention and comparison	Population	Outcomes	Comments
	Versus Control (n=63): Patients received standard general practice care.			
Collaboration Among Pharmacists and physicians To Improve Outcomes (CAPTION) trial: Carter 2015[39] Conducted in the US Cluster-RCT	Intervention 1 (n=194): At baseline, the pharmacist reviewed the medical record and performed a structured interview with the patient, including a detailed medication history; assessment of patient knowledge of BP medications, purpose of each medication, goals of therapy, medication dosages and timing, and potential medication side effects; potential contraindications to specific BP medications; and expectations for future dosage changes, monitoring, and issues that may become future barriers to BP control (for example, side effects, non-adherence, patient self-efficacy). The pharmacist supplied a wallet card listing all medications and doses, contact phone numbers and BP goals. The pharmacist created a care plan with treatment recommendations for the physician at the baseline visit so that an immediate change in medication can be made. If the physician agreed with the care plan or made a modification in the plan, the pharmacist implemented the plan. The suggested model included structured face-to-face visits with the patient at baseline, 1, 2, 4, 6, and 8 months; a telephone call at 2 weeks; and additional visits if BP remains uncontrolled. If BP is controlled, the recommended action was for the pharmacist to schedule the patient for routine follow-up every 3 to 6 months. If BP control is lost, the pharmacist was encouraged to increase visit frequency similar to the baseline schedule. Duration for 9 months. Versus	Identified for a list generated from each clinic with consecutive patients invited to participate. Inclusion - English or Spanish speaking, over 18 years of age. Hypertension and uncontrolled BP defined as 140 mmHg and over SBP or 90 mmHg and over diastolic BP (DBP) for uncomplicated hypertension. 130 mmHg and over SBG or 80 mmHg and over DPB for patients with diabetes or chronic kidney disease. Exclusion - Current signs of hypertensive emergency (acute angina, stroke or renal failure); SBP >200 or DBP >114 mmHg; history of myocardial infarction, stroke, or unstable angina in the prior 6 months; systolic dysfunction with a left ventricular ejection fraction <35% as documented by echocardiography, nuclear medicine study, or ventriculography; glomerular filtration rate <20 mL/min or proteinuria >1 g/day; cirrhosis, hepatitis B or C infection, or laboratory abnormalities (serum alanine aminotransferase or aspartate aminotransferase >2 bilirubin >1.5 mg/dL) in the prior 6 months;	Mortality. Serious adverse events at 2 years.	Randomised by community-based family medicine residency programs. Treatment for hypertension. Study closed early (no further details).

Study	Intervention and comparison	Population	Outcomes	Comments
	Intervention 2 (n=207): Identical to intervention 1, with duration extended to 24 months. Versus (n=224) Intervention 3: Usual care. Pharmacists in control sites do not provide the intervention for patients with hypertension but will continue to provide curbside consultations if physicians specifically ask questions about patients with hypertension.	pregnancy; pulmonary hypertension or sleep apnea (unless treated by continuous positive airway pressure); life. expectancy estimated at <2 years; residence in a nursing home or dementia; and inability to give informed consent or impaired cognitive function		
Heart Failure Optimal Outcomes from Pharmacy Study (HOOPS) trial: Lowrie 2012[129] (Lowrie 2011[130]) Conducted in the UK Cluster – RCT	Intervention (n=1092): Prior to commencing the intervention, all pharmacists attended 1, in-house training day (contact time 7.5 hours) covering the aetiology, symptoms and evidence-based management of heart failure. As part of routine continuing professional development, each pharmacist participated in a 3.5 hour peer-led session every month which involved group discussion of cases encountered in their medication review clinics. Patients from practices assigned to the intervention were offered a 30 minute appointment with a pharmacist. If there was agreement between the pharmacist and the patient during the consultation and subsequently with the family doctor, medications were initiated, discontinued, or modified by the pharmacist during 3–4 subsequent weekly or fortnightly consultations. Duration: single visit plus 3–4 subsequent weekly or fortnightly consultations if change in care plan. Versus Control (n=1077): Usual care. No instructions were given to family doctors in the usual care practices. The study pharmacists	A letter was sent inviting all 220 General Practices in the area to participate in the trial. Non-responding practices were re-invited, on up to 3 occasions, until the end of the recruitment period. After receiving written consent from a practice, study personnel arranged a visit to identify eligible patients, by searching practice electronic records to identify patients with possible LVSD using specific Read codes. Inclusion - Written, informed consent, aged ≥18 years and had left ventricular systolic dysfunction confirmed by cardiac imaging conducted at a local hospital (transthoracic echocardiography in 90% of cases). Exclusion - Concurrent serious systemic disease (other than heart failure) likely to reduce life-expectancy (for example, advanced malignancy), severe cognitive impairment, severe psychiatric illness,	Admissions. Mortality up to 6 years. Hazard ratio adjusted for age, creatinine, grade of left ventricular systolic dysfunction, atrial fibrillation, respiratory disease, total number of medical treatments, and diuretic use.	Randomised by GP practice. All participating pharmacists had between 3 and 16 years of post-qualification experience. All had experience delivering primary care-based medication review clinics for patients receiving multiple drug treatment. Seven pharmacists held post-graduate clinical pharmacy qualifications. Four pharmacists had hospital (ward-based) clinical pharmacy experience.

Study	Intervention and comparison	Population	Outcomes	Comments
	did not collect information on symptoms or examine the patients as this was not part of their professional training.	chronic renal impairment requiring dialysis, resident of long-term care facility, current registration with the nurse-led heart failure service.		
Lenander 2014[123] RCT	Intervention (n=107): The intervention group met a certified geriatric pharmacist prior to a scheduled GP appointment that performed a medication review, using a standard semi-structured protocol that was open for patients' questions and remarks. Computerised patients records were checked for prescriptions, drug indications and plans for evaluation. Drugs and dosages were evaluated to correlate with renal function, good practice and the drug formulary. A patient-centred technique was used, focusing on the patient's questionnaire answers to assess understanding of and concordance with drug treatment. Patients were also asked about prescribers other than their GP and use of non-prescription and herbal drugs. Concluding pharmaceutical advice was given to patients and entered into the computerised patient record. Versus Control (n=102): Usual care. No further details.	Inclusion - Aged 65 years or more with 5 or more medications; already scheduled for an appointment with a GP Exclusion - Not fluent in Swedish; could not answer for themselves; participated in earlier pilot study	Hospital admissions at 12 months	No SDs given
Magid 2013[135] Conducted in the USA RCT	Intervention (n=175): Patients were provided with a properly fitting home BP cuff; trained how to use it; assisted in establishing an account at the Heart360 website; and shown how to automatically upload BPs stored on home BP device into Heart360 account. They were asked to measure their BP at least 3 times weekly and upload BP readings at least weekly. These were automatically organised into summary reports for the	Inclusion - Adults 18 to 79 years of age with diagnosis of hypertension and 2 most recent clinic BP readings above goal (systolic 140mmHg or more, or diastolic 90mmHg or more, or for those with diabetes or CKD, 130 and 80mmHg respectively); prescribed 3 or fewer antihypertensive medications; had a	Number of ED presentations. Hospital admissions at 6 months.	Clinical pharmacist based in a primary care clinic. Permitted to initiate or change antihypertensive medications, to adjust medication

Study	Intervention and comparison	Population	Outcomes	Comments
	pharmacist, giving weekly BP averages and flagging patients with averages above goal. Patients met with a clinical pharmacy specialist who reviewed the home BP measurements, their current BP medications and adherence, provided counselling on lifestyle changes, and adjusted or changed antihypertensive medication as needed, communicating by phone or email. Any medication changes were communicated to the primary care physician through the electronic health record. Versus Control (n=173): Usual care - Patients were advised that their BP was elevated, received written educational materials on managing high BP, diet and physical activity, and were instructed to follow up with their primary care physician; physician was notified of the patient's elevated BP via a note sent to the electronic health record in-box of the physician.	primary care provider who worked at 1 of the 10 participating clinics; and were registered on the KPCO My Chart website Exclusion - Limited life expectancy (for example, in hospice or palliative care); 80 years or older, because aggressive BP reduction may not be appropriate for these patients; recent MI, stroke, PCI or CABG surgery because KPCO patients receive enhance hypertension care as part of intensive cardiac rehabilitation for 1 year after the event; end-stage renal disease, because hypertension care is provided for these patients by nephrology specialists instead of primary care providers; did not speak English; did not have access to the internet and a computer with a USB port and Internet Explorer 6.0 or higher; BP at baseline was already at goal; or home BP cuff could not be validated (for example, home BP reading not within 5mmHg of baseline BP).		doses, and to order laboratory tests related to medication monitoring.
Rozenfeld 2006[176] Conducted in the USA RCT	Intervention (n=230): Appointment with 1 of 5 primary care clinical pharmacy specialists. During the first visit the pharmacist reviewed the patient's prescribed drugs and lifestyle habits, assessed vital signs, screened for adverse drug reactions and other barriers to drug compliance, provided education, and optimised the antihypertensive regimen in keeping with pre-established collaborative hypertension management guidelines. Duration: single visit with	Identified from electronic medical record database. Inclusion - Over 18, office visit and blood pressure measurement within the past 2 years, ICD-9-CM diagnostic code and last documented systolic blood pressure of 160 mm Hg or greater and/or diastolic blood pressure of 100 mm Hg or	Mortality at 12 months.	Concurrent medication/care: treatment for hypertension.

Study	Intervention and comparison	Population	Outcomes	Comments
	subsequent visits or telephone calls scheduled at the discretion of the pharmacist. Versus Control (n=233) Usual care. Instructed to continue their normal schedule of care.	greater. Exclusion - No longer an active patient, refused consent, excluded by their primary care provider.		
Taylor 2003[199] RCT	Intervention (n=33): Four pharmacists joined the study to provide pharmaceutical care at the clinics 2 or 3 afternoons a week. Since the clinics did not have a pharmacy, interventions were limited to clinical services and patient education and did not include dispensing. Patients were asked to bring all their current medications; the pharmacists contacted local pharmacies for dispensing information as necessary. Patients typically met the pharmacist for 20 minutes before seeing a physician during scheduled office visits. Pharmaceutical care: uniform process for preventing or identifying and resolving problems related to drug therapy. Pharmacists were specifically trained to evaluate a therapy's indication, effectiveness and dosage as well as the correctness and practicality of directions, drug-drug interactions, drug-disease interactions, therapeutic duplication, and duration of treatment, untreated indications and expense. Pharmacist reviewed the medical record for medication-related problems, conducted a chart review to ensure that information on drug therapy and allergies was accurately documented, examined the medication history to determine compliance with and complications of medications, and provided comprehensive individualised patient education that included a brief review of the disease,	Inclusion - Adults (18 years or over) who received care at the participating clinics and were identified as being at high risk for medication-related adverse events. High risk: 3 or more of the following factors: 5 or more medications in drug regimen; 12 or more doses per day; 4 or more medication changes in previous year; 3 or more concurrent diseases; history of medication non-compliance; drugs requiring therapeutic monitoring (for example, warfarin, theophylline, phenytoin). Exclusion - Significant cognitive impairment, history of missed office visits, scheduling conflicts, life expectancy <1 year.	Mortality. Number of ED presentations. Hospital admissions at 1 year.	Unequal ED presentations at baseline – Intervention: 18; control: 6.

Study	Intervention and comparison	Population	Outcomes	Comments
	important lifestyle modifications and basic drug information. Pharmacists also provided drug and disease information during follow up visits and answered patients' questions. In addition, the pharmacists monitored patients' responses to drugs and attempted to improve compliance by consolidating medication regimens, reducing dosage frequency, devising medication reminders and teaching patient's techniques for using devices such as inhalers, peak flow meters, glucometers and pill boxes. Versus (n=36) Usual care. Medical record review and patient interviews at baseline and 1 year later performed by pharmacist, including compliance, medication misadventures and medication knowledge. A pharmacist evaluated pharmacotherapy and documented clinical outcomes but provided no advice or recommendation to patient or physician. Data were collected primarily from medical records to minimise contact with control patients.			
Zermansky 2001[229] Conducted in the UK RCT	Intervention (n=608): Clinical review by pharmacist: pharmacist invited patient to his clinic when next review due (or when convenient if no review date set; or at home if patient immobile). Data were gathered before the patient interview on drugs taken and active medical problems. Patient interview: discussed each condition being treated; asked about relevant symptoms (for example, swollen ankles/breathlessness in patients with heart failure); adherence and identify unaddressed problems; consider continuing need for drugs; identify sub-optimal treatment of recognised disease, side effects, drug interactions/contraindications;	Inclusion - Patients aged 65 and over receiving at least one drug on repeat prescription on 1 June 1999. Exclusion - In nursing or residential homes; terminal illness; in clinical trials.	Mortality. Hospital admissions GP attendances at 1 year.	Part of an HTA.

Study	Intervention and comparison	Population	Outcomes	Comments
	consider costs. In conditions for which clinical or pathological monitoring was due, pharmacist directed patient to the practice nurse or doctor. The pharmacist did not physically examine the patients but noted signs that were obvious (for example, swollen ankles, rash). Patients with new clinical problems referred to the doctor. Treatment recommendations were based on national, local and where applicable practice guidelines. The researchers agreed with each practice the level of intervention that the pharmacist could make without seeking prior approval. Versus Control (n=580) Usual care. No further details.			

Table 8: Clinical evidence summary: Community pharmacist based within a community pharmacy

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 Community pharmacist @ pharmacy versus usual care (95% CI)
Mortality	2989 (6 studies) 6 months	⊕⊖⊖⊖ VERY LOW[a,b,c] due to risk of bias, inconsistency, imprecision	RR 0.69 (0.46 to 1.02)	Moderate	
				32 per 1000	10 fewer per 1000 (from 17 fewer to 1 more)
ED presentations	2413 (7 studies) 3 months	⊕⊖⊖⊖ LOW[a,c] due to risk of bias, imprecision	RR 0.63 (0.53 to 0.76)	Moderate	
				93 per 1000	34 fewer per 1000 (from 22 fewer to 44 fewer)
ED presentations	314 (1 study) 12 months	⊕⊕⊖⊖ LOW[a] due to risk of bias		The mean ED presentations in the control groups was 2.68 days	The mean ED presentations in the intervention groups was 0.52 lower (1.43 lower to 0.39 higher)
Hospital admissions	1267 (7 studies) 3 months	⊕⊖⊖⊖ VERY LOW[a,b,c] due to risk of bias, inconsistency, imprecision	RR 0.92 (0.56 to 1.49)	Moderate	
				93 per 1000	7 fewer per 1000 (from 41 fewer to 46 more)
Mean number of hospitalisations	1612 (2 study) 6-12 months	⊕⊕⊕⊖ MODERATE[a] due to risk of bias		The mean number of hospitalisations in the control groups was 0.08 admissions	The mean number of hospitalisations in the intervention groups was 0.02 lower (0.05 lower to 0.1 higher)
GP visits	330 (2 studies) 2-3 months	⊕⊖⊖⊖ VERY LOW[a,b,c] due to risk of bias, inconsistency, imprecision	RR 0.6 (0.17 to 2.06)	Moderate	
				797 per 1000	319 fewer per 1000 (from 662 fewer to 845 more)

(a) Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias.

(b) Downgraded by 1 or 2 increments because: the point estimate varies widely across studies, unexplained by subgroup analysis.

(c) Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.

Narrative findings

Ali 2012: adverse events (total hypoglycaemic and hyperglycaemic events) at 12 months was 5/23 in the intervention group and 28/23 in the control.

Respect trial team 2010: emergency admission episodes per month at 2 years was modelled with the intervention effect estimate (SE): 0.049 (0.290) and the time-intervention effect estimate (SE): -0.042 (0.038).

BC Community pharmacy study: emergency visits during baseline and month 12: intervention - baseline: 0.165, final: 0.043, change: -0.122; control - baseline: 0.377, final: 0.213, change: -0.164.

BC Community pharmacy study: medical visits during baseline and month 12: intervention - baseline: 1.328, final: 0.386, change: -0.942; control - baseline: 1.429, final: 1.730, change: 0.301.

BC Community pharmacy study: hospitalisations during baseline and month 12: intervention - baseline: 0.123, final: 0.078, change: -0.045; control - baseline: 0.143, final: 0.160, change: 0.017.

Gordois 2007 (Armour 200): total GP visits at 6 months: intervention 309/162; control 278/185.

Table 9: Clinical evidence summary: Community pharmacist at the patients' homes

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 Community pharmacist @ home versus usual care (95% CI)
Mortality	427 (2 studies) 6 months	⊕⊕⊖⊖ LOW[a,b] due to risk of bias, imprecision	RR 1.19 (0.77 to 1.85)	Moderate	
				129 per 1000	25 more per 1000 (from 30 fewer to 110 more)
Hospital admissions	1254 (3 studies) 6 months	⊕⊕⊖⊖ LOW[a,b] due to risk of bias, imprecision	RR 1.12 (0.98 to 1.29)	Moderate	
				321 per 1000	39 more per 1000 (from 6 fewer to 93 more)
Quality of Life EQ-5D. Scale from: 0 to 1.	883 (2 study) 6 months	⊕⊕⊖⊖ LOW[a] due to risk of bias		The mean quality of life in the control groups was -0.116	The mean quality of life in the intervention groups was 0.03 higher (0.02 lower to 0.07 higher)

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 Community pharmacist @ home versus usual care (95% CI)
Quality of Life EQ-VAS. Scale from: 1 to 100.	883 (2 study) 6 months	⨁⨁⨀⨀ LOW[a] due to risk of bias		The mean quality of life in the control groups was -1.08	The mean quality of life in the intervention groups was -2.93 lower (6.06 lower to 0.21 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.

Table 10: Clinical evidence summary: Community pharmacist based within a GP practice

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 Community pharmacist @ GP versus usual care (95% CI)
Mortality	1281 (3 studies) 5-12 months	⨁⨀⨀⨀ VERY LOW[a,b] due to risk of bias, imprecision	RR 1.26 (0.54 to 2.96)	Moderate	
				15 per 1000	4 more per 1000 (from 7 fewer to 30 more)
Survival	674 (1 study) 12 months	⨁⨀⨀⨀ VERY LOW[a,b] due to risk of bias, imprecision	HR 0.78 (0.13 to 4.68)	974 per 1000	32 fewer per 1000 (from 956 fewer to 26 more)
ED presentations	260 (1 study) 12 months	⨁⨀⨀⨀ VERY LOW[a,b] due to risk of bias, imprecision	RR 0.98 (0.44 to 2.19)	Moderate	
				85 per 1000	2 fewer per 1000 (from 48 fewer to 101 more)
Mean number of ED visits	889 (1 study) 5 months	⨁⨁⨁⨁ HIGH		The mean number of ED visits in the control groups was 0.23 visits	The mean number of ED visits in the intervention groups was 0.03 lower (0.11 lower to 0.05 higher)

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 Community pharmacist @ GP versus usual care (95% CI)
Hospital admission	674 (1 study) 12 months	⊕⊖⊖⊖ VERY LOW[a,b] due to risk of bias, imprecision	HR 0.5 (0.12 to 2.08)	32 per 1000	16 fewer per 1000 (from 28 fewer to 34 more)
Hospital admissions	260 (1 study) 12 months	⊕⊖⊖⊖ VERY LOW[a,b] due to risk of bias, imprecision	RR 0.79 (0.22 to 2.87)	Moderate	
				39 per 1000	8 fewer per 1000 (from 30 fewer to 73 more)
Mean number of hospitalisations	889 (1 study) 5 months	⊕⊕⊕⊕ HIGH		The mean number of hospitalisations in the control groups was 0.11 admissions	The mean number of hospitalisations in the intervention groups was 0.03 higher (0.03 lower to 0.09 higher)
Mean number of GP visits	889 (1 study) 5 months	⊕⊕⊕⊕ HIGH		The mean number of GP visits in the control groups was 4.97 GP visits	The mean number of GP visits in the intervention groups was 0.19 higher (0.59 lower to 0.97 higher)
Adverse events	674 (1 study) 12 months	⊕⊖⊖⊖ VERY LOW[a,b] due to risk of bias, imprecision	RR 1.21 (0.94 to 1.57)	Moderate	
				236 per 1000	50 more per 1000 (from 14 fewer to 135 more)

(a) Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias.
(b) Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.

Table 11: Clinical evidence summary: Clinical pharmacist based within a community clinic

Outcomes	No of	Quality of the	Relative	Anticipated absolute effects

	Participants (studies) Follow up	evidence (GRADE)	effect (95% CI)	Risk with Control	Risk difference with Clinical pharmacist @ clinic versus usual care (95% CI)
Mortality	2561 (4 studies) 1-2 years	⊕⊕⊕⊖ MODERATE[b] due to imprecision	RR 0.8 (0.59 to 1.09)	Moderate	
				42 per 1000	8 fewer per 1000 (from 17 fewer to 4 more)
Mean number of ED visits	231 (2 studies) 1 years	⊕⊕⊖⊖ LOW[a] due to risk of bias		The mean number of ED visits in the control groups was 0.6 ED visits per patient	The mean number of ED visits in the intervention groups was 0.11 lower (0.37 lower to 0.15 higher)
Mean number of hospitalisations	338 (3 studies) 1-2 years	⊕⊕⊖⊖ LOW[a] due to risk of bias		The mean number of hospitalisations in the control groups was 0.5 admissions per person	The mean number of hospitalisations in the intervention groups was 0.12 standard deviations higher (0.1 lower to 0.33 higher)
Mean number of GP visits	231 (2 studies) 1 years	⊕⊕⊖⊖ LOW[a] due to risk of bias		The mean number of GP visits in the control groups was 2.8 GP visits per person	The mean number of GP visits in the intervention groups was 0.09 higher (0.18 lower to 0.37 higher)
Total hospitalisations	227 (1 study)	⊕⊕⊕⊖ MODERATE[b] due to risk of bias	RR 0.31 (0.17 to 0.58)	Moderate	
				310 per 1000	214 fewer per 1000 (from 130 fewer to 257 fewer)

(a) Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias.
(b) Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.

Table 12: Clinical evidence summary: Clinical pharmacist at the patients' homes

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 Clinical pharmacist @ home versus usual care (95% CI)

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 Clinical pharmacist @ home versus usual care (95% CI)
Mortality	154 (1 study) 6 months	⨁⨁⊖⊖ LOW[b] due to risk of imprecision	RR 1.21 (0.64 to 2.29)	182 per 1000	38 more per 1000 (from 66 fewer to 235 more)
Hospital admission	480 (1 study) 60 days	⨁⊖⊖⊖ VERY LOW[a,b] due to risk of bias, imprecision	HR 0.8 (0.6 to 1.07)	233 per 1000	**42 fewer per 1000 (from 86 fewer to 14 more)**
Hospital admission	486 (2 studies) 3-6 months	⨁⊖⊖⊖ VERY LOW[a,b] due to risk of bias, imprecision	RR 0.90 (0.68 to 1.19)	Moderate	
				317 per 1000	32 fewer per 1000 (from 101 fewer to 60 more)
GP visits	124 (1 study) 12 months	⨁⊖⊖⊖ VERY LOW[a,b] due to risk of bias, imprecision	RR 0.73 (0.55 to 0.95)	Moderate	
				746 per 1000	201 fewer per 1000 (from 37 fewer to 336 fewer)

(a) Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias.
(b) Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.

Table 13: Clinical evidence summary: Clinical pharmacist based within a GP practice

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 Clinical pharmacist @ GP versus usual care (95% CI)
Mortality	2581 (5 studies) 12 months	⨁⊖⊖⊖ VERY LOW[a,b,c] due to risk of bias, indirectness, imprecision	RR 0.58 (0.34 to 0.97)	Moderate	
				25 per 1000	11 fewer per 1000 (from 1 fewer to 16 fewer)
Mortality	1074 (1 study) 4.7 years	⨁⨁⨁⨁ HIGH	HR 0.96 (0.8 to 1.15)	308 per 1000	10 fewer per 1000 (from 53 fewer to 37 more)
ED presentations	69	⨁⊖⊖⊖	RR 0.73	Moderate	

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 Clinical pharmacist @ GP versus usual care (95% CI)
	(1 study) 1 years	VERY LOW[a,b] due to risk of bias, imprecision	(0.22 to 2.35)	167 per 1000	45 fewer per 1000 (from 130 fewer to 225 more)
Mean number of ED visits	326 (1 study) 6 months	⊕⊕⊕⊕ HIGH		The mean number of ED visits in the control groups was 0.05 ED visits per person	The mean number of ED visits in the intervention groups was 0.01 lower (0.06 lower to 0.04 higher)
Hospital admissions	1164 (4 studies) 12 months	⊕⊖⊖⊖ VERY LOW[a,b,c] due to risk of bias, indirectness, imprecision	RR 0.86 (0.32 to 2.32)	Moderate	
				96 per 1000	13 fewer per 1000 (from 65 fewer to 127 more)
Mean number of hospitalisations	326 (1 study) 6 months	⊕⊕⊕⊕ HIGH		The mean number of hospitalisations in the control groups was 0.04 Hospital admissions per person	The mean number of hospitalisations in the intervention groups was 0.01 lower (0.05 lower to 0.03 higher)
Hospital admission	1074 (1 study) 4.7 years	⊕⊕⊕⊕ HIGH	HR 0.97 (0.87 to 1.08)	647 per 1000	11 fewer per 1000 (from 51 fewer to 28 more)
Adverse events	506 (2 studies) 2 years	⊕⊖⊖⊖ VERY LOW[a,c] due to risk of bias, imprecision	RR 0.29 (0.03 to 2.8)	Moderate	
				9 per 1000	6 fewer per 1000 (from 9 fewer to 16 more)
GP visits	167 (2 studies) 6 months	⊕⊕⊖⊖ LOW[a] due to risk of bias	RR 0.96 (0.79 to 1.17)	Moderate	
				714 per 1000	29 fewer per 1000 (from 150 fewer to 121 more)

(a) Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias.

(b) Downgraded by 1 or 2 increments because: the majority of the evidence was from studies that had higher/lower drug doses than the recommended dose.

(c) Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.

10.4 Economic evidence

Published literature

Ten health economic studies were identified from eleven papers with the relevant comparison and have been included in this review.[26,53,61,63,79,94,103,151,161,172,191,214] These are summarised for each stratum in the health economic evidence profiles below (Table 14 to Table 17) and the health economic evidence tables in Appendix E.

Twelve 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 14: Health economic evidence profile: enhanced-role community pharmacists at community pharmacy versus usual care

Study	Applicability	Limitations	Other comments	Incremental cost	Incremental effects	Cost-effectiveness	Uncertainty
Bond 2007[53] & Scott 2007[187](UK)	Partially applicable[(a)]	Potentially serious limitation[(b)]	**Population:** Patients over 17 years with coronary heart disease (CHD)identified from general practice system **Study design**: economic evaluation alongside a randomised controlled trial (RCT), The Community Pharmacy Medicines Management Service RCT. **Follow-up**: 12 months **Intervention 1:** Standard care **Intervention 2:** Initial consultation with a community pharmacist who received training designed and delivered by the Centre for Pharmacy Postgraduate Education (CPPE) to review appropriateness of therapy, compliance life style, social and support issues.	£147	0.02 QALYs	Pharmacist intervention cost effective. ICER: £7,350 per QALY gained	A threshold analysis showed that reducing intervention cost per patient by 35 % to a mean cost of £76 (compared to £118 in the base case) will result in cost neutrality.
Gordois 2007 [79] (Australia)	Partially applicable[(c)]	Potentially serious limitations[(d)]	**Population:** Patients with asthma attending a community pharmacy who met certain criteria regarding the severity of their asthma for example, used reliever	£278	0.131 QALYs	Pharmacist intervention cost effective (ICER: £2,121 per QALY)	An analysis where no annual patient review was performed to maintain the improvement in asthma gained during the first 6 months of the program. The benefits were assumed to be

Study	Applicability	Limitations	Other comments	Incremental cost	Incremental effects	Cost-effectiveness	Uncertainty
			medication more than three times a week. **Study design:** Decision analytic model. **Intervention 1:** Usual care **Intervention 2:** Pharmacy Asthma Care Program				maintained but the costs of the annual reviews were not incurred. This resulted in a more favourable result for the community pharmacist intervention. Various one-way sensitivity analyses were performed including varying the time horizon, varying the costs and discount rates. The only analysis that changed the conclusion was when the time horizon was just 6 months (that is, the trial period) where the ICER was £28,953 per QALY gained.
Houle 2012[94] (Canada)	Partially applicable[(e)]	Potentially serious limitations [(f)]	**Population:** Patients with diabetes mellitus and uncontrolled hypertension **Study design:** Decision analytic model. **Intervention 1:** Usual care **Intervention 2:** Cardiovascular risk reduction counselling by a pharmacist-nurse team along with a hypertension education brochure.	Saves £150	Absolute risk reduction: 0.54% for myocardial infarction 0.66% for stroke 0.60% for development of heart failure exacerbation	Pharmacist intervention dominant due to improving measured health outcomes and reducing costs.	Sensitivity analysis explored the impact of assuming the blood pressure reduction lasted for only 6 months and then returned to the same levels in both arms. The pharmacist intervention remained dominant. Doubling time spent by the pharmacist still resulting in cost savings and thus dominance.

Study	Applicability	Limitations	Other comments	Incremental cost	Incremental effects	Cost-effectiveness	Uncertainty
Jodar-Sanchez 2015[103](Spain)	Partially applicable[(g)]	Potentially serious limitations [(h)]	**Population:** Older adults aged 65 years or over, with polypharmacy, defined as individuals taking five or more medications per day. **Study design:** cluster Randomised Clinical Trial (RCT)(ConSIGUE) **Follow-up**: 6 months **Intervention 1:** Normal dispensing with no pharmacist follow-up **Intervention 2:** Community pharmacies implemented a medication review and follow-up service where patients received 6 consultations, with a frequency of 1 visit every 1.2 months. In the first month, the pharmacist developed action plan that was shared with the patient's GP.	Saves £262	0.0156 QALYs	Pharmacist intervention dominant.	None reported
Respect trial team 2010A [172](UK)	Directly applicable [(i)]	Minor limitations [(j)]	**Population:** People aged > 75 years who are living at home, receiving repeat prescriptions for five or more medications. **Study design:** Randomised multiple interrupted time series analyses (clinical results reported in Respect Trail Team 2010[173],	£192	0.019 QALYs	Pharmacist intervention cost effective. ICER: £10,000 per QALY gained	Several scenario analyses were undertaken to test the effect of alternative assumptions on the results. None of these analyses changed the ICER or the probability of the intervention being cost effective. Heterogeneity between different types of patients was also

Study	Applicability	Limitations	Other comments	Incremental cost	Incremental effects	Cost-effectiveness	Uncertainty
			which was included in the clinical review) **Follow-up**: 12 months **Intervention 1:** Usual care **Intervention 2:** Pharmaceutical care adapted to British primary care. The intervention was provided by pharmacists who received training that covered the theory and practice of pharmaceutical care, practical exercises in collaborating with the GPs. Training took place just before the start of each 12 months period.				examined. Results were presented by type of patient and were as follows: 1- 75 year old with 5 repeat drugs: ICER £4,661 2- 80 year old with 7 repeat drugs: ICER £9,515 3- 85 year old with 10 repeat drugs: ICER £17,980 4- 90 year old with 15 repeat drugs: £35,185
Vegter 2014[214] (Netherland)	Partially applicable[(k)]	Potentially serious limitations[(l)]	**Population:** Patients initiating lipid lowering therapy for primary prevention (40%) or secondary prevention (60%) of cardiovascular events. **Study design:** Markov model **Time horizon:** Lifetime **Intervention 1: (n= 502)** Historic control receiving usual care	Saves £27	0.084 QALYs	Pharmacist intervention dominant.	The results were robust to changes in the model parameters and assumptions. The only parameters that resulted in a positive ICER were a higher age (ICER: £1,562), lower statin effectiveness (ICER: £1,079) and lower CVE incidence (ICER: £758)

Study	Applicability	Limitations	Other comments	Incremental cost	Incremental effects	Cost-effectiveness	Uncertainty
			Intervention 2: (n=500) Pharmaceutical care program delivered at 9 community pharmacies (MeMO [medication monitoring and optimisation) based on continuous monitoring and optimisation of lipid lowering therapy in new patients who are identified as non-adherent.				

Abbreviations: ICER: incremental cost-effectiveness ratio; QALY: quality-adjusted life years; RCT: randomised controlled trial.

(a) Some uncertainty regarding the applicability of resource use and cost data from 2004 to the current NHS context. The perspective used is NHS only, as opposed to NHS and PSS. QALYs were not reported but could be calculated from data reported in the paper.

(b) RCT based analysis, so by definition the evidence is based on one study and does not reflect all evidence in this area. Limited sensitivity analysis and no bootstrapping reported.

(c) The analysis is from an Australian healthcare perspective and may not be applicable to the UK NHS perspective.

(d) The transition probabilities in the model are derived from a single RCT with a follow up of just 6 months. Assumptions were made that the treatment effects would be maintained in the long term. The discount rate used was higher than the 3.5% in the NICE reference case, however, a sensitivity analysis with undiscounted costs and QALYs was done and the conclusion did not change. Quality of life was not measured using the EQ5D.

(e) The analysis is from a Canadian healthcare perspective and may not be applicable to the UK NHS perspective. QALYs are not estimated and impacts on quality of life and mortality are not assessed.

(f) The model uses an intermediate outcome taken from a randomised controlled trial to predict impacts on myocardial infarctions, stroke and heart failure. These outcomes are not directly measured and there is therefore some uncertainty regarding modelling process. None-the-less the model is built on good data.

(g) Some uncertainty regarding the applicability of resource use and costs from Spain in 2014 to current UK NHS perspective. The perspective used is that of the Spanish NHS.

(h) RCT based analysis, so by definition the evidence is based on 1 study and does not reflect all evidence in this area. The follow-up is 6 months, which is unlikely to capture all differences in costs and outcomes. No sensitivity analysis is presented.

(i) Some uncertainty regarding the applicability of resource use and costs from 2004-2005 to current NHS context.

(j) RCT based analysis, so by definition the evidence is based on one study and does not reflect all evidence in this area. Follow-up was for 12 months, which might not be long enough to capture all the differences in costs and outcomes.

(k) Some uncertainty regarding the applicability of resource use and costs from The Netherland in 2012 to current NHS context. Discount rates used for costs (4%) and outcomes (1.5%) are not in line with NICE Reference Case. Utilities were obtained from published studies.

(l) The source of intervention effectiveness estimate is from a single, non-randomised study, so by definition, does not reflect all evidence in this area. The Base case analysis assumes that intervention effectiveness persists over the lifetime time horizon. It is not clear if the unit costs used are from national or local sources, which might limit the generalisability of the results.

Table 15: Health economic evidence profile: enhanced-role community pharmacists at home versus usual care

Study	Applicability	Limitations	Other comments	Incremental cost	Incremental effects	Cost-effectiveness	Uncertainty
Desborough 2012 [61](UK)	Partially applicable[(a)]	Potentially serious limitations[(b)]	**Population:** Patients 65 years or older and registered with a GP in Norfolk, residing in their own home and referred to the service by anyone in their care that identified they were having difficulties managing their medication. **Study design:** Before and after study. **Follow up:** 6 months. **Intervention 1:** Usual care **Intervention 2:** Medicine management assessment and support service.	Saves £307	-0.019 QALYs	Usual care cost effective compared to pharmacist intervention (ICER: £16,157)	Sensitivity analyses were performed by varying some of the costs of inpatient stay and central administration costs. The results remained cost saving in favour of the community pharmacist intervention.
Pacini 2007[161] (UK)	Partially applicable[(c)]	Potentially serious limitations[(d)]	**Study design:** economic evaluation alongside a randomised controlled trial (RCT)[the HOMER trial[92]] **Population:** Patients aged > 80 years who were admitted to as an emergency to an acute or community hospital in Norfolk or Suffolk (for any cause), returning to their own home or warden-controlled accommodation and taking two or more drugs. **Follow-up:** 6 months	£407	0.0075 QALYs	Pharmacist intervention not cost effective. ICER: £54,454 per QALY gained	In all scenario analyses, the ICER was > £20,000/ QALY gained, except when only intervention cost was considered, where it was £17,070.

Study	Applicability	Limitations	Other comments	Incremental cost	Incremental effects	Cost-effectiveness	Uncertainty
			Intervention 1: Usual care **Intervention 2:** Two home visits by a community pharmacist within 2 and 8 weeks of discharge to educate the patients and carers about their drugs, remove out-of- date drugs, inform GP of drug reactions or interactions and inform local pharmacist if adherence aid was needed.				

Abbreviations: ICER: incremental cost-effectiveness ratio; QALY: quality-adjusted life years; RCT: randomised controlled trial.

(a) The study does not measure health benefits in QALYs and no baseline EQ5D was measured in the before intervention group so QALY calculations would rely on assumptions based on the baseline of the after intervention group.

(b) The analysis is based on a single before and after evaluation of the service change and so may be subject to confounding. A single patient group is used to assess the effects both before and after and so this increases the risk of bias further.

(c) Some uncertainty regarding the applicability of resource use and costs from the year 2000 to current NHS context.

(d) RCT based analysis, so by definition the evidence is based on one study and does not reflect all evidence in this area. Follow-up was for 6 months, which might not be long enough to capture all the differences in costs and outcomes.

Table 16: Health economic evidence profile: enhanced-role community pharmacists at GP practice versus usual care

Study	Applicability	Limitations	Other comments	Incremental cost	Incremental effects	Cost-effectiveness	Uncertainty
Simpson 2015[191] (Canada)	Partially applicable[(a)]	Potentially serious limitations[(b)]	**Population:** Patients with type 2 diabetes being treated in primary care. **Study design:** Within trial analysis (RCT)	Saves £102	0.26% reduction in UKPDS risk score.	Pharmacist intervention is dominant.	10,000 bootstrap replications were calculated from the main analysis to estimate confidence intervals. A multiple imputation was performed to estimate the full sample of 258 patients and 50,000

Study	Applicability	Limitations	Other comments	Incremental cost	Incremental effects	Cost-effectiveness	Uncertainty
			Follow up: 12 months. **Intervention 1:** Usual care **Intervention 2:** Addition of pharmacist to primary care teams.				bootstrap replications were calculated. No difference in the outcome was observed.

Abbreviations: ICER: incremental cost-effectiveness ratio; QALY: quality-adjusted life years; RCT: randomised controlled trial.

(a) Costs in this study may not be applicable to the UK NHS perspective and health benefits are not measured in QALYs.

(b) RCT based analysis, so by definition the evidence is based on one study and does not reflect all evidence in this area. Follow-up was for 12 months, which might not be long enough to capture all the differences in costs and outcomes.

Table 17: Health economic evidence profile: enhanced-role clinical pharmacists at GP practice versus usual care

Study	Applicability	Limitations	Other comments	Incremental cost	Incremental effects	Cost-effectiveness	Uncertainty
Neilson 2015 [151] (UK)	Partially applicable[(k)]	Potentially serious limitations[(l)]	**Population:** Patients who are 18 years or older, living in their own home and receiving medication for pain. **Study design:** Within trial analysis (RCT) **Follow up:** 6 months **Intervention 1** Usual care **Intervention 2** Pharmacy medication review only. **Intervention 3** Pharmacy medication review with pharmacist prescribing.	£54 for intervention 2 relative to usual care (£78 for intervention 3 relative to usual care)	0.0097 for intervention 2 relative to usual care (0.0069 QALYs for intervention 3 relative to usual care)	£5,567 per QALY for intervention 2 relative to usual care (£11,304 per QALY for intervention 3 relative to usual care)	Sensitivity analyses were performed on a data set with multiple imputations used where values were missing. The ICER for the non-prescribing pharmacist versus usual care would then increase to £19,000 per QALY and for the prescribing pharmacist versus usual care it would increase to £73,529 per QALY gained.

Abbreviations: ICER: incremental cost-effectiveness ratio; QALY: quality-adjusted life years; RCT: randomised controlled trial.

(a) The population is a specific population that may not fully represent people at risk of an acute medical emergencies population.

(b) The analysis is based on a single RCT with only a 6 month follow up period. Quality of life was not measured using the EQ5D. A probabilistic sensitivity analysis was not performed and may well change the conclusion of the analysis due to the small differences in quality of life scores.

10.5 Evidence statements

Clinical

Community pharmacist:

Fourteen studies comprising 2413 participants evaluated the role of community pharmacists (community pharmacist's strata) for improving outcomes in adults and young people at risk of an AME, or with a suspected or confirmed AME. The evidence suggested that enhanced role of a community pharmacists may provide a benefit in reduced mortality (6 studies, very low quality), ED presentations (7 studies, low quality), mean ED presentations (1 study, low quality), GP visits (2 studies, very low quality) and hospital admissions (7 studies, very low quality) and mean number of hospitalisation (2 studies, moderate quality).

Three studies comprising 1254 participants evaluated the role of community pharmacists (patient's home strata) for improving outcomes in adults and young people at risk of an AME, or with a suspected or confirmed AME. The evidence suggested that home visits from a community pharmacist were associated with higher mortality (2 studies, low quality) and more hospital admissions (3 studies, low quality) but no effect on quality of life (2 studies, low quality).

Four studies comprising 3824 participants evaluated the role of community pharmacists (GP practice strata) for improving outcomes in adults and young people at risk of an AME, or with a suspected or confirmed AME. The evidence suggested that the community pharmacist within a GP practice may provide a benefit in reduced hospital admissions (2 studies, very low quality). However, the evidence suggested there was no effect on survival (1 study, very low quality), ED presentations (1 study, very low quality), mean number of hospitalisations (1 study, high quality) and GP visits (1 study, high quality). The evidence suggested a possible increase in adverse events (1 study, very low quality) and mortality (3 studies, very low quality).

Clinical Pharmacist:

Five studies comprising 2805 participants evaluated the role of clinical pharmacists (community clinics strata) for improving outcomes in adults and young people at risk of an AME, or with a suspected or confirmed AME. The evidence suggested that clinical pharmacists provided a benefit in reduced mortality (4 studies, moderate quality), hospitalisations (1 study, moderate quality) and number of ED visits (2 studies, low quality). The evidence suggested there was no effect on the number of GP visits (2 studies, low quality) or mean number of hospitalisations (3 studies, low quality).

Four studies comprising 1765 participants evaluated the role of clinical pharmacists (patient's home strata) for improving outcomes in adults and young people at risk of an AME, or with a suspected or confirmed AME. The evidence suggested that home visits from a clinical pharmacist may provide a benefit in reduced hospital admission (3 studies; 2 report relative risk and 1 reports a hazard ratio, very low quality) and GP visits (1 study, very low quality). The evidence suggested that there was a possible increase in mortality (1 study, low quality) with clinical pharmacists.

Eight studies comprising 2581 participants evaluated the role of clinical pharmacists (GP practice strata) for improving outcomes in adults and young people at risk of an AME, or with a suspected or confirmed AME. The evidence suggested that adverse events (2 studies, very low quality) and hospital admissions (4 studies reporting a relative risk, very low quality) were reduced by use of a clinical pharmacist but no difference was seen for GP visits (2 studies, low quality) or hospitalisations

(1 study reporting a mean and 1 study reporting a hazard ratio (high quality). There was a possible decrease in mortality from 5 studies when reported as risk ratio (very low quality), but no difference from 1 study which reported a hazard ratio (high quality). There was a possible decrease in ED visits from 1 study which reported a dichotomous outcome (low quality), but no difference from one study which reported a continuous outcome (high quality).

Economic

- Two cost-utility analyses found that enhanced-role **community pharmacists** at community pharmacies dominated usual care by reducing costs and improving health outcomes. Both studies were assessed as being partially applicable with potentially serious limitations.
- One cost-effectiveness analysis found that enhanced-role community pharmacists at community pharmacies dominated usual care by reducing costs and improving health outcomes. The study was assessed as being partially applicable with potentially serious limitations.
- Three cost-utility analyses found that enhanced-role **community pharmacists** at community pharmacies were cost effective compared to usual care (ICERs: £7,350; £2,121 and £10,000 per QALY gained). Two of these studies were assessed as being partially applicable with potentially serious limitations; one of these studies was assessed as being directly applicable with minor limitations.
- One cost-utility analysis found that an enhanced role **community pharmacist at the patient's home** was not cost effective (£54,454 per QALY) compared with usual care. The study was assessed as being partially applicable with potentially serious limitations.
- One cost-utility analysis found that usual care was cost effective compared with **community pharmacist at the patient's home** (£16,157 per QALY). The study was assessed as being partially applicable with potentially serious limitations.
- One cost-effectiveness analysis found that enhanced-role **community pharmacists at the GP surgery** dominated usual care by reducing costs and improving health outcomes. The study was assessed as being partially applicable with potentially serious limitations.
- One cost-utility analysis found that an enhanced-role **clinical pharmacist at the GP surgery** was cost effective compared to usual care (ICER: £5,567 per QALY gained). This study was assessed as being partially applicable with potentially serious limitations.

10.6 Recommendations and link to evidence

Recommendations	**4. For people who are at increased risk of developing a medical emergency:** • **provide advanced community pharmacy-based services** • **consider providing advanced pharmacist services in general practices** **5. For people at risk of an acute medical emergency, do not commission pharmacists to conduct medication reviews in the home unless needed for logistical or clinical reasons.**
Research recommendations	**-**
Relative values of different outcomes	Mortality, avoidable adverse events, quality of life, patient and/or carer satisfaction, number of ED presentations and unplanned GP attendances were considered by the guideline committee to be critical outcomes. Hospital admissions were considered important outcomes.
Trade-off between benefits and harms	The review was separated into 6 strata split by both the provider of the intervention, either a community or clinical pharmacist, and the location. The locations of the intervention for the community pharmacist were at a community pharmacy, within the patient's home, or within a GP practice. The locations of the intervention for the clinical pharmacist were at a community clinic, within the patient's home, or within a GP practice. 'Community clinic' in this context refers to a service for patients with specific chronic conditions such as pulmonary disease or diabetes. Thirty seven studies from 56 papers were included overall. The majority of these contain some type of medication review and patient education intervention, though there was significant heterogeneity in the individual elements across the identified evidence. The majority of studies either recruited patients who had a specific long-term condition requiring medications, or a heterogeneous population taking varied medications. Several of the latter studies restricted the population to the elderly. <u>Community pharmacist:</u> Twenty one randomised controlled trials were included within the community pharmacist strata overall: **Community pharmacist based within a community pharmacy** Fourteen randomised controlled trials were included for the community pharmacy stratum with the evidence suggesting a benefit for enhanced roles for community pharmacists in reduced mortality, ED presentations, GP visits and hospital admissions. No evidence was identified for quality of life, GP attendances or patient and/or carer satisfaction. **Community pharmacist at the patients' homes** Three randomised controlled trials were included for the 'at patient's home' stratum. The evidence suggested that home visits from a community pharmacist were associated with higher mortality and more hospital admissions but no effect on quality of life. **Community pharmacist based within a GP practice** Four randomised controlled trials were included for the 'within a GP practice'

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Research recommendations	**-**
	stratum. The evidence suggested that the community pharmacist within a GP practice may provide a benefit in reduced hospital admissions. However, the evidence suggested there was no effect on survival, ED presentations, mean number of hospitalisations and GP visits. The evidence suggested a possible increase in adverse events and mortality. No evidence was identified for `quality of life or patient and/or carer satisfaction. <u>Clinical Pharmacist</u> Seventeen randomised controlled trials were included within the clinical pharmacist strata overall: **Clinical pharmacist based within a community clinic** Five randomised controlled trials were included for the 'within a community clinic' stratum. The evidence suggested that clinical pharmacists provided a benefit in reduced mortality, hospitalisations and number of ED visits. The evidence suggested there was no effect on the number of GP visits or hospitalisations (reported as a mean). No evidence was identified for avoidable adverse events, quality of life, or patient and/or carer satisfaction. **Clinical pharmacist at the patients' homes** Four randomised controlled trials were included for the 'at patient's home' stratum. The evidence suggested that home visits from a clinical pharmacist may provide a benefit in reduced hospital admission and GP visits. The evidence suggested a possible increase in mortality with clinical pharmacists. No evidence was identified for avoidable adverse events, ED visits, or patient and/or carer satisfaction. **Clinical pharmacist based within a GP practice** Eight randomised controlled trials were included for within a GP practice stratum. The evidence suggested that adverse events (serious adverse events) and hospital admissions (reported as a relative risk) were reduced by use of a clinical pharmacist but no difference was seen for GP visits or hospitalisations (reported as a mean and a hazard ratio). The outcomes were reported using different methods in the evidence. There was a possible decrease in mortality from 5 studies when reported as risk ratio, but no difference from 1 study which reported a hazard ratio. There was a possible decrease in ED visits from 1 study which reported a dichotomous outcome, but no difference from 1 study which reported a continuous outcome. No evidence was identified for quality of life or patient and/or carer satisfaction. The committee discussed this apparent inconsistency when making their recommendation, and noted that the higher quality evidence consistently showed no difference from using

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Research recommendations	**-**
	a clinical pharmacist in a GP practice. **Overall** The committee discussed the evidence and felt that given the body of evidence and consistency in benefit, a strong recommendation could be made for the enhanced use of community and clinical pharmacists with interventions based within the community pharmacy. The committee agreed that the evidence was generalisable to recommend for all people at increased risk of developing a medical emergency. Overall, there was evidence of effectiveness to consider introducing an advanced role for pharmacists within GP practices, however, without direct comparisons the committee were unable to make a judgement on the exact role or skills required when commissioning these services. The committee noted that there is a 3-year pilot study for clinical pharmacists in GP practice that has just started (The General Practice Forward View).[152] The committee discussed the evidence concerning pharmacists travelling and performing an intervention within a patient's home. They deemed that the evidence was weak, and often showed that these visits were detrimental compared to usual care (most often the usual service from a GP); even when clinical pharmacists were involved. They judged that a negative recommendation for the commissioning of services that take place at patients' homes would be most appropriate at this time.
Trade-off between net effects and costs	Ten economic evaluations were included in this review, of which 6 were in the stratum of community pharmacists based in community pharmacies, 1 was a community pharmacist in a general practice, 1 was a clinical pharmacist in a general practice and 2 were for community pharmacists at the patient's home. <u>Community pharmacists</u> For the community pharmacist interventions provided at a community pharmacy, the net costs ranged from cost saving to an increase in cost of £278 per patient. All the interventions showed a health benefit, which for all of the studies that showed an increase in costs was measured in QALYs, so cost effectiveness could be assessed. The ICERs went up to £10,000 per QALY and therefore this intervention was shown to be cost effective. Various sensitivity analyses showed that these results were robust to changes. The committee discussed the economic evidence and agreed that there is strong economic evidence to support the cost effectiveness of enhanced role community pharmacists' interventions at community pharmacies. The interventions described in the studies covered conducting medicines' use reviews and providing support for those starting on newly prescribed medicines. These interventions reflected the advanced services currently provided at community pharmacists in England, which have been established for some time and the accumulated evidence strongly support the continuation of their provision. Thus, the committee felt that enhancing the role

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Research recommendations	**-**
	of community pharmacists to allow the expansion in the provision of these services represents good value for money by improving health outcomes while being either cost saving or cost effective; with ICERs well below the cost effectiveness threshold. While all studies showed evidence of cost effectiveness, the ones in the UK (and in particular, the one study that was assessed as directly applicable and only minor limitations) indicated an increase in costs overall from this intervention. <u>Pharmacists at GP practices</u> For **community pharmacist** interventions at GP practices, 1 Canadian study showed that the intervention was dominant, as it led to saving of £102 per patient and improved health outcomes. However, the outcome was not measured in QALYs. For **clinical pharmacist** interventions at GP practices, 1 UK study showed the intervention was cost effective with an ICER of £5,567 per QALY gained. When the intervention was delivered by a prescribing pharmacist, the ICER increased to £11,304 per QALY gained. No evidence was found for clinical pharmacist interventions at any other community-based setting. The evidence for clinical pharmacists' interventions was either positive or neutral in terms of health outcomes and has been shown to be cost effective. The committee noted that although there were no differences between prescribing and non-prescribing pharmacists based on the clinical evidence, 1 UK economic evaluation showed that prescribing pharmacists were not considered cost effective compared to non-prescribing pharmacists. The committee discussed this particular finding in detail and concluded that this could be due to the cost of the prescribing qualification, which would possibly require longer follow-up to be offset by improvement in outcomes. The committee also noted that both the interventions delivered by prescribing and non-prescribing pharmacists were still cost effective when compared to usual GP-delivered care, so did not believe that prescriber status should be specified in the recommendation. Overall, the committee felt that clinical pharmacist interventions provided at GP practices were at least as effective as usual care and could potentially have an additional positive impact on GPs' workload by freeing up their time to focus on the more complex patients. The evidence from the clinical pharmacist role at community clinics, though not directly applicable to the UK setting, could also be extrapolated to the role at a GP practice. The committee was aware of the recently published GP Forward View, from NHS England, which supported this conclusion.[152] The report outlined plans to provide an additional 1500 clinical pharmacists to join the GP practice workforce by 2020, acknowledging their role in the GP practice workforce and their expected positive impact on GPs' workload. For community pharmacists' interventions at GP practices, the evidence of health benefit was weaker, with some outcomes showing harm (adverse events and mortality). However, the committee noted that this was based on low quality evidence, and could be interpreted as indicating that community pharmacists would

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Research recommendations	**-**
	need more training, in terms of their clinical skills (for example, physical examination and history taking), and more time to integrate into the GP practice team in order to realise the benefit of their adoption of practice-based roles. The committee was aware of current initiatives by NHS England supporting extended roles for pharmacists, including the introduction of the Pharmacy Integration Fund. This includes the recent creation of a new role of a "Practice Pharmacist", by which pharmacists from any practice background (hospital, community or primary care) could work at GP practices as long as they have the necessary skills and competencies. The committee also noted that, given the favourable economic evidence, the initial investment to enhance the skills of pharmacists to undertake these practice-based roles would show positive returns in the long term. <u>Home setting</u> For the community pharmacist interventions at the patient's home, 2 UK studies had contradictory results in terms of costs and health outcomes but had the same conclusion regarding cost effectiveness. One study showed that the intervention was cost saving (saving £307 per patient) but led to reduction in quality of life (loss of 0.019 QALYs), despite increasing adherence by 10%. The ICER for usual care in this study was calculated to be £16,157 per QALY gained, indicating that the pharmacist intervention was not cost effective compared to usual care. The second study showed that the pharmacist intervention increased cost (£407 per patient) and had a relatively small increase in QALYs of 0.0075, which meant it was not cost effective with an ICER of £54,454 per QALY. The evidence of health benefit was contradictory and the economic evidence showed that these interventions were not cost effective. There was no economic evidence relating to the clinical pharmacist interventions at patients' homes. Hence, the committee felt that these interventions should not be provided. The committee noted that the evidence, however, was primarily focused on visits to the patients' homes and may not apply to pharmacists' interventions at residential and care homes, the evidence for which was not specifically reviewed in this question. The committee was aware of on-going research in this area.
Quality of the evidence	<u>Community pharmacist</u> For the community pharmacy stratum the evidence was graded at low or very low due to a combination of risk of bias and imprecision. Three out of 4 outcomes containing a pooled estimate were further downgraded for inconsistency. These were the outcomes mortality, hospital admissions and GP visits. For the 'at home' stratum the majority of evidence was of moderate quality due to risk of bias, with the outcome mortality further downgraded for imprecision. For the 'within a GP practice' stratum the evidence was either very low or high quality, with evidence downgraded for a combination of risk of bias and imprecision. All economic studies of community pharmacists were assessed as partially applicable

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Research recommendations	**-**
	with potentially serious limitations. <u>Clinical pharmacist</u> For the clinical pharmacist in a community clinic stratum the evidence was graded at moderate or low due to risk of bias and/or imprecision. For the clinical pharmacist at patients home stratum the evidence was graded at low or very low due to a combination of risk of bias and imprecision. For the clinical pharmacist 'within a GP practice' stratum the majority of evidence was either very low or high quality, with evidence downgraded for a combination of risk of bias and imprecision. The outcomes mortality and hospital admissions were further downgraded for inconsistency. The committee assessed the applicability of evidence to the UK practice. In particular, they noted that the evidence supporting the use of clinical pharmacists working within a community clinic, such as a stand-alone haemodialysis clinic, would not be applicable to UK. Therefore, they judged that a recommendation in this area would not be appropriate. All economic studies of clinical pharmacists were assessed as partially applicable with potentially serious limitations.
Other considerations	Advanced community pharmacy based services are services such as the Medicines Use Reviews (MUR) and the New Medicines Service (NMS) as defined in the NHS Community Pharmacy Contractual Framework. Advanced pharmacist services in general practice are services such as level 3 clinical medication reviews where the pharmacist reviews the patient, illness and drug treatment during a consultation with access to patient notes, prescribing history, access to laboratory tests and with the patient present.[190] The committee noted that there is no clear distinction between a clinical pharmacist and a community pharmacist. Historically a community pharmacist has been based within a community pharmacy and a clinical pharmacist within a hospital ward; however, recently the distinction has become more blurred. The committee noted that within the studies identified, a community-based clinical pharmacist, particularly outside a GP practice, was more established in North America. The committee noted that in the future it is likely that these 2 roles are likely to diverge, even when located within the same setting, with the expectation that community pharmacists will concentrate on medication adherence and/or patient education and therefore supporting the role of the GP, whereas clinical pharmacists will have a greater clinical involvement with patients, therefore replacing the involvement of GPs in some situations. The committee noted that pharmacists should not be functioning in isolation and should be supported by other healthcare staff as appropriate, for example, the GP, hospital consultant or district/community nurse. In particular the committee judged

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Research recommendations	**-**
	that it would be more appropriate for a multi-disciplinary team led by other healthcare professionals, such as a district nurse, to be making home visits to patients, rather than a pharmacist but they could be supported by the pharmacist if needed. The committee noted that this review did not specifically look at care homes so this would not be included within the pharmacists 'at home' recommendation. The NICE guideline: Managing medicines in care homes (2014)[148] provides advice for this population group. The committee noted that the recommendations will be impacted by the General Practice Forward View published April 2016.[152] This report recommends an additional 1500 clinical pharmacists to be based within GP practices by 2020/21. This includes the current investment of £31 million to pilot 470 clinical pharmacists in over 700 practices, and is to be supplemented by a new central investment of £112 million to extend the programme for all practices not in the initial pilot. This is to be further supplemented with an additional pharmacy integration fund[153] to enable all pharmacists to provide more direct care to patients by expanding the range of clinical services they offer and integrating them into local care models outlined in the Five Year Forward View. The fund, worth £20 million in 2016 rising to a total of £300 million by 2020-21, is intended to help pharmacists and their teams to be fully incorporated across NHS planning and service delivery. In addition, the DH launched a package of reforms in October 2016 to modernise community pharmacy services.[60] There is an ongoing National Urgent Medicines Supply Advanced Service pilot for community pharmacy that runs from 1st December 2016 to 31st March 2018. At the end of the pilot an evaluation will be conducted by NHS England to test and evaluate the service in order to inform possible future commissioning.

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Appendices

Appendix A: Review protocol

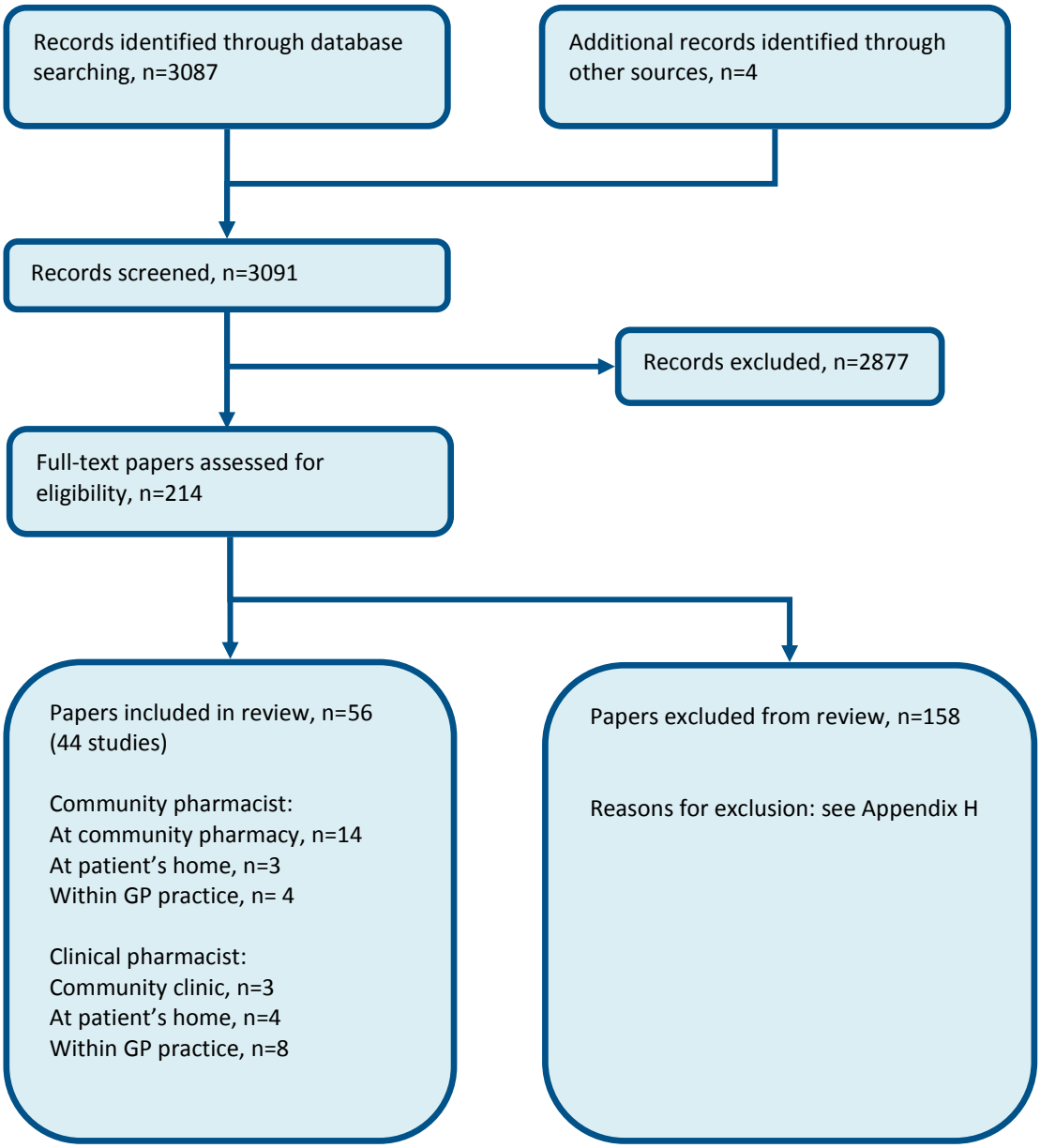
Table 18: Review protocol: Do enhanced roles of pharmacists in the community have clinical and cost-effectiveness benefits for patients at risk of an acute medical emergency or have a suspected or confirmed acute medical emergency?

Review question	Community pharmacist
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.
Review population	Adults or young people (>16 years of age) who are at risk of, or have a suspected or confirmed AME.
	Adults and young people (16 years and over).
	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)	Community pharmacists with enhanced roles in disease management; delivered at community clinics. Community pharmacists with enhanced roles in disease management; delivered at general practices. Community pharmacists with enhanced roles in disease management; delivered at patient's home. Community pharmacists with enhanced roles in disease management; delivered at community pharmacy. Community pharmacists with enhanced roles in disease management; intervention delivered at other community-based location. Clinical pharmacists with enhanced roles in disease management; delivered at community clinics. Clinical pharmacists with enhanced roles in disease management; delivered at general practices. Clinical pharmacists with enhanced roles in disease management; Delivered at patient's home. Clinical pharmacists with enhanced roles in disease management; delivered at community pharmacy. Clinical pharmacists with enhanced roles in disease management; intervention delivered at other community-based location. Usual care.
Outcomes	- Mortality within the study period (Dichotomous) CRITICAL - Avoidable adverse events (incorrect diagnosis and treatment) within the study period (Dichotomous) CRITICAL - Quality of life within the study period (Continuous) CRITICAL - Number of ED presentations within the study period (Dichotomous) CRITICAL - GP attendances within the study period (Dichotomous) CRITICAL - Hospital admissions within the study period (Dichotomous) IMPORTANT - Patient and/or carer satisfaction within the study period (Continuous) IMPORTANT
Review strategy	Systematic reviews (SRs) of RCTs, RCTs, observational studies only to be included if no relevant SRs or RCTs are identified.
Unit of randomisation	Patient. Pharmacist/Physician. Practice.
Crossover study	Permitted.
Minimum duration of	Not defined.

Review question	Community pharmacist
study	
Other stratifications	Type of pharmacist - clinical pharmacist, community pharmacist; location of the intervention.
Sensitivity/other analysis	Frail elderly. UK versus non-UK. Pre-specified study subgroups.
Subgroup analyses if there is heterogeneity	- Frail elderly (frail elderly; non-frail elderly); population differs. - UK versus non-UK (UK; non-UK); different practice. - Pre-specified study subgroups (pre-specified by study1; pre-specified by study 2); may be important. - Prescribing power (prescribing; non-prescribing); pharmacists who can prescribe may be more effective at community-based interventions.
Search criteria	Databases: Medline, Embase, the Cochrane Library. Date limits for search: 1990. Language: English.

Appendix B: Clinical study selection

Figure 1: Flow chart of clinical study selection for the review of Community-based pharmacists



Appendix C: Forest plots

C.1 Community pharmacist based within a community pharmacy

Figure 2: Mortality

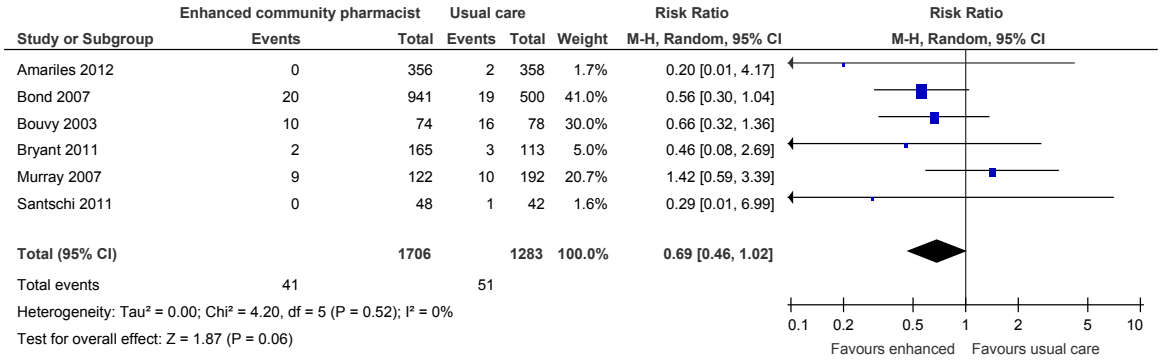


Figure 3: ED presentations

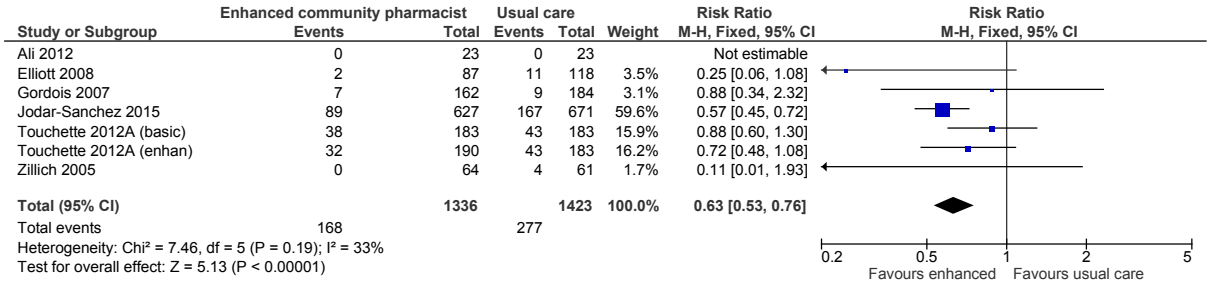


Figure 4: ED presentations

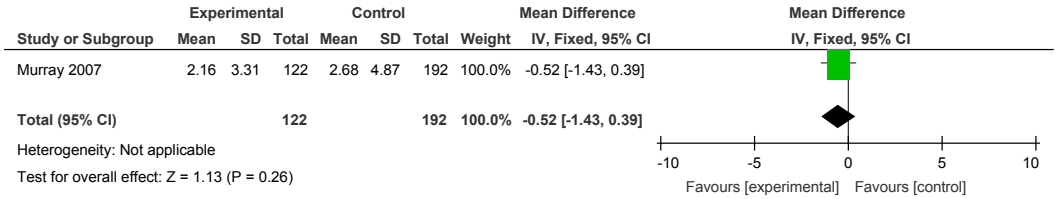


Figure 5: Hospital admissions

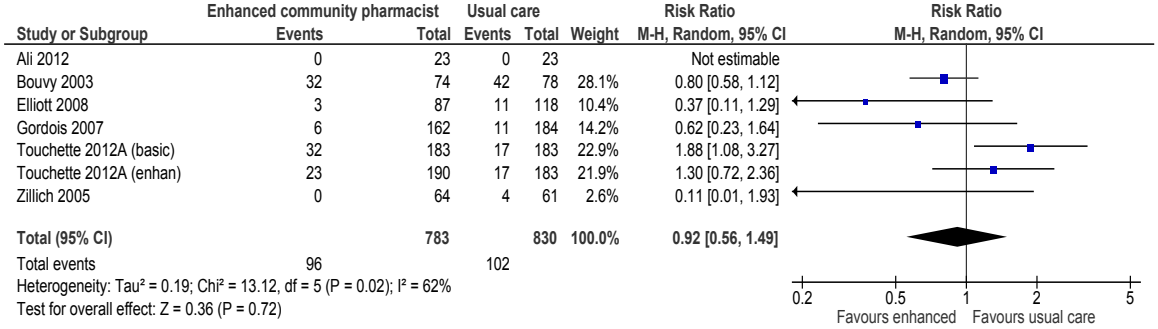


Figure 6: Hospital admissions

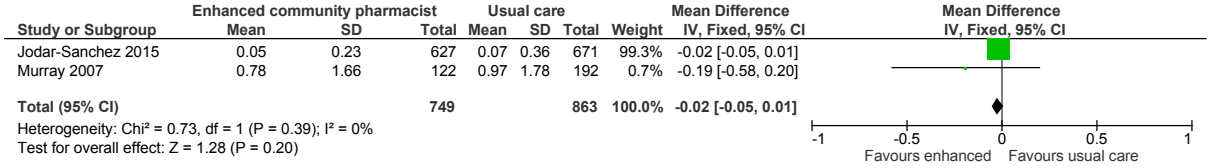
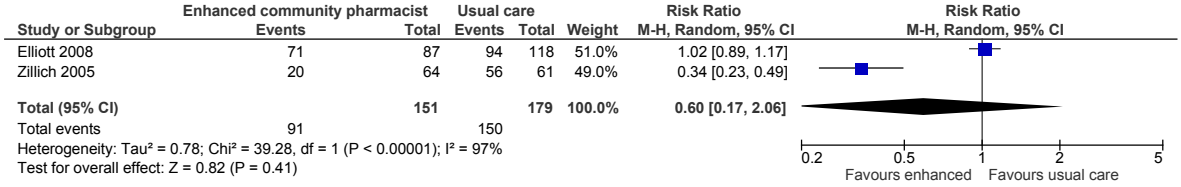


Figure 7: GP visits



C.2 Community pharmacist at the patients' homes

Figure 8: Mortality

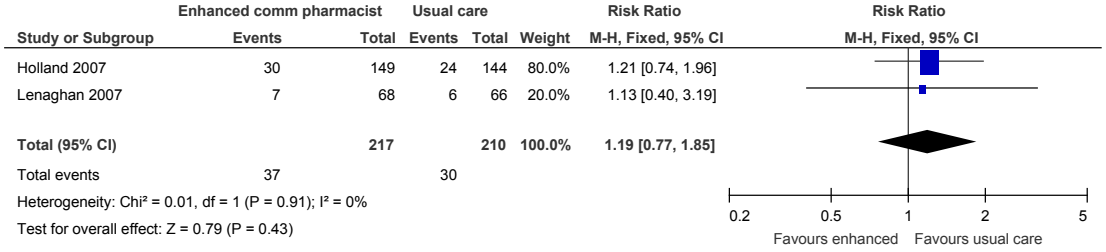


Figure 9: Hospital admissions

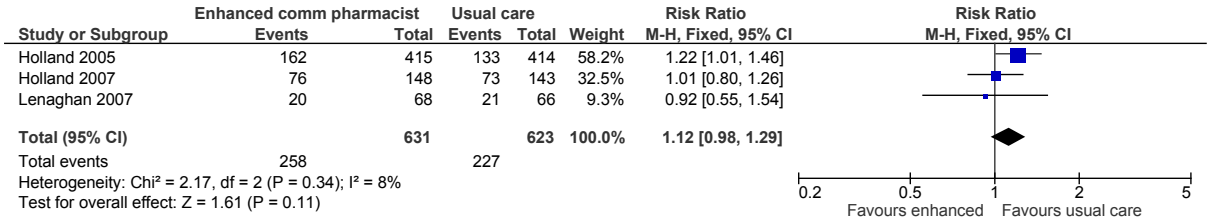


Figure 11: Quality of Life (EQ-5D)

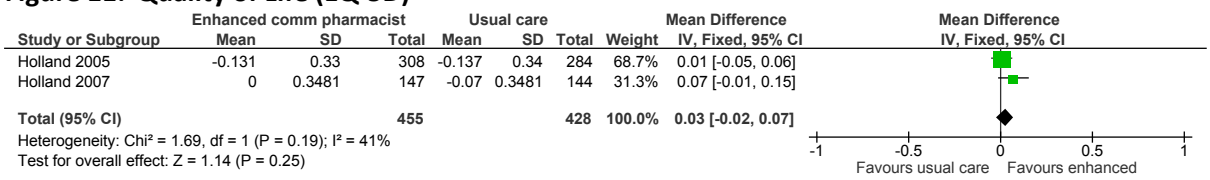
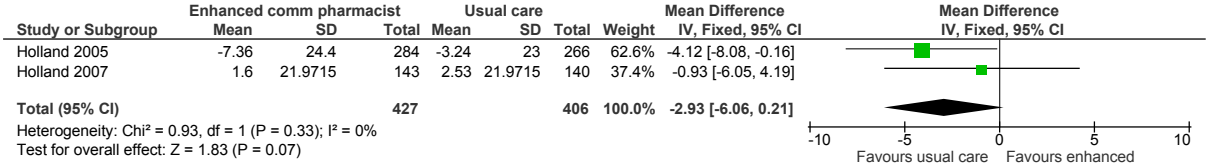


Figure 12: Quality of Life (EQ-VAS)



C.3 Community pharmacist based within a GP practice

Figure 10: Mortality

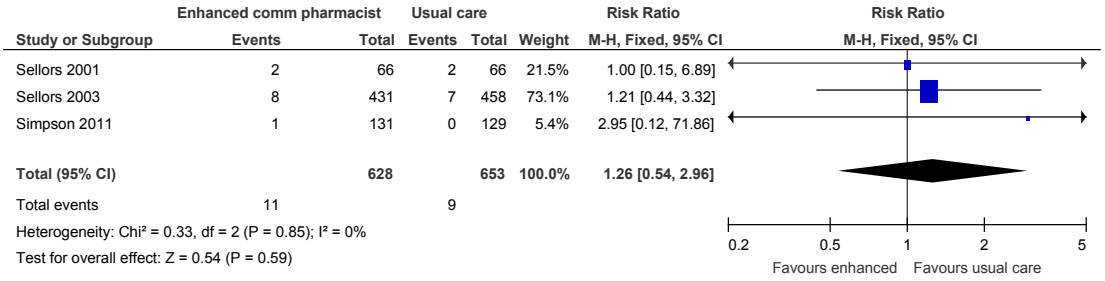
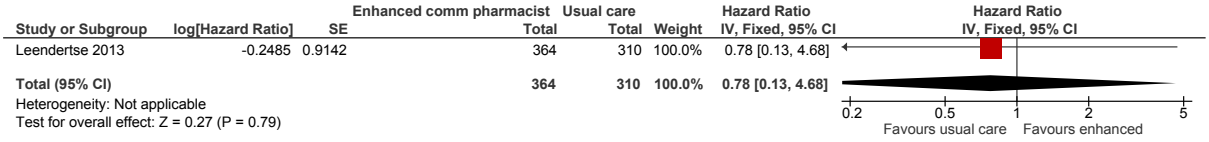


Figure 11: Survival



Adjusted for number of diseases.

Figure 12: ED presentations

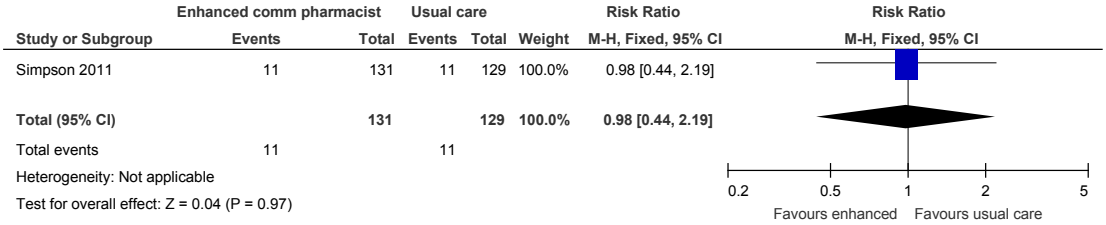


Figure 13: ED presentations

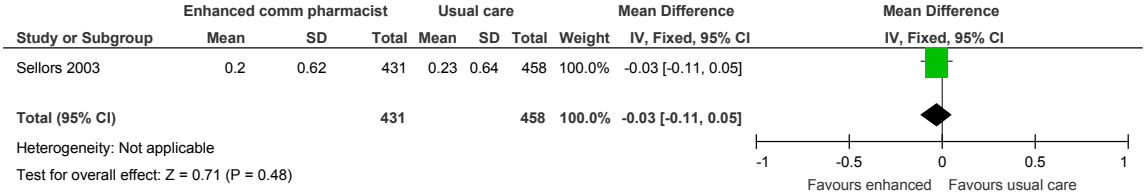


Figure 14: Hospital admissions

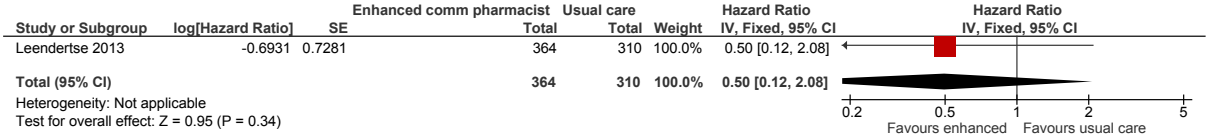


Figure 15: Hospital admissions

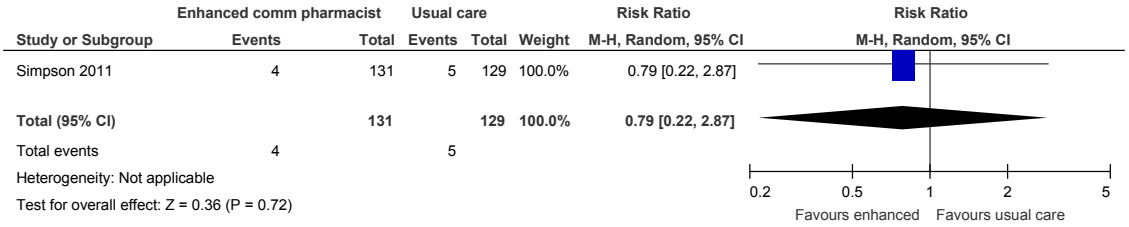


Figure 16: Hospital admissions

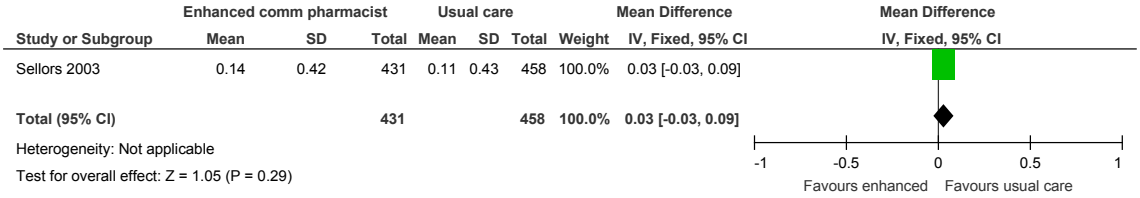


Figure 17: GP visits

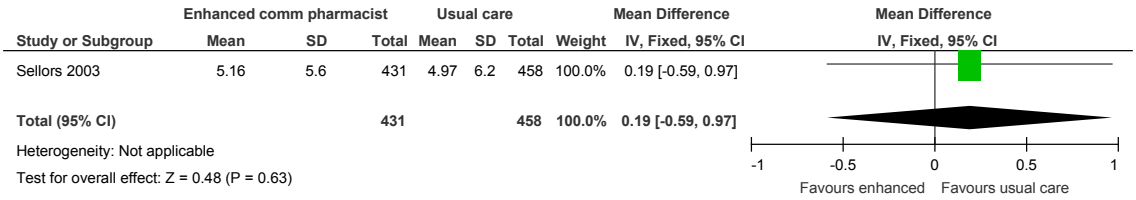


Figure 18: Adverse events

C.4 Clinical pharmacist based within a community clinic

Figure 19: Mortality

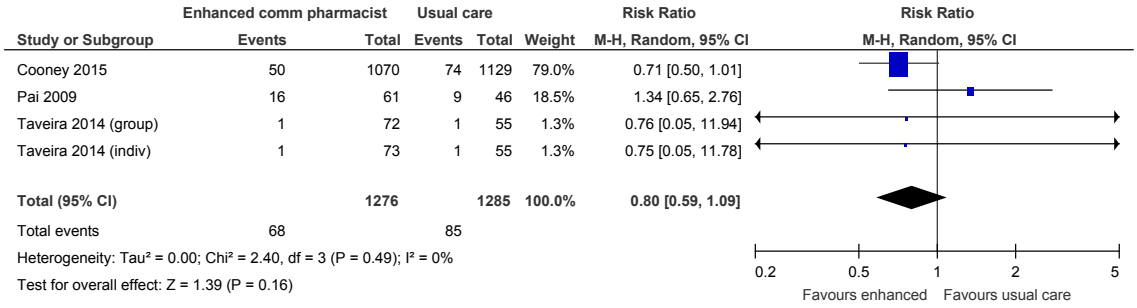


Figure 20: ED presentations

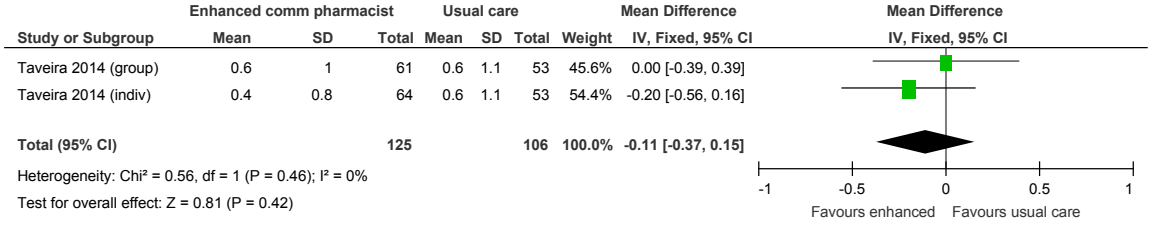


Figure 21: Hospital admissions

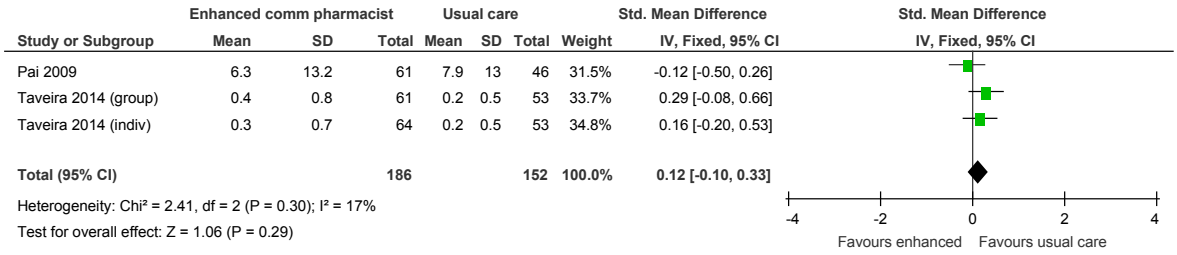


Figure 22: GP visits

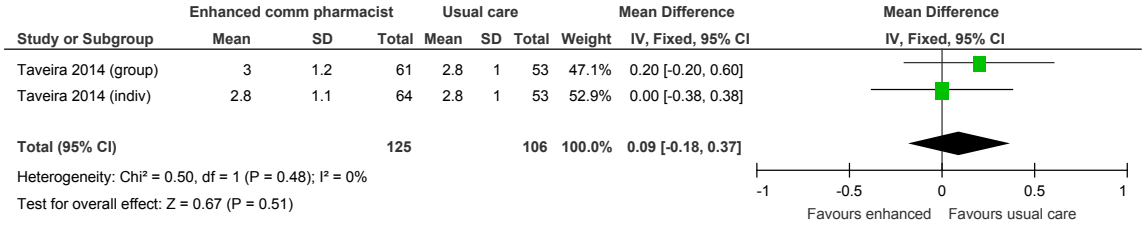
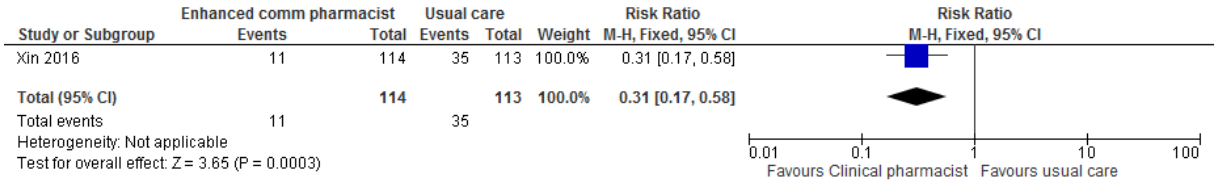


Figure 23: Total hospitalisations



C.5 Clinical pharmacist at the patients' homes

Figure 24: Mortality

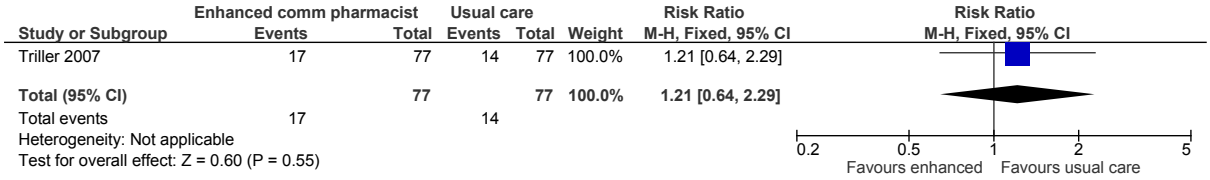
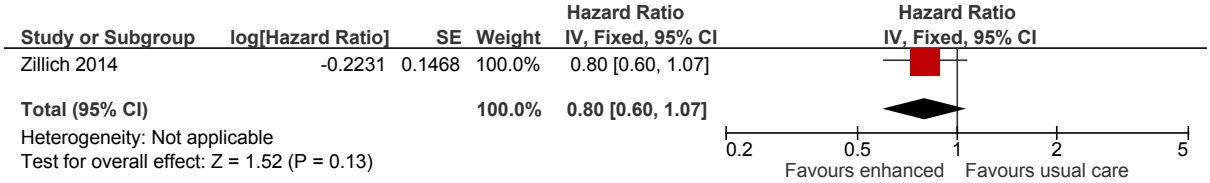


Figure 25: Hospital admission



Adjusted for CMS risk score for hospitalisation, patient age, total number of medication, ability to use a telephone, and detection of medication-related problems during initial in-home assessment

Figure 26: Hospital admission

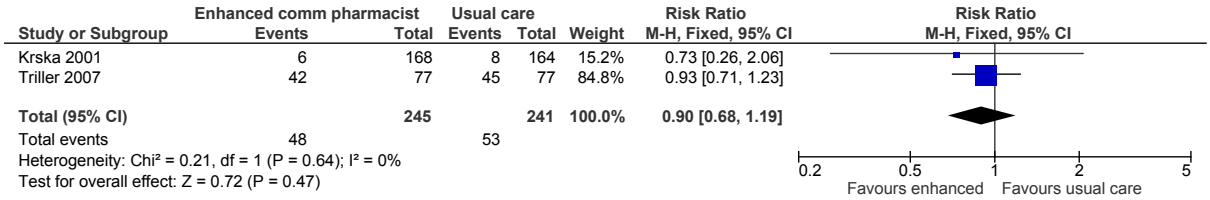
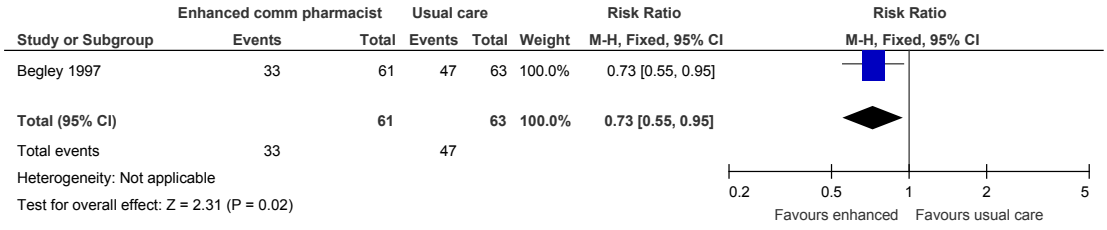


Figure 27: GP visits



C.6 Clinical pharmacist based within a GP practice

Figure 28: Mortality

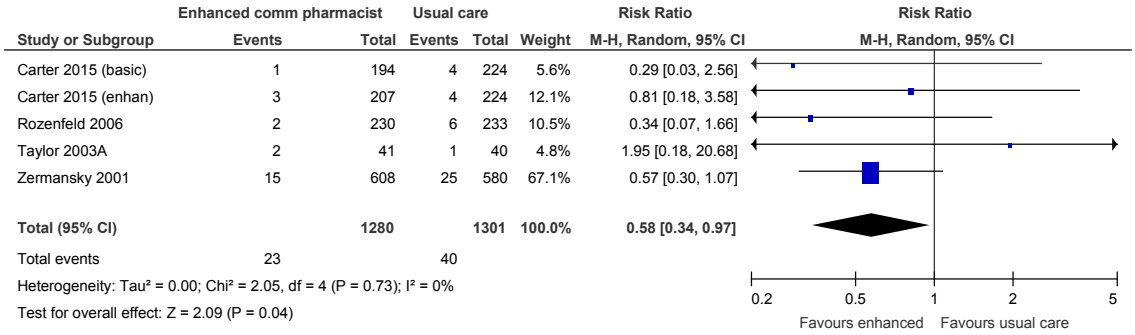
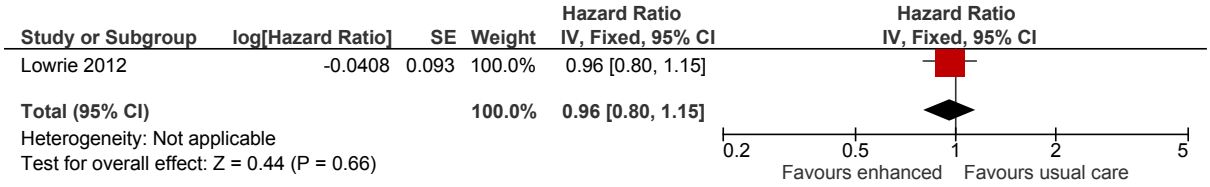


Figure 29: Mortality



Adjusted for age, creatinine, grade of left ventricular systolic dysfunction, atrial fibrillation, respiratory disease, total number of medical treatments, and diuretic use.

Figure 30: ED presentations

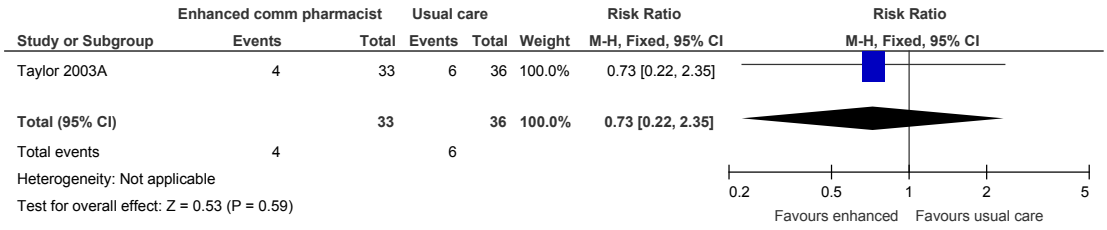


Figure 31: ED presentations

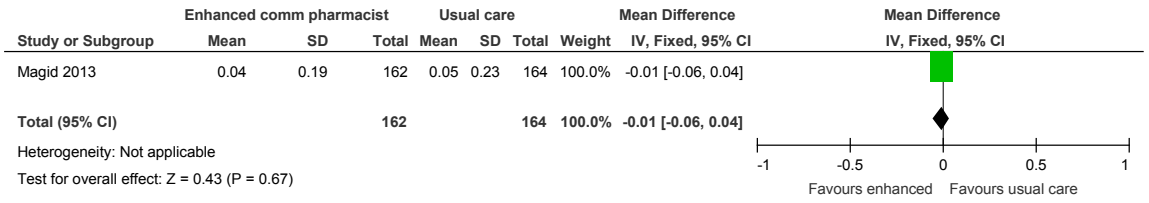


Figure 32: Hospital admissions

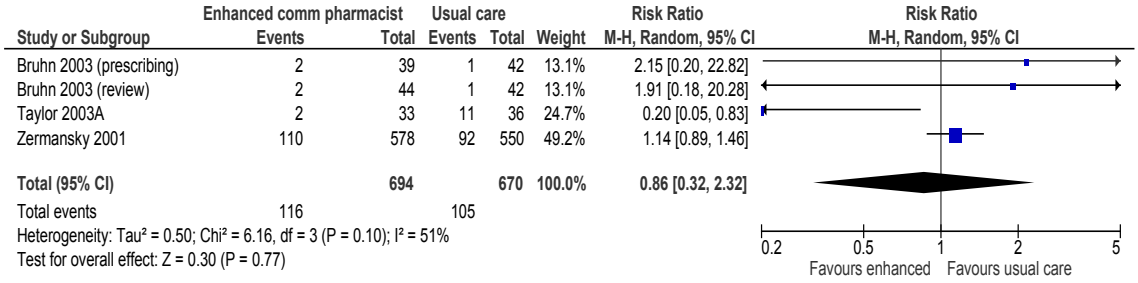


Figure 33: Hospital admissions

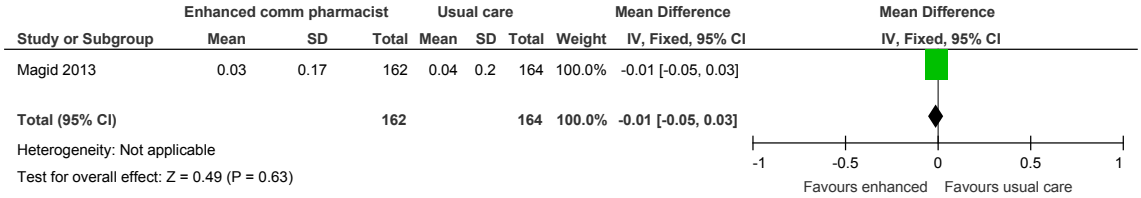
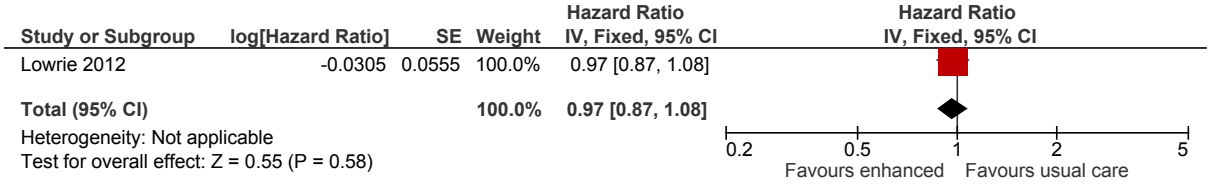


Figure 34: Hospital admissions



Adjusted for age, creatinine, grade of left ventricular systolic dysfunction, atrial fibrillation, respiratory disease, total number of medical treatments, and diuretic use.

Figure 35: Adverse events

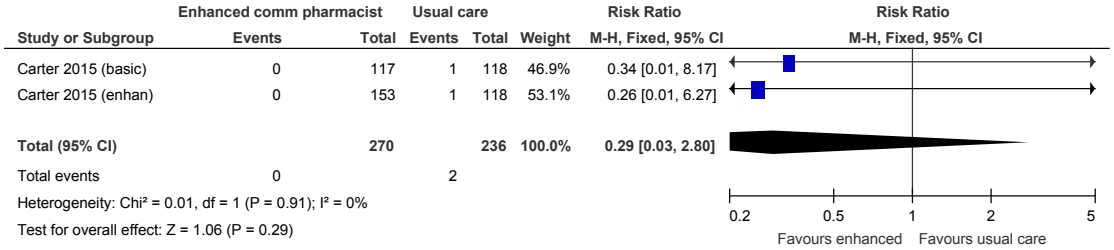
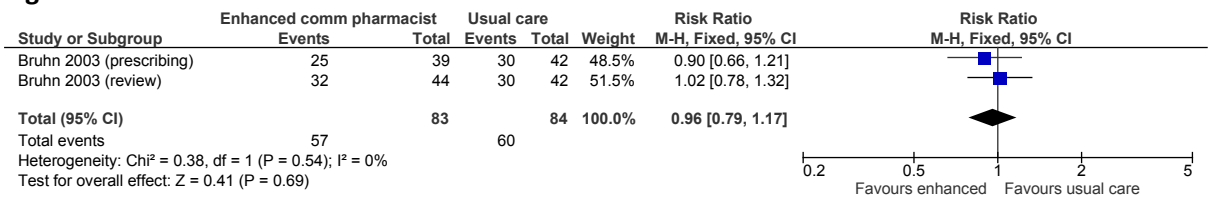


Figure 36: GP visits



Appendix D: Clinical evidence tables

Study	Ali 2012[5]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=48)
Countries and setting	Conducted in United Kingdom; Setting: Community pharmacy
Line of therapy	Not applicable
Duration of study	Intervention time: 12 months
Method of assessment of guideline condition	Partially adequate method of assessment/diagnosis: Type 2 diabetics recruited by posters and leaflets
Stratum	Overall: Type 2 diabetes
Subgroup analysis within study	Not applicable
Inclusion criteria	Type 2 diabetes mellitus on oral medication, not on insulin, over 18, HbA1c >53mmol/mol
Exclusion criteria	Significant co-morbidity, Involved in any trial/study during last 3 months
Recruitment/selection of patients	Solicited through posters and leaflets displayed in the pharmacies, and from computerized patient medication records held in the pharmacies, or by general practitioner referral. Patients were invited to take part by letter or at medication-dispensing opportunities
Age, gender and ethnicity	Age - Other: Group 1: < 45 - 0, 45-64 - 10, >65 - 13; Group 2: < 45 - 1, 45-64 - 13, >65 - 9. Gender (M:F): Group 1: 13:10; Group 2: 10:13. Ethnicity: Group 1: White - 19, South Asian - 2; Group 2: White - 23, South Asian - 0
Further population details	1. Frail elderly: Non-frail elderly (Age and morbidity of recruited population). 2. Pre-specified study subgroups: Not applicable/Not stated/Unclear. 3. UK versus non-UK: UK (UK).
Indirectness of population	No indirectness
Interventions	(n=25) Intervention 1: Community pharmacists with enhanced roles in disease management - Delivered at community pharmacy. Pharmaceutical care package designed for patients with Type 2 diabetes, with regular monitoring and consultations with the community pharmacist. Patients were seen every month for the first 2 months, and then every 3 months for the remainder of the 12 months, a total of six appointments. Pharmacists carried out a targeted medicine use review and lifestyle modification counselling with a referral to a general practitioner or healthcare professional where appropriate. Duration 12 months. Concurrent medication/care: Treatment for type 2 diabetes Further details: 1. Prescribing power: Not stated

Study	Ali 2012[5]
	(n=23) Intervention 2: Usual care. Usual service received from general practice plus assessment by a pharmacist at the beginning of the study and then after 12 months for an assessment of study outcomes. Duration 12 months. Concurrent medication/care: Treatment for type 2 diabetes Further details: 1. Prescribing power: Not stated
Funding	Study funded by industry (Department of Health, Merck Sharp and Dohme Ltd. Diagnostic equipment/kits supplied by Menarini Diagnostics)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DELIEVERED AT COMMUNITY PHARMACY versus USUAL CARE Protocol outcome 1: Avoidable adverse events (incorrect diagnosis and treatment) during the study period - Actual outcome: Total hypoglycaemic and hyperglycaemic events at 12 months; Group 1: 5/23, Group 2: 28/23; Risk of bias: All domain - Very high, Selection - Very high, Blinding - Very high, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Very high, Crossover - Low; Indirectness of outcome: ; Baseline details: smoking, gender, ethnic origin, age, mean duration of diabetes; Group 1 Number missing: 0; Group 2 Number missing: 2, Reason: 2 withdrew Protocol outcome 2: Number of ED presentations during the study period - Actual outcome: Emergency hospital visit at 12 months; Group 1: 0/23, Group 2: 0/23; Risk of bias: All domain - Very high, Selection - Very high, Blinding - High, Incomplete outcome data - High, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: smoking, gender, ethnic origin, age, mean duration of diabetes; Group 1 Number missing: 0; Group 2 Number missing: 2, Reason: 2 withdrew Protocol outcome 4: Hospital admissions during the study period - Actual outcome: Hospital admission at 12 months; Group 1: 0/23, Group 2: 0/23; Risk of bias: All domain - Very high, Selection - Very high, Blinding - High, Incomplete outcome data - High, Measurement - High, Crossover - Low; Indirectness of outcome: ; Baseline details: smoking, gender, ethnic origin, age, mean duration of diabetes; Group 1 Number missing: 0; Group 2 Number missing: 2, Reason: 2 withdrew	
Protocol outcomes not reported by the study	Mortality during the study period; Quality of life during the study period; Patient and/or carer satisfaction during the study period

Study	Begley 1997[17]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=149)

Study	Begley 1997[17]
Countries and setting	Conducted in United Kingdom; Setting: Patients' homes
Line of therapy	Not applicable
Duration of study	Intervention time: 12 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Over 75 with polypharmacy
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Aged 75 years or older, prescribed three or more different drugs, at least a twice daily dosage for one or more of the drugs, under the care of a participating consultant, consented to participate in the study, was returning to their own home following discharge
Exclusion criteria	None stated
Recruitment/selection of patients	Recruited from three hospitals within the district. Identified when discharge prescriptions which met the study inclusion criteria were presented in the hospital pharmacy
Age, gender and ethnicity	Age -: NR. Gender (M:F): NR. Ethnicity: NR
Further population details	1. Frail elderly: Frail elderly (Over 75 with polypharmacy). 2. Pre-specified study subgroups: Not applicable/Not stated/Unclear. 3. UK versus non-UK: UK (UK).
Indirectness of population	No indirectness
Interventions	(n=74) Intervention 1: Clinical pharmacists with enhanced roles in disease management - Delivered at patient's home. Patients were counselled on the correct use and storage of their drugs. The counselling included categorisation and a recall check at the end. Other practical strategies which have been validated to improve patient compliance were implemented. These included: Emphasising the importance of compliance, giving clear instruction on the exact treatment regimen (in writing if necessary), arranging dosing times to fit into the patient's daily routine, recognising the patient's effort to comply at each visit, simplifying the regimen if necessary. Duration 12 months. Concurrent medication/care: None detailed, but mean number of drugs (SD) per patient was 4.6 (1.8) Further details: 1. Prescribing power: Not stated (n=75) Intervention 2: Usual care. Received visits but no counselling. Duration 12 months. Concurrent medication/care: None detailed, but mean number of drugs (SD) per patient was 4.8 (1.6) Further details: 1. Prescribing power: Not stated
Funding	Funding not stated

Study	Begley 1997[17]
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DELIEVERED AT PATIENT'S HOME versus USUAL CARE Protocol outcome 1: GP attendances during the study period - Actual outcome: Proportion of patients who have contact with their GP at 3 - 12 months; Group 1: 33/61, Group 2: 47/63; Risk of bias: All domain - Very high, Selection - Very high, Blinding - High, Incomplete outcome data - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Control had higher number of patients who lived alone, 'hoarded' drugs, stored drugs incorrectly; Reason data missing: Overall: 7 death, 7 readmission, 10 admission to nursing home, 4 moved outside study area, 4 withdrew	
Protocol outcomes not reported by the study	Mortality during the study period; Avoidable adverse events (incorrect diagnosis and treatment) during the study period; Quality of life during the study period; Number of ED presentations during the study period; Hospital admissions during the study period; Patient and/or carer satisfaction during the study period

Study	Bouvy 2003[27]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=152)
Countries and setting	Conducted in Netherlands; Setting: Community pharmacy
Line of therapy	Unclear
Duration of study	Intervention time: 6 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Admitted to hospital with heart failure (ICD-9 428) or attended specialist heart failure clinic; diagnosis validated by hospital records including cardiac imaging
Stratum	Overall: Heart failure
Subgroup analysis within study	Not applicable
Inclusion criteria	Admitted to hospital with heart failure (ICD-9 428) or attended specialist heart failure clinic; diagnosis validated by hospital records including cardiac imaging. Treated with loop diuretics.
Exclusion criteria	Severe psychiatric problems or dementia, planned admission to a nursing home, did not take care of their own medication (for example, filled or administered by relatives or district nurses), life expectancy <3 months
Recruitment/selection of patients	Cardiologists informed patients about the study.
Age, gender and ethnicity	Age - Mean (SD): Intervention 69.1 (10.2); control 70.2 (11.2) years. Gender (M:F): 100:52. Ethnicity: Not stated
Further population details	1. Frail elderly: Not applicable/Not stated/Unclear. 2. Pre-specified study subgroups: Not applicable/Not stated/Unclear. 3. UK versus non-UK: Non-UK (Netherlands).

Study	Bouvy 2003[27]
Indirectness of population	No indirectness
Interventions	(n=74) Intervention 1: Community pharmacists with enhanced roles in disease management - Delivered at community pharmacy. Pharmacists received training for the intervention that consisted of a structured interview on the patient's first visit to the community pharmacy. A computerised medication history was used to discuss drug use, reasons for non-compliance (for example, possible adverse drug reactions and difficulties integrating medicine into daily life) to reinforce compliance. A short report of this interview was forwarded to the GP. Pharmacists contacted patients on a monthly basis for a maximum of 6 months. Duration 6 months. Concurrent medication/care: Loop diuretics Further details: 1. Prescribing power: not stated (n=78) Intervention 2: Usual care. Did not receive the structured interview or monthly follow up. Duration 6 months. Concurrent medication/care: Not stated Further details: 1. Prescribing power: not stated
Funding	Academic or government funding (Independent non-profit foundation for the efficient use of medicines (DGMN))
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: LONG-TERM CONDITIONS versus USUAL CARE Protocol outcome 1: Mortality during the study period - Actual outcome: Mortality at 6 months; Group 1: 10/74, Group 2: 16/78; Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness Protocol outcome 2: Hospital admissions during the study period - Actual outcome: Total number of hospital admissions at 6 months; Group 1: 32/74, Group 2: 42/78; Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Avoidable adverse events (incorrect diagnosis and treatment) during the study period; Quality of life during the study period; Number of ED presentations during the study period; GP attendances during the study period; Patient and/or carer satisfaction during the study period

Study (subsidiary papers)	Bruhn 2013[29] (Neilson 2015[151])
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=232)
Countries and setting	Conducted in United Kingdom; Setting: GP practices

Study (subsidiary papers)	Bruhn 2013[29] (Neilson 2015[151])
Line of therapy	Not applicable
Duration of study	Follow up (post intervention): 6 months
Method of assessment of guideline condition	Partially adequate method of assessment/diagnosis: computerised search
Stratum	Overall: Chronic pain
Subgroup analysis within study	Stratified then randomised: Prescribing versus non-prescribing
Inclusion criteria	Over 18 years of age, living in their own houses and receiving two or more acute prescriptions, and / or one repeat prescription within the last 120 days for an analgesic and/or NSAID
Exclusion criteria	Medications that can be used for analgesia but whose primary indication is not for chronic pain (for example, triptans, anti-epileptics or anti-depressants), concomitant severe mental health problem or terminal illness, suffered recent bereavement, had a known alcohol or drug addiction, suffered pain caused by cancer or other malignancy, were unable to give informed consent, other (unspecified) reasons
Recruitment/selection of patients	Identified by a computerised search and sent an invitation pack contain a letter, information sheet and consent form
Age, gender and ethnicity	Age - Mean (SD): Group 1: 66.1 (12.1); Group 2: 65.7 (14.2); Group 3: 64.9 (11.6). Gender (M:F): 73:120. Ethnicity: Caucasian: 190; Other: 1; Missing: 2
Further population details	1. Frail elderly: Non-frail elderly (Age and morbidity). 2. Pre-specified study subgroups: Not applicable/Not stated/Unclear. 3. UK versus non-UK: UK (UK).
Indirectness of population	No indirectness
Interventions	(n=70) Intervention 1: Clinical pharmacists with enhanced roles in disease management - Delivered at general practices. Pharmacists invited patients to a face-to-face consultation. Prior to the consultation, pharmacists completed a paper-based medication review of each patient's medical record and patients were asked to complete a pain diary to inform the consultation. A pharmaceutical care plan was agreed between the pharmacist and the patient. The plan assessed and documented relevant medical history and current conditions; known allergies and adverse drug reactions; relevant laboratory results; pain-related medications prescribed in the previous10 years; current pain-related prescription medications; current symptoms; lifestyle issues, including units of alcohol consumed per week; recommendations for changes to medication (if any); whether non-pharmaceutical treatments had been considered; and any other relevant issue. At the end of the consultation any required prescriptions for medicines were issued by the pharmacist. Owing to Controlled Drug (CD) regulations in place at the time, prescribing for CDs was performed using a supplementary prescribing clinical management plan rather than independent prescribing. Patients were followed up either by phone or face-to-face, at each pharmacist's discretion. Duration Single visit + follow-up at pharmacist's discretion. Concurrent medication/care: Treatment for chronic pain Further details: 1. Prescribing power: Prescribing (At the end of the consultation any required prescriptions for

Study (subsidiary papers)	Bruhn 2013[29] (Neilson 2015[151])
	medicines were issued by the pharmacist). (n=63) Intervention 2: Clinical pharmacists with enhanced roles in disease management - Delivered at general practices. The pharmacists conducted a paper-based medication review focussed on pain-related prescription medications, before creating a pharmaceutical care plan which detailed any recommendations for medication changes. The plan was passed to the patient's GP for implementation. The GPs were asked subsequently about actions taken as a result of the recommendations. Duration Single visit. Concurrent medication/care: Treatment for chronic pain Further details: 1. Prescribing power: Non-prescribing (Recommendations passed to GP). (n=63) Intervention 3: Usual care. Patients received standard general practice care. Duration 6 months. Concurrent medication/care: Treatment for chronic pain Further details: 1. Prescribing power: Not stated
Funding	Academic or government funding (Medical Research Council)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DELIEVERED AT GENERAL PRACTICES versus USUAL CARE Protocol outcome 1: GP attendances during the study period - Actual outcome: Proportion who had GP surgery consultations at 6 months; Group 1: 25/39, Group 2: 30/42; Risk of bias: All domain – very high, Selection - high, Blinding - high, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness Protocol outcome 2: Hospital admissions during the study period - Actual outcome: Proportion who had hospital admissions at 6 months; Group 1: 2/39, Group 2: 1/42; Risk of bias: All domain – very high, Selection - high, Blinding - high, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DELIEVERED AT GENERAL PRACTICES versus USUAL CARE Protocol outcome 1: GP attendances during the study period - Actual outcome: Proportion who had GP surgery consultations at 6 months; Group 1: 32/44, Group 2: 30/42; Risk of bias: All domain – very high, Selection - high, Blinding - high, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness Protocol outcome 2: Hospital admissions during the study period - Actual outcome: Proportion who had hospital admissions at 6 months; Group 1: 2/44, Group 2: 1/42; Risk of bias: All domain – very high, Selection - high, Blinding - high, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Mortality during the study period; Avoidable adverse events (incorrect diagnosis and treatment) during the study

Study (subsidiary papers)	Bruhn 2013[29] (Neilson 2015[151])
	period; Quality of life during the study period; Number of ED presentations during the study period; Patient and/or carer satisfaction during the study period

Study	Bryant 2011[30]
Study type	RCT (Pharmacist/Physician randomised; Parallel)
Number of studies (number of participants)	1 (n=498)
Countries and setting	Conducted in New Zealand; Setting: Community pharmacy
Line of therapy	Unclear
Duration of study	Intervention time: 6 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Identified by GP
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Age 65 or older; on 5 or more prescribed medicines; likely to be available for follow up for 1 year
Exclusion criteria	Not stated
Recruitment/selection of patients	All 76 pharmacists who had completed more than 5 care plans were invited to participate; those who agreed approached 2 GP practices and invited at least 1 GP (working 16 hours a week or more in general practice) from each practice. GPs invited eligible patients: starting on a different day each week, eligible patients were enrolled consecutively until 4 patients enrolled for that week. Each GP aimed to enrol 12 patients.
Age, gender and ethnicity	Age - Mean (range): Intervention 75.9 (64-92); control 74.9 (60-91) years. Gender (M:F): 141:209. Ethnicity: European 73.6%, Maori/Pacific people 4.2%, the rest "New Zealander" with no ethnic affiliation, other or not stated
Further population details	1. Frail elderly: Not applicable/Not stated/Unclear. 2. Pre-specified study subgroups: Not applicable/Not stated/Unclear. 3. UK versus non-UK: Non-UK (New Zealand).
Indirectness of population	No indirectness
Interventions	(n=269) Intervention 1: Community pharmacists with enhanced roles in disease management - Delivered at community pharmacy. The patients saw the study pharmacist for the Comprehensive Pharmaceutical Care (CPC) medication review consultation (at pharmacy or at home). It addressed patient concerns and expectations, adherence issues, provision of lifestyle and pharmacological advice and included a clinical assessment of medicine with recommendations if required to the GP in a pharmaceutical care plan. The pharmacist had access to the medical records from the GP and met with the GP after the patient consultation. The study pharmacist followed the patient at

Study	Bryant 2011[30]
	3 and 6 months, updating the pharmaceutical care plan as needed (interim meetings could be agreed if necessary). Duration 6 months. Concurrent medication/care: Not stated Further details: 1. Prescribing power: Non-prescribing (Discussed met with the general practitioner to discuss care plan). (n=229) Intervention 2: Usual care. No further details. Duration 6 months. Concurrent medication/care: Not stated Further details: 1. Prescribing power: Not stated
Funding	Academic or government funding (Health Funding Authority of New Zealand; Pharmaceutical Society of New Zealand)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: LONG-TERM CONDITIONS versus USUAL CARE Protocol outcome 1: Mortality during the study period - Actual outcome: Mortality at 6 months; Group 1: 2/165, Group 2: 3/113; Risk of bias: All domain - Very high, Selection - Very high, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Less males and more mental health co-morbidities in intervention; Group 1 Number missing: 32, Reason: 21 due to pharmacist withdrawal, 2 personal reasons, 3 unknown, 3 moved out of area, 3 changed general practitioner; Group 2 Number missing: 14, Reason: 1 personal reasons, 9 unknown, 1 too unwell, 3 changed general practitioner	
Protocol outcomes not reported by the study	Avoidable adverse events (incorrect diagnosis and treatment) during the study period; Quality of life during the study period; Number of ED presentations during the study period; GP attendances during the study period; Hospital admissions during the study period; Patient and/or carer satisfaction during the study period

Study	Collaboration Among Pharmacists and physicians To Improve Outcomes (CAPTION) trial: Carter 2015[39]
Study type	RCT (Practice randomised; Parallel)
Number of studies (number of participants)	1 (n=625)
Countries and setting	Conducted in USA; Setting: Primary care
Line of therapy	Not applicable
Duration of study	Intervention + follow up: Brief intervention: 9 month intervention + 15 month follow-up; Sustained intervention: 24 month intervention
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: hypertension as defined by seated BP (average of the second and third reading)

Study	Collaboration Among Pharmacists and physicians To Improve Outcomes (CAPTION) trial: Carter 2015[39]
Stratum	Overall: Uncontrolled hypertension
Subgroup analysis within study	Not applicable
Inclusion criteria	English or Spanish speaking, over 18 years of age, hypertension and uncontrolled BP defined as 140 mmHg and over SBP or 90 mmHg and over diastolic BP (DBP) for uncomplicated hypertension. 130 mmHg and over SBG or 80 mmHg and over DPB for patients with diabetes or chronic kidney disease
Exclusion criteria	Current signs of hypertensive emergency (acute angina, stroke or renal failure); SBP >200 or DBP >114 mmHg; history of myocardial infarction, stroke, or unstable angina in the prior 6 months; systolic dysfunction with a left ventricular ejection fraction <35% as documented by echocardiography, nuclear medicine study, or ventriculography; glomerular filtration rate <20 mL/min or proteinuria >1 g/day; cirrhosis, hepatitis B or C infection, or laboratory abnormalities (serum alanine aminotransferase or aspartate aminotransferase >2, bilirubin >1.5 mg/dL) in the prior 6 months; pregnancy; pulmonary hypertension or sleep apnea (unless treated by continuous positive airway pressure); life expectancy estimated at <2 years; residence in a nursing home or dementia; and inability to give informed consent or impaired cognitive function
Recruitment/selection of patients	Identified for a list generated from each clinic with consecutive patients invited to participate
Age, gender and ethnicity	Age - Mean (SD): Group 1: 61.8 (12.4); Group 2: 57.8 (11.8); Group 3: 61.8 (13.7). Gender (M:F): 248:377. Ethnicity: (%) Group 1: White - 49.0, Minority - 48.5; Group 2: White - 35.3, Minority - 63.8; Group 3: White - 49.6, Minority - 49.6;
Further population details	1. Frail elderly: Not applicable/Not stated/Unclear. 2. Pre-specified study subgroups: Not applicable/Not stated/Unclear. 3. UK versus non-UK: Non-UK (USA).
Extra comments	Primary care offices: 85.4% were located in family medicine residencies, 10.4% in internal medicine residencies and 4.2% in faculty practices
Indirectness of population	No indirectness
Interventions	(n=194) Intervention 1: Clinical pharmacists with enhanced roles in disease management - Delivered at general practices. At baseline, the pharmacist will review the medical record and perform a structured interview with the patient, including a detailed medication history; assessment of patient knowledge of BP medications, purpose of each medication, goals of therapy, medication dosages and timing, and potential medication side effects; potential contraindications to specific BP medications; and expectations for future dosage changes, monitoring, and issues that may become future barriers to BP control (for example, side effects, no adherence, patient self-efficacy). The pharmacist will supply a wallet card listing all medications and doses, contact phone numbers, and BP goals. The pharmacist will create a care plan with treatment recommendations for the physician at the baseline visit so that an immediate change in medication can be made. If the physician agrees with the care plan or makes a modification in the plan, the pharmacist will implement the plan. The study case report forms will capture whether the physician accepted the pharmacist's recommendations. The suggested model includes structured face-to-face visits with the

Study	Collaboration Among Pharmacists and physicians To Improve Outcomes (CAPTION) trial: Carter 2015[39]
	patient at baseline, 1, 2, 4, 6, and 8 months; a telephone call at 2 weeks; and additional visits if BP remains uncontrolled. If BP is controlled, the recommended action will be for the pharmacist to schedule the patient for routine follow-up every 3 to 6 months. If BP control is lost, the pharmacist is encouraged to increase visit frequency similar to the baseline schedule. Duration 9 months. Concurrent medication/care: Treatment for hypertension Further details: 1. Prescribing power: Not applicable/Not stated/Unclear. (If the physician agrees with the care plan or makes a modification in the plan, the pharmacist will implement the plan). (n=207) Intervention 2: Clinical pharmacists with enhanced roles in disease management - Delivered at general practices. At baseline, the pharmacist will review the medical record and perform a structured interview with the patient, including a detailed medication history; assessment of patient knowledge of BP medications, purpose of each medication, goals of therapy, medication dosages and timing, and potential medication side effects; potential contraindications to specific BP medications; and expectations for future dosage changes, monitoring, and issues that may become future barriers to BP control (for example, side effects, non-adherence, patient self-efficacy). The pharmacist will supply a wallet card listing all medications and doses, contact phone numbers, and BP goals. The pharmacist will create a care plan with treatment recommendations for the physician at the baseline visit so that an immediate change in medication can be made. If the physician agrees with the care plan or makes a modification in the plan, the pharmacist will implement the plan. The study case report forms will capture whether the physician accepted the pharmacist's recommendations. The suggested model includes structured face-to-face visits with the patient at baseline, 1, 2, 4, 6, and 8 months; a telephone call at 2 weeks; and additional visits if BP remains uncontrolled. If BP is controlled, the recommended action will be for the pharmacist to schedule the patient for routine follow-up every 3 to 6 months. If BP control is lost, the pharmacist is encouraged to increase visit frequency similar to the baseline schedule. Duration 24 months. Concurrent medication/care: Treatment for hypertension Further details: 1. Prescribing power: Not applicable/Not stated/Unclear. (If the physician agrees with the care plan or makes a modification in the plan, the pharmacist will implement the plan). (n=224) Intervention 3: Usual care. Pharmacists in control sites will not provide the intervention for patients with hypertension but will continue to provide curbside consultations if physicians specifically ask questions about patients with hypertension. Duration 24 months. Concurrent medication/care: Treatment for hypertension Further details: 1. Prescribing power: Not stated
Funding	Academic or government funding (National Heart, Lung, and Blood Institute)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DELIEVERED AT GENERAL PRACTICES versus USUAL CARE Protocol outcome 1: Mortality during the study period	

Study	Collaboration Among Pharmacists and physicians To Improve Outcomes (CAPTION) trial: Carter 2015[39]
- Actual outcome: Mortality at 24 months; Group 1: 1/194, Group 2: 4/224; Risk of bias: All domain - Very high, Selection - Very high, Blinding - Low, Incomplete outcome data - Very high, Crossover - Low, Other 1 - High; Indirectness of outcome: No indirectness ; Baseline details: Sustained intervention had more smokers, low-income patients, and those without health insurance versus control,; Group 1 Number missing: 76, Reason: 46 not observed due to early study closure, 31 early terminations (5 change in eligibility, 11 withdrew, 14 lost to follow-up, 1 other); Group 2 Number missing: 110, Reason: 57 not observed due to early study closure, 53 early terminations (6 change in eligibility, 114ithdrew, 24 lost to follow-up, 1 adverse event, 2 other) Protocol outcome 2: Avoidable adverse events (incorrect diagnosis and treatment) during the study period - Actual outcome: Adverse events at 24 months; Group 1: 0/117, Group 2: 1/118; Risk of bias: All domain - Very high, Selection - Very high, Blinding - Low, Incomplete outcome data - Very high, Crossover - Low, Other 1 - High; Indirectness of outcome: No indirectness ; Baseline details: Sustained intervention had more smokers, low-income patients, and those without health insurance versus control,; Group 1 Number missing: 76, Reason: 46 not observed due to early study closure, 31 early terminations (5 change in eligibility, 11 withdrew, 14 lost to follow-up, 1 other); Group 2 Number missing: 110, Reason: 57 not observed due to early study closure, 53 early terminations (6 change in eligibility, 114ithdrew, 24 lost to follow-up, 1 adverse event, 2 other) RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DELIEVERED AT GENERAL PRACTICES versus USUAL CARE Protocol outcome 1: Mortality during the study period - Actual outcome: Mortality at 24 months; Group 1: 3/207, Group 2: 4/224; Risk of bias: All domain - Very high, Selection - Very high, Blinding - Low, Incomplete outcome data - Very high, Crossover - Low, Other 1 - High; Indirectness of outcome: No indirectness ; Baseline details: Sustained intervention had more smokers, low-income patients, and those without health insurance versus control,; Group 1 Number missing: 76, Reason: 9 not observed due to early study closure, 45 early terminations (3 change in eligibility, 9 withdrew, 24 lost to follow-up, 6 other); Group 2 Number missing: 110, Reason: 57 not observed due to early study closure, 53 early terminations (6 change in eligibility, 114ithdrew, 24 lost to follow-up, 1 adverse event, 2 other) Protocol outcome 2: Avoidable adverse events (incorrect diagnosis and treatment) during the study period - Actual outcome: Adverse events at 24 months; Group 1: 0/153, Group 2: 1/118; Risk of bias: All domain - Very high, Selection - Very high, Blinding - Low, Incomplete outcome data - Very high, Crossover - Low, Other 1 - High; Indirectness of outcome: No indirectness ; Baseline details: Sustained intervention had more smokers, low-income patients, and those without health insurance versus control,; Group 1 Number missing: 76, Reason: 46 not observed due to early study closure, 31 early terminations (5 change in eligibility, 11 withdrew, 14 lost to follow-up, 1 other); Group 2 Number missing: 110, Reason: 57 not observed due to early study closure, 53 early terminations (6 change in eligibility, 114ithdrew, 24 lost to follow-up, 1 adverse event, 2 other)	
Protocol outcomes not reported by the study	Quality of life during the study period; Number of ED presentations during the study period; GP attendances during the study period; Hospital admissions during the study period; Patient and/or carer satisfaction during the study period

Study	Cooney 2015[54]
Study type	RCT (Practice randomised; Parallel)

Study	Cooney 2015[54]
Number of studies (number of participants)	1 (n=2199)
Countries and setting	Conducted in USA; Setting: Primary care in 13 Community Based Outpatient Clinics (CBOCs) in Veterans Affairs Medical Centres (VAMC)
Line of therapy	Unclear
Duration of study	Intervention time: 1 year
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: estimated glomerular filtration rate
Stratum	Overall: Chronic Kidney Disease
Subgroup analysis within study	Not applicable
Inclusion criteria	Moderate to severe chronic kidney disease (CKD) (calculated eGFR <45mL/min/1.73m2); GFR <60mL/min/1.73m2 between 90 days and 2 years prior to index GFR; at least 1 primary care visit in previous year
Exclusion criteria	End-stage renal disease (ESRD); ever referred for hospice care; >85 years or <18 years
Recruitment/selection of patients	Eligible patients in the primary care CBOCs
Age, gender and ethnicity	Age - Mean (SD): Intervention: 75.6 (8.2) years; Control: 75.7 (8.2) years. Gender (M:F): 2160:39. Ethnicity: 5% Black
Further population details	1. Frail elderly: Not applicable/Not stated/Unclear. 2. Pre-specified study subgroups: Not applicable/Not stated/Unclear. 3. UK versus non-UK: Non-UK (USA).
Indirectness of population	No indirectness
Interventions	(n=1070) Intervention 1: Clinical pharmacists with enhanced roles in disease management - Delivered at community clinics. The intervention included delivery system redesign which involved engaging pharmacists to interact with patients and collaborate electronically with primary care physicians; self-management support for patients in the form of an informational pamphlet regarding CKD (National Kidney Disease Education Program packet); and a CKD registry. The registry was used 1) to identify patients with CKD not receiving guideline adherent care; 2) by the pharmacist for decision support during the phone call with participants (phone script with branching logic); and 3) to facilitate documentation of the intervention (at the completion of the intervention phone call, the registry automatically generated a template note that was copied into the electronic medical record (EMR) as a progress note; only for study personnel, not used in daily practice). The registry was used to identify patients with an upcoming primary care appointment. Clinical pharmacists contacted subjects by phone prior to the appointment to discuss CKD and hypertension; they reviewed medication and lifestyle modifications, ordered KDOQI recommended laboratory tests and arranged nephrology consults for patients with severe CKD (eGFR <30mL/min/1.73m2); once lab results were completed, the pharmacist called the patient again to review any abnormal results and initiated appropriate medication changes to treat acidosis, hypophosphatemia, hyperparathyroidism, vitamin D deficiency, hyperkalaemia and anaemia. BP medications were not adjusted by the pharmacists but recommendations to primary care providers

Study	Cooney 2015[54]
	regarding hypertension management were included in the progress note. Duration 1 year. Concurrent medication/care: Not stated Further details: 1. Prescribing power: Non-prescribing (Medications were not adjusted by the pharmacist, but recommendations to primary care providers were included in the progress note). (n=1129) Intervention 2: Usual care. No further details. Duration 1 year. Concurrent medication/care: Treatment for CKD Further details: 1. Prescribing power: Not stated
Funding	Academic or government funding (Cleveland VA Medical Research & Education Foundation; National Institute of Diabetes and Digestive and Kidney Diseases)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: LONG-TERM CONDITIONS versus USUAL CARE Protocol outcome 1: Mortality during the study period - Actual outcome: Mortality at 1 year; Group 1: 50/1070, Group 2: 74/1129; Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Avoidable adverse events (incorrect diagnosis and treatment) during the study period; Quality of life during the study period; Number of ED presentations during the study period; GP attendances during the study period; Hospital admissions during the study period; Patient and/or carer satisfaction during the study period

Study	Elliott 2008[63]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=492)
Countries and setting	Conducted in United Kingdom; Setting: Community pharmacies
Line of therapy	Unclear
Duration of study	Intervention + follow up: Intervention = one-off; follow up 2 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Had a prescription for a chronic condition
Stratum	Long-term conditions
Subgroup analysis within study	Not applicable
Inclusion criteria	Receiving the first prescription for a new medicine for a chronic condition; age 75 years or older; stroke,

Study	Elliott 2008[63]
	cardiovascular disease, asthma, diabetes or rheumatoid arthritis
Exclusion criteria	Inability to understand written or spoken English or not having a telephone
Recruitment/selection of patients	Convenience sample: recruited opportunistically when patients presented a prescription in one of the 40 Moss pharmacies
Age, gender and ethnicity	Age - Mean (range): Intervention: 67 (28-88); control: 67 (34-85) years. Gender (M:F): 98:107. Ethnicity: Not stated
Further population details	1. Frail elderly: Frail elderly (75 years or older with chronic condition). 2. Pre-specified study subgroups: Not applicable/Not stated/Unclear. 3. UK versus non-UK: UK (England).
Indirectness of population	No indirectness
Interventions	(n=255) Intervention 1: Community pharmacists with enhanced roles in disease management - Delivered at community clinics. Two weeks after the patient presented to the pharmacy for a prescription for a new medicine for a chronic condition, they received a telephone call from a community pharmacist based on a semi-structured interview; pharmacist listened to patient's problems and gave advice or reassurance if needed; asked the patient how they were getting on with their medicines, any medicine-related problems, adherence to the new medicine and whether they required any further information. Duration One-off. Concurrent medication/care: Not stated Further details: 1. Prescribing power: not stated (n=237) Intervention 2: Usual care. No further details. Duration 2 months. Concurrent medication/care: Not stated Further details: 1. Prescribing power: not stated
Funding	Academic or government funding (DHHC London Research & Development Responsive Funding Programme)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: LONG-TERM CONDITIONS versus USUAL CARE

Protocol outcome 1: Number of ED presentations during the study period
- Actual outcome for Long-term conditions: Number of people with 1 or more A&E visits at 2 months; Group 1: 2/87, Group 2: 11/118; Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - Very high, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 168, Reason: Drop out or non-response; Group 2 Number missing: 119, Reason: Drop out or non-response

Protocol outcome 2: GP attendances during the study period
- Actual outcome for Long-term conditions: Number of people with 1 or more GP visits at 2 months; Group 1: 71/87, Group 2: 94/118; Risk of bias: All domain - Flawed, Selection - High, Blinding - Low, Incomplete outcome data - Very high, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 168, Reason: Drop out or non-response; Group 2 Number missing: 119, Reason: Drop out or non-response

Study	Elliott 2008[63]
Protocol outcome 3: Hospital admissions during the study period - Actual outcome for Long-term conditions: Number of people with 1 or more hospitalisations at 2 months; Group 1: 3/87, Group 2: 11/118; Risk of bias: All domain - Flawed, Selection - High, Blinding - Low, Incomplete outcome data - Very high, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 168, Reason: Drop out or non-response; Group 2 Number missing: 119, Reason: Drop out or non-response	
Protocol outcomes not reported by the study	Mortality during the study period; Avoidable adverse events (incorrect diagnosis and treatment) during the study period; Quality of life during the study period; Patient and/or carer satisfaction during the study period

Study	EMDADER-CV trial: Amariles 2012[6]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=714)
Countries and setting	Conducted in Spain; Setting: Community pharmacy
Line of therapy	Adjunctive to current care
Duration of study	Intervention time: 8 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: High or moderate CV risk according to the Systematic Coronary Risk Evaluation (SCORE) system and/or Wilson-Grundy method
Stratum	Overall: Cardiovascular disease or Cardiovascular risk
Subgroup analysis within study	Not applicable
Inclusion criteria	Patients aged 25 to 74 years; presented at the pharmacy with a prescription for at least 1 drug indicated for hypertension, hypercholesterolemia, CVD prophylaxis, or type 2 diabetes; High or moderate CV risk according to the Systematic Coronary Risk Evaluation (SCORE) system and/or Wilson-Grundy method
Exclusion criteria	Patients with BP of 180/110 or higher, history of myocardial infarction in the previous 3 months, a terminal disease, an intellectual or physical disability that prevented them from participating in the study, currently included in a cardiac rehabilitation program
Recruitment/selection of patients	Patients presenting at the pharmacy
Age, gender and ethnicity	Age - Mean (SD): 62.8 (8.1). Gender (M:F): 373:341. Ethnicity: NR
Further population details	1. Frail elderly: Non-frail elderly (Age and morbidity of patients). 2. Pre-specified study subgroups: Not applicable/Not stated/Unclear. 3. UK versus non-UK: Non-UK (Spain).

Study	EMDADER-CV trial: Amariles 2012[6]
Indirectness of population	No indirectness
Interventions	(n=356) Intervention 1: Community pharmacists with enhanced roles in disease management - Delivered at community pharmacy. The Dader method for pharmaceutical care: Pharmacists obtained patient data related to CV medical problems and current drug therapy, obtained by interviewing the patient and reviewing the drug and clinical records. Used the collected data to complete the assessment form, which was interpreted and evaluated once all the necessary information was added. Evaluated the patient's drug therapy outcomes to assess whether eh desired treatment goals for BP and TC were achieved. The pharmacist developed therapeutic plans that included interventions with the aim of achieving the desired clinical outcome. Conducted an intervention intended to directly prevent or resolve a Negative Outcomes associated with Medication (NOM). If the intervention was to modify drug therapy the recipient of the intervention was the physician. Completed a new assessment form to inform the physician of possible further modifications in the patient's care plan. Duration 8 months. Concurrent medication/care: Treatment for CVD. Verbal and written counselling regarding cardiovascular disease prevention (according to patient risk) Further details: 1. Prescribing power: Non-prescribing (If the intervention was to modify drug therapy the recipient of the intervention was the physician). (n=358) Intervention 2: Usual care. Usual care provided by the pharmacist. Duration 8 months. Concurrent medication/care: Treatment for CVD. Verbal and written counselling regarding cardiovascular disease prevention (according to patient risk) Further details: 1. Prescribing power: Not stated
Funding	Principal author funded by industry (Roche Diagnostics, SL, Spain; Stada Laboratory, SL, Spain)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DELIEVERED AT COMMUNITY PHARMACY versus USUAL CARE Protocol outcome 1: Mortality during the study period - Actual outcome: Mortality at 8 months; Group 1: 0/356, Group 2: 2/358; Risk of bias: All domain - Very high, Selection - Low, Blinding - Low, Incomplete outcome data - High, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0, Reason: 25 failed to attend the first scheduled appointment, 14 moved out of study area; Group 2 Number missing: 33, Reason: 25 failed to attend the first scheduled appointment, 8 moved out of study area	
Protocol outcomes not reported by the study	Avoidable adverse events (incorrect diagnosis and treatment) during the study period; Quality of life during the study period; Number of ED presentations during the study period; GP attendances during the study period; Hospital admissions during the study period; Patient and/or carer satisfaction during the study period

Study (subsidiary papers)	Gordois 2007[79] (Armour 2007[8])
Study type	RCT (Practice randomised; Parallel)
Number of studies (number of participants)	1 (n=396)
Countries and setting	Conducted in Australia; Setting: Community pharmacies
Line of therapy	Not applicable
Duration of study	Follow up (post intervention): 6 months
Method of assessment of guideline condition	Method of assessment /diagnosis not stated
Stratum	Overall: Asthma
Subgroup analysis within study	Not applicable
Inclusion criteria	age 18-75 years old, previous diagnosis of asthma, fulfilment of one or more of the following criteria: Use of a reliever medication >3 times a week over the previous 4 weeks, Waking at night or morning with cough/chest tightness on at least one occasion over the previous 4 weeks, Time off work/study because of asthma over the previous 4 weeks, Symptoms of asthma (cough, breathlessness, wheeze, etc.) at least once a week over the previous 4 weeks, and no visit to a doctor for asthma within the last 6 months
Exclusion criteria	terminal illness, were currently enrolled in another clinical trial, did not self-administer their inhaler and/or did not speak English well enough to communicate
Recruitment/selection of patients	Accredited pharmacies located within 300 km of any of the four participating institutions with inclusion criteria of: QCPP accreditation, availability of a computer system compatible with the spirometer software to be used in the study, ability to attend training sessions and a minimum of two pharmacists on duty at any one time. The exclusion criterion for pharmacies was current involvement in any other research project. Pharmacies were asked to recruit up to 10 subjects from their customers
Age, gender and ethnicity	Age - Mean (SD): Group 1: 50.4 (16.1); Group 2: 47.5 (17.1). Gender (M:F): Define. Ethnicity: NR
Further population details	1. Frail elderly: Non-frail elderly (Age and morbidity). 2. Pre-specified study subgroups: Not applicable/Not stated/Unclear. 3. UK versus non-UK: Non-UK (Australia).
Indirectness of population	No indirectness
Interventions	(n=191) Intervention 1: Community pharmacists with enhanced roles in disease management - Delivered at community clinics. Pharmacy Asthma Care Program which included targeted counselling and education on the condition, medication and lifestyle issues (such as trigger factors); review of inhaler technique; adherence assessment; detection of drug-related problems; goal setting and review; and referral to a GP as appropriate (for example, for a change in medication or dose). Duration 6 months. Concurrent medication/care: treatment for asthma

Study (subsidiary papers)	Gordois 2007[79] (Armour 2007[8])
	Further details: 1. Prescribing power: Non-prescribing (referral to a GP as appropriate (for example, for a change in medication or dose)). Comments: Intervention pharmacists were given an asthma education manual and were trained on risk assessment, pathophysiology of asthma, asthma medications, the NAC six-step asthma management plan, patient education, goal setting, adherence assessment, spirometer (by qualified respiratory scientists) and the PACP protocol during a 2-day workshop delivered by the research team (n=205) Intervention 2: Usual care. Received no intervention other than the pharmacist's usual care. Duration 6 months. Concurrent medication/care: treatment for asthma Further details: 1. Prescribing power: Not stated Comments: trained on risk assessment, spirometer and the control protocol during a 1-day workshop
Funding	Academic or government funding (Australian Department of Health)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DELIEVERED AT COMMUNITY CLINICS versus USUAL CARE Protocol outcome 1: Number of ED presentations during the study period - Actual outcome: Total ED visits at 6 months; Group 1: 7/162, Group 2: 9/184; Risk of bias: All domain - high, Selection - high, Blinding - high, Incomplete outcome data - low, Measurement - low, Crossover - Low; Indirectness of outcome: No indirectness Protocol outcome 2: GP attendances during the study period - Actual outcome: Total GP attendances at 6 months; Group 1: 309/162, Group 2: 278/185; Risk of bias: All domain - high, Selection - high, Blinding - high, Incomplete outcome data - low, Measurement - low, Crossover - Low; Indirectness of outcome: No indirectness Protocol outcome 3: Hospital admissions during the study period - Actual outcome: Total hospital admissions at 6 months; Group 1: 6/163, Group 2: 11/185; Risk of bias: All domain - high, Selection - high, Blinding - high, Incomplete outcome data - low, Measurement - low, Crossover - Low; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Mortality during the study period; Avoidable adverse events (incorrect diagnosis and treatment) during the study period; Quality of life during the study period; Patient and/or carer satisfaction during the study period

Study (subsidiary papers)	Heart Failure Optimal Outcomes from Pharmacy Study (HOOPS) trial: Lowrie 2012[129] (Lowrie 2011[130])
Study type	RCT (Practice randomised; Parallel)
Number of studies (number of participants)	1 (n=2164)
Countries and setting	Conducted in United Kingdom; Setting: Primary care practices

Study (subsidiary papers)	Heart Failure Optimal Outcomes from Pharmacy Study (HOOPS) trial: Lowrie 2012[129] (Lowrie 2011[130])
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 6 days - 6.2 years post randomisation
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: confirmed by cardiac imaging conducted at a local hospital
Stratum	Overall: Heart failure
Subgroup analysis within study	Not applicable
Inclusion criteria	Written, informed consent, aged ≥18 years and had left ventricular systolic dysfunction confirmed by cardiac imaging conducted at a local hospital (transthoracic echocardiography in 90% of cases)
Exclusion criteria	Concurrent serious systemic disease (other than heart failure) likely to reduce life-expectancy (for example, advanced malignancy), Severe cognitive impairment, Severe psychiatric illness, Chronic renal impairment requiring dialysis, Resident of long-term care facility, Current registration with the nurse-led heart failure service
Recruitment/selection of patients	A letter was sent inviting all 220 General Practices in the area to participate in the trial. Non-responding practices were re-invited, on up to three occasions, until the end of the recruitment period. After receiving written consent from a practice, study personnel arranged a visit to identify eligible patients, by searching practice electronic records to identify patients with possible LVSD using specific Read codes
Age, gender and ethnicity	Age - Mean (SD): Group 1: 70.6 (10.3); Group 2: 70.6 (10.1). Gender (M:F): 1520:649. Ethnicity: NR
Further population details	1. Frail elderly: Not applicable/Not stated/Unclear. 2. Pre-specified study subgroups: Not applicable/Not stated/Unclear. 3. UK versus non-UK: UK (UK).
Indirectness of population	No indirectness
Interventions	(n=1092) Intervention 1: Clinical pharmacists with enhanced roles in disease management - Delivered at general practices. Prior to commencing the intervention, all pharmacists attended one, in-house training day (contact time 7.5 h) covering the aetiology, symptoms, and evidence-based management of heart failure. As part of routine continuing professional development, each pharmacist participated in a 3.5-h peer-led session every month which involved group discussion of cases encountered in their medication review clinics. Patients from practices assigned to the intervention were offered a 30-min appointment with a pharmacist. If there was agreement between the pharmacist and the patient during the consultation and subsequently with the family doctor, medications were initiated, discontinued, or modified by the pharmacist during 3–4 subsequent weekly or fortnightly consultations. Duration Single visit plus 3–4 subsequent weekly or fortnightly consultations if change in care plan. Concurrent medication/care: Treatment for heart failure Further details: 1. Prescribing power: Prescribing (Pharmacist modified treatment during weekly or fortnightly consultations following agreement with GP). Comments: All participating pharmacists had between 3 and 16 years of post-qualification experience. All had

Study (subsidiary papers)	Heart Failure Optimal Outcomes from Pharmacy Study (HOOPS) trial: Lowrie 2012[129] (Lowrie 2011[130])
	experience delivering primary care-based medication review clinics for patients receiving multiple drug treatment. Seven pharmacists held post-graduate clinical pharmacy qualifications. Four pharmacists had hospital (ward-based) clinical pharmacy experience (n=1077) Intervention 2: Usual care. No instructions were given to family doctors in the usual care practices. The study pharmacists did not collect information on symptoms or examine the patients as this was not part of their professional training. Duration time-to-event (6 days - 6.2 years). Concurrent medication/care: Treatment for heart failure Further details: 1. Prescribing power: Not stated
Funding	Academic or government funding (NHS in Greater Glasgow and Clyde)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DELIEVERED AT GENERAL PRACTICES versus USUAL CARE Protocol outcome 1: Mortality during the study period - Actual outcome: Mortality at 6 days - 6.2 years post randomisation; 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 - Actual outcome: Admission at 6 days - 6.2 years post randomisation; Risk of bias: All domain - Low, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Avoidable adverse events (incorrect diagnosis and treatment) during the study period; Quality of life during the study period; Number of ED presentations during the study period; GP attendances during the study period; Hospital admissions during the study period; Patient and/or carer satisfaction during the study period

Study (subsidiary papers)	Holland 2005[91] (Holland 2006[92])
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=872)
Countries and setting	Conducted in United Kingdom; Setting: Patient's home
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 6 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Admitted as an emergency
Stratum	Long-term conditions

Study (subsidiary papers)	Holland 2005[91] (Holland 2006[92])
Subgroup analysis within study	Not applicable
Inclusion criteria	Over 80, admitted as an emergency, intended to be discharged to their own home or warden controlled accommodation, prescribed two or more drugs on discharge.
Exclusion criteria	Dialysis treatment and participation in an intensive discharge service on one site
Recruitment/selection of patients	Four general hospitals and six community hospitals
Age, gender and ethnicity	Age - Mean (SD): Group 1: 85.4 (4.0); Group 2: 85.5 (4.0). Gender (M:F): 321:534. Ethnicity: NR
Further population details	1. Frail elderly: Frail elderly (Age and morbidity). 2. Pre-specified study subgroups: Not applicable/Not stated/Unclear. 3. UK versus non-UK: UK (UK).
Indirectness of population	No indirectness
Interventions	(n=437) Intervention 1: Community pharmacists with enhanced roles in disease management - Delivered at patient's home. Initial referral to a review pharmacist included a copy of the patient's discharge letter. Pharmacists arranged home visits at times when they could meet patients and carers (mean was 7.2 days before visit). Pharmacists assessed patients' ability to self-medicate and drug adherence, and they completed a standardised visit form. Where appropriate, they educated the patient and carer, removed out of date drugs, reported possible drug reactions or interactions to the general practitioner, and reported the need for a compliance aid to the local pharmacist. One follow-up visit occurred at six to eight weeks after recruitment to reinforce the original advice. Duration Single visit + one follow-up. Concurrent medication/care: None stated Further details: 1. Prescribing power: Non-prescribing (Reported possible drug reactions or interactions to the general practitioner). (n=435) Intervention 2: Usual care. No further details. Duration 6 months. Concurrent medication/care: None stated Further details: 1. Prescribing power: Not stated
Funding	Academic or government funding (NHS eastern Region R&D and the University of East Anglia)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DELIEVERED AT PATIENT'S HOME versus USUAL CARE

Protocol outcome 1: Mortality during the study period
- Actual outcome: Mortality at 6 months; HR 0.75 (95%CI 0.52 to 1.1) 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 ; Group 1 Number missing: 22, Reason: 8 post-randomisation exclusion (reasons given for overall only), 2 moved out of study area, 12 withdrew from study; Group 2 Number missing: 21, Reason: 9 post-randomisation exclusion (reasons given for overall only), 4 moved out of study area, 8 withdrew from study

Study (subsidiary papers)	Holland 2005[91] (Holland 2006[92])
Protocol outcome 2: Quality of life during the study period - Actual outcome: Quality of life (EQ-5D) at 6 months; Group 1: mean -0.131 (SD 0.33); n=308, Group 2: mean -0.137 (SD 0.34); n=284; EQ-5D 0-1 Top=High is good outcome; Risk of bias: All domain - Very high, Selection - High, Blinding - Very high, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 22, Reason: 8 post-randomisation exclusion (reasons given for overall only), 2 moved out of study area, 12 withdrew from study; Group 2 Number missing: 21, Reason: 9 post-randomisation exclusion (reasons given for overall only), 4 moved out of study area, 8 withdrew from study - Actual outcome: Quality of life (VAS) at 6 months; Group 1: mean -7.36 (SD 24.4); n=308, Group 2: mean -3.24 (SD 23); n=284; Visual analogue scale 0-100 Top=High is good outcome; Risk of bias: All domain - Very high, Selection - High, Blinding - Very high, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 22, Reason: 8 post-randomisation exclusion (reasons given for overall only), 2 moved out of study area, 12 withdrew from study; Group 2 Number missing: 21, Reason: 9 post-randomisation exclusion (reasons given for overall only), 4 moved out of study area, 8 withdrew from study Protocol outcome 3: Hospital admissions during the study period - Actual outcome: Hospital readmission at 6 months; Group 1: 162/415, Group 2: 133/414; Risk of bias: All domain - 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: 22, Reason: 8 post-randomisation exclusion (reasons given for overall only), 2 moved out of study area, 12 withdrew from study; Group 2 Number missing: 21, Reason: 9 post-randomisation exclusion (reasons given for overall only), 4 moved out of study area, 8 withdrew from study	
Protocol outcomes not reported by the study	Avoidable adverse events (incorrect diagnosis and treatment) during the study period; Number of ED presentations during the study period; GP attendances during the study period; Patient and/or carer satisfaction during the study period

Study	Holland 2007[93]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=339)
Countries and setting	Conducted in United Kingdom; Setting: Patient's home
Line of therapy	Unclear
Duration of study	Intervention + follow up: Intervention 6-8 weeks; follow up to 6 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Diagnosed in hospital
Stratum	Long-term conditions: Heart failure
Subgroup analysis within study	Not applicable

Study	Holland 2007[93]
Inclusion criteria	Adults (over 18 years) admitted as an emergency in which heart failure was an important on-going clinical condition and prescribed two or more drugs (any class) on discharge.
Exclusion criteria	Living in residential or nursing home, awaiting surgery for ischaemic or valvular heart disease or heart transplant; terminal malignancy
Recruitment/selection of patients	Recruited from three large district general hospitals
Age, gender and ethnicity	Age - Mean (SD): Intervention: 77.6 (9.0); control: 76.4 (9.5) years. Gender (M:F): 186:107. Ethnicity: Not stated
Further population details	1. Frail elderly: Not applicable/Not stated/Unclear. 2. Pre-specified study subgroups: Not applicable/Not stated/Unclear. 3. UK versus non-UK: UK (England).
Indirectness of population	No indirectness
Interventions	(n=149) Intervention 1: Community pharmacists with enhanced roles in disease management - Delivered at patient's home. Community pharmacists with post-graduate qualification in pharmacy practice or recent CPD in therapeutics; not independent prescribers so could not directly modify drug regimen. Pharmacists provided with copy of discharge letter; arranged a home visit within 2 weeks of discharge; educated patient/carer about heart failure and drugs and gave basic exercise, dietary and smoking cessation advice; encouraged completion of simple sign and symptom monitoring diary cards (including weight); removed discontinued drugs; fed back recommendations to the GP; fed back to local pharmacist any need for drug adherence aid. Pharmacists were provided with detailed manual describing expected components of their visit and asked to deliver education in line with advice in the British Heart Foundation's booklet "Living with heart failure" which they left with the patients at the first visit. One follow-up visit occurred at 6-8 weeks after discharge to review progress and reinforce original advice. Duration 6-8 weeks. Concurrent medication/care: pharmacological treatment for heart failure (n=144) Intervention 2: Usual care. No further details. Duration 6 months. Concurrent medication/care: pharmacological treatment for heart failure
Funding	Other (British Heart Foundation, Great Yarmouth and Southern Norfolk Primary Care Trusts. Pfizer UK)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: LONG-TERM CONDITIONS versus USUAL CARE Protocol outcome 1: Mortality during the study period - Actual outcome for Long-term conditions: Mortality at 6 months; Group 1: 30/149, Group 2: 24/144; Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Baseline	

Study	Holland 2007[93]
details: Fewer intervention patients were from non-manual social classes (44% vs. 55%) and intervention patients more often used a drug adherence aid (27% vs. 16%) Protocol outcome 2: Quality of life during the study period - Actual outcome for Long-term conditions: EQ-5D at 6 months; Group 1: mean 0.58 (SD 0.29); n=108, Group 2: mean 0.52 (SD 0.34); n=104; EQ-5D -0.59 to +1 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, Subgroups - Low; Indirectness of outcome: No indirectness ; Baseline details: Fewer intervention patients were from non-manual social classes (44% vs. 55%) and intervention patients more often used a drug adherence aid (27% vs. 16%); Group 1 Number missing: 41, Reason: 1 moved out of area; the rest missing data; Group 2 Number missing: 40, Reason: 1 moved out of area; the rest missing data Protocol outcome 3: Hospital admissions during the study period - Actual outcome for Long-term conditions: Number of patients with any emergency hospital readmissions at 6 months; Group 1: 76/148, Group 2: 73/143; Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Baseline details: Fewer intervention patients were from non-manual social classes (44% vs. 55%) and intervention patients more often used a drug adherence aid (27% vs. 16%); Group 1 Number missing: 1, Reason: 1 moved out of area; Group 2 Number missing: 1, Reason: 1 moved out of area	
Protocol outcomes not reported by the study	Avoidable adverse events (incorrect diagnosis and treatment) during the study period; Number of ED presentations during the study period; GP attendances during the study period; Patient and/or carer satisfaction during the study period

Study	HOME study trial: Zillich 2005[233]
Study type	RCT (Practice randomised; Parallel)
Number of studies (number of participants)	1 (n=125)
Countries and setting	Conducted in USA; Setting: Community pharmacy
Line of therapy	Not applicable
Duration of study	Intervention time: 3 months
Method of assessment of guideline condition	Partially adequate method of assessment/diagnosis: Screening visit (no further details)
Stratum	Overall: Hypertension
Subgroup analysis within study	Not applicable
Inclusion criteria	Over 20 years of age with a diagnosis of hypertension, taking 1-3 BP medications with no changes in the regimen or dose within the past 4 weeks, receiving BP medication from the same physician for at least 2 consecutive months, and for non-diabetic patients SBP between 145 and 179 mmHg or DBO between 95 and 109 mmHg, for diabetic patients SBP between 135 and 179 mmHg or DBO between 90 and 109 mmHg

Study	HOME study trial: Zillich 2005[233]
Exclusion criteria	BP greater than 180/110 mmHg, a MI or Stroke within the last 6 months, serious renal or hepatic disease, pregnancy, dementia/cognitive impairment
Recruitment/selection of patients	Pharmacies were recruited based on commitment and willingness to participate (no further details). Patients receiving antihypertensive medications from participating pharmacies were informed of the study from a pharmacist or technician during medication refills
Age, gender and ethnicity	Age - Mean (SD): Group 1: 66.1 (13.8); Group 2: 64.0 (11.1). Gender (M:F): 49:76. Ethnicity: Group 1 - White: 98%, Other: 2%; Group 2 - White: 97%, Other: 3%
Further population details	1. Frail elderly: Not applicable/Not stated/Unclear. 2. Pre-specified study subgroups: Not applicable/Not stated/Unclear. 3. UK versus non-UK: Non-UK (USA).
Indirectness of population	No indirectness
Interventions	(n=64) Intervention 1: Community pharmacists with enhanced roles in disease management - Delivered at community pharmacy. Patients were scheduled to meet face-to-face with a pharmacist 4 times over 3 months. At each visit pharmacists provided patient-specific education about hypertension, including: disease process and complications, medication use and adherence, lifestyle modification, and home SBP monitor (SBPM) technique. During the baseline and third visit the patients were provided with a validated, fully automated home SBPM. Patients were instructed to perform 2 home BP measurements, separated by 5 minutes of rest, at least once daily in the morning. Home BP readings were recorded by the patient in the log book. During the second and fourth visit, logs and monitors were returned to the pharmacist who calculated weekly BP averages and used the measurements to develop written treatment recommendations for the patient's physician. If home BP weekly averages exceeded 140/90 mmHg (130/80mmHg for patients with diabetes and/or kidney disease), the pharmacists' recommended intensification of the medication regimen. Recommendations and BP logs were sent via facsimile to the physician and followed by a telephone call. Duration 3 months. Concurrent medication/care: Treatment for hypertension Further details: 1. Prescribing power: Non-prescribing (Recommendations sent to physician). (n=61) Intervention 2: Usual care. Patients met face-to-face with a trained pharmacist 3 times over 3 months. At each visit, patients' BP was measure by the pharmacist. In most cases, patients were told that their BP was above normal and they should contact their physician. These patients did not receive any other pharmacist education or home BP monitors. The BP measurements were sent via facsimile to the patients' physician without treatment recommendations. Duration 3 months. Concurrent medication/care: Treatment for hypertension Further details: 1. Prescribing power: Unclear
Funding	Other (Community Pharmacy Funding (non-profit))

Study	HOME study trial: Zillich 2005[233]
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DELIEVERED AT COMMUNITY PHARMACY versus USUAL CARE Protocol outcome 1: Number of ED presentations during the study period - Actual outcome: Total ER visits during the study period; Group 1: 0/64, Group 2: 4/61; Risk of bias: All domain - Very high, Selection - High, Blinding - High, Crossover - Low; Indirectness of outcome: No indirectness Protocol outcome 2: GP attendances during the study period - Actual outcome: Total physician office visits at 3 months; Group 1: 20/64, Group 2: 56/61; Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 3: Hospital admissions during the study period - Actual outcome: Total hospital admissions at 3 months; Group 1: 0/64, Group 2: 4/61; Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Mortality during the study period; Avoidable adverse events (incorrect diagnosis and treatment) during the study period; Quality of life during the study period; Patient and/or carer satisfaction during the study period

Study	Jodar-Sanchez 2015[103]
Study type	RCT (Practice randomised; Parallel)
Number of studies (number of participants)	1 (n=1403)
Countries and setting	Conducted in Spain; Setting: Community pharmacies
Line of therapy	Unclear
Duration of study	Intervention time: 6 months
Method of assessment of guideline condition	Partially adequate method of assessment/diagnosis: Pharmacist assessment
Stratum	Long-term conditions
Subgroup analysis within study	Not applicable
Inclusion criteria	Older adults aged 65 years or over with polypharmacy, that is, taking 5 or more officially registered (prescribed or over-the-counter) medicines per day.
Exclusion criteria	Not stated
Recruitment/selection of patients	Pharmacists selected eligible patients
Age, gender and ethnicity	Age - Mean (SD): Intervention: 75.36 (6.48); control: 74.91 (6.58) years. Gender (M:F): 553:850. Ethnicity: Not stated

Study	Jodar-Sanchez 2015[103]
Further population details	1. Frail elderly: Not applicable/Not stated/Unclear. 2. Pre-specified study subgroups: Not applicable/Not stated/Unclear. 3. UK versus non-UK: Non-UK (Spain).
Indirectness of population	No indirectness
Interventions	(n=688) Intervention 1: Community pharmacists with enhanced roles in disease management - Delivered at patient's home. Pharmacists allocated into the intervention group received a 3-day off-site training course and on-site visits by a facilitator during the 6 months follow up, to assist pharmacists in the provision of the service and ensuring quality and homogeneity of the interventions. Pharmacists and patients had follow-up visits every 1-2 months. Duration 6 months. Concurrent medication/care: Not stated (n=715) Intervention 2: Usual care. No further details. Duration 6 months. Concurrent medication/care: Not stated
Funding	Other (Spanish General Council of Official Colleges of Pharmacists and CINFA Laboratory)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: LONG-TERM CONDITIONS versus USUAL CARE

Protocol outcome 1: Quality of life during the study period
- Actual outcome for Long-term conditions: EQ-5D-3L at 6 months; Group 1: mean 0.0528 (SD 0.2); n=627, Group 2: mean -0.0022 (SD 0.24); n=671; EQ-5D-3L 0-1 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, Subgroups - Low; Indirectness of outcome: No indirectness ; Baseline details: Level of education: 27% intervention vs. 18.6% controls had no formal education, p<0.001; mean number of prescribed medications: 7.74 in intervention group and 7.39 for controls, p=0.009; Group 1 Number missing: 61, Reason: Drop out; Group 2 Number missing: 44, Reason: Drop out

Protocol outcome 2: Number of ED presentations during the study period
- Actual outcome for Long-term conditions: Numbers of patients who visited A&E at least once at 6 months; Group 1: 89/627, Group 2: 167/671; Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Baseline details: Level of education: 27% intervention vs. 18.6% controls had no formal education, p<0.001; mean number of prescribed medications: 7.74 in intervention group and 7.39 for controls, p=0.009; Group 1 Number missing: 61, Reason: Drop out; Group 2 Number missing: 44, Reason: Drop out

Protocol outcome 3: Hospital admissions during the study period
- Actual outcome for Long-term conditions: Mean number of admissions at 6 months; Group 1: mean 0.05 (SD 0.23); n=627, Group 2: mean 0.07 (SD 0.36); n=671; Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Baseline details: Level of education: 27% intervention vs. 18.6% controls had no formal education, p<0.001; mean

Study	Jodar-Sanchez 2015[103]
number of prescribed medications: 7.74 in intervention group and 7.39 for controls, p=0.009; Group 1 Number missing: 61, Reason: Drop out; Group 2 Number missing: 44, Reason: Drop out	
Protocol outcomes not reported by the study	Mortality during the study period; Avoidable adverse events (incorrect diagnosis and treatment) during the study period; GP attendances during the study period; Patient and/or carer satisfaction during the study period

Study (subsidiary papers)	Krska 2001[115] (Krska 2007[116])
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=381)
Countries and setting	Conducted in United Kingdom; Setting: Patient's home
Line of therapy	Not applicable
Duration of study	Intervention: 3 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Over 65s with polypharmacy and two chronic conditions
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Aged at 65 years, regular request for at least four medicines via the computerised repeat prescribing system and at least two chronic conditions
Exclusion criteria	Dementia and being considered by the GP to be unable to cope with the study
Recruitment/selection of patients	All medical practices within the area with at least 500 patients aged 65 years or over were stratified into three levels by the deprivation status (Jarman index) of their practice population and by fund holder status (yes/no). Using random number tables, one practice from each of the six resultant categories was selected and invited to participate. One practice refused and a further practice was randomly selected
Age, gender and ethnicity	Age - Mean (SD): Group 1: 74.8 (6.2); Group 2: 75.2 (6.6). Gender (M:F): Group 1: 73:95; Group 2: 58:106. Ethnicity: NR
Further population details	1. Frail elderly: Frail elderly (Over 65s with polypharmacy and two chronic conditions). 2. Pre-specified study subgroups: Not applicable/Not stated/Unclear. 3. UK versus non-UK: UK (UK).
Indirectness of population	No indirectness

Study (subsidiary papers)	Krska 2001[115] (Krska 2007[116])
Interventions	(n=168) Intervention 1: Clinical pharmacists with enhanced roles in disease management - Delivered at patient's home. Clinically-trained pharmacists completed a detailed profile for each patient using medical notes and practice computer records. All patients were then interviewed in their own home about their use of and responses to medication, and their use of health and social services. A pharmaceutical care plan was drawn up for each intervention group patient, copies of the plan were inserted in the patients' medical notes and given to their GP, who was asked to indicate their level of agreement with each Pharmaceutical Care Issues identified and with the suggested actions. The pharmacist then implemented all agreed actions, assisted by other practice staff where appropriate. Duration Single visit. Concurrent medication/care: treatment for at least two chronic conditions Further details: 1. Prescribing power: Not stated (n=164) Intervention 2: Usual care. Control patients were similarly interviews and PCIs identified, although no pharmaceutical care plan was implemented. Patients were advised to consult any with any usual carers or health-care professionals in response to direct queries during interview. When a pharmacist considered a PCI to potentially serious, an independent medical assessor decided on the need to withdraw the patient from the study on clinical grounds. Duration Single visit. Concurrent medication/care: treatment for at least two chronic conditions Further details: 1. Prescribing power: Not stated
Funding	Academic or government funding (Grampian Healthcare NHS trust)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DELIEVERED AT PATIENT'S HOME versus USUAL CARE Protocol outcome 1: Hospital admissions during the study period - Actual outcome: Emergency hospital admissions at 3 months; Group 1: 6/168, Group 2: 8/164; Risk of bias: All domain - Very high, Selection - Very high, Blinding - High, Incomplete outcome data - High, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Intervention patients experience both more baseline elective (13) and emergency admissions (23) than control (five elective and 11 emergency); Group 1 Number missing: 24, Reason: 24: mainly due to hospital admission, ill health or holiday ; Group 2 Number missing: 25, Reason: 25: 1 withdrawn by independent assessor (unclear if blinded), 24 mainly due to hospital admission, ill health or holiday	
Protocol outcomes not reported by the study	Mortality during the study period; Avoidable adverse events (incorrect diagnosis and treatment) during the study period; Quality of life during the study period; Number of ED presentations during the study period; Patient and/or carer satisfaction during the study period

Study	Lenaghan 2007[122]
Study type	RCT (Patient randomised; Parallel)

Study	Lenaghan 2007[122]
Number of studies (number of participants)	1 (n=136)
Countries and setting	Conducted in United Kingdom; Setting: General practice
Line of therapy	Unclear
Duration of study	Intervention + follow up: Intervention 6-8 weeks, follow up to 6 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: GP assessment
Stratum	Long-term conditions
Subgroup analysis within study	Not applicable
Inclusion criteria	Patients over 80 years, living in their own homes, prescribed at least 4 oral daily medicines plus at least one of the following criteria: living alone; record of confused mental state, vision or hearing impairment; prescribed medicines associated with medication-related morbidity; or prescribed >7 regular oral medicines
Exclusion criteria	Residents in a care home or documented use of adherence aid
Recruitment/selection of patients	Recruited from a dispensing general practice
Age, gender and ethnicity	Age - Mean (SD): Intervention: 84.5; control: 84.1 years (no SDs given). Gender (M:F): 46:88. Ethnicity: Not stated
Further population details	1. Frail elderly: Frail elderly (Over 80 years prescribed at least 4 oral daily medicines). 2. Pre-specified study subgroups: Not applicable/Not stated/Unclear. 3. UK versus non-UK: UK (England).
Indirectness of population	No indirectness
Interventions	(n=69) Intervention 1: Community pharmacists with enhanced roles in disease management - Delivered at community clinics. One community pharmacist experienced in home-based medication reviews, with a post-graduate qualification in pharmacy practice, visited patients. The referral to the review pharmacist included a copy of the participant's current medication and medical history; this was used to highlight areas to be addressed including possible drug interactions, adverse effects or storage issues. Whenever possible, the home visit was arranged for a time when the pharmacist could meet any carers who helped with the patient's medications. The pharmacist educated the patient, removed out-of-date drugs and assessed the need for an adherence aid. The pharmacist and GP held regular meetings. Possible changes to the patient's prescribed medication were discussed and agreed amendments were put in place by the GP or delegated to the practice dispensing team. A follow up visit occurred 6-8 weeks later to reinforce the original advice and assess whether there were any further pharmaceutical care issues to address with the GP. Duration 6-8 weeks. Concurrent medication/care: Not stated Further details: 1. Prescribing power: not stated (n=67) Intervention 2: Usual care. No further details. Duration 6 months. Concurrent medication/care: Not stated Further details: 1. Prescribing power: not stated

Study	Lenaghan 2007[122]
Funding	Academic or government funding (NHS Executive Eastern Region)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: LONG-TERM CONDITIONS versus USUAL CARE Protocol outcome 1: Mortality during the study period - Actual outcome for Long-term conditions: Mortality at 6 months; Group 1: 7/68, Group 2: 6/66; Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 1, Reason: Withdrew; Group 2 Number missing: 1, Reason: Withdrew Protocol outcome 2: Hospital admissions during the study period - Actual outcome for Long-term conditions: Unplanned hospital admissions at 6 months; Group 1: 20/68, Group 2: 21/66; Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 1, Reason: Withdrew; Group 2 Number missing: 1, Reason: Withdrew	
Protocol outcomes not reported by the study	Avoidable adverse events (incorrect diagnosis and treatment) during the study period; Quality of life during the study period; Number of ED presentations during the study period; GP attendances during the study period; Patient and/or carer satisfaction during the study period

Study	Lenander 2014[123]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=209)
Countries and setting	Conducted in Sweden; Setting: Primary care centre
Line of therapy	Unclear
Duration of study	Intervention + follow up: Intervention = one-off; follow up to 12 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: GP assessment
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Aged 65 years or more with 5 or more medications; already scheduled for an appointment with a GP

Study	Lenander 2014[123]
Exclusion criteria	Not fluent in Swedish; could not answer for themselves; participated in earlier pilot study
Recruitment/selection of patients	Patients identified through GP and contacted by phone and invited to participate
Age, gender and ethnicity	Age - Other: Intervention mean 79.0 (95% CI 77.8 to 80.2); control: 79.7 (78.4 to 81.1) years. Gender (M:F): 69:140. Ethnicity: Not stated
Further population details	1. Frail elderly: Not applicable/Not stated/Unclear. 2. Pre-specified study subgroups: Not applicable/Not stated/Unclear. 3. UK versus non-UK: Non-UK (Sweden).
Indirectness of population	No indirectness
Interventions	(n=107) Intervention 1: Clinical pharmacists with enhanced roles in disease management - Delivered at general practices. The intervention group met a certified geriatric pharmacist prior to a scheduled GP appointment who performed a medication review, using a standard semi-structured protocol that was open for patients' questions and remarks. Computerised patients records were checked for prescriptions, drug indications and plans for evaluation. Drugs and dosages were evaluated to correlate with renal function, good practice and the drug formulary. A patient-centred technique was used, focusing on the patient's questionnaire answers to assess understanding of and concordance with drug treatment. Patients were also asked about prescribers other than their GP and use of non-prescription and herbal drugs. Concluding pharmaceutical advice was given to patients and entered into the computerised patient record. Duration One-off. Concurrent medication/care: Not stated Further details: 1. Prescribing power: Unclear (n=102) Intervention 2: Usual care. No further details. Duration 12 months. Concurrent medication/care: Not stated Further details: 1. Prescribing power: Unclear
Funding	Academic or government funding (Stockholm County Council, Stockholm Drug and Therapeutics Committee, Apoteket AB)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: LONG-TERM CONDITIONS versus USUAL CARE Protocol outcome 1: Hospital admissions during the study period - Actual outcome for Long-term conditions: Mean number of hospitalisations per patient at 12 months; Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Baseline details: Patients in the intervention group used a greater number of drugs (8.6 vs. 7.4 per patient, p<0.05); Group 1 Number missing: 32, Reason: 10 withdrew, 22 non-response to questionnaire; Group 2 Number missing: 36, Reason: 20 withdrew, 16 non-response to questionnaire	
Protocol outcomes not reported by the study	Mortality during the study period; Avoidable adverse events (incorrect diagnosis and treatment) during the study

Study	Lenander 2014[123]
	period; Quality of life during the study period; Number of ED presentations during the study period; GP attendances during the study period; Patient and/or carer satisfaction during the study period

Study	Magid 2013[135]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=348)
Countries and setting	Conducted in USA; Setting: Primary care clinics
Line of therapy	Unclear
Duration of study	Intervention time: 6 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: GP assessment
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Adults 18 to 79 years of age with 1) diagnosis of hypertension and 2 most recent clinic BP readings above goal (systolic 140mmHg or more, or diastolic 90mmHg or more, or for those with diabetes or CKD, 130 and 80mmHg respectively); 2) prescribed 3 or fewer antihypertensive medications; 3) had a primary care provider who worked at one of the 10 participating clinics; and 4) were registered on the KPCO My Chart website (which suggested that they had access to a computer and the internet).
Exclusion criteria	1) Limited life expectancy (for example, in hospice or palliative care); 2) 80 years or older, because aggressive BP reduction may not be appropriate for these patients; 3) recent MI, stroke, PCI or CABG surgery because KPCO patients receive enhance hypertension care as part of intensive cardiac rehabilitation for 1 year after the event; 4) end-stage renal disease, because hypertension care is provided for these patients by nephrology specialists instead of primary care providers; 5) did not speak English; 6) did not have access to the internet and a computer with a USB port and Internet Explorer 6.0 or higher; 7) BP at baseline was already at goal; or 8) home BP cuff could not be validated (for example, home BP reading not within 5mmHg of baseline BP).
Recruitment/selection of patients	Identified by screening BP measurements and other clinical data recorded in electronic health record
Age, gender and ethnicity	Age - Mean (SD): Intervention: 59.1 (10.9); Control: 60.0 (11.3) years. Gender (M:F): 210:138. Ethnicity: Race: White: Intervention: 84.4%, control: 81.7%; Black: I: 6.1%, C: 8.6%; Asian: I: 0.6%; C: 2.9%; Other: I: 6.9%; C: 6.9%. Ethnicity: Hispanic: I: 5.8%; C: 9.1%
Further population details	1. Frail elderly: Not applicable/Not stated/Unclear. 2. Pre-specified study subgroups: Not applicable/Not

Study	Magid 2013[135]
	stated/Unclear. 3. UK versus non-UK: Non-UK (USA).
Indirectness of population	No indirectness
Interventions	(n=175) Intervention 1: Clinical pharmacists with enhanced roles in disease management - Delivered at general practices. Patients were provided with a properly fitting home BP cuff; trained how to use it; assisted in establishing an account at the Heart360 website; and shown how to automatically upload BPs stored on home BP device into Heart360 account. They were asked to measure their BP at least 3 times weekly and upload BP readings at least weekly. These were automatically organised into summary reports for the pharmacist, giving weekly BP averages and flagging patients with averages above goal. Patients met with a clinical pharmacy specialist who reviewed the home BP measurements, their current BP medications and adherence, provided counselling on lifestyle changes, and adjusted or changed antihypertensive medication as needed, communicating by phone or email. Any medication changes were communicated to the primary care physician through the electronic health record. Duration 6 months. Concurrent medication/care: Not stated Further details: 1. Prescribing power: Any medication changes were communicated to the primary care physician through the electronic health record. (n=173) Intervention 2: Usual care. Patients were advised that their BP was elevated, received written educational materials on managing high BP, diet and physical activity, and were instructed to follow up with their primary care physician; physician was notified of the patient's elevated BP via a note sent to the electronic health record in-box of the physician. Duration 6 months. Concurrent medication/care: Not stated Further details: 1. Prescribing power: not stated
Funding	Academic or government funding (American Heart Association)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: LONG-TERM CONDITIONS versus USUAL CARE Protocol outcome 1: Number of ED presentations during the study period - Actual outcome for Long-term conditions: Mean number of ED visits at 6 months; Group 1: mean 0.04 (SD 0.19); n=162, Group 2: mean 0.05 (SD 0.23); n=164; Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 13, Reason: Lost to follow up ; Group 2 Number missing: 9, Reason: Lost to follow up Protocol outcome 2: Hospital admissions during the study period - Actual outcome for Long-term conditions: Mean number of hospitalisations at 6 months; Group 1: mean 0.03 (SD 0.17); n=162, Group 2: mean 0.04 (SD 0.2); n=164; Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 13, Reason: Lost to follow up ; Group 2 Number missing: 9, Reason: Lost to	

Study	Magid 2013[135]
follow up	
Protocol outcomes not reported by the study	Mortality during the study period; Avoidable adverse events (incorrect diagnosis and treatment) during the study period; Quality of life during the study period; GP attendances during the study period; Patient and/or carer satisfaction during the study period

Study	Murray 2007[146]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=314)
Countries and setting	Conducted in USA; Setting: Community pharmacy
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 9 months + 3 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Identification from Medical Record System
Stratum	Overall: Congestive Heart Failure
Subgroup analysis within study	Not applicable
Inclusion criteria	Diagnosis of heart failure confirmed by their primary care physicians, 50 years or older, planned to receive all their care, including prescribed medications at within the study health service, regularly used at least 1 cardiovascular medication for heart failure, had access to a working telephone.
Exclusion criteria	Using or planning to use a medication aid (for example, a pill box), dementia
Recruitment/selection of patients	Weekly list of eligible patients were created by using the Medical Record System. Clinically stable patients were invited to participate (no further details)
Age, gender and ethnicity	Age - Mean (SD): Group 1: 61.4 (7.7); Group 2: 62.6 (8.8). Gender (M:F): 104:210. Ethnicity: Group 1 - Black: 45.1, White: 54.1, Other: 0.8; Group 2 - Black: 52.1, White: 46.9, Other: 1.0
Further population details	1. Frail elderly: Not applicable/Not stated/Unclear. 2. Pre-specified study subgroups: Not applicable/Not stated/Unclear. 3. UK versus non-UK: Non-UK (USA).
Extra comments	229 patients identified from general internal medicine practices, 15 from a cardiology clinic, and 70 at discharge from hospital. study pharmacy was adjacent to an ambulatory care centre
Indirectness of population	No indirectness

Study	Murray 2007[146]
Interventions	(n=122) Intervention 1: Community pharmacists with enhanced roles in disease management - Delivered at community pharmacy. A pharmacist delivered the intervention using a protocol that included a baseline medication history of all prescriptions and over the counter drugs and dietary supplements taken by patients, and the results of an assessment of patient medication knowledge and skills. When medications were dispensed, the pharmacist provided patient-centred verbal instructions and written materials about the medications. We assigned each medication category an icon (for example, the icon for ACE inhibitors was a red ace of hearts). The same icon appeared on the container label and lid and on the written patient instructions. Written instructions were aimed at patients with low health literacy and contained an easy-to-follow timeline to remind patients when to take their medications. The pharmacist monitored patients' medication use, health care encounters, body weight, and other relevant data by using a study database. Relevant information was communicated as needed to clinic nurses and primary care physicians by face-to-face visits, telephone, paging, and email. Duration 9 months. Concurrent medication/care: Treatment for congestive heart failure Further details: 1. Prescribing power: Non-prescribing Comments: Pharmacist delivered approximately 2 months' worth of medications per visit. The pharmacist was trained by an interdisciplinary team of investigators including pharmacists with advanced trading in patient education and cardiovascular pharmacotherapy, a geriatrician, a cardiologist with expertise in heart failure, a behavioural scientist, and a cognitive psychologist. (n=192) Intervention 2: Usual care. Patients received their prescription services from pharmacists who rotated through the study pharmacy. These pharmacists had not received the specialised training provided by the interdisciplinary team to the intervention pharmacist and did not have access to the patient-centred study materials. Duration 12 months. Concurrent medication/care: Treatment for congestive heart failure Further details: 1. Prescribing power: Not stated
Funding	Academic or government funding (National Institutes of Health)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DELIEVERED AT COMMUNITY PHARMACY versus USUAL CARE Protocol outcome 1: Mortality during the study period - Actual outcome: Mortality at 12 months; Group 1: 9/122, Group 2: 10/192; 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 ; Baseline details: more co-morbidities in usual care group; Group 1 Number missing: 18, Reason: 14 lost to follow up, 2 declined interview, 2 no longer eligible; Group 2 Number missing: 11, Reason: 3 lost to follow up, 2 declined interview, 2 no longer eligible, 9 died	

Study	Murray 2007[146]
Protocol outcome 2: Number of ED presentations during the study period - Actual outcome: Emergency Department visits at 12 months; Group 1: mean 2.16 (SD 3.31); n=122, Group 2: mean 2.68 (SD 4.87); n=192; Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Comments - Unclear if outcomes was measured for patients who were not analysed (dropped out) for the primary outcome; Indirectness of outcome: No indirectness ; Baseline details: more co-morbidities in usual care group; Group 1 Number missing: 18, Reason: 14 lost to follow up, 2 declined interview, 2 no longer eligible; Group 2 Number missing: 11, Reason: 3 lost to follow up, 2 declined interview, 2 no longer eligible, 9 died Protocol outcome 3: Hospital admissions during the study period - Actual outcome: Hospital admissions at 12 months; Group 1: mean 0.78 (SD 1.66); n=122, Group 2: mean 0.97 (SD 1.78); n=192; Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Comments - Unclear if outcomes was measured for patients who were not analysed (dropped out) for the primary outcome; Indirectness of outcome: No indirectness ; Baseline details: more co-morbidities in usual care group; Group 1 Number missing: 18, Reason: 14 lost to follow up, 2 declined interview, 2 no longer eligible; Group 2 Number missing: 11, Reason: 3 lost to follow up, 2 declined interview, 2 no longer eligible, 9 died	
Protocol outcomes not reported by the study	Avoidable adverse events (incorrect diagnosis and treatment) during the study period; Quality of life during the study period; GP attendances during the study period; Patient and/or carer satisfaction during the study period

Study	Pai 2009[162]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=107)
Countries and setting	Conducted in USA; Setting: Community-based haemodialysis clinic
Line of therapy	Not applicable
Duration of study	Intervention time: 2 years
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Undergoing haemodialysis
Stratum	Overall: Renal disease
Subgroup analysis within study	Not applicable
Inclusion criteria	Over 18 years of age, stable haemodialysis regimen for at least 3 months
Exclusion criteria	No informed consent, English not primary language
Recruitment/selection of patients	Not stated (assumed recruitment though attending normal haemodialysis sessions)

Study	Pai 2009[162]
Age, gender and ethnicity	Age - Mean (SD): Group 1: 55.8 (15.1); Group 2: 60.0 (15.0). Gender (M:F): Group 1: 38:23; Group 2: 18:28. Ethnicity: Group 1 - Black: 3%, Hispanic: 17%, Native American 15%, White 15%; Group 2 - Black: 5%, Hispanic: 13%, Native American 5%, White 16%
Further population details	1. Frail elderly: Non-frail elderly (Age and morbidity). 2. Pre-specified study subgroups: Not applicable/Not stated/Unclear. 3. UK versus non-UK: Non-UK (USA).
Extra comments	Six haemodialysis shifts that comprise the entire haemodialysis population were randomly assigned to receive pharmaceutical care or usual care. Two morning shifts and one evening shift was assigned the intervention, and two afternoons and one evening shift was assigned the control. Patients remained in their shift group throughout the study duration
Indirectness of population	No indirectness
Interventions	(n=61) Intervention 1: Clinical pharmacists with enhanced roles in disease management - Delivered at community clinics. Patients had medication reviews conducted by a nephrology-trained clinical pharmacist or one of two pharmacists completing postdoctoral training in nephrology pharmacotherapy. These patients were asked to bring in their medications every 8 weeks. At each session the clinical pharmacist would conduct a one-on-one patient interview, generate a current medication profile, identify and address various DRPs through review of medication, chart, and laboratory data, and provide healthcare provider and patient education. Duration 2 years. Concurrent medication/care: Haemodialysis Further details: 1. Prescribing power: Not stated (n=46) Intervention 2: Usual care. Periodic medication profile updates by dialysis nursing staff as mandated by the dialysis clinic policy and procedure. These are typically brief interactions where patients are queried as to whether any medications have changed since the last review. Duration 2 years. Concurrent medication/care: Haemodialysis Further details: 1. Prescribing power: Not stated
Funding	Other (PhRMAa Foundation)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DELIEVERED AT COMMUNITY CLINICS versus USUAL CARE Protocol outcome 1: Mortality during the study period - Actual outcome: Mortality at 2 years; Group 1: 16/61, Group 2: 9/46; Risk of bias: All domain - Very high, Selection - Very high, Blinding - High, Incomplete outcome data - High, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 17, Reason: transplant: 5, transfer to another clinic or shift: 12; Group 2 Number missing: 10, Reason: transplant 0, transfer to another clinic or shift: 10 Protocol outcome 2: Hospital admissions during the study period - Actual outcome: Mean number of hospitalisations at 2 years; Group 1: mean 6.3 (SD 13.2); n=61, Group 2: mean 7.9 (SD 13); n=46; Risk of bias: All domain - Very high,	

Study	Pai 2009[162]
Selection - Very high, Blinding - High, Incomplete outcome data - High, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 33, Reason: transplant: 5, transfer to another clinic or shift: 12, death: 16; Group 2 Number missing: 19, Reason: transplant 0, transfer to another clinic or shift: 10, death 9	
Protocol outcomes not reported by the study	Avoidable adverse events (incorrect diagnosis and treatment) during the study period; Quality of life during the study period; Number of ED presentations during the study period; GP attendances during the study period; Patient and/or carer satisfaction during the study period

Study (subsidiary papers)	Preventing hospital admissions by reviewing medication (PHARM) trial: Leendertse 2013[120] (Leendertse 2011[121])
Study type	RCT (Pharmacist/Physician randomised; Parallel)
Number of studies (number of participants)	1 (n=674)
Countries and setting	Conducted in Netherlands; Setting: Community pharmacy
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 12 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Patients with a high risk of medication-related hospital admissions (based on age, polypharmacy, type of drug class used, and non-adherence)
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	65 years or older, had five or more chronically prescribed drugs of which at least one was filled with a refill rate of less than 80% or more than 120% as a measure of non-adherence, and were dispensed one or more drugs from the Anatomical Therapeutic Chemical (ATC) class A or class B (therapeutics that act on the alimentary tract, metabolism, blood or blood-forming organs)
Exclusion criteria	Residing in a nursing home, life expectancy less than 3 months, or refused informed consent
Recruitment/selection of patients	All Dutch GPs and community pharmacist working in primary care were eligible and invited to participate. Randomisation at a GP level takes place after informed consent of the participating GPs and pharmacists and before the selection of patients. Eligible patients were extracted from the pharmacy computer system and included in the order they appeared on this list
Age, gender and ethnicity	Age - Other: Linear mixed-effects model mean (95%CI) Group 1: 75.8 (74.9-76.4); Group 2: 75.7 (75.1-76.7). Gender (M:F): Generalised mixed-effects model (% male) - Group 1: 44%; Group 2: 40%. Ethnicity: NR
Further population details	1. Frail elderly: Frail elderly (Patients with a high risk of medication-related hospital admissions (based on age, polypharmacy, type of drug class used, and non-adherence)). 2. Pre-specified study subgroups: Not applicable/Not

Study (subsidiary papers)	Preventing hospital admissions by reviewing medication (PHARM) trial: Leendertse 2013[120] (Leendertse 2011[121])
	stated/Unclear. (Not stated). 3. UK versus non-UK: Non-UK (Netherlands).
Indirectness of population	No indirectness
Interventions	(n=364) Intervention 1: Community pharmacists with enhanced roles in disease management - Delivered at general practices. Patients receive a multi-step intervention consisting of pharmaceutical anamnesis (information gathering), a review of patients' pharmacotherapy, the formulation and execution of a pharmaceutical care plan combined with the monitoring and follow up evaluation of the care plan and pharmacotherapy. Duration interventions completed within 1 month with follow-up at 3 and 6 months. Concurrent medication/care: All patients on therapeutics that act on the alimentary tract, metabolism, blood, or blood-forming organs Further details: 1. Prescribing power: Not stated (n=310) Intervention 2: Usual care. Dispensing of repeat prescriptions and automated medication surveillance according to current clinical guidelines. Patients do not routinely see a pharmacist when they go to their GP. Duration 12 months. Concurrent medication/care: therapeutics that act on the alimentary tract, metabolism, blood or blood-forming organs Further details: 1. Prescribing power: Not stated
Funding	Academic or government funding (Patient Safety Program of the Netherlands Organisation for Health Research and Development (ZonMw)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DELIEVERED AT GENERAL PRACTICES versus USUAL CARE Protocol outcome 1: Mortality during the study period - Actual outcome: Survival at 12 months; HR 0.78 (95%CI 0.13 to 1.94) Reported; Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: adjusted for comorbidites; Group 1 Number missing: 17, Reason: 17 moved out of area; Group 2 Number missing: 17, Reason: 17 moved out of area Protocol outcome 2: Avoidable adverse events (incorrect diagnosis and treatment) during the study period - Actual outcome: adverse drug events at 12 months; Group 1: 104/364, Group 2: 73/310; 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 ; Baseline details: adjusted for comorbidites; Group 1 Number missing: 17, Reason: 17 moved out of area; Group 2 Number missing: 17, Reason: 17 moved out of area Protocol outcome 3: Hospital admissions during the study period - Actual outcome: Hospital admissions related to Medication (HARM) at 12 months; HR 0.5 (95%CI 0.12 to 1.59) 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 ; Baseline details: adjusted for comorbidites; Group 1 Number missing: 17, Reason: 17 moved out of area; Group 2 Number missing: 17, Reason: 17 moved out of area	

Study (subsidiary papers)	Preventing hospital admissions by reviewing medication (PHARM) trial: Leendertse 2013[120] (Leendertse 2011[121])
Protocol outcomes not reported by the study	Quality of life during the study period; Number of ED presentations during the study period; GP attendances during the study period; Patient and/or carer satisfaction during the study period

Study	ProFiL trial: Santschi 2011[182]
Study type	RCT (Pharmacist/Physician randomised; Parallel)
Number of studies (number of participants)	1 (n=89)
Countries and setting	Conducted in Canada; Setting: Community pharmacy
Line of therapy	Unclear
Duration of study	Intervention time: 6 months
Method of assessment of guideline condition	Partially adequate method of assessment/diagnosis: Identified at Laval predialysis clinic
Stratum	Overall: CKD
Subgroup analysis within study	Not applicable
Inclusion criteria	Estimated CrCl over 60 ml/min, they were followed at a community pharmacy participating in the ProFil study and agreed to use the same pharmacy's services for the duration of the study, covered by the Quebec government drug plan 6 months prior to the study and throughout the duration and they spoke and wrote French
Exclusion criteria	None stated
Recruitment/selection of patients	Community pharmacies were recruited if they attended the workshop if assigned to the ProFil group, and willing to give researchers copies of the written recommendations they sent to physicians and of the pharmacy's record. Patients were recruited consecutively from Laval predialysis clinics
Age, gender and ethnicity	Age - Mean (SD): Group 1: 71.9 (10.4); Group 2: 73.3 (7.7). Gender (M:F): Define. Ethnicity: NR
Further population details	1. Frail elderly: Not applicable/Not stated/Unclear. 2. Pre-specified study subgroups: Not applicable/Not stated/Unclear. 3. UK versus non-UK: Non-UK (Canada).
Indirectness of population	No indirectness
Interventions	(n=48) Intervention 1: Community pharmacists with enhanced roles in disease management - Delivered at community pharmacy. Community pharmacist attended a 3-h training workshop on clinical presentations of CKD, management of DRPs among CKD outpatients, presentations of the programme and clinical tools, and discussion of two real clinical cases. There was communication of clinical information (laboratory test results and medications documented by the nephrologist) between the predialysis clinic and community pharmacies and a pharmaceutical consultation service by

Study	ProFiL trial: Santschi 2011[182]
	hospital [clinical] pharmacists with expertise in nephrology was made available to the community pharmacists. Duration 6 months. Concurrent medication/care: CKD treatment Further details: 1. Prescribing power: Non-prescribing (Written recommendations on DRP management were passed to physician). (n=42) Intervention 2: Usual care. Pharmacists did not have access to the ProFiL programme and were asked to provide usual care. Duration 6 months. Concurrent medication/care: Treatment for CKD Further details: 1. Prescribing power: Not stated
Funding	Study funded by industry (Pfizer Canada and Merck Frosst. Bristol-Myers Squbb, Pro Doc Ltee, LEO Pharma, Sabex, Hoffmann-LaRoche, Shire Biochem, Pharmaceutical Partners of Canada)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DELIEVERED AT COMMUNITY PHARMACY versus USUAL CARE Protocol outcome 1: Mortality during the study period - Actual outcome: Mortality at 6 months; Group 1: 0/48, Group 2: 1/42; Risk of bias: All domain - Very high, Selection - Very high, Blinding - Low, Incomplete outcome data - High, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Avoidable adverse events (incorrect diagnosis and treatment) during the study period; Quality of life during the study period; Number of ED presentations during the study period; GP attendances during the study period; Hospital admissions during the study period; Patient and/or carer satisfaction during the study period

Study (subsidiary papers)	RESPECT trial: Respect trial team 2010[173] (Respect trial team 2010[172])
Study type	RCT (Practice randomised; Parallel)
Number of studies (number of participants)	1 (n=760)
Countries and setting	Conducted in United Kingdom; Setting: Community pharmacy
Line of therapy	Unclear
Duration of study	Intervention time: 12 months
Method of assessment of guideline condition	Partially adequate method of assessment/diagnosis: practice records (no further details)
Stratum	Long-term conditions
Subgroup analysis within study	Not applicable
Inclusion criteria	Aged 75 or over, taking five or more repeat drugs (excluding any taken 'when required), living at home, scored 7 or

Study (subsidiary papers)	RESPECT trial: Respect trial team 2010[173] (Respect trial team 2010[172])
	over on the Abbreviated Mental Test, GP gave consent, community pharmacist was taking part in the RESPECT trial, able to provide written consent
Exclusion criteria	Living in in a residential or nursing home, their GP and community pharmacist were not in the same PCT, taken part in a local feasibility study
Recruitment/selection of patients	All general practices and all community pharmacies with a permanent pharmacist in the five PCTs were invited to participate. Eight practices from the largest PCT and four practices for the other PCTs were selected, all stratified by practice size. Practice records were search for patients meeting the inclusion criteria. Potential participants were interviewed in their home or at their GP's surgery.
Age, gender and ethnicity	Age - Mean (SD): Total: 80.4 (4.11). Gender (M:F): 432:328. Ethnicity: NR
Further population details	1. Frail elderly: Frail elderly (Age and comorbidity). 2. Pre-specified study subgroups: Not applicable/Not stated/Unclear. 3. UK versus non-UK: UK (UK).
Indirectness of population	No indirectness
Interventions	(n=563) Intervention 1: Community pharmacists with enhanced roles in disease management - Delivered at community clinics. Pharmaceutical care was undertaken by community pharmacists who interviewed patients, developed and implemented pharmaceutical care plans together with patients' GPs and thereafter undertook monthly medication reviews. Pharmacists and GPs attended training before the intervention. Duration 12 months. Concurrent medication/care: None stated Further details: 1. Prescribing power: Not stated (n=760) Intervention 2: Usual care. PCTs were randomised to receive usual care for 3, 5, 7, 9, or 11 months. Training for the intervention phase began 2 months prior to control period finishing. Duration 3-11 months. Concurrent medication/care: None stated Further details: 1. Prescribing power: Not stated
Funding	Academic or government funding
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DELIEVERED AT COMMUNITY CLINICS versus USUAL CARE Protocol outcome 1: Hospital admissions during the study period - Actual outcome: Emergency admission episodes per month at 2 years; Intervention effect estimate: 0.049 (0.290); Time-intervention effect estimate: -0.042 (0.038) Risk of bias: All domain - low, Selection - low, Blinding - Low, Incomplete outcome data - low, Crossover - Low; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Mortality during the study period; Avoidable adverse events (incorrect diagnosis and treatment) during the study period; Quality of life during the study period; Number of ED presentations during the study period; GP attendances

Study (subsidiary papers)	RESPECT trial: Respect trial team 2010[173] (Respect trial team 2010[172])
	during the study period; Patient and/or carer satisfaction during the study period

Study	Rozenfeld 2006[176]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=463)
Countries and setting	Conducted in USA; Setting: Primary care
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 12 months +/- 3 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: ICD-9-CM diagnostic code and last documented systolic blood pressure of 160 mm Hg or greater and/or diastolic blood pressure of 100 mm Hg or greater
Stratum	Overall: Hypertension
Subgroup analysis within study	Not applicable
Inclusion criteria	Over 18, office visit and blood pressure measurement within the past 2 years, ICD-9-CM diagnostic code and last documented systolic blood pressure of 160 mm Hg or greater and/or diastolic blood pressure of 100 mm Hg or greater
Exclusion criteria	No longer an active patient, refused consent, excluded by their primary care provider
Recruitment/selection of patients	Identified from electronic medical record database
Age, gender and ethnicity	Age - Mean (SD): Group 1: 69 (12); Group 2: 68 (13). Gender (M:F): 164:299. Ethnicity: NR
Further population details	1. Frail elderly: Non-frail elderly (Age and morbidity of patients). 2. Pre-specified study subgroups: Not applicable/Not stated/Unclear. 3. UK versus non-UK: Non-UK (USA).
Indirectness of population	No indirectness
Interventions	(n=230) Intervention 1: Clinical pharmacists with enhanced roles in disease management - Delivered at general practices. Appointment with one of five primary care clinical pharmacy specialists. During the first visit the pharmacist reviewed the patient's prescribed drugs and lifestyle habits, assessed vital signs, screened for adverse drug reactions and other barriers to drug compliance, provided education, and optimised the antihypertensive regimen in keeping with pre-established collaborative hypertension management guidelines. Duration Single visit with subsequent visits or telephone calls scheduled at the discretion of the pharmacist. Concurrent medication/care: Antihypertensive regimen Further details: 1. Prescribing power: Prescribing (Optimisation of the antihypertensive regimen).

Study	Rozenfeld 2006[176]
	(n=233) Intervention 2: Usual care. Instructed to continue their normal schedule of care. Duration 12 months +/- 3months. Concurrent medication/care: Treatment for hypertension Further details: 1. Prescribing power: Not stated
Funding	Study funded by industry (Boehringer Ingelheim)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DELIEVERED AT GENERAL PRACTICES versus USUAL CARE Protocol outcome 1: Mortality during the study period - Actual outcome: Mortality at 12 months; Group 1: 2/230, Group 2: 6/233; 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: 86, Reason: 32 active withdrawal, 2 transfer of care, 37 failed to return for exit visit, 10 phone disconnected; Group 2 Number missing: 97, Reason: 21 active withdrawal, 7 transfer of care, 60 failed to return for exit visit, 9 phone disconnected	
Protocol outcomes not reported by the study	Avoidable adverse events (incorrect diagnosis and treatment) during the study period; Quality of life during the study period; Number of ED presentations during the study period; GP attendances during the study period; Hospital admissions during the study period; Patient and/or carer satisfaction during the study period

Study	Sellors 2001[188]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=132)
Countries and setting	Conducted in Canada; Setting: Family physician practice
Line of therapy	Not applicable
Duration of study	Intervention time: 6 months
Method of assessment of guideline condition	Method of assessment /diagnosis not stated
Stratum	Long-term conditions
Subgroup analysis within study	Not applicable
Inclusion criteria	Over 65 and taking four medications regularly
Exclusion criteria	Refused to provide written informed consent
Recruitment/selection of patients	Presentation for office visits at four family practices

Study	Sellors 2001[188]
Age, gender and ethnicity	Age: NR. Gender (M:F): NR. Ethnicity: NR
Further population details	1. Frail elderly: Frail elderly (Age and co-morbidities). 2. Pre-specified study subgroups: Not applicable/Not stated/Unclear. 3. UK versus non-UK: Non-UK (Canada).
Extra comments	One pharmacist performed the intervention. He was trained by the investigators and usually worked in a community pharmacy
Indirectness of population	No indirectness
Interventions	(n=66) Intervention 1: Community pharmacists with enhanced roles in disease management - Delivered at general practices. After reviewing the family practice chart, the pharmacist consultant met once with each participant, reviewed the patient's medications, and developed a written summary and recommendations for the family physician. The pharmacist then met with the family physician to present and discuss the written recommendations. To follow changes in the medication regimen and to identify potential DRPs, the pharmacist contacted each participant in the group using a semi structured telephone interview at two weeks and monthly after the face to face meeting with the patient. Duration 6 months. Concurrent medication/care: Non-stated Further details: 1. Prescribing power: Non-prescribing (Recommendations passed to family physician). (n=66) Intervention 2: Usual care. Did not meet with the study pharmacist. No further details. Duration 6 months. Concurrent medication/care: None stated Further details: 1. Prescribing power: Not stated
Funding	Academic or government funding (Ministry of Health of Ontario)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DELIEVERED AT GENERAL PRACTICES versus USUAL CARE Protocol outcome 1: Mortality during the study period - Actual outcome: Mortality at 6 months; Group 1: 2/66, Group 2: 2/66; Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 3, Reason: 1 moved, 1 changed physician, 1 did not see pharmacist; Group 2 Number missing: 4, Reason: 1 moved, 3 refused	
Protocol outcomes not reported by the study	Avoidable adverse events (incorrect diagnosis and treatment) during the study period; Quality of life during the study period; Number of ED presentations during the study period; GP attendances during the study period; Hospital admissions during the study period; Patient and/or carer satisfaction during the study period

Study	Sellors 2003[189]

Study	Sellors 2003[189]
Study type	RCT (Pharmacist/Physician randomised; Parallel)
Number of studies (number of participants)	1 (n=889)
Countries and setting	Conducted in Canada; Setting: Community pharmacy
Line of therapy	Unclear
Duration of study	Intervention time: 5 months
Method of assessment of guideline condition	Partially adequate method of assessment/diagnosis: GP records assessed by office staff
Stratum	Long-term conditions
Subgroup analysis within study	Not applicable
Inclusion criteria	Aged 65 years or more, taking 5 or more medications, seen by GP within past 12 months, no evidence of cognitive impairment, could understand English
Exclusion criteria	Planned surgery, on nursing home waiting list, receiving palliative care
Recruitment/selection of patients	About 20 randomly chosen eligible senior citizens recruited in each family physician practice by office staff
Age, gender and ethnicity	Age - Mean (SD): Intervention: 74.0 (6.1); Control: 74.0 (6.0) years. Gender (M:F): 331:558. Ethnicity: Not stated
Further population details	1. Frail elderly: Not applicable/Not stated/Unclear. 2. Pre-specified study subgroups: Not applicable/Not stated/Unclear. 3. UK versus non-UK: Non-UK (Canada).
Indirectness of population	No indirectness
Interventions	(n=431) Intervention 1: Community pharmacists with enhanced roles in disease management - Delivered at community clinics. Specially trained community pharmacists who had received additional post-university training in the prevention, identification and resolution of drug-related problems completed structured drug therapy assessments with patients in the offices of their family physicians. The pharmacist wrote a consultation letter to the physician that summarised the patient's medications, identified drug-related problems and recommended actions to resolve any such problems. The pharmacist and physician met to discuss the letter. Physicians used a data collection form to indicate which recommendations they intended to implement and when. The pharmacist and physician met again 3 months later to discuss progress in implementing the recommendations. 5 months after the initial visit, they met again to determine which recommendations had been put in place. 1 and 3 months after the meeting the physician, the pharmacist monitored the patient's drug therapy using a semi-structured patient interview. Duration 5 months. Concurrent medication/care: Not stated Further details: 1. Prescribing power: Non-prescribing (pharmacist passed recommendations to physician). (n=458) Intervention 2: Usual care. No further details. Duration 5 months. Concurrent medication/care: Not stated

Study	Sellors 2003[189]
	Further details: 1. Prescribing power: Not stated
Funding	Academic or government funding (Health Transition Fund, Health Canada)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: LONG-TERM CONDITIONS versus USUAL CARE Protocol outcome 1: Mortality during the study period - Actual outcome: Mortality at 5 months; Group 1: 8/431, Group 2: 7/458; Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness Protocol outcome 2: Number of ED presentations during the study period - Actual outcome for Long-term conditions: Emergency/urgent care visits and ambulance use at 5 months; Group 1: mean 0.2 (SD 0.62); n=431, Group 2: mean 0.23 (SD 0.64); n=458; Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness Protocol outcome 3: GP attendances during the study period - Actual outcome for Long-term conditions: Physician visits at 5 months; Group 1: mean 5.16 (SD 5.6); n=431, Group 2: mean 4.97 (SD 6.2); n=458; Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness Protocol outcome 4: Hospital admissions during the study period - Actual outcome for Long-term conditions: Hospital admissions at 5 months; Group 1: mean 0.14 (SD 0.42); n=431, Group 2: mean 0.11 (SD 0.43); n=458; Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Avoidable adverse events (incorrect diagnosis and treatment) during the study period; Patient and/or carer satisfaction during the study period

Study (subsidiary papers)	Simpson 2011[192] (Simpson 2015[191])
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=260)
Countries and setting	Conducted in Canada; Setting: Primary care network
Line of therapy	Not applicable
Duration of study	Follow up (post intervention): 1 year

Study (subsidiary papers)	Simpson 2011[192] (Simpson 2015[191])
Method of assessment of guideline condition	Unclear method of assessment/diagnosis: Inclusion criteria does not specify cut-off for hypertension. Blood pressure not measured for inclusion in study
Stratum	Overall: Hypertensive type 2 diabetics
Subgroup analysis within study	Not applicable
Inclusion criteria	Type 2 diabetes, regularly seen by the primary care team, did not qualify for an urgent referral and assessment (fasting blood glucose >17mmol/l, blood pressure >220/120 mmHg, or triglycerides >15mmol/l)
Exclusion criteria	Followed in speciality clinics for diabetes, hypertension and dyslipidaemia; cognitively impaired; not responsible for their own medication; unable to communicate in English.
Recruitment/selection of patients	Patients who use the primary care network and who were identified from the clinic roster
Age, gender and ethnicity	Age - Mean (SD): Group 1: 59.4 (12.1); Group 2: 58.8 (11.1). Gender (M:F): 111:149. Ethnicity: NR
Further population details	1. Frail elderly: Not applicable/Not stated/Unclear. 2. Pre-specified study subgroups: Not applicable/Not stated/Unclear. 3. UK versus non-UK: Non-UK (Canada).
Indirectness of population	No indirectness
Interventions	(n=131) Intervention 1: Community pharmacists with enhanced roles in disease management - Delivered at general practices. In-person visit to measure height weight, blood pressure, and to identify all prescription, non-prescription, complementary, and alternative medications. Pharmacists then formulated guideline-concordant recommendations to optimise medication management of blood pressure and other cardiovascular risk factors. Pharmacist then worked independently with the patient to implement these changes. Duration 1 year. Concurrent medication/care: Medication for hypertension and type two diabetes Further details: 1. Prescribing power: Non-prescribing (Recommendations were discussed with the primary care physician who was responsible for authorising medication changes). (n=129) Intervention 2: Usual care. Control patients received usual care by the primary care team without contributions from study pharmacists, except for standardised blood pressure measurements at the end of the follow-up period. Duration 1 year. Concurrent medication/care: Medication for hypertension and type two diabetes Further details: 1. Prescribing power: Not stated
Funding	Academic or government funding (Canadian Diabetes Association, Institute of Health Economics, Alberta Heritage Foundation for Medical Research (AHFMR))
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DELIEVERED AT GENERAL PRACTICES versus USUAL CARE	

Study (subsidiary papers)	Simpson 2011[192] (Simpson 2015[191])
Protocol outcome 1: Mortality during the study period - Actual outcome: Mortality at 1 year; Group 1: 1/131, Group 2: 0/129; Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 20, Reason: 14 withdrew, 6 lost to follow-up; Group 2 Number missing: 16, Reason: 10 withdrew, 6 lost to follow-up Protocol outcome 2: Number of ED presentations during the study period - Actual outcome: 1 or more ED visits at 1 year; Group 1: 11/131, Group 2: 11/129; Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 20, Reason: 14 withdrew, 6 lost to follow-up; Group 2 Number missing: 16, Reason: 10 withdrew, 6 lost to follow-up Protocol outcome 3: Hospital admissions during the study period - Actual outcome: 1 or more hospital admissions at 1 year; Group 1: 4/131, Group 2: 5/129; Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 20, Reason: 14 withdrew, 6 lost to follow-up; Group 2 Number missing: 16, Reason: 10 withdrew, 6 lost to follow-up	
Protocol outcomes not reported by the study	Avoidable adverse events (incorrect diagnosis and treatment) during the study period; Quality of life during the study period; GP attendances during the study period; Patient and/or carer satisfaction during the study period

Study	Taveira 2014[198]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=200)
Countries and setting	Conducted in USA; Setting: Cardiovascular risk reduction clinic (CRRC); a pharmacist-coordinated care model comprising monthly clinic visits with a pharmacist in addition to standard primary care, that integrates management of hypertension, hyperlipidaemia and hyperglycaemia into a single treatment plan
Line of therapy	Unclear
Duration of study	Intervention time: 12 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Cardiovascular risk reduction clinic (CRRC)
Stratum	Long-term conditions
Subgroup analysis within study	Not stratified but pre-specified: Patients with and without diabetes analysed separately; minimal information on those without diabetes (only 22 patients)
Inclusion criteria	Actively enrolled in cardiovascular risk reduction clinic (CRRC); documented CVD or diabetes; meeting discharge criteria (HbA1c 7% or less; BP 140/80mmHg or less for those with diabetes and 140/90mmHg or less without diabetes; LDL cholesterol 2.59mmol/L or less)

Study	Taveira 2014[198]
Exclusion criteria	Had a condition that may limit long-term adherence to study visits (for example, severe dementia, acute psychiatric decompensation in previous 6 months, unstable psychiatric illness, metastatic cancer or terminal illness, or life expectancy <1 year
Recruitment/selection of patients	Recruited from CRRC clinic
Age, gender and ethnicity	Age - Mean (SD): CRRC individual sessions: 64.6 (10.0); group medical visits 64.5 (10.2); usual care: 66.6 (10.2) years. Gender (M:F): 173:5. Ethnicity: Not stated
Further population details	1. Frail elderly: Not applicable/Not stated/Unclear. 2. Pre-specified study subgroups: Not applicable/Not stated/Unclear. 3. UK versus non-UK: Non-UK (USA).
Extra comments	Male: female ratio shown for subgroup with diabetes (n=178) but not for those with CVD without diabetes (n=22)
Indirectness of population	No indirectness
Interventions	(n=72) Intervention 1: Clinical pharmacists with enhanced roles in disease management - Delivered at community clinics. Attended 4 sessions, 3-monthly for 1 year, with 6-8 participants (plus family members/members of social support); sessions facilitated by clinical pharmacist: education for first hour (self-management for example, healthy eating or physical activity), then behavioural (individualised behavioural change goal for example, exercise, diet, blood glucose or BP monitoring) and pharmacological interventions (initiating or titrating medications according to algorithm) for second hour for hyperglycaemia, hypertension and dyslipidaemia, based on individualised cardiovascular risk report card containing medical history, current medications, vitals and laboratory values, updated every 3 months. Demonstration and coaching were used to increase the frequency of self-care skills for example, blood glucose monitoring, logging dietary intake. Participants were contacted by phone as needed to follow up on pertinent laboratory values or to reinforce self-care monitoring or medication changes. Duration 1 year. Concurrent medication/care: Not stated Further details: 1. Prescribing power: No prescription change (n=73) Intervention 2: Clinical pharmacists with enhanced roles in disease management - Delivered at community clinics. 30-minute visit with clinical pharmacist every 3 months to assess medication adherence, obtain vitals and laboratory parameters and titrate medications to address BP, hyperlipidaemia and diabetes. Participants were referred to nutritionist or physical therapist for an individual diet and exercise programmes needed. Duration 1 year. Concurrent medication/care: Not stated Further details: 1. Prescribing power: Prescribing (titration of medications). (n=55) Intervention 3: Usual care. Follow up in primary care, on average 3-4 times a year; laboratory and vital signs obtained at the discretion and frequency of primary care provider, who had referral access to the nutrition and physical therapy and the same consultation services as the CRRC clinic provider (except patients were not referred to

Study	Taveira 2014[198]
	the CRRC for the study year). Duration 1 year. Concurrent medication/care: Not stated Further details: 1. Prescribing power: Not stated
Funding	Study funded by industry (Merck and Co)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: LONG-TERM CONDITIONS: GROUP MEDICAL VISITS versus USUAL CARE

Protocol outcome 1: Mortality during the study period
- Actual outcome for Long-term conditions: Mortality at 1 year; Group 1: 1/72, Group 2: 1/55; Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - High; Indirectness of outcome: No indirectness ; Group 1 Number missing: 11, Reason: These people in the other subgroup (without diabetes); Group 2 Number missing: 2, Reason: These people in the other subgroup (without diabetes)

Protocol outcome 2: Number of ED presentations during the study period
- Actual outcome for Long-term conditions: ED visits at 1 year; Group 1: mean 0.6 (SD 1); n=61, Group 2: mean 0.6 (SD 1.1); n=53; Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - High; Indirectness of outcome: No indirectness ; Group 1 Number missing: 11, Reason: These people in the other subgroup (without diabetes); Group 2 Number missing: 2, Reason: These people in the other subgroup (without diabetes)

Protocol outcome 3: GP attendances during the study period
- Actual outcome for Long-term conditions: Primary care provider visits at 1 year; Group 1: mean 3 (SD 1.2); n=61, Group 2: mean 2.8 (SD 1); n=53; Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - High; Indirectness of outcome: No indirectness ; Group 1 Number missing: 11, Reason: These people in the other subgroup (without diabetes); Group 2 Number missing: 2, Reason: These people in the other subgroup (without diabetes)
Protocol outcome 4: Hospital admissions during the study period
- Actual outcome for Long-term conditions: Hospitalisations at 1 year; Group 1: mean 0.4 (SD 0.8); n=61, Group 2: mean 0.2 (SD 0.5); n=53; Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - High; Indirectness of outcome: No indirectness ; Group 1 Number missing: 11, Reason: These people in the other subgroup (without diabetes); Group 2 Number missing: 2, Reason: These people in the other subgroup (without diabetes)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: LONG-TERM CONDITIONS: INDIVIDUAL CLINIC SESSIONS versus USUAL CARE

Protocol outcome 1: Mortality during the study period

Study	Taveira 2014[198]
- Actual outcome for Long-term conditions: Mortality at 1 year; Group 1: 1/73, Group 2: 1/55; Risk of bias; Indirectness of outcome: No indirectness Protocol outcome 2: Number of ED presentations during the study period - Actual outcome for Long-term conditions: ED visits at 1 year; Group 1: mean 0.4 (SD 0.8); n=64, Group 2: mean 0.6 (SD 1.1); n=53; Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - High; Indirectness of outcome: No indirectness ; Group 1 Number missing: 9, Reason: These people in the other subgroup (without diabetes); Group 2 Number missing: 2, Reason: These people in the other subgroup (without diabetes) Protocol outcome 3: GP attendances during the study period - Actual outcome for Long-term conditions: Primary care provider visits at 1 year; Group 1: mean 2.8 (SD 1.1); n=64, Group 2: mean 2.8 (SD 1); n=53; Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - High; Indirectness of outcome: No indirectness ; Group 1 Number missing: 9, Reason: These people in the other subgroup (without diabetes); Group 2 Number missing: 2, Reason: These people in the other subgroup (without diabetes) Protocol outcome 4: Hospital admissions during the study period - Actual outcome for Long-term conditions: Hospitalisations at 1 year; Group 1: mean 0.3 (SD 0.7); n=64, Group 2: mean 0.2 (SD 0.5); n=53; Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - High; Indirectness of outcome: No indirectness ; Group 1 Number missing: 9, Reason: These people in the other subgroup (without diabetes); Group 2 Number missing: 2, Reason: These people in the other subgroup (without diabetes)	
Protocol outcomes not reported by the study	Avoidable adverse events (incorrect diagnosis and treatment) during the study period; Quality of life during the study period; Patient and/or carer satisfaction during the study period

Study	Taylor 2003[199]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=69)
Countries and setting	Conducted in USA; Setting: Community-based physician offices
Line of therapy	Unclear
Duration of study	Intervention time: 1 year
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Medical records
Stratum	Overall

Study	Taylor 2003[199]
Subgroup analysis within study	Not applicable
Inclusion criteria	Adults (18 years or over) who received care at the participating clinics and were identified as being at high risk for medication-related adverse events. High risk: 3 or more of the following factors: 5 or more medications in drug regimen; 12 or more doses per day; 4 or more medication changes in previous year; 3 or more concurrent diseases; history of medication non-compliance; drugs requiring therapeutic monitoring (for example, warfarin, theophylline, phenytoin).
Exclusion criteria	Significant cognitive impairment, history of missed office visits, scheduling conflicts, life expectancy <1 year
Recruitment/selection of patients	Patients identified by participating pharmacists through manual evaluation of clinic medical records and review of computerised medical records in physician offices.
Age, gender and ethnicity	Age - Mean (SD): Intervention: 64.4 (13.7); control: 66.7 (12.3) years. Gender (M:F): 22:47. Ethnicity: 61% White
Further population details	1. Frail elderly: Not applicable/Not stated/Unclear. 2. Pre-specified study subgroups: Not applicable/Not stated/Unclear. 3. UK versus non-UK: Non-UK (USA).
Indirectness of population	No indirectness
Interventions	(n=41) Intervention 1: Clinical pharmacists with enhanced roles in disease management - Delivered at general practices. Four pharmacists joined the study to provide pharmaceutical care at the clinics 2 or 3 afternoons a week. Since the clinics did not have a pharmacy, interventions were limited to clinical services and patient education and did not include dispensing. Patients were asked to bring all their current medications; the pharmacists contacted local pharmacies for dispensing information as necessary. A patient typically met the pharmacist for 20 minutes before seeing a physician during scheduled office visits. Pharmaceutical care: uniform process for preventing or identifying and resolving problems related to drug therapy. Published therapeutic algorithms and guidelines were used as the basis for the pharmacist's recommendations. Pharmacists were specifically trained to evaluate a therapy's indication, effectiveness and dosage as well as the correctness and practicality of directions, drug-drug interactions, drug-disease interactions, therapeutic duplication, and duration of treatment, untreated indications and expense. Pharmacist reviewed the medical record for medication-related problems, conducted a chart review to ensure that information on drug therapy and allergies was accurately documented, examined the medication history to determine compliance with and complications of medications, and provided comprehensive individualised patient education that included a brief review of the disease, important lifestyle modifications and basic drug information. Therapeutic recommendations were communicated to physicians through discussions or progress notes. Pharmacists also provided drug and disease information during follow up visits and answered patients' questions. Written materials were provided. In addition, the pharmacists monitored patients' responses to drugs and attempted to improve compliance by consolidating medication regimens, reducing dosage frequency, devising medication reminders and teaching patient’s techniques for using devices such as inhalers, peak flow meters, glucometers and pill boxes.

Study	Taylor 2003[199]
	Duration 1 year. Concurrent medication/care: Not stated Further details: 1. Prescribing power: Unclear (n=40) Intervention 2: Usual care. Medical record review and patient interviews at baseline and 1 year later performed by pharmacist, including compliance, medication misadventures and medication knowledge. A pharmacist evaluated pharmacotherapy and documented clinical outcomes but provided no advice or recommendation to patient or physician. Data were collected primarily from medical records to minimise contact with control patients. Duration 1 year. Concurrent medication/care: Not stated Further details: 1. Prescribing power: Not stated
Funding	Academic or government funding (ASHP Research and Education Foundation)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: LONG-TERM CONDITIONS versus USUAL CARE

Protocol outcome 1: Mortality during the study period
- Actual outcome: Mortality at 1 year; Group 1: 2/41, Group 2: 1/40; Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Baseline details: Hospitalisation in previous year: intervention group: 24, control: 11; ED visits I: 18, C: 6 ; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcome 2: Number of ED presentations at Define
- Actual outcome for Long-term conditions: ED visits at 1 year; Group 1: 4/33, Group 2: 6/36; Comments: Baseline - Group 1: 18; Group 2: 6
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Baseline details: Hospitalisation in previous year: intervention group: 24, control: 11; ED visits I: 18, C: 6 ; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcome 3: Number of ED presentations during the study period
- Actual outcome for Long-term conditions: ED visits at 1 year; Group 1: 4/33, Group 2: 6/36; Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Baseline details: Hospitalisation in previous year: intervention group: 24, control: 11; ED visits I: 18, C: 6 ; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcome 4: Hospital admissions during the study period
- Actual outcome for Long-term conditions: Hospitalisations at 1 year; Group 1: 2/33, Group 2: 11/36; Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Baseline details: Hospitalisation in previous year: intervention group: 24, control: 11; ED visits I: 18, C: 6 ; Group 1 Number missing: 0; Group 2 Number missing: 0

Study	Taylor 2003[199]
Protocol outcomes not reported by the study	Avoidable adverse events (incorrect diagnosis and treatment) during the study period; GP attendances during the study period; Patient and/or carer satisfaction during the study period

Study	The BC Community Pharmacy Asthma Study trial: Mclean 2003[141]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=405)
Countries and setting	Conducted in Canada; Setting: Community pharmacy
Line of therapy	Not applicable
Duration of study	Intervention time: 9-12 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Diagnosis of asthma confirmed with physician
Stratum	Overall: Asthma
Subgroup analysis within study	Not applicable
Inclusion criteria	provided consent and diagnosis confirmed with their physician
Exclusion criteria	None stated
Recruitment/selection of patients	Recruited in the local community by each pharmacist. methods included store notices, communication with local physicians and clinics, and information provided by BC
Age, gender and ethnicity	Age - Mean (range): 48 (7-84). Gender (M:F): 83:141. Ethnicity: NR
Further population details	1. Frail elderly: Not applicable/Not stated/Unclear. 2. Pre-specified study subgroups: Not applicable/Not stated/Unclear. 3. UK versus non-UK: Non-UK (Canada).
Extra comments	Cluster-randomisation by pharmacy for subsection of patients
Indirectness of population	No indirectness
Interventions	(n=235) Intervention 1: Community pharmacists with enhanced roles in disease management - Delivered at community clinics. EC patients received usual care plus pharmaceutical care, which included education on disease, identification of triggers and pharmacist-patient developed action plan, patient participation in decision making, patient monitoring of own therapy (PEFRs and using calendar/diary), pharmacist responsibility for outcomes, pharmacist promotion of evidence-based care, pharmacist-patient interaction at appointment in a private consultation area. The physician was informed or consulted regarding all results and interventions. Duration 9-12 months. Concurrent medication/care: Treatment for asthma

Study	The BC Community Pharmacy Asthma Study trial: Mclean 2003[141]
	Further details: 1. Prescribing power: unclear - physician informed or consulted regarding all results and interventions (n=214) Intervention 2: Usual care. Initial interview with the patient to complete a symptom, drug utilisation and knowledge assessment. The patient was taught proper inhaler technique, and the pharmacist answered any questions the patient had about the project. Patients were asked to complete a monthly asthma calendar/diary. A second interview was conducted at the end of the study. Duration 9-12 months. Concurrent medication/care: Treatment for asthma Further details: 1. Prescribing power: Not stated
Funding	Academic or government funding (Health Transition Fund, Health Canada)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DELIEVERED AT COMMUNITY CLINICS versus USUAL CARE Protocol outcome 1: Number of ED presentations during the study period - Actual outcome: Emergency visits during baseline and month 12; Group 1 - baseline: 0.165, final: 0.043, change: -0.122; Group 2 - baseline: 0.377, final: 0.213, change: -0.164; ; Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness Protocol outcome 2: GP attendances during the study period - Actual outcome: Medical visits during baseline and month 12; Group 1 - baseline: 1.328, final: 0.386, change: -0.942; Group 2 - baseline: 1.429, final: 1.730, change: 0.301; ; Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness Protocol outcome 3: Hospital admissions during the study period - Actual outcome: Hospitalisations during baseline and month 12; Group 1 - baseline: 0.123, final: 0.078, change: -0.045; Group 2 - baseline: 0.143, final: 0.160, change: 0.017; ; Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Mortality during the study period; Avoidable adverse events (incorrect diagnosis and treatment) during the study period; Quality of life during the study period; Patient and/or carer satisfaction during the study period

Study (subsidiary papers)	The MEDMAN Study trial: Bond 2007[53] (Tinelli 2007[202], Tinelli 2011[201])
Study type	RCT (Patient randomised; Parallel)

Study (subsidiary papers)	The MEDMAN Study trial: Bond 2007[53] (Tinelli 2007[202], Tinelli 2011[201])
Number of studies (number of participants)	1 (n=1614)
Countries and setting	Conducted in United Kingdom; Setting: Community pharmacy
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: General practice recruited CHD patients
Stratum	Long-term conditions: Coronary Heart Disease
Subgroup analysis within study	Not applicable
Inclusion criteria	Over 17, with CHD (previous myocardial infarction, angina, coronary artery bypass graft and/or angioplasty)
Exclusion criteria	illiterate/innumerate, history of alcohol/drug misuse, terminal/serious illness, severe mental illness and unable to provide informed consent or otherwise unsuitable for the trial
Recruitment/selection of patients	Nine study site purposively selected from a list of 33 volunteer primary care organisations in England, selected on the basis of local knowledge to include a range of population, general practice and community pharmacy characteristics
Age, gender and ethnicity	Age - Mean (SD): Group 1: 68.7 (9.2), Group 2: 68.8 (9.1). Gender (M:F): 141:200. Ethnicity: NR
Further population details	1. Frail elderly: Not applicable/Not stated/Unclear. 2. Pre-specified study subgroups: Not applicable/Not stated/Unclear. 3. UK versus non-UK: UK (England).
Indirectness of population	No indirectness
Interventions	(n=980) Intervention 1: Community pharmacists with enhanced roles in disease management - Delivered at community pharmacy. Medicines management service delivered from community pharmacy premises, by community pharmacists who had received training designed and delivered by the Centre for Pharmacy Post-Graduate Education. Initial consultation informed by the extracted medical data supplied by the researchers. Further consultations included assessments of the following: therapy, medication compliance, lifestyle (for example, smoking cessation, exercise and diet), and social support (for example, difficulties in collecting prescriptions and opening bottles). Recommendations were recorded on a referral form which was sent to the GP, who returned annotated copies to the pharmacists. Duration 12 months from first pharmacy appointment. Concurrent medication/care: Treatment for CHD Further details: 1. Prescribing power: Non-prescribing (Recommendations passed to GP). (n=513) Intervention 2: Usual care. Standard treatment from GP and community pharmacist. Duration estimated equivalent follow-up (12 months from first intervention appointment). Concurrent medication/care: Treatment for CHD Further details: 1. Prescribing power: Not stated

Study (subsidiary papers)	The MEDMAN Study trial: Bond 2007[53] (Tinelli 2007[202], Tinelli 2011[201])
Funding	Academic or government funding (Department of Health for England and Wales)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: LONG-TERM CONDITIONS versus USUAL CARE Protocol outcome 1: Mortality during the study period - Actual outcome: Mortality at 12 months; Group 1: 20/941, Group 2: 19/500; 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: 15, Reason: 9 withdrew, 6 not stated; Group 2 Number missing: 12, Reason: 38 withdrew but only 12 clinical record forms unreturned	
Protocol outcomes not reported by the study	Avoidable adverse events (incorrect diagnosis and treatment) during the study period; Quality of life during the study period; Number of ED presentations during the study period; GP attendances during the study period; Hospital admissions during the study period; Patient and/or carer satisfaction during the study period

Study	Touchette 2012[205]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=637)
Countries and setting	Conducted in USA; Setting: Community pharmacy
Line of therapy	Unclear
Duration of study	Intervention + follow up: Intervention 3 months and follow up to 6 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: GP records
Stratum	Long-term conditions
Subgroup analysis within study	Not applicable
Inclusion criteria	Age 65 or older, primary use of English for written and oral communication, access to a telephone, 3 or more chronic comorbid conditions associated with increased health care use (for example, congestive heart failure, diabetes, COPD, hypertension), 2 or more visits to a clinic provider during previous year, 6 or more chronic prescription medications in previous 6 months, 1 or more recent situations placing patient at high risk of drug-related problems (that is, 3 or more different healthcare providers visited in previous 12 months, any change in medication, new physician visit, ED visit, hospitalisation or invasive procedure requiring stopping medications in previous 30 days).
Exclusion criteria	Presence of a terminal condition with life expectancy 6 months or less or previous enrolment in a medication therapy management (MTM) programme involving comprehensive medication review in previous 12 months

Study	Touchette 2012[205]
Recruitment/selection of patients	Identified through administrative and pharmacy databases; recruited via letter, telephone calls or in person from family practice clinics
Age, gender and ethnicity	Age - Mean (SD): 74.6 (6.7) years. Gender (M:F): 216:421. Ethnicity: Race: 51.2% Black, 47.7% White, 0.8% Asian, 0.3% American Indian; Ethnicity: Non-Hispanic 95.6%, Hispanic: 4.4%
Further population details	1. Frail elderly: Frail elderly (Age 65 or older with 3 or more chronic comorbid conditions associated with increased health care use). 2. Pre-specified study subgroups: Not applicable/Not stated/Unclear. 3. UK versus non-UK: Non-UK (USA).
Indirectness of population	No indirectness
Interventions	(n=211) Intervention 1: Community pharmacists with enhanced roles in disease management - Delivered at community clinics. Basic Medication Therapy Management (MTM): two scheduled visits (0 and 3 months); MTM pharmacist performed a comprehensive medication review and drug-related problem (DRP) assessment with no access to clinical information except from the patient. All medications were documented with directions for use and actual patient use; DRPs were classified using previously validated Pharmaceutical Care Network Europe (PCNE) classification. Pharmacist attempted to resolve as many DRPS as possible through patient education and/or physician notification. Unless DRPs required urgent attention, DRPs were sent to physician by fax. Urgent DRPs and those for which a response had not been received by a physician were communicated to an appropriate representative from the physician's office via telephone. Study pharmacists underwent a 90-minute training session to ensure the MTM intervention was conducted in a similar manner among all sites. Training included study background and methods, good clinical research practice, identifying and clarifying DRPs, documenting DRPs using the PCNE checklist, use of the MTM interview tool and a protocol for emergent events. MTM pharmacists were not allowed to access patients' electronic medical records (like a typical community pharmacy). Duration 3 months. Concurrent medication/care: Not stated Further details: 1. Prescribing power: Not stated (n=218) Intervention 2: Community pharmacists with enhanced roles in disease management - Delivered at community clinics. Enhanced Medication Therapy Management (MTM): two scheduled visits (0 and 3 months); MTM pharmacist performed a comprehensive medication review and drug-related problem (DRP) assessment. All medications were documented with directions for use and actual patient use; DRPs were classified using previously validated Pharmaceutical Care Network Europe (PCNE) classification. Pharmacist attempted to resolve as many DRPS as possible through patient education and/or physician notification. Unless DRPs required urgent attention, DRPs were sent to physician by fax. Urgent DRPs and those for which a response had not been received by a physician were communicated to an appropriate representative from the physician's office via telephone. Study pharmacists underwent a 90-minute training session to ensure the MTM intervention was conducted in a similar manner among all

Study	Touchette 2012[205]
	sites. Training included study background and methods, good clinical research practice, identifying and clarifying DRPs, documenting DRPs using the PCNE checklist, use of the MTM interview tool and a protocol for emergent events. MTM pharmacists were not allowed to access patients' electronic medical records (like a typical community pharmacy). In the enhanced TM group, pharmacists were provided with a two-page clinical summary (extracted from electronic medical record by a research assistant within 10 minutes) containing basic data on the patient's medical history (including 2 most recent BP and heart rate measurements), laboratory values (electrolytes, liver tests, INR, complete blood count, lipid panel, thyroid panel, glycosylated haemoglobin, drug levels and dates) and current medication regimens including OTC and herbal medications where listed in the chart. Duration 3 months. Concurrent medication/care: Not stated Further details: 1. Prescribing power: Not stated (n=208) Intervention 3: Usual care. Patients received medication counselling according to their pharmacy's normal routine. Duration 6 months. Concurrent medication/care: Not stated Further details: 1. Prescribing power: Not stated
Funding	Academic or government funding (Agency for Healthcare Research and Quality, US Department of Health and Human Services)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: LONG-TERM CONDITIONS: BASIC MTM versus USUAL CARE Protocol outcome 1: Avoidable adverse events (incorrect diagnosis and treatment) during the study period - Actual outcome for Long-term conditions: Adverse drug events at Between 3 and 6 months; Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 28, Reason: 24 withdrew, 4 lost to follow up; Group 2 Number missing: 25, Reason: 10 withdrew, 15 lost to follow up Protocol outcome 2: Number of ED presentations during the study period - Actual outcome for Long-term conditions: Participants with 1 or more ED visits at Between 3 and 6 months; Group 1: 38/183, Group 2: 43/183; Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 28, Reason: 24 withdrew, 4 lost to follow up; Group 2 Number missing: 25, Reason: 10 withdrew, 15 lost to follow up Protocol outcome 3: GP attendances during the study period - Actual outcome for Long-term conditions: Number of GP visits per patient at Between 3 and 6 months; Group 1: mean 2.24 (SD 2.08); n=183, Group 2: mean 2.19 (SD 2.19); n=183; Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 28, Reason: 24 withdrew, 4 lost to follow up; Group 2 Number missing: 25,	

Study	Touchette 2012[205]
Reason: 10 withdrew, 15 lost to follow upProtocol outcome 4: Hospital admissions during the study period - Actual outcome for Long-term conditions: Participants with 1 or more hospitalisations at Between 3 and 6 months; Group 1: 32/183, Group 2: 17/183; Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 28, Reason: 24 withdrew, 4 lost to follow up; Group 2 Number missing: 25, Reason: 10 withdrew, 15 lost to follow up RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: LONG-TERM CONDITIONS: ENHANCED MTM versus USUAL CARE Protocol outcome 1: Avoidable adverse events (incorrect diagnosis and treatment) during the study period - Actual outcome for Long-term conditions: Adverse drug events at Between 3 and 6 months; Risk of bias; Indirectness of outcome: No indirectness Protocol outcome 2: Number of ED presentations during the study period - Actual outcome for Long-term conditions: Participants with 1 or more ED visits at Between 3 and 6 months; Group 1: 32/190, Group 2: 43/183; Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 28, Reason: 18 withdrew, 10 lost to follow up; Group 2 Number missing: 25, Reason: 10 withdrew, 15 lost to follow up Protocol outcome 3: GP attendances during the study period - Actual outcome for Long-term conditions: Number of GP visits per patient at Between 3 and 6 months; Group 1: mean 2.14 (SD 2.08); n=190, Group 2: mean 2.19 (SD 2.19); n=183; Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 28, Reason: 18 withdrew, 10 lost to follow up; Group 2 Number missing: 25, Reason: 10 withdrew, 15 lost to follow up Protocol outcome 4: Hospital admissions during the study period - Actual outcome for Long-term conditions: Participants with 1 or more hospitalisations at Between 3 and 6 months; Group 1: 23/190, Group 2: 17/183; Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 28, Reason: 18 withdrew, 10 lost to follow up; Group 2 Number missing: 25, Reason: 10 withdrew, 15 lost to follow up	
Protocol outcomes not reported by the study	Mortality during the study period; Quality of life during the study period; Patient and/or carer satisfaction during the study period

Study	Triller 2007[207]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=154)
Countries and setting	Conducted in USA; Setting: Patient's Home
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: diagnosis of heart failure documented in the medical record or billing system
Stratum	Overall: Heart failure
Subgroup analysis within study	Not applicable
Inclusion criteria	Primary or secondary diagnosis of heart failure, aged 21 years or older, residence in the catchment area
Exclusion criteria	residing outside the defined geographic area, without telephone service, disability or illness, lacked the mental capacity to provide informed consent
Recruitment/selection of patients	Identified by discharge nurses before hospital discharge
Age, gender and ethnicity	Age - Mean (SD): Group 1: 81.3 (9.3); Group 2: 78.1 (11.2). Gender (M:F): 43:111. Ethnicity: Group 1 - White: 97%, Other: 3%; Group 2 - White: 88%, Other: 12%
Further population details	1. Frail elderly: Not applicable/Not stated/Unclear. 2. Pre-specified study subgroups: Not applicable/Not stated/Unclear. 3. UK versus non-UK: Non-UK (USA).
Extra comments	Study participants must receive at least 3 days of home care and 1 pharmacist visit if in the intervention arm to be included in the final analysis
Indirectness of population	No indirectness
Interventions	(n=77) Intervention 1: Clinical pharmacists with enhanced roles in disease management - Delivered at patient's home. Usual home-based care plus three home visits from a clinical pharmacist. Role included initial comprehensive in-home medication assessment (concurrent with the initial usual care admission process). The follow-up visits were conducted at day 7-10 and 18-21 and were contingent on the patient's continue use of the home-based care service. During the initial visit, the pharmacist catalogued all medications and interviewed the patient regarding their medication use. The pharmacist sought to improve patient progress toward meeting pertinent pharmacotherapy goals related to heart failure and also endeavoured to reduce the use of inappropriate medications, encourage smoking cessations, suggest improvements in diet, and promote medication adherence. Throughout the 21 days the pharmacist accessed and reviewed all pertinent physician notes and laboratory test values via the NEH data system and interacted with prescribers on behalf of the patients. Individual physicians were not part of the trial and were not required to act on

Study	Triller 2007[207]
	the pharmacist's recommendations. The physicians were contacted either by phone or by fax. Duration 21 days. Concurrent medication/care: Treatment for heart failure Further details: 1. Prescribing power: Non-prescribing (Recommendations passed to physician). (n=77) Intervention 2: Usual care. Received the home-based services typically provided by the visiting nurse association. These include basic nursing care, a brief physical assessment and medical history. Duration Not stated. Concurrent medication/care: Treatment for heart failure Further details: 1. Prescribing power: Not stated
Funding	Other (Jacob and Valeria Langeloth foundation)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DELIEVERED AT PATIENT'S HOME versus USUAL CARE Protocol outcome 1: Mortality during the study period - Actual outcome: Mortality at 180 days; Group 1: 17/77, Group 2: 14/77; 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 Protocol outcome 2: Hospital admissions during the study period - Actual outcome: Hospital admission at 180 days; Group 1: 42/77, Group 2: 45/77; Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Avoidable adverse events (incorrect diagnosis and treatment) during the study period; Quality of life during the study period; Number of ED presentations during the study period; GP attendances during the study period; Patient and/or carer satisfaction during the study period

Study	Xin 2016[227]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=244)
Countries and setting	Conducted in China; Setting: Community clinic
Line of therapy	1st line
Duration of study	Intervention + follow up: 12 months follow-up
Method of assessment of guideline condition	Adequate method of assessment/diagnosis

Study	**Xin 2016[227]**
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	age >35 years, diagnosis of COPD, regular visit to pharmacist, no previous diagnosis of uncontrolled psychiatric disease, and no previous diagnosis of severe liver or kidney disease.
Exclusion criteria	Patients who were pregnant or analphabetic were excluded
Recruitment/selection of patients	Patients were recruited between Jan 2015 and Dec 2015 from Tongde Hospital.
Age, gender and ethnicity	Age - Mean (SD): PMC group- 64.2 (14.2); control group-64.6 (14.5). Gender (M:F): PMC group-44:70; control group-42:71. Ethnicity:
Further population details	1. Frail elderly: 2. Pre-specified study subgroups: 3. UK versus non-UK.
Indirectness of population	No indirectness
Interventions	(n=122) Intervention 1: Clinical pharmacists with enhanced roles in disease management - Delivered at community clinics. Pharmacy managed clinic (PMC) The pharmacist was mainly responsible for individualised education, and developing a comprehensive pharmaceutical care programme. At first the pharmacist discussed with the patients about the definition of COPD, pathophysiology of the disease, the importance of medication adherence, and the importance of smoking cessation. Then the pharmacist taught the patients on how to take the prescribed drugs and use the respiratory devices effectively, explained the possible ADR, the possible effect of drug combination, the importance of a well-balanced diet with sufficient intake of fruits and vegetables, and the necessity of timely follow-up by physicians. In order to help the patients understand easily the education plan, the pharmacists prepared many drug education materials. During telephone or network counselling, the pharmacist asked the patients about the effect of medication, explained the examination results, the possible ADR and reminded when the patients should visit their doctor. Duration 12 months. Concurrent medication/care: No. of medications: PMC group - mean (SD) 6.4 (1) Further details: 1. Prescribing power: Not stated (n=122) Intervention 2: Usual care. Usual care delivered by the doctor, but no prescription services by the clinical pharmacist. Duration 12 months. Concurrent medication/care: No of medications- 6.2 (1) Further details: 1. Prescribing power: Not stated
Funding	Academic or government funding

Study	Xin 2016[227]
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DELIEVERED AT COMMUNITY CLINICS versus USUAL CARE Protocol outcome 1: Hospital admissions at end of follow-up - Actual outcome: Total hospitalisations at 12 months; Group 1: 11/114, Group 2: 35/113; Risk of bias: All domain - High, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Mortality at end of follow-up; Avoidable adverse events (incorrect diagnosis and treatment) at end of follow-up; Quality of life at end of follow-up; Number of ED presentations at end of follow-up; GP attendances at end of follow-up; Patient and/or carer satisfaction at end of follow-up

Study (subsidiary papers)	Zermansky 2001[229] (Zermansky 2002[230])
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=1188)
Countries and setting	Conducted in United Kingdom; Setting: General practices
Line of therapy	Unclear
Duration of study	Intervention + follow up: Intervention = one-off, follow up to 12 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: GP records
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Patients aged 65 and over receiving at least one drug on repeat prescription on 1 June 1999
Exclusion criteria	In nursing or residential homes; terminal illness; in clinical trials
Recruitment/selection of patients	General practices recruited by selecting randomly from a list of all practices in Leeds Health Authority with 4 or more partners, computerised repeat prescribing, no previous or current clinical pharmacist involvement and prescribing costs close to average; approached in random order until 4 participated.
Age, gender and ethnicity	Age - Mean (SD): Intervention: 74 (6.6); control 72 (6.4) years. Gender (M:F): 524:664. Ethnicity: Not stated
Further population details	1. Frail elderly: Not applicable/Not stated/Unclear. 2. Pre-specified study subgroups: Not applicable/Not stated/Unclear. 3. UK versus non-UK: UK
Indirectness of population	No indirectness

Study (subsidiary papers)	Zermansky 2001[229] (Zermansky 2002[230])
Interventions	(n=608) Intervention 1: Community pharmacists with enhanced roles in disease management - Delivered at community clinics. Clinical review by pharmacist: pharmacist invited patient to his clinic when next review due (or when convenient if no review date set; or at home if patient immobile). Data were gathered before the patient interview on drugs taken and active medical problems. Patient interview: discussed each condition being treated; asked about relevant symptoms (for example, swollen ankles/breathlessness in patients with heart failure); adherence and identify unaddressed problems; consider continuing need for drugs; identify sub-optimal treatment of recognised disease, side effects, drug interactions/contraindications; consider costs. In conditions for which clinical or pathological monitoring was due, pharmacist directed patient to the practice nurse or doctor. The pharmacist did not physically examine the patients but noted signs that were obvious (for example, swollen ankles, rash). Patients with new clinical problems referred to the doctor. Treatment recommendations were based on national, local and where applicable practice guidelines. The researchers agreed with each practice the level of intervention that the pharmacist could make without seeking prior approval. Duration 1 year. Concurrent medication/care: Not stated Further details: 1. Prescribing power: Not stated (n=580) Intervention 2: Usual care. No further details. Duration 1 year. Concurrent medication/care: Not stated Further details: 1. Prescribing power: Not stated
Funding	Academic or government funding (NHS Research and Development National Coordinating Centre for Health Technology Assessment)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: LONG-TERM CONDITIONS versus USUAL CARE Protocol outcome 1: Mortality during the study period - Actual outcome for Long-term conditions: Death at 1 year; Group 1: 15/608, Group 2: 25/580; Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness Protocol outcome 2: GP attendances during the study period - Actual outcome for Long-term conditions: Median (IQR) GP consultations at 1 year; Ri Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 27/608 = 4%, Reason: Died or left the list; Group 2 Number missing: 30/580 = 5%, Reason: Died or left the list Protocol outcome 3: Hospital admissions during the study period - Actual outcome for Long-term conditions: Number of patients admitted to hospital at least once at 1 year; Group 1: 110/578, Group 2: 92/550; Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness	

Study (subsidiary papers)	Zermansky 2001[229] (Zermansky 2002[230])
of outcome: No indirectness ; Group 1 Number missing: 27/608 = 4%, Reason: Died or left the list; Group 2 Number missing: 30/580 = 5%, Reason: Died or left the list	
Protocol outcomes not reported by the study	Avoidable adverse events (incorrect diagnosis and treatment) during the study period; Quality of life during the study period; Number of ED presentations during the study period; Patient and/or carer satisfaction during the study period

Study	Zillich 2014[232]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=895)
Countries and setting	Conducted in USA; Setting: Unclear - Pharmacists from a for-profit corporation contacted patients in their homes by phone
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 60 days
Method of assessment of guideline condition	Method of assessment /diagnosis not stated
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	All patients on plan, including those receiving physical/ occupational therapy services only)
Exclusion criteria	Reoccurring episode of care within the past 12 months were excluded
Recruitment/selection of patients	Patients admitted into Medicare's defined 70-day home health care episode
Age, gender and ethnicity	Age - Mean (SD): Group 1: 73 (13); Group 2: 73 (13). Gender (M:F): 358:537. Ethnicity: White: 75%; Black: 22%; Hispanic: 2%; Other: 1%
Further population details	1. Frail elderly: Not applicable/Not stated/Unclear. 2. Pre-specified study subgroups: Not applicable/Not stated/Unclear. 3. UK versus non-UK: Non-UK (USA).
Indirectness of population	No indirectness
Interventions	(n=475) Intervention 1: Clinical pharmacists with enhanced roles in disease management - Delivered at patient's home. Upon completion of the home health nurse's (who was blinded to the assignment of the patient) admission assessment on day one of the home health care episode, the patient's current medication information was faxed to the MTM intervention provider (HealthStat Rx). Following a pre-MTM call by a pharmacy technician to verify medication information, there was an initial telephone call to the patient and/or caregiver from a trained pharmacist. During this telephone call, the pharmacist completed a comprehensive medication therapy review to identify any

Study	Zillich 2014[232]
	medication-related problems, constructed a written personal medication record for the patient and providers, and developed a medication-related action plan. The action plan served as a patient-centred document to assist the patient and pharmacist in the resolution of identified medication-related problems. The duration of the initial pharmacist telephone call with the patient was approximately 30 minutes. The pharmacist also spent 15 minutes reviewing patient information prior to the call and 15 minutes after the call to complete documentation pertaining to the encounter. For all patients, pharmacists provided a follow-up telephone call on day seven to continue resolving medication-related problems according to the medication action plan and to identify any new medication-related problems. Additional telephone follow-up was provided as needed during the first 30 days of the 60-day home health care episode. The duration of each follow-up encounter was approximately 20 minutes. Duration 30 days. Concurrent medication/care: None stated Further details: 1. Prescribing power: Unclear (n=486) Intervention 2: Usual care. Usual care - no further details. Duration 60 days. Concurrent medication/care: None stated Further details: 1. Prescribing power: Not stated
Funding	Study funded by industry (Amedisys Inc.)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DELIEVERED AT PATIENT'S HOME versus USUAL CARE Protocol outcome 1: Hospital admissions during the study period - Actual outcome: Time to first hospital admission at 60 days; HR 0.8 (95%CI 0.6 to 1.06) Reported; Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Very high, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 60, Reason: 59 unable to contact for MTM, 1 lost to follow-up; Group 2 Number missing: 6, Reason: 6 lost to follow-up	
Protocol outcomes not reported by the study	Mortality during the study period; Avoidable adverse events (incorrect diagnosis and treatment) during the study period; Quality of life during the study period; Number of ED presentations during the study period; GP attendances during the study period; Patient and/or carer satisfaction during the study period

Appendix E: Health economic evidence tables

E.1 Community pharmacists based within a community pharmacy

Study	Bond 2007[53] & Scott 2007[187]			
Study details	**Population & interventions**	**Costs**	**Health outcomes**	**Cost-effectiveness**
Economic analysis: CUA (health outcome: QALYs) **Study design**: Economic evaluation alongside a **r**andomised controlled trial (RCT), The Community Pharmacy Medicines Management Service RCT. **Approach to analysis:** Analysis of individual level data for resource use. Unit costs applied. Analysis was conducted on an intention-to treat basis. Multiple regression analysis, adjusting for baseline covariates was used to analyse the differences in costs and outcomes. **Perspective:** UK NHS **Follow-up**: 12 months **Treatment effect duration:**[(a)] 12 months **Discounting:** Costs: n/a;	**Population:** Patients over 17 years with coronary heart disease (CHD)identified from general practice system **Cohort settings: (n=1493)** Mean age: Intervention 1: 68.8 years Intervention 2: 68.7 years Male: Intervention 1: 70.6% Intervention 2: 67.4% **Intervention 1: (n=513)** Standard care **Intervention 2: (n=980)** Initial consultation with a community pharmacist who received training designed and delivered by the Centre for Pharmacy Postgraduate Education (CPPE) to review appropriateness of therapy, compliance life style, social and support issues.	**Total costs (mean per patient):** Intervention 1: NR Intervention 2: NR Incremental (2−1): NR (95% CI: NR; p=NR) **Total costs - baseline (mean per patient):** Intervention 1: £1243 Intervention 2: £1410 Incremental (2−1): £167 (95% CI: NR; p=NR) **Total costs- follow up (mean per patient)[(b)]:** Intervention 1: £1286 Intervention 2: £1433 Incremental (2−1): £147 (95% CI: NR; p=NR) **Currency & cost year:** 2003-2004 UK pounds **Cost components incorporated:**	**QALYs[(c)] (mean per patient):** Intervention 1: NR Intervention 2: NR Incremental (2−1): 0.02 (95% CI: NR; p=NR)	**ICER (Intervention 2 versus Intervention 1):** £7,350 per QALY gained (da)[(d)] 95% CI: NR Probability Intervention 2 cost-effective (£20K/30K threshold): NR **Analysis of uncertainty:** A threshold analysis was conducted to examine the sensitivity of the results to variations in the intervention costs. The results showed that reducing intervention cost per patient by 35 % to a mean cost of £76 (compared to £118 in the base case) will result in cost neutrality.

Outcomes: n/a		Intervention cost (training and intervention sites) NHS treatment costs (cost of medicines, hospitalisation and other health consultations)		
Data sources				
Health outcomes: Data collected within the context of the RCT. baseline data collected from patient medical records and self-completed patient questionnaires. These included health-related quality-of-life measured using SF-36 and EQ-5D. data were also collected on 5-year risk of death from CHD using a modified score accounting for absence of data on stroke history and creatinine clearance. Baseline and Follow-up data were collected for 12 months. **Quality-of-life weights:** SF-36 and EQ-5D [UK tariff]. **Cost sources:** Not reported.				
Comments				
Source of funding: Department of Health England and Wales. **Applicability and limitations:** some uncertainty regarding the applicability of resource use and cost data from 2004 to the current NHS context. The perspective used is NHS only, as opposed to NHS and PSS. QALYs were not reported but could be calculated from data reported in the paper. RCT based analysis, so by definition the evidence is based on one study and does not reflect all evidence in this area. Limited sensitivity analysis and no bootstrapping reported.				
Overall applicability:[e] Partially applicable **Overall quality**[f] Potentially serious limitation				

Abbreviations: 95% CI: 95% confidence interval; CUA: cost-utility analysis; da: deterministic analysis; EQ-5D: Euroqol 5 dimensions (scale: 0.0 [death] to 1.0 [full health], negative values mean worse than death); ICER: incremental cost-effectiveness ratio; n/a: not applicable; NHS: national health service; NR: not reported; pa: probabilistic analysis; PSS: personal social services; QALYs: quality-adjusted life years; RCT: randomised controlled trial.

(a) For studies where the time horizon is longer than the treatment duration, an assumption needs to be made about the continuation of the study effect. For example, does a difference in utility between groups during treatment continue beyond the end of treatment and if so for how long.

(b) NGC calculation based on mean total cost reported in Scott 2007.[187]

(c) NGC calculation based on reported incremental adjusted mean difference in EQ-5D of 0.04and a follow-up period of 12 months.

(d) NGC calculation based on the unadjusted difference in mean total cost at follow-up only (£147) as reported in Scott 2007[187] and incremental adjusted mean difference in EQ-5D. We used the highest incremental cost of all the reported time points, to have a conservative estimate of cost effectiveness.

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

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

Study	**Gordois 2007[79]**			
Study details	**Population & interventions**	**Costs**	**Health outcomes**	**Cost-effectiveness**

Economic analysis: CUA **Study design:** Deterministic decision analytic model. **Approach to analysis:** A Markov model with 6-monthly cycles was developed to extrapolate the effects of the outcomes of a 6 month RCT. [8] **Perspective:** Australian healthcare. **Time horizon:** 5 years. **Treatment effect duration:** 6 months.(a) **Discounting:** Costs: 5%; Outcomes: 5%	**Population:** Patients with asthma attending a community pharmacy who met certain criteria regarding the severity of their asthma for example, used reliever medication more than three times a week. **Cohort settings:** N: n/a Mean age: 49 years Male: 36% **Intervention 1:** Usual care **Intervention 2:** Pharmacy Asthma Care Program	**Total costs (mean per patient):** Intervention 1: £676 Intervention 2: £953 Incremental (2−1): £278 (95% CI: NR; p=NR) **Currency & cost year:** 2006 Australian Dollars (presented here as 2006 UK pounds).(b) **Cost components incorporated:** Service costs, asthma treatment costs, ED visits, hospital admissions, GP visits.	**QALYs (mean per patient):** Intervention 1: 3.312 Intervention 2: 3.443 Incremental (2−1): 0.131 (95% CI: NR; p=NR)	**ICER (Intervention 2 versus Intervention 1):** £2,121 per QALY gained. 95% CI: n/a **Analysis of uncertainty:** An analysis where no annual patient review was performed to maintain the improvement in asthma gained during the first 6 months of the program. The benefits were assumed to be maintained but the costs of the annual reviews were not incurred. This resulted in a more favourable result for intervention 2. Various one-way sensitivity analyses were performed including varying the time horizon, varying the costs and discount rates. The only analysis that changed the conclusion was when the time horizon was just 6 months (that is, the trial period) where the ICER was £28,953 per QALY gained.
Data sources				
Health outcomes: Measured by Armour et al. 2007 (RCT).[8] **Quality-of-life weights:** AQoL. **Cost sources:** Australian Government, Department of Health and Ageing.				
Comments				
Source of funding: Australian Department of Health and Ageing. **Applicability and limitations:** The analysis is from an Australian healthcare perspective and may not be applicable to the UK NHS perspective. The transition probabilities in the model are derived from a single RCT with a follow up of just 6 months. Assumptions were made that the treatment effects would be maintained in the long term. The discount rate used was higher than the 3.5% in the NICE reference case, however, a sensitivity analysis with undiscounted costs and QALYs was done and the conclusion did not change. Quality of life was not measured using the EQ5D.				
Overall applicability:(c) Partially applicable **Overall quality**(d) Potentially serious limitations.				

Abbreviations: AQoL: Assessment of Quality of Life; CUA: cost-effectiveness analysis; 95% CI: 95% confidence interval; ICER: incremental cost-effectiveness ratio; NR: not reported; PSSRU: Personal Social Services Research Unit; QALYs: quality-adjusted life years; RCT: randomised controlled trial.

(a) Treatment effect was assumed to be maintained.

(b) Converted using 2006 purchasing power parities.[160]

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

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

Study	**Houle 2012[94]**			
Study details	**Population & interventions**	**Costs**	**Health outcomes**	**Cost-effectiveness**
Economic analysis: CEA **Study design:** Decision analytic model. **Approach to analysis:** Cost and health outcomes associated with a reduction in systolic blood pressure from an RCT were calculated. **Perspective:** Canadian healthcare. **Time horizon:** 1 year. **Treatment effect duration:** 1 year with a sensitivity analysis looking at 6 months.[(a)] **Discounting:** NA	**Population:** Patients with diabetes mellitus and hypertension. **Cohort settings:** N: n/a Mean age: NR Male: NR **Intervention 1:** Usual care **Intervention 2:** Cardiovascular risk reduction counselling by a pharmacist-nurse team along with a hypertension education brochure.	**Total costs (mean per patient):** Intervention 1: NR Intervention 2: NR Incremental (2−1): £150 (95% CI: NR; p=NR) **Currency & cost year:** 2011 Canadian Dollars (presented here as 20011 UK pounds).[(b)] **Cost components incorporated:** Myocardial infarction, stroke, heart failure hospitalisation.	**Absolute risk reduction for those receiving intervention:** 0.54% for myocardial infarction 0.66% for stroke 0.60% for development of heart failure exacerbation	**ICER (Intervention 2 versus Intervention 1):** Intervention 2 dominated. 95% CI: n/a **Analysis of uncertainty:** Sensitivity analysis explored the impact of assuming the blood pressure reduction lasted for only 6 months and then returned to the same levels in both arms. The pharmacist intervention remained dominant. Doubling time spent by the pharmacist still resulting in cost savings and thus dominance.
Data sources				
Health outcomes: Measured by McClean et al. 2008 (RCT).[140] **Quality-of-life weights:** NA. **Cost sources:** Canadian Institute for Health Information.				
Comments				
Source of funding: NR. **Applicability and limitations:** The analysis is from a Canadian healthcare perspective and may not be applicable to the UK NHS perspective. QALYs are not estimated and impacts on quality of life and mortality are not assessed. The model uses an intermediate outcome taken from a randomised controlled trial to predict impacts on myocardial infarctions, stroke and heart failure. These outcomes are not directly measured and there is therefore some uncertainty regarding modelling process. Only costs related to the intervention, stroke, myocardial infarction and heart failure are included, therefore resource use associated with				

unscheduled healthcare utilisation is not included, though it would seem likely that the exclusion of these costs would make the intervention less cost effective. None-the-less the model is built on good data.	
Overall applicability:(c) Partially applicable	**Overall quality**(d) Potentially serious limitations.

Abbreviations: AQoL: Assessment of Quality of Life; CUA: cost-effectiveness analysis; 95% CI: 95% confidence interval; ICER: incremental cost-effectiveness ratio; NR: not reported; PSSRU: Personal Social Services Research Unit; QALYs: quality-adjusted life years; RCT: randomised controlled trial.

(a) Treatment effect was assumed to be maintained for only the stated duration.

(b) Converted using 2011 purchasing power parities.[160]

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

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

Study	**Jodar-Sanchez 2015[103]**			
Study details	**Population & interventions**	**Costs**	**Health outcomes**	**Cost-effectiveness**
Economic analysis: CUA (health outcome: QALYs) **Study design:** cluster Randomised Clinical Trial (RCT)(ConSIGUE) **Approach to analysis:** Economic evaluation alongside RCT with individual patient level data for costs and outcomes analysed using multiple regression analysis, adjusting for baseline utility and characteristics. **Perspective:** Spanish NHS **Follow-up:** 6 months **Treatment effect duration:**(a) 12 months	**Population:** Older adults, aged 65 years or over, with polypharmacy, defined as individuals taking five or more medications per day. **Cohort settings: (n=1403)** Mean age: Intervention 1: 74.9 years Intervention 2: 75.4 years Male: Intervention 1: 38.3% Intervention 2: 39.9% **Intervention 1: (n=715)** Normal dispensing with no pharmacist follow-up **Intervention 2: (n=688)**	**Total costs (mean per patient- unadjusted):** Intervention 1: £1,022 Intervention 2: £1,226 Incremental (2−1): £205 (95% CI: NR; p=NR) **Total costs (mean per patient- adjusted):** Intervention 1: NR Intervention 2: NR Incremental (2−1): -£262 (95% CI: -£615 to £60; p=NR) **Currency & cost year:** 2014 Euro (presented here as 2014 UK pounds(b)) **Cost components incorporated:**	**QALYs (mean per patient-unadjusted):** Intervention 1: 0.3488 Intervention 2: 0.3721 Incremental (2−1): 0.0233 (95% CI: NR; p=0.002) **QALYs (mean per patient-adjusted):** Intervention 1: NR Intervention 2: NR Incremental (2−1): 0.0156 (95% CI: 0.008 to 0.023; p=NR)	**ICER (Intervention 2 versus Intervention 1):** Intervention 2 dominant Probability Intervention 2 cost-effective (£20K/30K threshold): NR Probability Intervention 2 cost-effective (£31,352/£47,029 threshold: 100% **Analysis of uncertainty:** None reported.

Discounting: Costs: n/a; Outcomes: n/a	178 community pharmacies implemented a medication review and follow-up service where patients received 6 consultations, with a frequency of 1 visit every 1.2 months. In the first month, the pharmacist developed action plan that was shared with the patient's GP. Pharmacist allocated to the intervention received a 3-day off-site training course and on-site visits by a facilitator during the 6 months follow-up. The function of the facilitator were assisting pharmacists in the provision of the service and ensuring quality and homogeneity of the service.	Intervention costs (pharmacist time, set-up costs) Medication Accident and emergency visits GP visits Hospital admissions		
Data sources				
Health outcomes: Baseline and follow-up data collected during patient interviews conducted every 1.2 months **Quality-of-life weights:** EQ-5D Spanish Tariff. **Cost sources:** National unit costs including official list of drug prices, Spanish DRGs and Spanish community pharmacy agreement. Costs from previous years adjusted for inflation using the Spanish consumer price index.				
Comments				
Source of funding: Spanish General Council of Official Colleges of Pharmacists and CINFA Laboratory **Applicability and limitations:** Some uncertainty regarding the applicability of resource use and costs from Spain in 2014 to current UK NHS perspective. The perspective used is that of the Spanish NHS. RCT based analysis, so by definition the evidence is based on one study and does not reflect all evidence in this area. The follow-up is 6 months, which is unlikely to capture all differences in costs and outcomes. No sensitivity analysis is presented.				
Overall applicability:[(c)] Partially applicable **Overall quality**[(d)] Potentially serious limitations				

Abbreviations: 95% CI: 95% confidence interval; CUA: cost-utility analysis; da: deterministic analysis; EQ-5D: Euroqol 5 dimensions (scale: 0.0 [death] to 1.0 [full health], negative values mean worse than death); GP: general practitioner; ICER: incremental cost-effectiveness ratio; n/a: not applicable; NHS: national health service, NR: not reported; pa: probabilistic analysis; QALYs: quality-adjusted life years; RCT: randomised controlled trial.

(a) For studies where the time horizon is longer than the treatment duration, an assumption needs to be made about the continuation of the study effect. For example, does a difference in utility between groups during treatment continue beyond the end of treatment and if so for how long.

(b) Converted using 2014 purchasing power parities.[160]

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

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

Study	**Respect trial team 2010A [172]**			
Study details	**Population & interventions**	**Costs**	**Health outcomes**	**Cost-effectiveness**
Economic analysis: CUA (health outcome: QALYs) **Study design:** Randomised multiple interrupted time series analyses (clinical results reported in Respect Trail Team 2010[173], which was included in the clinical review) **Approach to analysis:** The analysis was undertaken using a "difference in difference" econometric model, as the data was collected before and after the introduction of the intervention across the 5 PCTs in a stepped manner. **Perspective:** UK NHS **Follow-up**: 12 months **Treatment effect**	**Population:** People aged > 75 years who are living at home, receiving repeat prescriptions for five or more drugs and registered with practices that used the Egton Medical information System (EMIS) across five primary care trusts (PCTs). **Cohort settings: (n=760 ITT, 598 PP)** Mean age: 80.4 years (ITT) Male: 56.8% (ITT) **Intervention 1:** Usual care **Intervention 2:** Pharmaceutical care adapted to British primary	**Total costs (mean per patient):** Intervention 1: £1,809 Intervention 2: £2,001 Incremental (2−1): £192 (95% CI: -£150 to 579; p=NR) **Currency & cost year:** 2004-2005 UK pounds **Cost components incorporated:** Intervention costs (pharmacist time) GP consultations Home visits Telephone consultations GP and nurse time Medication costs Laboratory tests Inpatient admissions	**QALYs (mean per patient):** Intervention 1: 0.595 Intervention 2: 0.614 Incremental (2−1): 0.019 (95% CI: -0.023 to 0.102; p=NR)	**ICER (Intervention 2 versus Intervention 1):** £10,000 per QALY gained (pa) 95% CI:NR Probability Intervention 2 cost-effective (£20K/30K threshold): 77.5%/81.2% **Analysis of uncertainty:** Several scenario analyses were undertaken to test the effect of alternative assumptions on the results. These included alternative methods of costing visits, depending on the effect on pharmacies of patient non-attendance and whether they used locums. None of these analyses changed the ICER of the probability of the intervention being cost effective. Heterogeneity between different types of patients was also examined. Results were presented by type of patient and were as follows: 5- 75 year old with 5 repeat drugs: ICER £4,661 6- 80 year old with 7 repeat drugs: ICER

duration:[(a)] 12 months **Discounting:** Costs: n/a; Outcomes: n/a	care. The intervention was provided by pharmacists who received training that covered the theory and practice of pharmaceutical care, practical exercises in collaborating with the GPs. Training took place just before the start of each 12 months period. Forty-five practices and 62 community pharmacists participated in the study	Outpatient visits		£9,515 7- 85 year old with 10 repeat drugs: ICER £17,980 8- 90 year old with 15 repeat drugs: £35,185
Data sources				
Health outcomes: Participants completed EQ-5D questionnaire at 5 points in time: at recruitment, immediately before intervention start, 3 and 12 months thereafter and at the end of the study period (some at 3 years after the start of recruitment). **Quality-of-life weights:** EQ-5D UK tariff. **Cost sources:** National unit costs from standard source including PSSRU, NHS Reference Costs, drug tariff and Chemist and Druggist.				
Comments				
Source of funding: MRC (charity funding), with extra funding from primary care trusts. **Applicability and limitations:** Some uncertainty regarding the applicability of resource use and costs from 2004-2005 to current NHS context. RCT based analysis, so by definition the evidence is based on one study and does not reflect all evidence in this area. Follow-up was for 12 months, which might not be long enough to capture all the differences in costs and outcomes.				
Overall applicability:[(c)] Partially applicable **Overall quality**[(d)] Potentially serious limitations				

Abbreviations: 95% CI: 95% confidence interval; CUA: cost-utility analysis; da: deterministic analysis; EQ-5D: Euroqol 5 dimensions (scale: 0.0 [death] to 1.0 [full health], negative values mean worse than death); ICER: incremental cost-effectiveness ratio; n/a: not applicable; NR: not reported; pa: probabilistic analysis; QALYs: quality-adjusted life years.

(a) For studies where the time horizon is longer than the treatment duration, an assumption needs to be made about the continuation of the study effect. For example, does a difference in utility between groups during treatment continue beyond the end of treatment and if so for how long?

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

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

Study	**Vegter 2014[214]**			
Study details	**Population & interventions**	**Costs**	**Health outcomes**	**Cost-effectiveness**
Economic analysis: CUA (health outcome: QALYs)	**Population:** Patients initiating lipid lowering therapy for	**Total costs (mean per patient-overall population):** Intervention 1: £16,554	**QALYs (mean per patient-overall population):** Intervention 1: 9.36	**ICER (Intervention 2 versus Intervention 1):** Intervention 2 dominant 95% CI: NR

Study design: Markov model **Approach to analysis:** A time-dependent Markov model was developed based on the results of a single interventional study to extrapolate the results to a lifetime time horizon. The following events were modelled: non-fatal MI, fatal MI, non-fatal stroke, fatal stroke, and revascularisation. The model consisted of three interlinked models: primary prevention, secondary prevention and secondary prevention after stroke. **Perspective:** Dutch Healthcare payer perspective **Time horizon:** Lifetime **Treatment effect duration:**[(a)] 12 months **Discounting:** Costs: 4%; Outcomes: 1.5%	primary prevention (40%) or secondary prevention (60%) of cardiovascular events. **Cohort settings: (n=1002)** Start age: 61.3 years Male: 54.6% **Intervention 1: (n= 502)** Historic control receiving usual care **Intervention 2: (n=500)** Pharmaceutical care program delivered at 9 community pharmacies (MeMO [medication monitoring and optimisation) based on continuous monitoring and optimisation of lipid lowering therapy in new patients who are identified as non-adherent.	Intervention 2: £16,528 Incremental (2−1): -£27 (95% CI: NR; p=NR) **Total costs (mean per patient-secondary prevention population):** Intervention 1: £25,437 Intervention 2: £25,251 Incremental (2−1): -£187 (95% CI: NR; p=NR) **Total costs (mean per patient-primary prevention population):** Intervention 1: £3,230 Intervention 2: £3,444 Incremental (2−1): £213 (95% CI: NR; p=NR) **Currency & cost year:** 2012 euros (presented here as 2012 UK pounds[(b)]) **Cost components incorporated:** Intervention costs (not including start-up costs such as training costs) Drug costs GP visits Laboratory tests	Intervention 2: 9.44 Incremental (2−1): 0.084 (95% CI: NR; p=NR) **QALYs (mean per patient-secondary prevention population):** Intervention 1: 6.86 Intervention 2: 6.97 Incremental (2−1): 0.105 (95% CI: NR; p=NR) **QALYs (mean per patient-primary prevention population):** Intervention 1: 13.10 Intervention 2: 13.15 Incremental (2−1): 0.052 (95% CI: NR; p=NR)	Probability Intervention 2 cost-effective (£20K/30K threshold): NR Probability Intervention 2 cost-effective (£16,744K/£41,861K threshold): 100%/100% Probability Intervention 2 cost-saving: 60.7% **ICER (Intervention 2 versus Intervention 1-secondary prevention):** Intervention 2 dominant 95% CI: NR Probability Intervention 2 cost-effective (£20K/30K threshold): NR Probability Intervention 2 cost-effective (£16,744K/£41,861K threshold): 100%/100% Probability Intervention 2 cost-saving: 94.1% **ICER (Intervention 2 versus Intervention 1-primary prevention):** £3,839 per QALY gained 95% CI: NR Probability Intervention 2 cost-effective (£20K/30K threshold): NR

				Probability Intervention 2 cost-effective (£16,744K/£41,861K threshold): 91.7%/98.1% Probability Intervention 2 cost-saving: 5.3% **Analysis of uncertainty:** The model was run probabilistically in the base case analysis. Additionally, a sensitivity analysis using shorter time horizon was undertaken. A large number of other model parameters were varied by 25% in univariate SAs. The only parameters that resulted in a positive ICER were a higher age (ICER: £1,562), lower statin effectiveness (ICER: £1,079) and lower CVE incidence (ICER: £758) Scenario analyses were undertaken, varying the duration of the program effect, costs of the intervention, baseline risk of vascular disease in patients without history of a cardiovascular event. Assuming no effect from the intervention beyond the first year still resulted in QALY gain and cost saving (that is, intervention 2 remained dominant). Doubling the intervention cost gave similar results as well as increasing the risk of CVE.
Data sources				
Health outcomes: statin efficacy estimates were based on published RCTs (WOSCOP study for patients with hyper-cholesterolaemia but without history of cardiovascular event, HPS study for patients with history of CVE except stroke or diabetes mellitus and SPARCL study for patients with a history of stroke. Baseline risk of cardiovascular events in patients without a history of one was based on a large observational Dutch database. For other populations, RCT data was used. Incidence rates of stroke and MI were taken from large observational studies. Non-cardiovascular mortality rates were based on Dutch overall population data and were age and				

sex specific. The impact of adherence (defined as continuation/persistence at 2 years) on statin efficacy was calculated based on the difference in adherence reported in the trials at 2 years and that in an observational database. A proportional reduction in efficacy was applied based on this difference, which was 59.2%. **Quality-of-life weights:** data on disutility values used in the model were based on published studies and a Dutch burden of disease study. **Cost sources:** cost data were based on published studies. Drug costs were based on GIPdatbank, a national source of unit costs for drugs in the Netherland.	
Comments	
Source of funding: Royal Dutch Pharmaceutical Society and the Dutch PRISMA Network. **Applicability and limitations:** Some uncertainty regarding the applicability of resource use and costs from The Netherland in 2012 to current NHS context. Discount rates used for costs (4%) and outcomes (1.5%) are not in line with NICE Reference Case. Utilities were obtained from published studies. The source of intervention effectiveness estimate is from a single, non-randomised study, so by definition, does not reflect all evidence in this area. The Base case analysis assumes that intervention effectiveness persists over the lifetime time horizon. It is not clear if the unit costs used are from national or local sources, which might limit the generalisability of the results.	
Overall applicability:[c] partially applicable	**Overall quality**[d] potentially serious limitations

Abbreviations: 95% CI: 95% confidence interval; CUA: cost-utility analysis; CVE: cardiovascular event; da: deterministic 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; pa: probabilistic analysis; QALYs: quality-adjusted life years.

(a) The difference in treatment effect was assumed to continue over the life-time time horizon. This assumption was tested in sensitivity analysis.

(b) Converted using 2012 purchasing power parities.[160]

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

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

E.2 Community pharmacist at the patient's home

Study	**Desborough 2012[61]**			
Study details	**Population & interventions**	**Costs**	**Health outcomes**	**Cost-effectiveness**
Economic analysis: CCA **Study design:** Before and after evaluation of NMSS. **Approach to analysis:** Healthcare costs were measured in a single group of patients 6 months before and 6 months after the intervention was	**Population:** Patients 65 years or older and registered with a GP in Norfolk, residing in their own home and referred to the service by anyone in their care that identified they were having difficulties managing their medication. **Cohort settings:** N: 117	**Total costs (mean per patient):** Intervention 1: £2,190 Intervention 2: £1,883 Incremental (2−1): -£307 (95% CI: - £1,269 to £655; p=NR) **Currency & cost year:** 2006 UK pounds[a]	**QALYS (mean per patient):** Intervention 1: NR Intervention 2: NR Incremental (2−1): - 0.019[b] (95% CI: NR; p=NR)	**ICER (Intervention 1 versus Intervention 2):** £16,157 (Usual care is cost effective compared to pharmacist intervention) 95% CI: n/a **Analysis of uncertainty:** Sensitivity analyses were performed by varying some of the costs of inpatient stay and central administration costs. The results remained cost saving in favour of

introduced. EQ5D was measured at just before the intervention started and after 6 months. **Perspective:** UK NHS. **Time horizon/Follow-up** 6 months. **Treatment effect duration:** 6 months. **Discounting:** Costs: n/a; Outcomes: n/a	Mean age: NR Male: NR **Intervention 1:** Usual care **Intervention 2:** Medicine management assessment and support service.	**Cost components incorporated:** Pharmacist fee, travel expenses, administrative costs, medication costs, ambulance costs and admissions.		intervention 2.
Data sources				
Health outcomes: Within the before and after study. **Quality-of-life weights:** EQ5D UK tariff. **Cost sources:** NMSS, NHS Drug Tariff, PSSRU Unit Costs of Health and Social Care 2006, and HES.				
Comments				
Source of funding: Norfolk primary care trust and The Harold and Marjorie Charitable Trust. **Applicability and limitations:** The analysis is based on a single before and after evaluation of the service change and so may be subject to confounding. A single patient group is used to assess the effects both before and after and so this increases the risk of bias further.				
Overall applicability:(c) Partially applicable **Overall quality**(d) Potentially serious limitations.				

Abbreviations: CCA: cost-consequence analysis; 95% CI: 95% confidence interval; ICER: incremental cost-effectiveness ratio; NMSS: Norfolk Medicines Support Service; NR: not reported; PSSRU: Personal Social Services Research Unit; QALYs: quality-adjusted life years.

(a) Converted using 2014 purchasing power parities.[160]

(b) NGC calculation based on utility loss of 0.038 over 6 month's follow-up.

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

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

Study	**Pacini 2007[161]**			
Study details	**Population & interventions**	**Costs**	**Health outcomes**	**Cost-effectiveness**
Economic analysis: CUA (health outcome: QALYs) **Study design:** randomised	**Population:** Patients aged > 80 years who were admitted to as an emergency to an acute or	**Total costs (mean per patient-complete case analysis):** Intervention 1: £579	**QALYs (mean change per patient-complete case analysis):** Intervention 1: -0.0569	**ICER (Intervention 2 versus Intervention 1):** £54,454 per QALY gained (pa) 95% CI: NR Probability Intervention 2 cost-effective

controlled trial (RCT)[the HOMER trial[92]] **Approach to analysis:** Analysis of individual patient level data on costs and outcomes. **Perspective:** UK NHS **Follow-up:** 6 months **Treatment effect duration:**[(a)] 6 months **Discounting:** Costs: n/a; Outcomes: n/a	community hospital in Norfolk or Suffolk (for any cause), returning to their own home or warden-controlled accommodation and taking two or more drugs. **Cohort settings: (n=872 [ITT])** Mean age: NR Male: NR **Intervention 1: (n= 414 for cost data, 344 for QoL data)** Usual care (no further details given) **Intervention 2: (n=415 for cost data, 354 for QoI data)** Two home visits by a community pharmacist within 2 and 8 weeks of discharge to educate the patients and carers about their drugs, remove out-of-date drugs, inform GP of drug reactions or interactions and inform local pharmacist if adherence aid was needed. Pharmacists had either a postgraduate qualification in Pharmacy Practice or	Intervention 2: £986 Incremental (2−1): £407 (95% CI: £179 to £635; p=NR) **Currency & cost year:** 2000 UK pounds **Cost components incorporated:** Intervention costs (training and pharmacist time and adherence aid costs) Emergency hospital admissions (including ambulance transfer for all) Primary care costs (only for a subset of patients where data were collected)	Intervention 2: -0.0494 Incremental (2−1): 0.0075 (95% CI: -0.0064 to 0.0214; p=NR)	(£20K/30K threshold): NR%/25% **Analysis of uncertainty:** Sensitivity analyses were conducted to explore the impact of changing the following variables: 1- Cost of hospital stay: using a generic per-diem cost rather than a geriatric specific and using fixed cost per admission rather than based on length of stay multiplied by per-diem cost 2- Including community hospital and primary care costs for all patients by imputation (base case analysis considered these costs for only a subset of patients for whom data were available) 3- Imputing QoL data for those patients who did not complete it at 6 months and were alive at the end 4- Considering intervention costs only and assuming all other costs equal 5- Baseline assumption of geriatric bed-day cost only without the cost of ambulance In all scenario analyses, the ICER was > £20,000/ QALY gained, except when only intervention cost was considered, where it was £17,070.

	recent continuing professional development in therapeutics participated in the trial. They also attended 2-day training course that included lectures on prescribing for the elderly, adverse drug reactions, improving adherence and communication skills.			
Data sources				
Health outcomes: data were collected for both the control and intervention groups at baseline and at 6 months. These included mortality, hospital admission, HRQoL complete QoL data were available for 698 patients only. **Quality-of-life weights:** UK EQ-5D. **Cost sources:** resource use data were collected from hospital Episode Statistics (HES) data, GP medical records. Unit costs were based on standard national unit costs such as the NHS reference cots and PSSRU. Complete cost data were available for 829 patients only.				
Comments				
Source of funding: NHS Eastern Region R&D and Academic Pharmacy Practice Unit of the University of East Anglia. **Applicability and limitations:** Some uncertainty regarding the applicability of resource use and costs from the year 2000 to current NHS context. RCT based analysis, so by definition the evidence is based on one study and does not reflect all evidence in this area. Follow-up was for 6 months, which might not be long enough to capture all the differences in costs and outcomes. The economic evaluation was based only on patients that had complete QoL data, who showed a larger mean difference in cost than the overall group.				
Overall applicability:[(c)] Partially applicable **Overall quality**[(d)] Potentially serious limitations				

Abbreviations: 95% CI: 95% confidence interval; CUA: cost-utility analysis; da: deterministic analysis; EQ-5D: Euroqol 5 dimensions (scale: 0.0 [death] to 1.0 [full health], negative values mean worse than death); ICER: incremental cost-effectiveness ratio; n/a: not applicable; NR: not reported; pa: probabilistic analysis; QALYs: quality-adjusted life years.

(a) For studies where the time horizon is longer than the treatment duration, an assumption needs to be made about the continuation of the study effect. For example, does a difference in utility between groups during treatment continue beyond the end of treatment and if so for how long.

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

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

E.3 Community pharmacist based within a GP practice

Study	**Simpson 2015[191]**

Study details	Population & interventions	Costs	Health outcomes	Cost-effectiveness
Economic analysis: CEA (health outcome: improvement in cardiovascular risk) **Study design:** Within trial analysis (RCT). **Approach to analysis:** Cost analysis of intervention and resources used with the trial compared against the improvement in cardiovascular risk. **Perspective:** Canadian healthcare. **Time horizon/Follow-up** 12 months. **Treatment effect duration:** 12 months. **Discounting:** Costs: n/a; Outcomes: n/a	**Population:** Patients with type 2 diabetes treated in primary care. **Cohort settings:** N: 123 Mean age: 62 years. Male: 38% **Intervention 1:** Usual care **Intervention 2:** Addition of pharmacist to primary care teams.	**Total costs (mean per patient):** Intervention 1: £1,071 Intervention 2: £969 Incremental (2−1): -£102 (95% CI: - £560 to £360; p=NR) **Currency & cost year:** 2014 Canadian dollars (presented here as 2014 UK pounds[(b)]) **Cost components incorporated:** Pharmacist intervention cost, medications, healthcare services, ED visits and hospitalisations.	**Reduction in UKPDS risk score (% per patient):** Intervention 1: 0.06% Intervention 2: 0.33% Incremental (2−1): 0.26% (95% CI: NR; p=NR)	**ICER (Intervention 2 versus Intervention 1):** Intervention 2 dominates intervention 1. 95% CI: n/a Probability Intervention 2 is dominant: 66% **Analysis of uncertainty:** 10,000 bootstrap replications were calculated from the main analysis to estimate confidence intervals. A multiple imputation was performed to estimate the full sample of 258 patients and 50,000 bootstrap replications were calculated. No difference in the outcome was observed.
Data sources				
Health outcomes: Within the RCT. **Quality-of-life weights:** n/a **Cost sources:** Hospital staff salaries and the Alberta drugs benefit list.				
Comments				
Source of funding: Canadian Diabetes Association, Institute of Health Economics, and Alberta Heritage Foundation for Medical Research (AH-FMR). **Applicability and limitations:** Costs in this study may not be applicable to the UK NHS perspective and health benefits are not measured in QALYs.				
Overall applicability:[(c)] Partially applicable **Overall quality**[(d)] Potentially serious limitations.				

Abbreviations: CEA: cost-effectiveness analysis; 95% CI: 95% confidence interval; ICER: incremental cost-effectiveness ratio; NR: not reported; QALYs: quality-adjusted life years.

(a) Converted using 2014 purchasing power parities.[160]

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

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

E.4 Clinical pharmacist based within a GP practice

Study	Neilson 2015[151]			
Study details	**Population & interventions**	**Costs**	**Health outcomes**	**Cost-effectiveness**
Economic analysis: CUA **Study design:** Within trial analysis (RCT). **Approach to analysis:** Regression analysis of costs and outcomes from an RCT on an intention-to-treat basis for patients with complete quality of life data. **Perspective:** UK NHS. **Time horizon:** 6 months. **Treatment effect duration:** 6 months. **Discounting:** Costs: n/a; Outcomes: n/a.	**Population:** Patients who are 18 years or older. living in their own home and receiving medication for pain.[(a)] **Cohort settings:** Mean age: NR Male: NR **Intervention 1 (N=42):** Usual care **Intervention 2 (N=44):** Pharmacy medication review only. **Intervention 3 (N=39):** Pharmacy medication review with pharmacist prescribing.	**Total costs (mean incremental cost per patient relative to intervention 1):** Intervention 1: n/a Intervention 2: £54 Intervention 3: £78 (95% CI: NR; p=NR) **Currency & cost year:** 2010 UK pounds. **Cost components incorporated:** Pharmacist training, staff time for delivering intervention, pain related hospitalisation, primary care visits for chronic pain, primary care telephone contacts for chronic pain, prescribed and non-prescribed medication.	**QALYs (mean incremental cost per patient relative to intervention 1):** Intervention 1: n/a Intervention 2: 0.0097 Intervention 3: 0.0069 (95% CI: NR; p=NR)	**ICER (Intervention 2 versus Intervention 1):** £5,567 per QALY gained. 95% CI: NR **ICER (Intervention 3 versus Intervention 1):** £11,304 per QALY gained. 95% CI: NR **ICER (Intervention 3 versus Intervention 2):** Intervention 2 dominates intervention 3. 95% CI: NR **Analysis of uncertainty:** Sensitivity analyses were performed on a data set with multiple imputations used where values were missing. When excluding the costs of patients who had inpatient stay and adjusting only for baseline cost and SF6D score, the incremental costs increased to £125 and £76 for intervention 3 and intervention 2 respectively, relative to intervention 1. The incremental QALYs were 0.0017 and 0.0040 respectively. The ICER for intervention 2 versus intervention 1 would then increase to £19,000 per QALY and for intervention 3 versus intervention 1 it would increase to £73,529 per QALY gained. Intervention would remain dominant over intervention 3.
Data sources				

Health outcomes: Within RCT. **Quality-of-life weights:** SF-6D. **Cost sources:** British National Formulary, Scottish Health Service Costs Book, and PSSRU.
Comments
Source of funding: Medical Research Council. **Applicability and limitations:** The analysis is based on a single RCT with only a 6 month follow up period. Quality of life was not measured using the EQ5D. A probabilistic sensitivity analysis was not performed and may well change the conclusion of the analysis due to the small differences in quality of life scores.
Overall applicability:[c] Partially applicable **Overall quality**[d] Potentially serious limitations.

Abbreviations: CUA: cost-effectiveness analysis; 95% CI: 95% confidence interval; ICER: incremental cost-effectiveness ratio; NR: not reported; PSSRU: Personal Social Services Research Unit; QALYs: quality-adjusted life years; RCT: randomised controlled trial.

(a) Defined as receiving within the previous 120 days either 2 or more acute prescriptions, and/or one repeat prescription for an analgaesic and/or a non-steroidal anti-inflammatory drug (NSAID).

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

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

Appendix F: GRADE tables

Table 19: Clinical evidence profile: Community pharmacist based within a community pharmacy

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Community pharmacist @ pharmacy versus usual care	Control	Relative (95% CI)	Absolute		
Mortality												
6	randomised trials	very serious[1]	serious[2]	no serious indirectness	serious[3]	None	41/1706 (2.4%)	3.2%	RR 0.69 (0.46 to 1.02)	10 fewer per 1000 (from 17 fewer to 1 more)	⊕OOO VERY LOW	CRITICAL
ED presentations												
7	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	168/1336 (12.6%)	9.3%	RR 0.63 (0.53 to 0.76)	34 fewer per 1000 (from 22 fewer to 44 fewer)	⊕⊕OO LOW	CRITICAL
ED presentations (follow-up 12 months; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	None	122	192	-	MD 0.52 lower (1.43 lower to 0.39 higher)	⊕⊕OO LOW	CRITICAL
Hospital admissions												
7	randomised trials	very serious[1]	serious[2]	no serious indirectness	very serious[3]	None	90/621 (14.5%)	9.3%	RR 0.92 (0.56 to 1.49)	7 fewer per 1000 (from 41 fewer to 46 more)	⊕OOO VERY LOW	IMPORTANT
Mean number of hospitalisations (follow-up 12 months; Better indicated by lower values)												
2	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	749	863	-	MD 0.02 lower (0.05 lower to 0.01 higher)	⊕⊕⊕O MODERATE	IMPORTANT

GP visits												
2	randomised trials	very serious[1]	serious[2]	no serious indirectness	very serious[3]	None	91/151 (60.3%)	79.7%	RR 0.6 (0.17 to 2.06)	319 fewer per 1000 (from 662 fewer to 845 more)	⊕OOO VERY LOW	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 or 2 increments because: The point estimate varies widely across studies, unexplained by subgroup analysis.
[3] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs.

Table 20: Clinical evidence profile: Community pharmacist at the patients' homes

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Community pharmacist @ home versus usual 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	37/217 (17.1%)	12.9%	RR 1.19 (0.77 to 1.85)	25 more per 1000 (from 30 fewer to 110 more)	⊕⊕OO LOW	CRITICAL
Hospital admissions												
3	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	None	258/631 (40.9%)	32.1%	RR 1.12 (0.98 to 1.29)	39 more per 1000 (from 6 fewer to 93 more)	⊕⊕OO LOW	CRITICAL
Quality of Life EQ-5D (Better indicated by lower values)												
2	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	455	428	-	MD 0.03 higher (0.02 lower to 0.07 higher)	⊕⊕OO LOW	CRITICAL
Quality of Life EQ-VAS (Better indicated by lower values)												
2	randomised	very	no serious	no serious	no serious	none	427	406	-	MD 2.93 lower (6.06	⊕⊕OO	CRITICAL

	trials	serious[1]	inconsistency	indirectness	imprecision					lower to 0.21 higher)	LOW	

[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.

Table 21: Clinical evidence profile: Community pharmacist based within a GP practice

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Community pharmacist @ GP versus usual care	Control	Relative (95% CI)	Absolute		
Mortality (follow-up 5-12 months)												
3	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	11/628 (1.8%)	1.5%	RR 1.26 (0.54 to 2.96)	4 more per 1000 (from 7 fewer to 29 more)	⊕OOO VERY LOW	CRITICAL
Survival (follow-up 12 months)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	0/364 (0%)	302/310 (97.4%)	HR 0.78 (0.13 to 4.68)	32 fewer per 1000 (from 596 fewer to 26 more)	⊕OOO VERY LOW	CRITICAL
ED presentations (follow-up 12 months)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	11/131 (8.4%)	8.5%	RR 0.98 (0.44 to 2.19)	2 fewer per 1000 (from 48 fewer to 101 more)	⊕OOO VERY LOW	CRITICAL
Mean number of ED visits (follow-up 5 months; Better indicated by lower values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	431	458	-	MD 0.03 lower (0.11 lower to 0.05 higher)	⊕⊕⊕⊕ HIGH	CRITICAL
Hospital admission (follow-up 12 months)												

1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	0/364 (0%)	10/310 (3.2%)	HR 0.5 (0.12 to 2.08)	16 fewer per 1000 (from 28 fewer to 34 more)	⊕OOO VERY LOW	IMPORTANT
Hospital admissions (follow-up 12 months)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	4/131 (3.1%)	3.9%	RR 0.79 (0.22 to 2.87)	8 fewer per 1000 (from 30 fewer to 73 more)	⊕OOO VERY LOW	IMPORTANT
Mean number of hospitalisations (follow-up 5 months; Better indicated by lower values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	431	458	-	MD 0.03 higher (0.03 lower to 0.09 higher)	⊕⊕⊕⊕ HIGH	IMPORTANT
Mean number of GP visits (follow-up 5 months; Better indicated by lower values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	431	458	-	MD 0.19 higher (0.59 lower to 0.97 higher)	⊕⊕⊕⊕ HIGH	CRITICAL
Adverse events (follow-up 12 months)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	104/364 (28.6%)	23.6%	RR 1.21 (0.94 to 1.57)	50 more per 1000 (from 14 fewer to 135 more)	⊕OOO VERY LOW	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.

Table 22: Clinical evidence profile: Clinical pharmacist based within a community clinic

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Clinical pharmacist @ clinic versus usual care**	**Control**	**Relative (95% CI)**	**Absolute**		

Mortality (follow-up 1-2 years)												
4	randomised trials	no serious risk of bias[1]	no serious inconsistency	no serious indirectness	serious[2]	none	68/1276 (5.3%)	4.2%	RR 0.8 (0.59 to 1.09)	8 fewer per 1000 (from 17 fewer to 4 more)	⊕⊕⊕O MODERATE	CRITICAL
Mean number of ED visits (follow-up 1 years; Better indicated by lower values)												
2	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	125	106	-	MD 0.11 lower (0.37 lower to 0.15 higher)	⊕⊕OO LOW	CRITICAL
Mean number of hospitalisations (follow-up 1-2 years; Better indicated by lower values)												
3	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	186	152	-	SMD 0.12 higher (0.1 lower to 0.33 higher)	⊕⊕OO LOW	IMPORTANT
Mean number of GP visits (follow-up 1 year; Better indicated by lower values)												
2	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	125	106	-	MD 0.09 higher (0.18 lower to 0.37 higher)	⊕⊕OO LOW	CRITICAL
Total hospitalisations (follow-up 1 year; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	11/114 (9.6%)	31%	RR 0.31 (0.17 to 0.58)	214 fewer per 1000 (from 130 fewer to 257 fewer)	⊕⊕⊕O MODERATE	IMPORTANT

[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.

Table 23: Clinical evidence profile: Clinical pharmacist at the patients' homes

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Clinical pharmacist @ home versus usual care**	**Control**	**Relative (95% CI)**	**Absolute**		

Mortality (follow-up 6 months)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	17/77 (22.1%)	18.2%	RR 1.21 (0.64 to 2.29)	38 more per 1000 (from 66 fewer to 235 more)	⊕⊕OO LOW	CRITICAL
Hospital admission (follow-up 60 days)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	None	-	112/480 (23.3%)	HR 0.8 (0.6 to 1.07)	42 fewer per 1000 (from 86 fewer to 14 more)	⊕OOO VERY LOW	IMPORTANT
Hospital admission (follow-up 3-6 months)												
2	randomised trials	serious[1]	serious[3]	no serious indirectness	serious[1]	None	48/245 (19.6%)	31.7%	RR 0.9 (0.68 to 1.19)	32 fewer per 1000 (from 101 fewer to 60 more)	⊕OOO VERY LOW	IMPORTANT
GP visits (follow-up 12 months)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	None	33/61 (54.1%)	74.6%	RR 0.73 (0.55 to 0.95)	201 fewer per 1000 (from 37 fewer to 336 fewer)	⊕OOO VERY LOW	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: The point estimate varies widely across studies, unexplained by subgroup analysis.

Table 24: Clinical evidence profile: Clinical pharmacist based within a GP practice

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Clinical pharmacist @ GP versus usual care**	**Control**	**Relative (95% CI)**	**Absolute**		
Mortality												

5	randomised trials	very serious[1]	no serious inconsistency	serious indirectness[2]	serious[3]	none	23/1280 (1.8%)	2.5%	RR 0.58 (0.34 to 0.97)	11 fewer per 1000 (from 1 fewer to 16 fewer)	⊕OOO VERY LOW	CRITICAL
Mortality (follow-up median 4.7 years)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	331/1074 (30.8%)	HR 0.96 (0.8 to 1.15)	10 fewer per 1000 (from 53 fewer to 37 more)	⊕⊕⊕⊕ HIGH	CRITICAL
ED presentations (follow-up 1 years)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[3]	none	4/33 (12.1%)	16.7%	RR 0.73 (0.22 to 2.35)	45 fewer per 1000 (from 130 fewer to 225 more)	⊕OOO VERY LOW	CRITICAL
Mean number of ED visits (follow-up 6 months; Better indicated by lower values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	162	164	-	MD 0.01 lower (0.06 lower to 0.04 higher)	⊕⊕⊕⊕ HIGH	CRITICAL
Hospital admissions												
4	randomised trials	very serious[1]	no serious inconsistency	serious indirectness[2]	serious[3]	none	116/694 (16.7%)	15.7%	RR 0.86 (0.32 to 2.32)	22 fewer per 1000 (from 107 fewer to 207 more)	⊕OOO VERY LOW	IMPORTANT
Mean number of hospitalisations (follow-up 6 months; Better indicated by lower values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	162	164	-	MD 0.01 lower (0.05 lower to 0.03 higher)	⊕⊕⊕⊕ HIGH	CRITICAL
Hospital admission (follow-up median 4.7 years)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	695/1074 (64.7%)	HR 0.97 (0.87 to 1.08)	11 fewer per 1000 (from 51 fewer to 28 more)	⊕⊕⊕⊕ HIGH	IMPORTANT
Adverse events (follow-up 2 years)												
2	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[3]	none	0/270 (0%)	0.9%	RR 0.29 (0.03 to 2.8)	6 fewer per 1000 (from 9 fewer to 16 more)	⊕OOO VERY LOW	CRITICAL

GP visits(follow-up 6 months												
2	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	57/83 (68.7%)	71.4%	RR 0.96 (0.79 to 1.17)	29 fewer per 1000 (from 150fewer to 121 more)	⊕⊕OO LOW	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 or 2 increments because: The majority of the evidence was from studies that had higher/lower drug doses than the recommended dose
[3] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.

Appendix G: Excluded clinical studies

Table 25: Studies excluded from the clinical review

Study	Exclusion reason
ABULOHA 2016[2]	Paper not available
ADAMS2015[3]	Inappropriate intervention- supervised undergraduate pharmacy student-led medication review (third year pharmacy students)
Aguiar2016[4]	Incorrect setting- hospital affiliated secondary clinic. No extractable outcomes
Anon 2005[1]	Paper not available
Armour 2008[7]	Systematic review: quality assessment is inadequate
Aslani 2009[9]	Systematic review: quality assessment is inadequate
Avery 2009[11]	No outcomes of interest
Avery 2012[10]	No outcomes of interest
Bacchus 2009[12]	Systematic review: study designs inappropriate
Ballantyne 2011[13]	Commentary not primary study
Barr 2012[15]	Review non-systematic
Bayoumi 2009[16]	Systematic review: study designs inappropriate
Bell 2005[19]	Systematic review: quality assessment is inadequate
Bell 2010[18]	Systematic review: quality assessment is inadequate
Benavides 2009[20]	Systematic review: quality assessment is inadequate
BLACKBURN2016[22]	No extractable outcomes (outcome reported in the study- statin adherence)
Blenkinsopp 2005[23]	Systematic review: study designs inappropriate
Bogden 1998[24]	Incorrect interventions. Hospital-based outpatient clinic
Bond 2000[25]	Not review population
Bond 2007[26]	No outcomes of interest
Butt 2016[31]	Incorrect setting -private counselling room of a medical centre
Cameli 2013[32]	Not available

Caro 2002[33]	Commentary not primary study
Carrier 2009[34]	Commentary not primary study
Carter 2001[37]	Incorrect setting: hospital-based ambulatory care
Carter 2004[38]	Systematic review: quality assessment is inadequate
Carter 2008[36]	Incorrect interventions. 2/5 sites were hospital-based clinics. No outcomes of interest
Carter 2009[35]	Not protocol outcomes
Carter 2010[40]	Editorial not primary study
Carter 2015[41]	Incorrect interventions. 2/5 clinics were hospital based. No outcomes of interest
Casteel 2011[42]	Does not report any of our outcomes
Cheema 2014[43]	Not protocol outcomes
Chin 2011[44]	Systematic review: quality assessment is inadequate
Choe 2005[45]	Incorrect interventions. Ambulatory care clinic
Chrischilles 2014[46]	Inappropriate comparison. No comparison of Medication management therapy versus usual care. Unknown number of patients received the intervention at a hospital
Clark 2007[47]	No outcomes of interest
Clyne2015[48]	No extractable outcomes (outcome reported in the study- inappropriate prescribing)
Coburn2016[49]	Inappropriate setting- ambulatory clinics. Inappropriate population- adult patients with gout
Cohen 2011[50]	No outcomes of interest
Coleman 1999[52]	Incorrect interventions. MDT with a majority team nurse component
Coleman 2001[51]	Incorrect interventions. Nurse led MDT
Crawford-faucher 2012[55]	Commentary not primary study
Davidson 2000[56]	Incorrect study design
De smet 2004[57]	Systematic review: quality assessment is inadequate
Delate 2008[58]	Incorrect study design
Dennis 2009[59]	Systematic review: quality assessment is inadequate

Doucette 2009[62]	No outcomes of interest
ELLIOTT2016[64]	No extractable outcomes (outcome reported in the study- self-reported adherence in people starting a new medicine for long term conditions)
Elliott 2012[65]	Inappropriate comparison. Pharmacist-led home medication review versus GP-led home medication review. No outcomes of interest
Evans 2011[66]	No extractable outcomes
Fathima 2013[67]	Systematic review: quality assessment is inadequate
Fish 2002[68]	Systematic review: no papers of interest
Fornos 2006[70]	No outcomes of interest
Freemantle 2002[71]	No outcomes of interest
Gallagher 2015[72]	Not protocol outcomes
Gattis 1999[74]	Incorrect setting- general cardiology faculty clinic
Garcao 2002[73]	No outcomes of interest
George 2008[76]	Systematic review: no papers of interest
George 2010[77]	SR: not all RCTs, no extractable data
George 2011[75]	Literature review
Glynn 2010[78]	Systematic review is not relevant to review question or unclear PICO. SR: combines nurse-led and pharmacist-led programmes
Gourley 1998[80]	Not community pharmacy
Graffen 2004[81]	No extractable data
Grymonpre 2001[82]	Not protocol outcomes
Health 2009[83]	Systematic review: all papers included
Heisler 2010[84]	Incorrect interventions. Hospital-based outpatient primary care clinic
Heisler 2012[85]	Incorrect interventions. Hospital-based outpatient primary care clinic
Hennessy 2006[87]	No outcomes of interest
Hirsch 2014[88]	Incorrect interventions. Hospital-based primary care clinic
Ho 2014[89]	Incorrect interventions. Hospital-based clinical pharmacist
Hogg 2009[90]	Incorrect interventions. Nurse practitioner led MDT
Hugtenburg 2009[95]	Incorrect study design

Ifeanyi 2015[96]	Systematic review: study designs inappropriate
Jacobs 2012[97]	Not community pharmacy; not protocol outcomes
Jokanovic 2016[104]	Overview of systematic reviews on pharmacist led medication review in community settings- checked for relevant references
Jahangardrad- Rafsanjani 2015[98]	No extractable outcomes
Jalal 2014[99]	Systematic review: screened for relevant references
Jarab 2012[102]	Incorrect setting -out-patient clinic of a hospital
Jameson 2010[100]	No outcomes of interest
Jamieson 2010[101]	Crossover trial; no data first period intervention versus Control
Jones 2000[105]	Not comparing intervention and control patients using same outcome measures
Kaur 2009[106]	Systematic review: quality assessment is inadequate
Khdour 2009[108]	Incorrect setting: hospital-based outpatient clinic
Khdour 2011[107]	Not community pharmacy
Kirwin 2010[109]	No outcomes of interest. Incorrect setting: hospital-based clinic
Kjeldsen 2015[110]	No extractable outcomes
Kraemer 2012[111]	No outcomes of interest
Krass 2006[112]	No outcomes of interest
Kritikos 2007[113]	Not typical community pharmacy
Krska 2008[114]	No comparator
Kucukarslan 2011[117]	SR: no extractable data
Kwint 2011[118]	Not protocol outcomes
Lambert-kerzner 2012[119]	Incorrect interventions. Hospital-based clinical pharmacist
Lim 2014[124]	Incorrect setting: hospital-based clinic
Lindenmeyer 2006[125]	Systematic review is not relevant to review question or unclear PICO
Lipton 1992[126]	Not community pharmacy
Lowe 2000[127]	No extractable outcomes (results from arms reported in combined format)
Lowrie 2010[131]	Education of primary care professionals. Incorrect interventions. No

	outcomes of interest
Lowrie 2014[128]	No outcomes of interest
Lund 2010[132]	Incorrect setting: hospital-based primary care clinic
Machado 2007[133]	Systematic review: study designs inappropriate
Mackeigan 2008[134]	Systematic review: quality assessment is inadequate
Mansell 2016[136]	No outcomes of interest
Martin 2015[137]	Protocol only
Mcalister 2014[138]	Not protocol outcomes
Mclean 2006[139]	No outcomes of interest
Mclean 2008[140]	No outcomes of interest
Milos 2013[142]	Hospital-based pharmacist (remote intervention)
Mohammed 2012[143]	Excluded by committee subgroup
Mossialos 2013[144]	Systematic review: study designs inappropriate
Mott 2016[145]	No extractable outcomes
Mott 2016[145]	No outcomes of interest
Murray 2004[147]	Incorrect setting: hospital-based primary care clinic
Nazar 2015[150]	Systematic review of the role of community pharmacies in improving transition from secondary to primary care- checked for relevant references
Naunton 2003[149]	Non-OECD country
Nkansah 2010[154]	SR - no extractable data
Obarcanin 2015[155]	Inappropriate population- adolescents –mean age 14.5 years
Okamoto 2001[156]	Incorrect interventions. Not community pharmacy
Okumura 2014[157]	Systematic review: no papers of interest
Olson 2009[158]	Incorrect interventions. Hospital-based pharmacist (remote intervention)
Omran 2015[159]	No outcomes of interest
Parker 2014[163]	No comparator
Paudyal 2013[164]	Systematic review: quality assessment is inadequate
Paulos 2005[165]	No outcomes of interest

Petkova 2009[166]	Not review population. Arthritis patients - not at risk of an AME
Pinto 2014[167]	No outcomes of interest
Planas 2009[169]	No outcomes of interest
Planas 2012[168]	No outcomes of interest
Polack 2008[170]	No outcomes of interest. Inappropriate comparison
Renders 2009[171]	Systematic review: study designs inappropriate. SR: not all RCTs
Rothman 2005[174]	Incorrect interventions. General internal medicine practice
Royal 2006[175]	SR: not all RCTs
Rubio-valera 2014[177]	Review non-systematic
Saastamoinen 2009[178]	No outcomes of interest
Sadik 2005[179]	Incorrect setting- hospital based
Saini 2004[181]	Incorrect study design
Santschi 2011[183]	Systematic review: no papers of interest
Santschi 2012[185]	Systematic review: no papers of interest
Santschi 2014[184]	Systematic review: no papers of interest
Schneiderhan 2014[186]	No outcomes of interest
Sorensen 2004[193]	Incorrect interventions. MDT with a large clinical pharmacist component
Spinewine 2012[194]	Systematic review: quality assessment is inadequate
Stewart 2014[195]	Not protocol outcomes
Stuurman-bieze 2014[196]	Incorrect study design
Tan 2014[197]	SR: no extractable data for our outcomes
Tjia 2013[203]	Not protocol outcomes
Tonna 2007[204]	Not protocol outcomes
Touchette 2012[206]	Not protocol outcomes
Tsuyuki 2004[209]	Incorrect interventions. Significant pre-discharge intervention component
Tsuyuki 2015[208]	No outcomes of interest
Van boven 2014[210]	SR: not RCTs

Van der meer 2015[211]	Protocol only
Van wijk 2005[212]	Systematic review: study designs inappropriate
Varma 1999[213]	Incorrect setting- hospital based
Vera 2014[215]	Protocol
Vermeire etienne 2005[216]	SR: no extractable data for our outcomes
Viswanathan 2015[217]	Systematic review: study designs inappropriate
Vivian 2002[219]	Not typical community pharmacy
Vivian 2007[218]	Systematic review is not relevant to review question or unclear PICO
Wagner 2001[220]	No information on the role of the pharmacist
Watson 2001[221]	Incorrect interventions. Educational outreach for GPs
Wentzlaff 2011[222]	No outcomes of interest
Westberg 2014[223]	Incorrect study design
Willeboordse 2014[224]	Protocol only
Zermansky 2009[231]	Systematic review: quality assessment is inadequate
Community Pharmacy Medicines Management Project Evaluation Team, [53]	Duplicate of the study[53]

Appendix H: Excluded health economic studies

Table 26: Studies excluded from the health economic review

Reference	Reason for exclusion
Bevan 2013[21]	This study was assessed as partially applicable with very serious limitations. The analysis was a partial economic analysis that only focused on costs. The analysis built largely off assumptions and was not underpinned by a controlled study. A UK randomised controlled trial included in the review analysed the impact of pharmacists in the GP so more applicable evidence was available.
Baqir 2011[14]	This study was assessed as partially applicable with very serious limitations. A cost minimisation analysis was undertaken, assuming equivalent health outcomes, with no supporting evidence of equivalence. The comparator used in the study was a hypothetical scenario based on patient report. Intervention costs were not fully incorporated in the analysis.
Brown 2016[28]	This study was a non-UK study based on non-RCT data. Given there was more relevant data included in this review this evidence was excluded from this review.
Elliott 2008[63]	This study was assessed as partially applicable with very serious limitations. The main outcome of the paper was improvement in adherence. This is a very variable outcome that is likely to significantly change over time, meaning the 4 week analysis was likely not sufficient to capture the long term impacts. There is also uncertainty regarding the applicability of resource use and costs from 2004 to current NHS context. The evidence is based on one study and does not reflect all evidence in this area. The source of the unit costs used is not reported. It is unclear if the costs were calculated using national or local unit costs, which may limit generalisability. The follow-up is very short and different for health outcomes (4 weeks) and costs (2 months). It was assumed the effectiveness of the intervention persists beyond the 4 weeks and up to 2 months, with no evidence to support this assumption.
Elliott 2016[64]	This study was assessed as partially applicable with very serious limitations. The main outcome of the paper was improvement in adherence. This is a very variable outcome that is likely to significantly change over time, meaning the 10 week analysis was likely not sufficient to capture the long term impacts. EQ-5D was collected but not assessed. Although the intervention was cost saving the cost of medication had been excluded from the analysis, this is still a cost to the health service and should be included, making the cost saving conclusions potentially misleading.
Formoso 2013[69]	This study was a non-UK study based on non-RCT data. Given there was more relevant data included in this review this evidence was excluded from this review.

Reference	Reason for exclusion
Hendrie 2014[86]	This study was a non-UK study based on non-RCT data. Given there was more relevant data included in this review this evidence was excluded from this review.
Krska 2001[115]	This study was assessed as partially applicable with very serious limitations as hospital attendances were not included in the costs. Only medication costs were included.
Lenander 2014[123]	This study was assessed as partially applicable with very serious limitations as only the cost of the intervention was reported.
Saini 2008[180]	This study was assessed as partially applicable with very serious limitations. The perspective of the analysis is not reported and QALYs are not used as an outcome. Not all important health outcomes are reported. Intervention costs are not included in the analysis and the source of unit costs is not reported. No sensitivity analysis reported. Follow-up is short (6 months).
Taylor 2005A[200]	This study was assessed as not applicable. The intervention is delivered by both hospital and community pharmacists in a hospital based clinic, rural and urban community pharmacies. The data was not reported separately for the community pharmacy-based intervention to allow estimating its cost effectiveness.
Wright 2015[225,226]	This study (2 papers) was assessed as partially applicable with potentially serious limitations. However, the Committee judged that other available evidence was of greater applicability and methodological quality, and therefore this study was selectively excluded. The economic evaluation in the RESPECT trial[172] was in the same strata but had a more generalizable population and was based on randomised evidence with a larger sample size.
Zermansky 2006[228]	This study was assessed as partially applicable with very serious limitations as the cost of GP visits and hospitalisations were not included.