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Professional, structural and organisational interventions in primary care for reducing medication errors (Review)

Khalil H, Bell B, Chambers H, Sheikh A, Avery AJ

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Professional, structural and organisational interventions in primary care for reducing medication errors.
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[Intervention Review]

Professional, structural and organisational interventions in primary care for reducing medication errors

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ABSTRACT

Background

Medication-related adverse events in primary care represent an important cause of hospital admissions and mortality. Adverse events could result from people experiencing adverse drug reactions (not usually preventable) or could be due to medication errors (usually preventable).

Objectives

To determine the effectiveness of professional, organisational and structural interventions compared to standard care to reduce preventable medication errors by primary healthcare professionals that lead to hospital admissions, emergency department visits, and mortality in adults.

Search methods

We searched CENTRAL, MEDLINE, Embase, three other databases, and two trial registries on 4 October 2016, together with reference checking, citation searching and contact with study authors to identify additional studies. We also searched several sources of grey literature.

Selection criteria

We included randomised trials in which healthcare professionals provided community-based medical services. We also included interventions in outpatient clinics attached to a hospital where people are seen by healthcare professionals but are not admitted to hospital. We only included interventions that aimed to reduce medication errors leading to hospital admissions, emergency department visits, or mortality. We included all participants, irrespective of age, who were prescribed medication by a primary healthcare professional.

Data collection and analysis

Three review authors independently extracted data. Each of the outcomes (hospital admissions, emergency department visits, and mortality), are reported in natural units (i.e. number of participants with an event per total number of participants at follow-up). We presented all outcomes as risk ratios (RRs) with 95% confidence intervals (CIs). We used the GRADE tool to assess the certainty of evidence.

Main results

We included 30 studies (169,969 participants) in the review addressing various interventions to prevent medication errors; four studies addressed professional interventions (8266 participants) and 26 studies described organisational interventions (161,703 participants). We did not find any studies addressing structural interventions. Professional interventions included the use of health information technology to identify people at risk of medication problems, computer-generated care suggested and actioned by a physician, electronic notification systems about dose changes, drug interventions and follow-up, and educational interventions on drug use aimed at physicians to improve drug prescriptions. Organisational interventions included medication reviews by pharmacists, nurses or physicians, clinician-led clinics, and home visits by clinicians.

There is a great deal of diversity in types of professionals involved and where the studies occurred. However, most (61%) of the interventions were conducted by pharmacists or a combination of pharmacists and medical doctors. The studies took place in many different countries; 65% took place in either the USA or the UK. They all ranged from three months to 4.7 years of follow-up, they all took place in primary care settings such as general practice, outpatients' clinics, patients' homes and aged-care facilities. The participants in the studies were adults taking medications and the interventions were undertaken by healthcare professionals including pharmacists, nurses or physicians. There was also evidence of potential bias in some studies, with only 18 studies reporting adequate concealment of allocation and only 12 studies reporting appropriate protection from contamination, both of which may have influenced the overall effect estimate and the overall pooled estimate.

Professional interventions

Professional interventions probably make little or no difference to the number of hospital admissions (risk ratio (RR) 1.24, 95% confidence interval (CI) 0.79 to 1.96; 2 studies, 3889 participants; moderate-certainty evidence). Professional interventions make little or no difference to the number of participants admitted to hospital (adjusted RR 0.99, 95% CI 0.92 to 1.06; 1 study, 3661 participants; high-certainty evidence). Professional interventions may make little or no difference to the number of emergency department visits (adjusted RR 0.71, 95% CI 0.50 to 1.02; 2 studies, 1067 participants; low-certainty evidence). Professional interventions probably make little or no difference to mortality in the study population (adjusted RR 0.98, 95% CI 0.82 to 1.17; 1 study, 3538 participants; moderate-certainty evidence).

Organisational interventions

Overall, it is uncertain whether organisational interventions reduce the number of hospital admissions (adjusted RR 0.85, 95% CI 0.71 to 1.03; 11 studies, 6203 participants; very low-certainty evidence). Overall, organisational interventions may make little difference to the total number of people admitted to hospital in favour of the intervention group compared with the control group (adjusted RR 0.92, 95% CI 0.86 to 0.99; 13 studies, 152,237 participants; low-certainty evidence. Overall, it is uncertain whether organisational interventions reduce the number of emergency department visits in favour of the intervention group compared with the control group (adjusted RR 0.75, 95% CI 0.49 to 1.15; 5 studies, 1819 participants; very low-certainty evidence. Overall, it is uncertain whether organisational interventions reduce mortality in favour of the intervention group (adjusted RR 0.94, 95% CI 0.85 to 1.03; 12 studies, 154,962 participants; very low-certainty evidence.

Authors' conclusions

Based on moderate- and low-certainty evidence, interventions in primary care for reducing preventable medication errors probably make little or no difference to the number of people admitted to hospital or the number of hospitalisations, emergency department visits, or mortality. The variation in heterogeneity in the pooled estimates means that our results should be treated cautiously as the interventions may not have worked consistently across all studies due to differences in how the interventions were provided, background practice, and culture or delivery of the interventions. Larger studies addressing both professional and organisational interventions are needed before evidence-based recommendations can be made. We did not identify any structural interventions and only four studies used professional interventions, and so more work needs to be done with these types of interventions. There is a need for high-quality studies describing the interventions in more detail and testing patient-related outcomes.

PLAIN LANGUAGE SUMMARY

Actions to reduce medication errors in adults in primary care

What is the aim of this review?

The aim of this Cochrane Review was to find out the best way to reduce medication errors by primary healthcare professionals in adult patients that lead to hospital admissions, emergency department visits, and death. We wanted to know whether targeting individual health professionals (e.g. with educational materials and reminders about drug dosage etc.), changing the organisation of primary care (e.g. revising professional roles, such as nurse- or pharmacist-led prescribing etc.), or structural actions, such as organising quality monitoring services can reduce medication errors by primary healthcare professionals. We collected and analysed relevant studies to answer this question and found 30 studies.

Key messages

The 30 studies (169,969 participants) in this Cochrane Review showed that actions aimed at reducing medication errors, such as medication reviews by pharmacists or physicians probably make little or no difference to the number of people admitted to hospital, number of hospital admissions, number of emergency department visits, or death. In general, all the actions described in the review were found to have unclear benefits. We did not find any studies that fitted the criteria of structural actions. The main limitation of this review is the small number of studies addressing each method and the low-certainty of the evidence.

What was studied in the review?

Prescribing medications is one of the most powerful tools available to general practitioners (GPs) in the prevention and treatment of disease. Medication-related adverse events could be the result of people either experiencing adverse drug reactions (not usually preventable) or as a result of medication errors (usually preventable). We studied the effectiveness of professional and organisational methods compared to standard care in primary care settings (examples of primary care settings include general practices, community pharmacies, patient homes, community settings, outpatient clinics, and aged-care facilities) to reduce preventable medication errors that lead to hospital admissions, emergency department visits, and death in adults who are prescribed medication in primary care.

What are the main results of the review?

We included 30 studies in our analysis. We classified 26 studies as organisational and the remaining four as professional actions. We found no structural actions in our search. The studies included in this Cochrane Review showed that based on moderate- and low-certainty evidence, actions in primary care for reducing preventable medication errors probably make little or no difference to the number of people admitted to hospital or the number of hospitalisations, emergency department visits, or death. Most of the studies took place in the UK and the USA; studies undertaken in high-income countries with disadvantaged populations, and in low- and middle-income countries, were underrepresented. This might affect the generalisation of the results.

Certainty of the evidence

We found the overall certainty of evidence for the professional actions to vary considerably across the reported outcomes: moderate-certainty for number of hospital admissions, high-certainty for number of people admitted to hospital, low-certainty for number of emergency department visits, and moderate-certainty for deaths. The certainty of evidence for organisational actions was less varied: very low-certainty for number of hospital admissions, low-certainty for number of people admitted to hospital, and very low-certainty for number of emergency department visits and deaths.

More work needs to be done in improving the quality of the studies regarding selection of participants and adequate blinding of participants and study assessors. Participants dropping out of the studies was another concern in the certainty of evidence. Funding of the included studies came from various sources and it is difficult to decide whether the funding affected the results of the studies.

How up-to-date is this review?

We searched for studies that had been published up to 4 October 2016.

SUMMARY OF FINDINGS FOR THE MAIN COMPARISON [Explanation]

Professional interventions compared to standard/usual care for prevention of medication errors

Patient or population: adults receiving medication in primary care
Setting: primary and community care
Intervention: professional interventions (using health information technology to identify people at risk or using it to generate a patient care plan)
Comparison: standard/usual care

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with standard/ usual care	Risk with professional interventions				
Number of hospital admissions	Study population		RR 1.24 (0.79 to 1.96)	3889 (2 RTs)	⊕⊕⊕◯ Moderate[1]	The two studies had wide confidence intervals.
	17 per 1000	21 per 1000 (13 to 33)				
Number of people admitted to hospital	Study population		RR 0.99 (0.92 to 1.06)	3661 (1 RT)	⊕⊕⊕⊕ High[2]	
	448 per 1000	443 per 1000 (412 to 475)				
Number of emergency department visits	Study population		RR 0.71 (0.50 to 1.02)	1067 (2 RTs)	⊕⊕◯◯ Low[1,3]	The two studies had wide confidence intervals and selection bias
	118 per 1000	85 per 1000 (59 to 121)				
Mortality	Study population		RR 0.98 (0.82 to 1.17)	3538 (1 RT)	⊕⊕⊕◯ Moderate[3]	
	122 per 1000	119 per 1000 (100 to 142)				

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: confidence interval; **RR**: risk ratio; **RT**: randomised trial

GRADE Working Group grades of evidence
High-certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate-certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low-certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low-certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect

[1]We downgraded one level due to imprecision.
[2]We did not downgrade the outcomes because all included studies had low risk of bias and narrow confidence intervals.
[3]We downgraded one level due to risk of bias (selection bias).

BACKGROUND

Description of the condition

Medication-related (drug-related) adverse events in primary care represent an important cause of hospital admissions and mortality (Howard 2003). Medication-related adverse events could be the result of people either experiencing adverse drug reactions (not usually preventable) or as a result of medication errors (usually preventable) (Bates 1995; Ioannidis 2001).

According to Edwards 2000, adverse drug reactions can be defined as "an appreciably harmful or unpleasant reaction resulting from an intervention related to the use of a medicinal product." Medication errors on the other hand, are mostly preventable. A medication error is defined by Ferner 2006 as "a failure in the treatment process that leads to, or has the potential to lead to, harm to the patient." They are mainly due to prescribing or medication management errors. A reduction of these types of prescribing/medication errors has been a high priority for healthcare policy in order to improve the safety profile of the healthcare delivery system (Howard 2003; Soe 2013).

A prospective cohort study has shown that within four weeks of receiving a primary care prescription, 25% of participants experienced an adverse drug event, 11% of which were judged preventable (Gandhi 2003). A systematic review and meta-analysis by Winterstein 2002 reported that a median 7.1% (inter-quartile range 5.7% to 16.2%) of hospital admissions resulted from drug-related problems, of which 59% were considered preventable (i.e. attributable to error), while Howard 2007 reported that a median of 3.7% of hospital admissions were preventable and drug-related. Improving patient safety is, as a consequence, now a government priority in many high-income and middle- and low-income countries, including the UK, USA and five African countries; Egypt, South Africa, Morocco, Tanzania and Zimbabwe (Brown 2008; WHO 2004).

Description of the intervention

In this review we examined interventions in primary care to reduce preventable medication errors that resulted in hospital admissions, emergency department visits, and mortality. The three main types of interventions that we examined included professional, organisational, and structural interventions as described by Cochrane Effective Practice and Organisation of Care (EPOC) (Appendix 1). Professional interventions included quality assurance tools that provided educational interventions for practitioners or participants, such as teaching the use of structured assessments with general practitioners (GPs). Organisational interventions included revision of professional roles (e.g. nurse- or pharmacist-led chronic disease clinics and nurse prescribing) and revision of clinical multidisciplinary teams (e.g. pharmacist-managed medication reviews). Structural interventions included the organisation of quality monitoring services. We used these interventions for any type of primary care-based population, irrespective of their characteristics. The comparator was no intervention or standard or usual care. The selected outcomes included in the review were the number of hospital admissions, emergency department visits, and mortality. These outcomes were selected as they are tangible and mostly reported in primary studies. We did not consider patient-oriented or patient-mediated outcomes in this review due to the complexity of the included interventions. We will consider these outcomes in the updated review.

How the intervention might work

The three main interventions, mentioned above, used different approaches to achieve a reduction in medication errors that led to hospital admissions, emergency department visits, and mortality. Professional interventions included continuing education and quality assurance that provided educational interventions for practitioners or participants, such as teaching the use of structured assessments with GPs. Other examples of professional interventions included drug education programmes for physicians that were run by physicians, electronic health record systems that provided information about drugs and gave recommendations about changing doses, health technology that identified care home residents at risk of falls, and computer-based drug-ordering systems that gave suggestions to physicians and pharmacists.

Organisational interventions included revision of professional roles (e.g. nurse- or pharmacist-led chronic disease clinics and nurse prescribing) and revision of clinical multidisciplinary teams (e.g. pharmacist-managed medication reviews). Organisational interventions may have included telephone consultations along with home-based medication reviews by pharmacists or nurses. Such interventions aimed at engaging workers in the management of risk to increase patient safety.

Structural interventions included the organisation of quality monitoring services. Examples of these interventions included structural approaches such as social, economic, and political interventions that could improve public health outcomes by increasing the willingness and ability of individuals to practice prevention. An example of the latter would be the introduction of financial incentives to healthcare workers to reduce medication errors. By looking at all of these interventions in the current review, we can begin to address the multiple perspectives of various stakeholders who provide health care to individuals in primary care (Benning 2011).

Why it is important to do this review

Prescribing medications is one of the most powerful tools available to GPs in the prevention and treatment of disease, and allevia-

tion of symptoms (Spencer 2014). However, medication-related adverse events arising as a result of primary care prescribing are an important source of participant morbidity, much of which could be prevented by higher-quality prescribing and medicines management (Howard 2007). To date, there is little information on the interventions mentioned above, aimed at reducing preventable medication-related adverse events in primary care due to errors. A review undertaken by Ioannidis 2001, addressed interventions of all types of medical errors in both primary and secondary care. It highlighted the complexity in studying those types of interventions aimed at minimising errors in healthcare delivery. Other reviews by Durieux 2012 and O'Brien 2008 focused on interventions to improve professional practice and healthcare outcomes, including prescribing. A review by Royal 2006 found that there was weak evidence to support pharmacist-led medication interventions being effective in reducing hospital admissions. However, none of these reviews have focused on other types of interventions at the professional, organisational or structural level that could possibly reduce medication errors in the primary care setting.

Given that preventable medication errors in primary care are associated with hospital admissions, emergency department visits, and mortality, it is important to know whether there are any interventions that have been found to be effective in reducing the occurrence of these outcomes. While members of our team published a related systematic review on this topic (Royal 2006), there has been no Cochrane Review of interventions aimed at reducing the incidence of preventable medication errors that lead to hospital admissions, emergency department visits, and mortality.

OBJECTIVES

To determine the effectiveness of professional, organisational and structural interventions compared to standard care to reduce preventable medication errors by primary healthcare professionals that lead to hospital admissions, emergency department visits, and mortality in adults.

METHODS

Criteria for considering studies for this review

Types of studies

We included randomised trials in this review. We excluded controlled before-after studies and other non-randomised designs as they provided much weaker evidence due to the non-randomisation of participants to experimental and control groups. We did not impose any restriction on the language or country in which studies were carried out.

Types of participants

We included studies directed at healthcare professionals and organisations involved in the provision of primary care in the community setting who were authorised to prescribe, sell or administer medications, including primary care physicians (general practitioners (GPs), family doctors, family physicians, family practitioners), dental practitioners, community nurses, nurse practitioners, community pharmacists, dispensers in community pharmacies and any other relevant healthcare providers. We included all adult participants who were receiving a medication through the intervention of the aforementioned primary healthcare professionals. Examples of community settings included general practice, community pharmacies, and nursing and residential homes. We excluded studies of interventions for outpatients in a clinic attached to a hospital or a day hospital unless these were specifically described as primary care clinics.

Types of interventions

Using the taxonomy of interventions developed by EPOC, we categorised interventions that improved patient safety by reducing hospital admissions, emergency department visits, and mortality (Appendix 1). We compared the interventions with inactive control interventions such as no treatment, or standard or conventional care. We divided interventions into the following categories.

Professional interventions

Professional interventions included the use of health information technology to identify people at risk of medication problems, computer-generated care suggested and actioned by a physician, electronic notification systems about dose changes, drug interventions and follow-up, and educational interventions on drug use aimed at physicians to improve drug prescriptions.

Organisational interventions

Examples of organisational interventions included medication reviews by pharmacists, nurses or physicians, clinician-led clinics, and home visits by clinicians.

Structural interventions

Structural interventions included the organisation of quality monitoring services. Structural approaches included social, economic, and political interventions that could improve public health outcomes by increasing the willingness and ability of individuals to practice prevention. An example of the latter would be the introduction of financial incentives to healthcare workers to reduce medication errors.

Types of outcome measures

We included studies that addressed preventable medication errors with the following outcomes. All the outcomes below are included in Summary of findings for the main comparison and Summary of findings 2.

Primary outcomes

- Number of hospital admissions (this outcome takes into account that one patient can have multiple admissions)
- Number of people admitted to hospital (this outcome reports on the number of people admitted to hospital irrespective of the number of times they were admitted during the study period)

Secondary outcomes

- Number of emergency department visits
- Mortality

Search methods for identification of studies

EPOC's Information Specialist, Paul Miller, developed the search strategies in consultation with the review authors. The Information Specialist searched the Cochrane Database of Systematic Reviews and the Database of Abstracts of Reviews of Effects (DARE) for related systematic reviews, and the databases listed below for primary studies.

Electronic searches

We searched the following databases on 4 October 2016.

- Cochrane Central Register of Controlled Trials (CENTRAL; 2016, Issue 9), in the Cochrane Library.
- MEDLINE Ovid (including epub ahead of print, in-process and other non-indexed citations) (1946 to 4 October 2016).
- Embase, Ovid (1974 to 3 October 2016).
- Health Technology Assessment Database (NHSEED; 2015, Issue 2), in the Cochrane Library.
- NHS Economic Evaluation Database (NHSEED; 2015, Issue 2), in the Cochrane Library.
- CINAHL EBSCO (Cumulative Index to Nursing and Allied Health Literature; 1981 to 4 October 2016).

Search strategies are comprised of keywords and controlled vocabulary terms. We applied no language or time limits. We searched all databases from database start date to date of search. All search strategies used are provided in Appendix 2.

Searching other resources

Grey literature

On 4 October 2016 we conducted a grey literature search to identify studies not indexed in the databases listed above. Sources included the sites listed below. We documented additional sources, if any, in the review.

- Open Grey (opengrey.eu).
- Grey Literature Report (New York Academy of Medicine) (greylit.org).
- Agency for Healthcare Research and Quality (AHRQ) (ahrq.gov).
- Joanna Briggs Institute (joannabriggs.edu.au).
- National Institute for Health and Care Excellence (NICE) (nice.org.uk).

Trial registries

We searched the following trial registries on 4 October 2016.

- International Clinical Trials Registry Platform (ICTRP), Word Health Organization (WHO) (who.int/ictrp).
- ClinicalTrials.gov, US National Institutes of Health (NIH) (clinicaltrials.gov).

We undertook the following.

- Screened individual journals and conference proceedings (e.g. handsearch).
- Reviewed reference lists of all included studies, relevant systematic reviews/primary studies/other publications.
- Contacted authors of relevant studies or reviews to clarify reported published information/seek unpublished results/data.
- Contacted researchers with expertise relevant to the review topic/EPOC interventions.
- Conducted cited reference searches for all included studies in citations indexes.

Data collection and analysis

Selection of studies

Three review authors (HK, HC and BB) independently screened the titles and abstracts to assess studies against the inclusion criteria. We obtained full-text copies of all papers considered to be of potential relevance and we contacted first authors of studies for clarification, where necessary. We resolved disagreements about relevance by discussion between the review authors. We entered all included studies in Review Manager 5 software (Review Manager 2014).

Data extraction and management

Three review authors (HK, HC and BB) independently completed data extraction using a customised version of the EPOC data collection checklist (EPOC 2017a). All three review authors met frequently to discuss progress, with discrepancies resolved by discussion between the review authors. We grouped studies together on the basis of similar interventions and common outcomes and used Review Manager 5 software to manage and pool data (Review Manager 2014), as mentioned in chapter 7 of the *Cochr ane Handbook for Systematic Reviews of Interventions* (Higgins 2011a). We documented the selection process in sufficient detail to complete a PRISMA flow chart (Liberati 2009), and a Characteristics of excluded studies table.

Assessment of risk of bias in included studies

Three review authors (HK, HC and BB) independently assessed the risk of bias of all included studies using the criteria described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011b). We resolved differences through discussion.
We assessed seven parameters including random sequence generation, allocation concealment, blinding of participants and outcome assessors, incomplete outcome data, selective reporting, and other bias including protection against contamination and publication bias. We discussed the inclusion of the selected studies in the meta-analysis based on their risk of bias. We assessed studies on the basis of having low, unclear or high risk of bias. We included all trials in the final meta-analysis.

Measures of treatment effect

For each of the primary outcomes listed above, we reported outcomes for each study in natural units (i.e. number of participants with an event per total number of participants at follow-up). We examined funnel plots for evidence of publication bias and analysed data using Review Manager 5 (Review Manager 2014). We presented results with 95% confidence intervals (CIs) and estimates for dichotomous data (number of people admitted to hospital) as risk ratios (RRs).

Unit of analysis issues

We examined the methods of analysis of all study types critically. All randomised trials were appropriately analysed. We analysed cluster-randomised trials at the same level as the allocation, thereby avoiding unit-of-analyses errors (Alvarez 2001; Coleman 1999; Gernant 2016; Kaczorowski 2011; Lapane 2011; Lowrie 2012; Malet-Larrea 2016; Roberts 2001). Therefore, we did not need to reanalyse the results and it was appropriate to combine them with other randomised trials.

Dealing with missing data

We did not exclude any studies from the meta-analysis due to a differential loss to follow-up or missing data. Most studies had adequate reporting of the participants in their samples. We were able to extract all the data needed for analysis from the included studies. We did not need to contact any study authors for more information.

Assessment of heterogeneity

Because trials may not have been carried out according to a common protocol, there were usually variations in participant groups, clinical settings, concomitant care, etc. Therefore, we assessed heterogeneity between trial results. We considered trial data to be heterogeneous where the I^2 statistic was greater than 40% (Higgins 2003). For analyses, we used the random-effects method. We attempted to explain the differences between studies on the basis of the characteristics of interventions in the included studies.

Assessment of reporting biases

We carefully assessed all studies for reporting bias. Reporting bias was especially likely with outcomes that used participant self-reports or self-administered surveys.

Data synthesis

We carried out statistical analysis using Review Manager 5 software (Review Manager 2014). We used a random-effects meta-analysis for combining data due to the clinical and methodological heterogeneity between studies. We grouped studies based on the two main interventions (i.e. professional and organisational). Where appropriate, we carried out meta-analyses to establish the effects of interventions on medication-related hospital admissions, emergency department visits, and mortality. We found no studies addressing structural interventions and hence no analysis was undertaken.

'Summary of findings table' and GRADE

We included two 'Summary of findings' tables for the main intervention comparisons: 'professional interventions compared to usual care' (Summary of findings for the main comparison); and 'organisational interventions compared to usual care' (Summary of findings 2). The 'Summary of findings' tables include the justification for our decisions to downgrade or upgrade the evidence for an outcome, along with comments to help the reader understand the process. We included the following outcomes in the 'Summary of findings' tables: number of hospital admissions, number of people admitted to hospital, number of emergency department visits, and mortality.
Three review authors (HK, HC and BB) used the GRADE tool to independently judge the certainty of the evidence (high, moder-

ate, low, and very low) with respect to five criteria (risk of bias, inconsistency, indirectness, imprecision, and publication bias), with disagreements resolved through discussion (Guyatt 2008). We used methods and recommendations described in Section 8.5 and Chapter 11 of the *Cochrane Handbook for Systematic Reviews of interventions* and GRADEpro GDT software (GRADE pro GDT 2015; Higgins 2011b; Schünemann 2011). In addition, we used the EPOC worksheets to write plain language statements to report these findings in the review (EPOC 2017b).

Subgroup analysis and investigation of heterogeneity

We conducted the analyses based on the types of interventions (professional, organisational, structural) as described by Deeks 2011. We undertook analyses for the following interventions.

1. Professional interventions, such as provision of educational interventions for practitioners or participants.
2. Organisational interventions, including revision of professional roles (e.g. nurse- or pharmacist-led chronic disease clinics, nurse prescribing) and clinical multidisciplinary teams (e.g. pharmacist-managed medication reviews).

We found no studies addressing structural interventions and therefore, we did not include this type of intervention in our review. There was no other subgroup analysis undertaken in the review.

Sensitivity analysis

We used a sensitivity analysis to explore the influence of the following on effect size: repeating the analysis; and excluding any high risk of bias studies to see how they influenced the results. We did this in order to help understand whether the results of the review are robust.

RESULTS

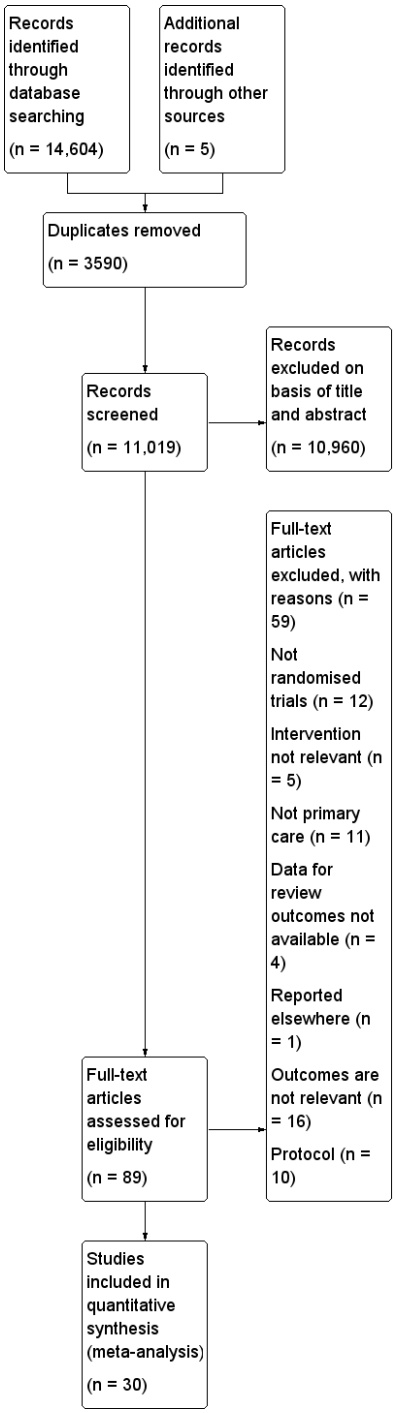
Description of studies

Results of the search

Searches of the main electronic databases led to identification of 14,604 titles. A search of the grey literature and of trial registries yielded a total of five articles that did not make it in the final included studies. Handsearching of the references listed did not yield new studies.

We identified a total of 11,019 references after removal of duplicates. From reading titles and abstracts, we eliminated 10,960 as being not relevant to the review. Reasons for exclusions included irrelevant interventions, study designs and populations (i.e. not primary care settings). We obtained full papers for 89 references. From these 89 papers, we excluded 59 papers for reasons such as study design, study reported elsewhere and study not conducted in a primary care setting, irrelevant outcomes and protocols (see Characteristics of excluded studies). We included a total of 30 papers reporting on 30 trials (see Characteristics of included studies). We have provided an overview of the selection process in a PRISMA flow diagram, Figure 1 (Liberati 2009).

Figure 1. Study flow diagram



Included studies

Method (design)

We included a total of 30 studies (169,969 participants) in this review. Four studies addressed professional interventions (8266 participants) and 26 studies described organisational interventions (161,703 participants). Overall, there were eight cluster-randomised trials (Alvarez 2001; Coleman 1999; Gernant 2016; Kaczorowski 2011; Lapane 2011; Lowrie 2012; Malet-Larrea 2016; Roberts 2001), and 22 randomised trials (Bernsten 2001; Campins 2016; Frankenthal 2014; Garcia-Gollarte 2014; Gurwitz 2014; Hawes 2014; Holland 2005; Ibrahim 2013; Korajkic 2011; Krska 2001; Lenaghan 2007; Malone 2000; Moertl 2009; Murray 2004; Nabagiez 2013; Okamoto 2001; Olesen 2014; Pai 2009; Rytter 2010; Triller 2007; Zermansky 2001; Zermansky 2006. They all ranged from three months to 4.7 years of follow-up. A full description of the interventions of each study is included in the 'Characteristics of included studies', Table 1 and Table 2. All cluster-randomised trials were appropriately analysed. Alvarez 2001 reported randomisation at the pharmacy level. They used adjusted Pearson's Chi^2 to compare means. Coleman 1999 used statistical techniques that accounted for potential within-practice correlation that results from randomisation of practices. For continuous variables, they used a mixed model analysis of covariance and regression analysis and for binary values, they used generalised estimating equations. They derived P values from a t-distribution rather than a normal distribution. Gernant 2016 used a multivariable logistic regression model using generalised estimating equations to examine the effect of the intervention on the probability of 60-day all-cause emergency department utilisation. The analysis was approved by the Purdue University Institutional Review Board. Kaczorowski 2011 fitted linear regression models by using the Poisson distribution. Lapane 2011 analysed their results using a Poisson regression model and accounted for the cluster trial design to provide estimates adjusted for potential confounders. In contrast, Lowrie 2012 compared the main outcomes between the intervention and control groups using a Cox proportional hazards frailty model, which accounted for the cluster-randomisation design. Malet-Larrea 2016 included a random intercept for pharmacies nested within a group, to account for clustering of participants within pharmacies, and was adjusted by covariate that could affect hospital admissions (age, gender and number of health problems). Differences between groups in hospital costs were analysed by hospital admission and by participant, and the latter ones adjusted by analysis of covariance (ANCOVA) for the number of health problems. Roberts 2001 used robust variance estimation techniques (SUDAAN 2012), in which the effect of clustering within nursing homes on the variance was accounted for.

Participants and study setting

There is a great deal of diversity in types of professionals involved and where the studies occurred. However, most (61%) of the interventions were conducted by pharmacists or a combination of pharmacists and medical doctors. The studies took place in many different countries; 65% took place in either the USA or the UK. The study settings included general practices (Coleman 1999; Gurwitz 2014; Krska 2001; Lowrie 2012; Murray 2004; Zermansky 2001), community pharmacies (Alvarez 2001; Bernsten 2001; Malet-Larrea 2016), patient homes or community settings (Campins 2016; Gernant 2016; Kaczorowski 2011; Holland 2005; Ibrahim 2013; Lenaghan 2007; Olesen 2014; Rytter 2010; Triller 2007), outpatient clinics (Hawes 2014; Korajkic 2011; Malone 2000; Moertl 2009; Okamoto 2001; Pai 2009), and aged care facilities (Frankenthal 2014; Garcia-Gollarte 2014; Lapane 2011; Roberts 2001; Triller 2007; Zermansky 2006).

Interventions

We included a total of 30 studies (169,969 participants) in this review.

Four studies (8266 participants) reported on professional interventions (Garcia-Gollarte 2014; Gurwitz 2014; Lapane 2011; Murray 2004). Two of these studies (3889 participants) reported on the number of hospital admissions (Lapane 2011; Murray 2004), one study (3661 participants) reported on the number of people admitted to hospital (Gurwitz 2014), one study (3538 participants) reported on mortality (Lapane 2011), and two studies (1067 participants) reported on the number of emergency department visits (Garcia-Gollarte 2014; Murray 2004).

A total of 26 studies (161,703 participants) reported on organisational interventions (Alvarez 2001; Bernsten 2001; Campins 2016; Coleman 1999; Frankenthal 2014; Gernant 2016; Hawes 2014; Holland 2005; Ibrahim 2013; Kaczorowski 2011; Korajkic 2011; Krska 2001; Lenaghan 2007; Lowrie 2012; Malet-Larrea 2016; Malone 2000; Moertl 2009; Nabagiez 2013; Okamoto 2001; Olesen 2014; Pai 2009; Roberts 2001; Rytter 2010; Triller 2007; Zermansky 2001; Zermansky 2006). Eleven trials (6203 participants) reported on number of hospital admissions (Coleman 1999; Holland 2005; Ibrahim 2013; Krska 2001; Lenaghan 2007; Lowrie 2012; Malone 2000; Moertl 2009; Nabagiez 2013; Okamoto 2001; Rytter 2010). A total of 13 studies (152,237 participants) reported on the number of people admitted to hospital (Alvarez 2001; Bernsten 2001; Campins 2016; Frankenthal 2014; Hawes 2014; Kaczorowski 2011; Korajkic

2011; Malet-Larrea 2016; Nabagiez 2013; Olesen 2014; Triller 2007; Zermansky 2001; Zermansky 2006). Five studies (1819 participants) reported on emergency department visits (Alvarez 2001; Coleman 1999; Gernant 2016; Hawes 2014; Ibrahim 2013), and 12 studies (154,962 participants) reported on mortality (Campins 2016; Holland 2005; Kaczorowski 2011; Lenaghan 2007; Lowrie 2012; Moertl 2009; Olesen 2014; Pai 2009; Roberts 2001; Triller 2007; Zermansky 2001; Zermansky 2006).

We did not find any studies that fitted the criteria of structural interventions. This was in concordance with the EPOC taxonomy of interventions (Appendix 1).

The 'Characteristics of included studies' tables provide a summary of the interventions and comparisons. The interventions varied. Professional interventions included the use of health information technology to identify people at risk of medication problems: computer-generated care suggested and actioned by physicians; electronic notification system about dose changes, drug interventions and follow-up; and educational interventions on drug use aimed at physicians to improve drug prescriptions. Organisational interventions included medication reviews by pharmacists, nurses or physicians, clinician-led clinics and home visits by clinicians.

Outcomes

The primary outcomes were number of hospital admissions and number of people admitted to hospital. A total of 13 studies (10,092 participants) reported on number of hospital admissions (Coleman 1999; Holland 2005; Ibrahim 2013; Krska 2001; Lapane 2011; Lenaghan 2007; Lowrie 2012; Malone 2000; Moertl 2009; Murray 2004; Nabagiez 2013; Okamoto 2001; Rytter 2010); and 14 studies (155,898 participants) reported on number of people admitted to hospital (Alvarez 2001; Bernsten 2001; Campins 2016; Frankenthal 2014; Kaczorowski 2011; Gurwitz 2014; Hawes 2014; Korajkic 2011; Malet-Larrea 2016; Nabagiez 2013; Olesen 2014; Triller 2007; Zermansky 2001; Zermansky 2006).

The secondary outcomes were the number of emergency department visits and mortality. Seven studies (2886 participants) reported on the number of emergency department visits (Alvarez 2001; Coleman 1999; Garcia-Gollarte 2014; Gernant 2016; Hawes 2014; Ibrahim 2013; Murray 2004); and 13 studies (158,500 participants) reported on mortality (Campins 2016; Holland 2005; Kaczorowski 2011; Lenaghan 2007; Lapane 2011; Lowrie 2012; Moertl 2009; Olesen 2014; Pai 2009; Roberts 2001; Triller 2007; Zermansky 2001; Zermansky 2006).

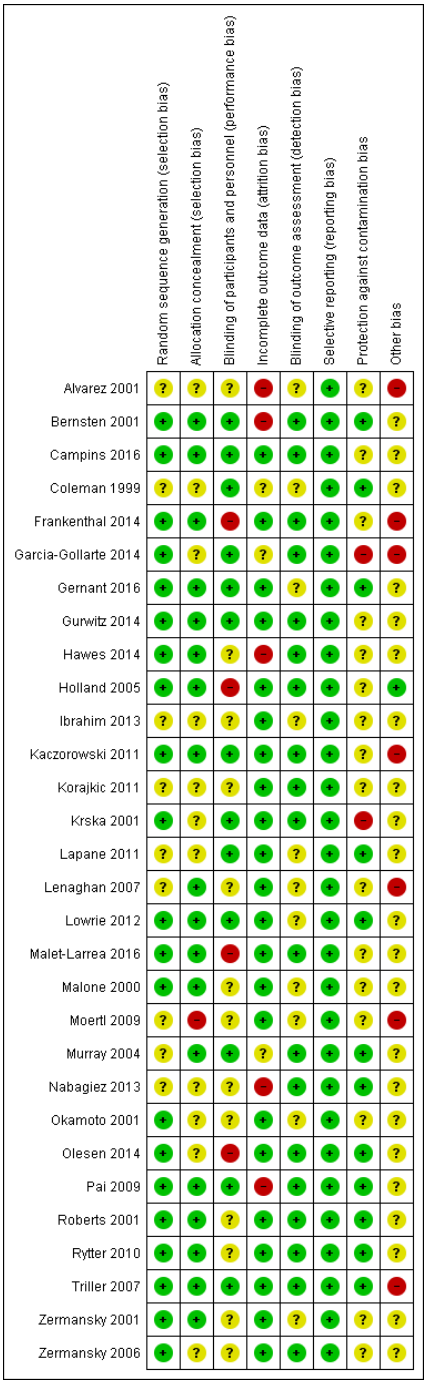
Excluded studies

We have summarised the 59 excluded studies, with the reasons for their exclusion in the 'Characteristics of excluded studies' table. We excluded studies with an unsuitable design (Furniss 2000; Graffen 2004; Hugtenburg 2009; Lee 1996; Leendertse 2011; Leendertse 2013; Mills 2001; Montero-Balosa 2016; Moreno 2016; Ni 2016; Safran 1993; Saltzberg 2011). Other reasons for exclusion were studies that did not occur in a primary care setting (Alassaad 2014; Barker 2012; Bell 2016; Bonnet-Zamponi 2013; Briggs 2015; Gorgas 2012; Hanlon 1996; Keane 2014; Naunton 2003; Neven 2016; Xin 2014); results reported elsewhere (Sturgess 2003); data for outcomes not available (Cowper 1998; Knowlton 1994; Liu 2010; Yuan 2003); interventions not relevant to the review (Al-Arifi 2014; Benard-Laribiere 2015; Carrington 2013; Fredericks 2013; Pinnock 2013); outcomes not relevant to the review (Barker 2016; Barnes 2014; Basheti 2016; Billington 2015; Clyne 2015; Clyne 2016; Dhalla 2014; Geurts 2016; Guthrie 2016; Hallsworth 2016; Huiskes 2014; Malin 2016; Perula 2014; Setter 2009; Sinnott 2015; Wolf 2015); and 10 studies were published protocols (Alicic 2016; Bhatt 2014; Clyne 2013; Desveaux 2016; Elliott 2014; Forster 2015; Phung 2013; Przytula 2015; Stingl 2016; Wooster 2016), as described in the PRISMA diagram (see Figure 1).

Risk of bias in included studies

We have presented details of risk of bias in Figure 2.

Figure 2. Risk of bias summary: review authors' judgements about each risk of bias item for each included study



Allocation

A total of 21 studies reported adequate sequence generation (Bernsten 2001; Campins 2016; Frankenthal 2014; Garcia-Gollarte 2014; Gernant 2016; Gurwitz 2014; Hawes 2014; Holland 2005; Kaczorowski 2011; Krska 2001; Lowrie 2012; Malet-Larrea 2016; Malone 2000; Okamoto 2001; Olesen 2014; Pai 2009; Roberts 2001; Rytter 2010; Triller 2007; Zermansky 2001; Zermansky 2006); and 18 reported adequate concealment of allocation (Bernsten 2001; Campins 2016; Frankenthal 2014; Gernant 2016; Gurwitz 2014; Hawes 2014; Holland 2005; Kaczorowski 2011; Lenaghan 2007; Lowrie 2012; Malone 2000; Malet-Larrea 2016; Murray 2004; Pai 2009; Roberts 2001; Rytter 2010; Triller 2007; Zermansky 2001).

Blinding

Thirteen studies adequately blinded measurements of participants and personnel delivering the intervention (Bernsten 2001; Campins 2016; Coleman 1999; Garcia-Gollarte 2014; Gernant 2016; Gurwitz 2014; Kaczorowski 2011; Krska 2001; Lapane 2011; Lowrie 2012; Murray 2004; Pai 2009; Triller 2007), whereas adequate blinding of outcome assessment was undertaken in 19 studies (Bernsten 2001; Campins 2016; Frankenthal 2014; Garcia-Gollarte 2014; Gurwitz 2014; Hawes 2014; Holland 2005; Kaczorowski 2011; Korajkic 2011; Krska 2001; Malet-Larrea 2016; Murray 2004; Nabagiez 2013; Olesen 2014; Pai 2009; Roberts 2001; Rytter 2010; Triller 2007; Zermansky 2006). Eleven studies reported an unclear risk of detection bias (Alvarez 2001; Coleman 1999; Gernant 2016; Ibrahim 2013; Lapane 2011; Lenaghan 2007; Lowrie 2012; Malone 2000; Moertl 2009; Okamoto 2001; Zermansky 2001).

Incomplete outcome data

A total of five studies had high risk of attrition bias (Alvarez 2001; Bernsten 2001; Hawes 2014; Nabagiez 2013; Pai 2009). Twenty-two studies adequately addressed problems with incomplete outcomes (Campins 2016; Frankenthal 2014; Gernant 2016; Gurwitz 2014; Holland 2005; Ibrahim 2013; Kaczorowski 2011; Korajkic 2011; Krska 2001; Lapane 2011; Lenaghan 2007; Lowrie 2012; Malet-Larrea 2016; Malone 2000; Moertl 2009; Okamoto 2001; Olesen 2014; Roberts 2001; Rytter 2010; Triller 2007; Zermansky 2001; Zermansky 2006), that is, these studies reported complete outcome data or they replaced any missing outcome data using a recognised statistical method, such as last observation carried forward with participants remaining in the group to which they had been allocated.

Selective reporting

There was no selective reporting in the included studies. All studies assessed their predefined primary and secondary outcomes.

Other potential sources of bias

Other potential sources of bias included protection against contamination, publication bias and other bias.

Protection against contamination bias

A total of 12 studies adequately protected against contamination bias (Bernsten 2001; Coleman 1999; Gernant 2016; Lapane 2011; Lowrie 2012; Murray 2004; Nabagiez 2013; Olesen 2014; Pai 2009; Roberts 2001; Rytter 2010; Triller 2007); whereas 16 studies, had unclear risk of protection against contamination (Alvarez 2001; Campins 2016; Frankenthal 2014; Gurwitz 2014; Hawes 2014; Holland 2005; Ibrahim 2013; Kaczorowski 2011; Korajkic 2011; Lenaghan 2007; Malet-Larrea 2016; Malone 2000; Moertl 2009; Okamoto 2001; Zermansky 2001; Zermansky 2006), and two studies clearly did not adequately protect against contamination bias (Garcia-Gollarte 2014; Krska 2001). Contamination bias occurs when members of the control group are inadvertently exposed to the intervention, thus potentially minimising the difference in outcomes between the two groups (Higgins 2011b).

Publication bias

Publication bias did not take place amongst the professional interventions due to the small number of studies included in the review. We have shown funnel plots of the main outcomes for the organisational interventions as follows: number of hospital admissions (Figure 3); number of people admitted to hospital (Figure 4); number of emergency department visits (Figure 5); and mortality (Figure 6). There was no evidence of publication bias.

Figure 3. Funnel plot of comparison: 2 Organisational interventions, outcome: 2.1 Number of hospital admissions

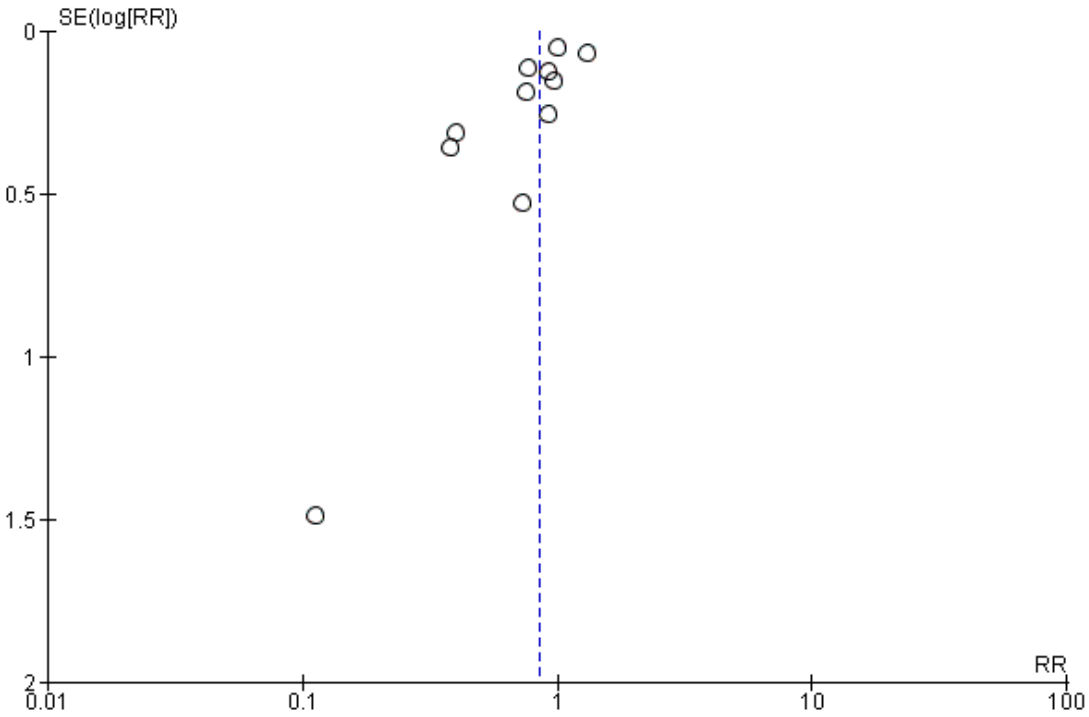


Figure 4. Funnel plot of comparison: 2 Organisational interventions, outcome: 2.2 Number of people admitted to hospital

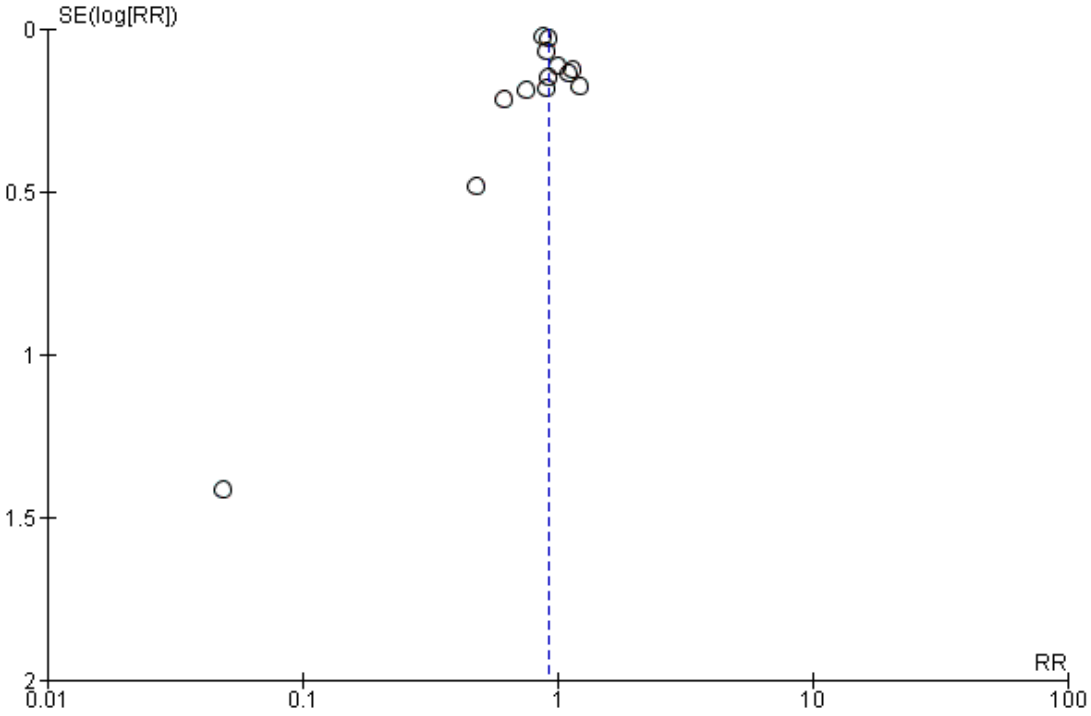


Figure 5. Funnel plot of comparison: 2 Organisational interventions, outcome: 2.3 Number of emergency department visits

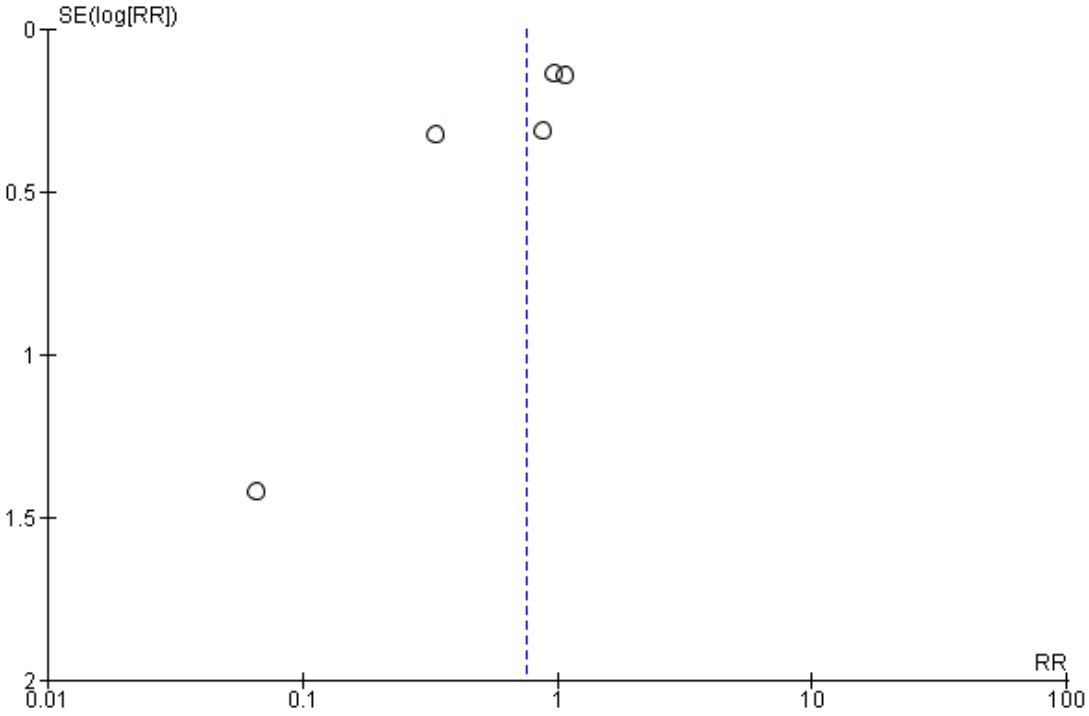
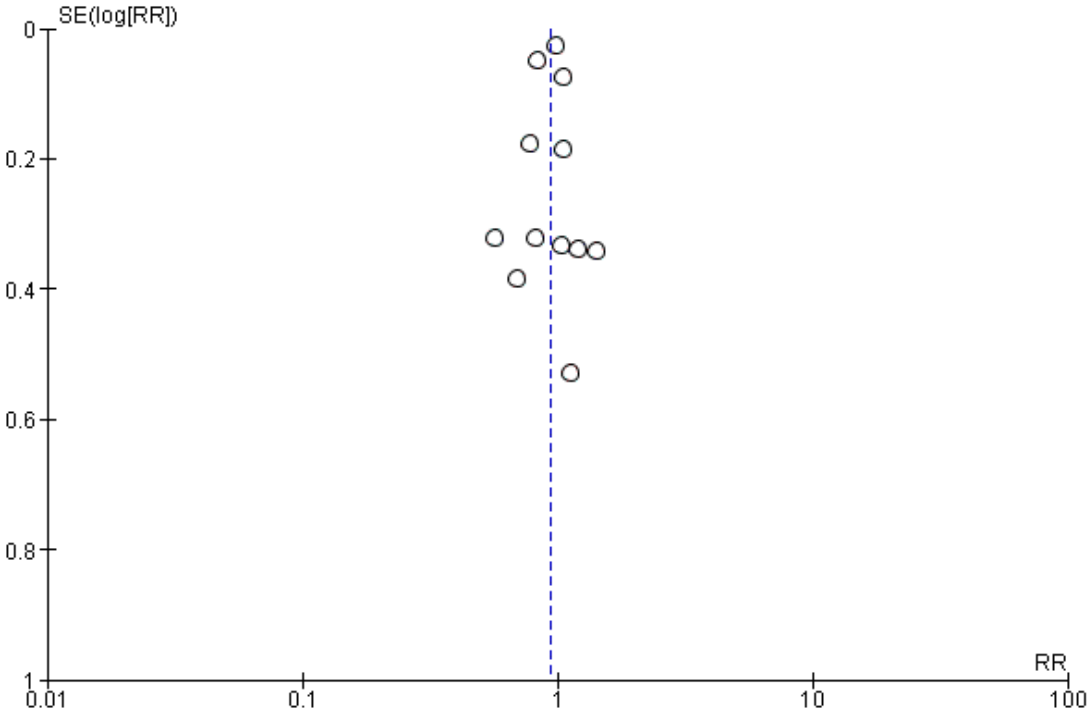


Figure 6. Funnel plot of comparison: 2 Organisational interventions, outcome: 2.4 Mortality



Other bias

A total of 22 studies had an unclear risk of 'other bias' (Bernsten 2001; Campins 2016; Coleman 1999; Gernant 2016; Gurwitz 2014; Hawes 2014; Ibrahim 2013; Korajkic 2011; Krska 2001; Lapane 2011; Lowrie 2012; Malet-Larrea 2016; Malone 2000; Murray 2004; Nabagiez 2013; Okamoto 2001; Olesen 2014; Pai 2009; Roberts 2001; Rytter 2010; Zermansky 2001; Zermansky 2006). Seven studies had a high risk of 'other bias' (Alvarez 2001; Frankenthal 2014; Garcia-Gollarte 2014; Kaczorowski 2011; Lenaghan 2007; Moertl 2009; Triller 2007), while only one study had a low risk of 'other bias' (Holland 2005). Other biases included inappropriate administration of the intervention, such as the method of training used to deliver the intervention or level of knowledge of the health professional delivering the intervention. Short length of the intervention was a bias in some studies (Kaczorowski 2011; Triller 2007), with the level of knowledge of the pharmacist or health professional delivering the intervention a bias in other studies. For example, in the study by Lenaghan 2007, research was carried out in one rural general practice with a single experienced review pharmacist, which may have had a bearing on the generalisability of the results.

In Bernsten 2001, one aspect of the study that was not rigorously controlled was the training of participating pharmacists. A study manual was provided to each participating pharmacist, followed by a one-day training session. Further training was provided in individual countries; however, the extent of this was driven by available resources. Other biases include small sample sizes in the intervention arms; with 48 participants in Moertl 2009 and 77 participants in Triller 2007, and poor pharmacist-prescriber communication, which may have reduced the efficacy of the intervention (Triller 2007). Alvarez 2001 did not report on any pre-intervention data for most of the outcome measures. Garcia-Gollarte 2014 had a short intervention of a six-month period and a short follow-up of three months. Frankenthal 2014 conducted the study in only one geriatric centre.

There was a total of eight cluster-randomised studies included in the review (Alvarez 2001; Coleman 1999; Gernant 2016; Kaczorowski 2011; Lapane 2011; Lowrie 2012; Malet-Larrea 2016; Roberts 2001). Cluster-randomised studies include other potential biases such as recruitment bias and complete loss of a cluster in a trial. The extent of this type of bias was not fully reported and therefore we considered it under this section.

Effects of interventions

See: **Summary of findings for the main comparison** Professional interventions compared to standard/usual care for prevention of medication errors; **Summary of findings 2** Organisational interventions compared to standard/usual care for prevention of medication errors

Professional interventions

We performed a meta-analysis on the number of hospital admissions and the number of emergency department visits, as they were the only outcomes reported by more than one study. We have presented effect estimates and certainty of evidence for each outcome in Summary of findings for the main comparison (see Appendix 3 for the full GRADE evidence profile). We obtained all reported data from the published papers.

Primary outcomes

We measured hospital admissions as either the number of hospital admissions or the number of people admitted to hospitals.

1. Number of hospital admissions

Two studies (3889 participants) reported on the number of hospital admissions (Lapane 2011; Murray 2004). Overall, professional interventions in health information technology to identify people at risk of medication problems in the case of Lapane 2011, or the computer-generated care suggested and actioned by the physician described by Murray 2004, reported an increase in the number of hospital admissions, but the 95% confidence interval (CI) indicates that it probably makes little or no difference (risk ratio (RR) 1.24, 95% CI 0.79 to 1.96; moderate-certainty evidence). There was no significant heterogeneity (I^2 = 0%, P = 0.44) across the studies, as shown in Summary of findings for the main comparison.

2. Number of people admitted to hospital

One study (3661 participants) reported on number of people admitted to hospital (Gurwitz 2014). The study authors found that the intervention, which included an electronic notification system about dose changes, drug interactions, and follow-up, made little or no difference to the number of people admitted to hospital (adjusted RR 0.99, 95% CI 0.92 to 1.06; high-certainty evidence).

Secondary outcomes

1. Number of emergency department visits

Two studies (1067 participants) reported on this outcome (Garcia-Gollarte 2014; Murray 2004). Garcia-Gollarte 2014 described an educational intervention on drug use aimed at physicians to improve drug prescriptions. Murray 2004 described an intervention including computer-generated care suggested and actioned by the physician. Both professional interventions described by the study authors may make little or no difference to the number of emergency department visits (adjusted RR 0.71, 95% CI 0.50 to 1.02; low-certainty evidence). There was no significant heterogeneity among the two studies (I^2 = 0%, P = 0.64).

2. Mortality

One study (3538 participants) reported on the number of deaths (Lapane 2011). The health information technology to identify people at risk of medication problems probably makes little or no difference to the number of deaths in the study population (adjusted RR 0.98, 95% CI 0.82 to 1.17; moderate-certainty evidence).

Organisational interventions

We performed a meta-analysis on the number of hospital admissions, number of people admitted to hospital, the number of emergency department visits, and mortality. We have presented effect estimates and certainty of evidence for each outcome in Summary of findings 2 (see Appendix 4 for the full GRADE evidence profile). We obtained all reported data from the published papers.

Primary outcome

1. Number of hospital admissions

Eleven trials (6203 participants) reported on the number of hospital admissions (Coleman 1999; Holland 2005; Ibrahim 2013; Krska 2001; Lenaghan 2007; Lowrie 2012; Malone 2000; Moertl 2009; Nabagiez 2013; Okamoto 2001; Rytter 2010). The organisational interventions included medication reviews by pharmacists, nurses or physicians, clinician-led clinics, and home visits by clinicians. Most interventions included optimisation of the medications that participants were taking or home visits by healthcare practitioners, or both. Overall, it is uncertain whether organisational interventions (which included pharmaceutical care or medication reviews by a doctor, a pharmacist, or a nurse, home visits, educational interventions with a pharmacist) reduce the number of hospital admissions (adjusted RR 0.85, 95% CI 0.71 to 1.03; very low-certainty evidence. There was significant heterogeneity (I^2 = 75%, P < 0.0001) across the studies (Analysis 2.1). The direction of the effect was consistent in 10 out of 11 trials. Holland 2005 reported an increase in the total number of hospital admissions (adjusted RR 1.31, 95% CI 1.13 to 1.50; based on very low-certainty evidence. The study authors explained these findings by indicating that their study was not statistically powered to detect changes in hospital admissions and new admissions. The study authors explained the unusual increase in hospital admissions among

participants by concluding that the participants were better informed about adverse events through the pharmacist intervention, and this promoted help-seeking behaviour, which resulted in an admission.

We undertook a sensitivity analysis by removing studies at high risk of bias (Holland 2005; Krska 2001; Moertl 2009; Nabagiez 2013), and again it is uncertain whether organisational interventions (which included pharmacist home visits, pharmaceutical care plan, home-based nurse care and home visits by physician assistants) reduce the number of hospital admissions (adjusted RR 0.86, 95% CI 0.72 to 1.03). Ibrahim 2013, Moertl 2009 and Rytter 2010 showed a reduction in hospital admissions with a relatively narrow confidence interval: adjusted RR 0.40, 95% CI 0.22 to 0.74 (Ibrahim 2013); RR 0.38, 95% CI 0.19 to 0.72 (Moertl 2009); and RR 0.76, 95% CI 0.61 to 0.95 (Rytter 2010), in favour of the interventions. These three studies were characterised by frequent follow-up by the clinical pharmacists. In the case of Ibrahim 2013, there was a three-month follow-up and a once-a-week telephone conversation; Moertl 2009 had frequent follow-up by the clinical pharmacists at three, six, nine, and 12 months; and Rytter 2010 also had three follow-up contacts by GPs and district nurses.

2. Number of people admitted to hospital

A total of 13 studies (152,237 participants) reported on the number of people admitted to hospital (Alvarez 2001; Bernsten 2001; Campins 2016; Frankenthal 2014; Hawes 2014; Kaczorowski 2011; Korajkic 2011; Malet-Larrea 2016; Nabagiez 2013; Olesen 2014; Triller 2007; Zermansky 2001; Zermansky 2006). Most of the organisational interventions described included medication reviews by pharmacists, nurses or physicians, clinician-led clinics, and home visits by clinicians. Overall, organisational interventions may make little or no difference to the total number of people admitted to hospital in favour of the intervention group compared with the control group (adjusted RR 0.92, 95% CI 0.86 to 0.99; low-certainty evidence) with significant heterogeneity (I^2 = 47%, P = 0.03). Three studies showed that the organisational interventions reduced the total number of people admitted to hospital, as the RR was less than 1 (Bernsten 2001; Hawes 2014; Malet-Larrea 2016).

We undertook a sensitivity analysis by removing studies at high risk of bias (Alvarez 2001; Bernsten 2001; Frankenthal 2014; Hawes 2014; Kaczorowski 2011; Malet-Larrea 2016; Nabagiez 2013; Triller 2007), and again, the intervention made little or no difference to the number of people admitted to hospital (adjusted RR 0.98, 95% CI 0.85 to 1.13) with low, non-significant heterogeneity between studies (I^2 = 28%, P = 0.23).

Secondary outcomes

1. Number of emergency department visits

Five studies (1819 participants) reported on emergency department visits (Alvarez 2001; Coleman 1999; Gernant 2016; Hawes 2014; Ibrahim 2013). Overall, it is uncertain whether organisational interventions including medication reviews by pharmacists, nurses or physicians, clinician-led clinics, and home visits by clinicians reduce emergency department visits in favour of the intervention group compared with the control group (adjusted RR 0.75, 95% CI 0.49 to 1.15; very low-certainty evidence). Please refer to Summary of findings 2.

There was also significant heterogeneity between the studies (I^2 = 73%, P = 0.005). We undertook a sensitivity analysis by removing studies at high risk of bias (Alvarez 2001; Hawes 2014). Pharmaceutical care and care transition clinic interventions may make little or no difference in emergency department visits (adjusted RR 0.68, 95% CI 0.37 to 1.27) with significant heterogeneity between studies (I^2 = 79%, P = 0.009).

All studies showed wide confidence intervals, and although Alvarez 2001 showed an increase in the number of emergency department visits in favour of the intervention, this study had high risk of bias as there was a high proportion of incomplete data in the outcomes measured.

2. Mortality

A total of 12 studies (154,962 participants) reported on mortality (Campins 2016; Holland 2005; Kaczorowski 2011; Lenaghan 2007; Lowrie 2012; Moertl 2009; Olesen 2014; Pai 2009; Roberts 2001; Triller 2007; Zermansky 2001; Zermansky 2006). Overall, it is uncertain whether organisational interventions, which included medication reviews by pharmacists, nurses or physicians, clinician-led clinics, and home visits by clinicians reduce mortality in favour of the intervention group (adjusted RR 0.94, 95% CI 0.85 to 1.03; very low-certainty evidence) with non-significant heterogeneity (I^2 = 37%, P = 0.10). Please refer to Summary of findings 2.

We undertook sensitivity analysis by removing studies at high risk of bias (Holland 2005; Kaczorowski 2011; Lenaghan 2007; Moertl 2009; Olesen 2014; Roberts 2001), and we found that interventions addressing home visits by pharmacists, educational sessions to assess cardiovascular risk, medication reviews, home-based nurse care, and nurse education probably made little or no difference to mortality (adjusted RR 1.02, 95% CI 90 to 1.17). There was no significant heterogeneity between studies after the removal of the six studies (I^2 = 0%, P = 0.45).

Structural interventions

We did not find any studies that fitted the criteria of structural interventions.

ADDITIONAL SUMMARY OF FINDINGS [Explanation]

Organisational interventions compared to standard/usual care for prevention of medication errors

Patient or population: adults receiving medication in primary care
Setting: primary care
Intervention: organisational interventions (provision of pharmaceutical care, medication reviews, follow-up visits by a healthcare professional including a pharmacist, nurse or physician)
Comparison: standard/usual care

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with standard/usual care	Risk with organisational interventions				
Number of hospital admissions	Study population		RR 0.85 (0.71 to 1.03)	6203 (11 RTs)	⊕◯◯◯ Very low[1,2,3]	Some studies had unclear risk of bias (selection and attrition), high heterogeneity and wide confidence intervals
	274 per 1000	233 per 1000 (194 to 282)				
Number of people admitted to hospital	Study population		RR 0.92 (0.86 to 0.99)	152,237 (13 RTs)	⊕⊕◯◯ Low[1,3]	Some studies had unclear risk of bias (selection, attrition and performance bias) and wide confidence intervals
	13 per 1000	13 per 1000 (11 to 14)				
Number of emergency department visits	Study population		RR 0.75 (0.49 to 1.15)	1819 (5 RTs)	⊕◯◯◯ Very low[1,2,3]	Studies had unclear risk of bias (selection, performance and attrition bias), high heterogeneity and wide confidence intervals
	234 per 1000	176 per 1000 (115 to 269)				

Mortality	Study population		RR 0.94 (0.85 to 1.03)	154,962 (12 RTs)	⊕◯◯◯ Very low[3,4]	Studies had high risk of selection, attrition and performance bias and wide confidence intervals
	50 per 1000	47 per 1000 (43 to 52)				

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the __relative effect__ of the intervention (and its 95% CI).
CI: confidence interval; **RR:** risk ratio; **RT**: randomised trial.

GRADE Working Group grades of evidence
High-certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate-certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low-certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low-certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect

[1]We downgraded one level for unclear risk of bias (selection and attrition bias).
[2]We downgraded one level for inconsistency (high heterogeneity across studies).
[3]We downgraded one level for imprecision.
[4]We downgraded two levels for high risk of bias (selection, performance and attrition bias).

DISCUSSION

Summary of main results

The studies included in this Cochrane Review showed that, based on moderate- and low-certainty evidence, interventions in primary care for reducing preventable medication errors probably make little or no difference to the number of people admitted to hospital or the number of hospitalisations, emergency department visits, or mortality. Most of the interventions took place in the UK and the USA; studies undertaken in high-income countries with disadvantaged populations, and in low- and middle-income countries, were underrepresented. This might affect the generalisability of the results. We undertook sensitivity analysis by removing studies at high risk of bias and detecting whether there was any difference on the overall effect size. Overall, there is no evidence of an effect in any of the outcomes.

Overall completeness and applicability of evidence

The types of interventions included in this review were based on the taxonomy of interventions developed by Cochrane EPOC (Appendix 1); four studies used professional interventions and 26 studies used organisational interventions. The professional interventions included the use of health information technology to identify people at risk of medication problems: computer-generated care suggested and actioned by a physician; electronic notification systems about dose changes, drug interventions and follow-up; and educational interventions on drug use aimed at physicians to improve drug prescriptions. Organisational interventions consisted of medication reviews by pharmacists, nurses or physicians, clinician-led clinics and home visits by clinicians.

The interventions described in the review were complex and generally multifaceted, which resulted in significant heterogeneity. The variation in heterogeneity in the pooled estimates means that our results should be treated cautiously as the interventions may not have worked consistently across all studies due to differences in how the interventions were provided, background practice, setting, healthcare system, or delivery of the interventions. Another potential limitation is the quality of the studies. The methods sections of the studies provided varying levels of detail on how complex interventions were developed, the design of the trials or how staff were trained to deliver the interventions. There was also evidence of potential bias in some studies, with only 18 studies reporting adequate concealment of allocation and only 12 studies reporting appropriate protection from contamination, both of which may have influenced the overall effect estimate and the overall pooled estimate.

Certainty of the evidence

The certainty of the evidence obtained from the 'Summary of findings' tables using the GRADE system highlights the very low to high certainty of the evidence reported by the studies. The primary outcomes of number of hospital admissions and number of people admitted to hospital were reported to have very low- to high-certainty evidence, respectively. Mortality was reported in 13 studies (1 study involving professional interventions, moderate-certainty evidence; and 12 studies involving organisational interventions, very low-certainty evidence), with the main type of biases being detection and performance bias. We considered studies reporting on emergency department visits to have low-certainty evidence for professional interventions and very low-certainty evidence for organisational interventions using the GRADE system, due to study design and heterogeneity. Further research and better study designs are likely to change the overall estimate reported using these outcomes.

The Methods sections provided few details about study methodology and how complex interventions were delivered. The overall quality of the evidence presented in this review is either at high risk or unclear risk of bias. The main limitations were the heterogeneity between studies, the imprecision in results due to the wide confidence intervals amongst studies, unclear selection bias, performance and detection bias, and attrition bias.

Potential biases in the review process

The number of studies that we were able to combine in the meta-analysis was somewhat small due to subclassification of the interventions and because not all studies reported on all the outcomes of interest mentioned in the review. We did not place any language restrictions on the search strategy. The review included one study written in Spanish (Alvarez 2001). We were able to pool the data from this study with the help of a Spanish-speaking colleague. Despite the limited number of studies that were included, funnel plots of studies reporting the outcomes of interest showed no apparent publication bias (Figure 3; Figure 4; Figure 5; Figure 6). Another limitation of the review included the definitions of 'pharmaceutical care' and 'pharmaceutical review' described in the studies, which may have led to different interventions. We also did not consider studies where participants were treated in the emergency department of hospitals, although we are aware that at times people could receive treatment in the emergency department without being admitted to hospital. We will consider these types of studies in our updated review. Finally, a sensitivity analysis with a separate comparison of cluster- and individual randomised trials may have yielded different results, and we will consider including this in our updated review.

Agreements and disagreements with other studies or reviews

Few studies have examined whether the types of interventions that were investigated in this review lead to reductions in hospital admissions, emergency department visits, or mortality. One of the few reviews that studied this problem (Royal 2006), found that pharmacist-led medication reviews were effective in reducing hospital admissions, although restricting the analysis to randomised trials did not produce a significant benefit.

Previous observational studies addressing similar interventions also provide limited evidence of their effectiveness. A controlled study by Hugtenburg 2009, which included 37 community pharmacists and 715 participants, and examined the impact of medication reviews and participant counselling at discharge from the hospital by community pharmacists, found that the intervention was not effective at reducing mortality. Another open controlled study, conducted by Leendertse 2013, examined the effect of reviewing medications in primary care by pharmacists. They found that the intervention did not significantly reduce medication-related hospital admissions. Moreover, a study by Safran 1993 examined the effect of an electronic medical record used by physicians to care for people with HIV on hospitalisation, emergency visits and mortality. The study authors found that the intervention was significant for emergency department visits, but not for mortality or hospitalisations. Our study mirrors these findings in that the interventions investigated in this review had little or no effect on the number of people admitted to hospital, number of hospital admissions, number of emergency department visits, or mortality.

AUTHORS' CONCLUSIONS

Implications for practice

The evidence from this review does not fully support the benefits of interventions to reduce medication-related preventable errors with respect to any of the outcomes of interest that were reported in this review. Both professional and organisational interventions had little or no significant effect on the outcomes of interest. Therefore, organisations implementing interventions to improve medication safety in primary care should be aware that the evidence endorsing these interventions is limited, both in number and methodological quality.

Implications for research

Larger studies addressing both professional and organisational interventions and reporting on the number of people admitted to hospital and emergency department visits are needed before evidence-based recommendations can be made, given that only one study with 3661 participants addressing professional interventions and 13 studies with 8960 participants reported on the number of people admitted to hospital in primary care following organisational interventions. Emergency department visits were only reported by two studies (1067 participants) describing professional interventions and five studies (1819 participants) describing organisational interventions.

Further, large studies exploring which interventions involving healthcare professionals (nurse, physician or pharmacist) are likely to have a beneficial effect in preventing errors in primary care should also be addressed. Furthermore, longer time frames for interventions and a focus on high risk participants/therapies would also help. The quality of the studies needs to be improved as the certainty of the evidence was very low to high. The methods sections of the studies provided varying levels of detail on how complex interventions were developed, the design of the trials, or how staff were trained to deliver the interventions. We did not identify any structural interventions and only four studies used professional interventions, so more work needs to be done with these types of interventions. Most of the studies did not provide details of what constituted 'usual care', so this can also be improved in future studies.

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Alvarez 2001

Methods	Cluster-RT (randomisation at the pharmacy level) Study duration: 1 year
Participants	735 at beginning of the study, 600 at the end of the study (data are on the 600 reported below) Setting: community pharmacies Diagnostic criteria: CHD Age (years) (mean): intervention group: 64.8 years; control group: 65.8 years Sex female n (%): intervention group: 79 (29.5%); control group: 94 (29%) Country: Spain Comorbidity: not reported Sociodemographics: not reported Ethnicity: not reported Date of study: not reported
Interventions	1 intervention group Intervention group: pharmacies allocated to that group provided pharmaceutical care, consisting of the prevention, identification and solution of medication-related problems Control group: care as usual Pharmaceutical care consisted of the following: offering the pharmaceutical care service to participants and to their corresponding GPs, initial interview and assessment of the therapeutic plan, registration of data during the subsequent visits in order to allow the identification of medication-related problems, and intervention to solve the problem
Outcomes	• Frequency of hospital emergency room visits, number of people admitted to hospital and length-of-stay in ICU, all of them due to coronary causes (data obtained from external sources) • Health-related QoL score (SF-36, measured before and after the intervention) • Participant knowledge of CHD risk factors (only measured at the end of the study) • Participant knowledge of their drugs, and subjective perception of the anticoagulant drugs and beta-blockers (only measured at the end of the study) • Satisfaction with pharmaceutical care service and perception of pharmacist's professional competence (only measured at the end of the study)
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported

Alvarez 2001 (*Continued*)

Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported. Pharmacists may have been blinded, as they all received training on methods to treat CHD (in order to ensure that differences after the intervention are due to the intervention per se and not due to differences in theoretical knowledge on methods to treat CHD)
Incomplete outcome data (attrition bias) All outcomes	High risk	High proportion of incomplete outcome data for most to the measures
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Selective reporting (reporting bias)	Low risk	All outcomes were reported
Protection against contamination bias	Unclear risk	Unclear
Other bias	High risk	For most of the outcome measures no pre-intervention data were collected. We considered other bias due to cluster randomisation

Bernsten 2001

Methods	RT Study duration: 18 months Setting: community pharmacy
Participants	2454 participants were recruited: 1290 intervention participants and 1164 control participants were assessed at baseline although there were subsequent dropouts Diagnostic criteria: participants were eligible if they were ≥ 65 years, taking 4 or more prescribed medicines, and oriented with respect to time, place, and person. They were required to be community dwelling and regular visitors to a community pharmacy. Participants could not be housebound or in a nursing facility Age (years) (mean ± SD): intervention: 735 (58%); control: 663 (57%); no significant difference Sex female n (%): intervention: 735 (58%); control: 663 (57%); no significant difference Country: 7 European countries; Denmark, Germany, The Netherlands, Northern Ireland (co-ordinating centre), Portugal, Republic of Ireland and Sweden Comorbidity: there were no significant differences between intervention and control participants at baseline Sociodemographics: none of note, although participants from 2 countries (Republic of Ireland and Portugal) did not complete the study Ethnicity: not reported

Bernsten 2001 (*Continued*)

	Date of study: unclear although published in 2001
Interventions	104 intervention pharmacies A pharmaceutical care programme was involved and a manual was distributed to all the intervention sites detailing the intervention. Pharmacists assessed participants to identify drug-related problems using a structured approach. Pharmacists used several sources of information including informal questioning of the participant, the participant's GP, and pharmacy records. Pharmacists also formulated a monitoring and intervention plan for each participant, which included participant education about drugs and their medical condition, using improvement in medication compliance strategies, and simplifying drug regimens Control group: participants were treated as per the usual care with no pharmaceutical care plan provided
Outcomes	Data relating to health and economic outcomes were collected for each participant at baseline, 6, 12 and 18 months. These included hospital admissions
Notes	The study authors note that the training of pharmacists was not rigorously controlled. Although a study manual was provided along with a 1-day training session, additional training was not consistently provided

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Sites were randomly allocated as control or intervention sites
Allocation concealment (selection bias)	Low risk	Concealment was adequate as sites rather than individual participants were randomly allocated. Also, all units were allocated at the start of the study
Blinding of participants and personnel (performance bias) All outcomes	Low risk	As pharmacies were the unit of randomisation, this appears to be low risk. Control pharmacists provided usual care and intervention pharmacists only provided the intervention
Incomplete outcome data (attrition bias) All outcomes	High risk	Those participants who withdrew from the study were significantly older and in poorer health
Blinding of outcome assessment (detection bias) All outcomes	Low risk	This is less important for our purpose as we are looking at objective outcomes (hospitalisations, ED visits, and mortality)
Selective reporting (reporting bias)	Low risk	No evidence of selective reporting

Bernsten 2001 (*Continued*)

Protection against contamination bias	Low risk	No evidence of contamination of the intervention group with the control
Other bias	Unclear risk	1 aspect of the study that was not rigorously controlled was the training of participating pharmacists. A study manual was provided to each participating pharmacist, followed by a 1-day training session. Further training was provided in individual countries; however, the extent of this was driven by the available resources

Campins 2016

Methods	RT 15 months
Participants	503 participants: 252 intervention, 251 control; final sample 242 intervention, 246 control Setting: primary care centres Diagnostic criteria: elderly people (> 70 years) on ≥ 8 drugs
Interventions	The intervention consisted of 3 consecutive phases. First, a trained and experienced clinical pharmacist evaluated all drugs prescribed to each participant using the GP-GP algorithm and based their decision about appropriateness on the STOPP/START criteria. Second, the pharmacist discussed recommendations for each drug with the participant's physician in order to come up with a final set of recommendations. Finally, these recommendations were discussed with the participant, and a final decision was agreed by physicians and their patients in a face-to-face visit Control group participants followed the usual treatments and control procedures of their physicians
Outcomes	Main outcome measures regarding intervention effectiveness were as follows • number of medications prescribed at 3, 6 and 12 months • (treatment restart ratio (after discontinuation) • primary care and emergency department consultation rate for acute conditions • hospitalisation rate • mortality rate • baseline, 3-month and 6-month self-reported QoL (measured using EuroQoL-5D, www.euroqol.org) • baseline, 3-month and 6-month treatment Adherence was measured using the Morisky-Green test.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement

Campins 2016 (*Continued*)

Random sequence generation (selection bias)	Low risk	Participants were blindly randomised to 1 or other of the 2 study arms. Assignment was based on a list of random numbers generated by a statistical programme
Allocation concealment (selection bias)	Low risk	Each family physician received 10 sealed, opaque envelopes with identification numbers (assigned consecutively in strict chronological order of recruitment) on the back. Each envelope contained a card with the same identification number and the intervention group to which the subject was assigned. Envelopes were not prepared in primary care centres but in the research unit
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Low risk because pharmacists only treated intervention participants and did not know that the participants they interacted with were in a study. Also, participants did not appear to know whether they were receiving an intervention or not
Incomplete outcome data (attrition bias) All outcomes	Low risk	Very few people dropped out.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcomes of interest were objective
Selective reporting (reporting bias)	Low risk	No evidence of selective reporting
Protection against contamination bias	Unclear risk	Prescribing physicians who received recommendations from the pharmacist regarding intervention group participants also had participants in the control group, so the control group could have benefited from the intervention
Other bias	Unclear risk	Study has limited statistical power to detect effects for outcomes of interest

Coleman 1999

Methods	Cluster-RT. The unit of randomisation was the physician practice Study duration: 2 years
Participants	Total participants: 169 participants, 9 physician groups Participants aged ≥ 65 in ambulatory setting, chronic-care clinics Age: intervention 77.3%; control 77.4%; no SD provided; P = 0.70 Sex female (%): intervention 47.9%; control 49.6%; no SD provided; P = 0.81 Country: USA Diabetes: intervention 53.2%; control 48.6%; P = 0.62 Education > 12 years: intervention 77.1%; control 66.7%; P = 0.1 Married: intervention 55.2%; control 58.3%; P = 0.63 Income < USD 15,000: intervention 15.8%; control 14%; P = 0.75

Coleman 1999 (*Continued*)

	Hospitalised in prior year: intervention 46.7%; control 39.7%; P = 0.15 Mean chronic disease score: intervention 7.3; control 7.7; P = 0.06 Mean risk score: intervention 0.55; control 0.53; P = 0.35 Ethnicity: non-white: intervention 2.8%; control 4.1%; P = 0.54
Interventions	Intervention practices (5 physicians, 96 participants) held half-day, chronic-care clinics every 3-4 months. These clinics included an extended visit with the physician and nurse dedicated to planning chronic-disease management, a pharmacist visit that emphasised reduction of polypharmacy and high-risk medications, and a patient self-management group Control practices (4 physicians, 73 participants) received usual care
Outcomes	Emergency visits (mean/year) and hospitalisations
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Randomisation was not mentioned nor how it was done.
Allocation concealment (selection bias)	Unclear risk	Allocation was not mentioned nor how it was done.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	This would be impossible.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Some participants did not complete the study and were reported in the study
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No explanation given
Selective reporting (reporting bias)	Low risk	All outcomes were reported.
Protection against contamination bias	Low risk	It is hard to determine if the intervention group interacted with the control group
Other bias	Unclear risk	Unclear. We considered other bias due to cluster randomisation

Frankenthal 2014

Methods	RT 18 months Chronic-care geriatric facility
Participants	359 participants: 183 intervention, 176 control; final sample: 160 intervention, 146 control
Interventions	The intervention consisted of a medication review by the study pharmacist for all residents at study opening and 6 and 12 months later using the The STOPP/START criteria. Interventional recommendations that the study pharmacist made for residents in the intervention group but not in the control group were discussed with the chief physician at study opening and after 6 months. The chief physician decided whether to accept these recommendations and implement prescribing changes Control: usual care
Outcomes	Outcome measures included: • average number of falls • hospitalisations • QoL as assessed using the Medical Outcomes Study 12-item SF-12 and the costs of medications • functioning was also assessed using the Functional Independence Measure, 20, which rates 18 ADL Outcomes were measured at the beginning of the study and at the 12-month follow-up
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Fixed, stratified randomisation was used to allocate residents to groups according to the 3 types of residents: ADL-dependent, ADL-independent, and primarily cognitively impaired. Participants who were ADL-dependent with impaired cognition were assigned to the ADL-dependent group. Randomisation for each level was according to simple list randomisations
Allocation concealment (selection bias)	Low risk	A physician who was not part of the study randomised participants. Group allocation was concealed from the study pharmacist, and participants were assigned to 1 of the 2 groups using sealed envelopes
Blinding of participants and personnel (performance bias) All outcomes	High risk	Pharmacists were aware that they were interacting with the intervention group

Frankenthal 2014 (*Continued*)

Incomplete outcome data (attrition bias) All outcomes	Low risk	Most participants completed the study and there was no apparent difference between intervention and control group
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Number of hospitalisations is an objective measure.
Selective reporting (reporting bias)	Low risk	No evidence of selective reporting
Protection against contamination bias	Unclear risk	The intervention pharmacist only interacted with intervention participants, but may have interacted with pharmacists in the control group
Other bias	High risk	Only 1 geriatric centre was investigated

Garcia-Gollarte 2014

Methods	RT
Participants	1018 residents: 516 intervention, 502 control Final sample: 59 physicians, 716 nursing home residents Intervention: 29 doctors, 372 nursing home residents Control: 30 doctors, 344 nursing home residents Diagnostic criteria: residents aged ≥ 65 years and clinically stable (no change in prescription in last 2 months) Setting: private organisation
Interventions	6 months professional intervention A nursing home physician, expert in drug use in older people, delivered a structured educational intervention The programme included: general aspects of prescription and drug use in geriatric patients, how to reduce the number of drugs, to perform a regular review of medications, to avoid inappropriate drug use, to discontinue drugs that do not show benefits, and to avoid under-treatment with drugs that have shown benefits. It also discussed in detail some drugs frequently related to adverse drug reactions in older people. Educational material and references were given to participants Finally, two, 1-h workshops reviewed practical, real life cases and promoted practice changes in participants. The educator offered further on-demand advice on prescriptions for the next 6 months. This intervention was reinforced through a single review by the researchers, using standard appropriateness criteria, STOPP-START Control: physicians in the control group did not receive any intervention or information about an educational intervention delivered in other centres
Outcomes	Outcome measures were as follows: • appropriateness and quality of drug use. The STOPP-START criteria were used to assess the drugs that were actively used by each resident at the beginning of the study

	and 9 months later (3 months after the intervention was finished). The number of individuals with potentially inappropriate prescriptions, duplicate class of drugs, and antipsychotic use are reported here. • incidence of selected geriatric syndromes. The number of falls and the number of episodes of delirium were recorded for the 3-month period before the intervention started, and the 3-month period immediately after the 6-month intervention finished. This allowed for comparing the control and the intervention group, and also for assessing time changes in both groups. Falls and delirium are systematically registered in the clinical records of all the participant nursing homes. • health resource utilisation. The number of visits to physicians and nurses, the number of visits to an emergency room, and the total number of days spent in hospital were also recorded for the 3-month period before the intervention started, and the 3-month period after the 6-month intervention finished. These are also regularly registered in the clinical records of all the participant nursing homes.
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Randomisation was done using random number tables.
Allocation concealment (selection bias)	Unclear risk	There was no mention made of sequence concealment.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Physicians in both groups were informed that there was a company programme aimed to improve drug prescription (to explain why data on prescriptions was collected in their centres) but were blinded to the fact that the educational intervention was being assessed. Also, participants did not know they were receiving an intervention
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	30% of participants were lost to the study, but it is unclear if there was differential attrition in intervention and control groups
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Number of emergency room visits and length of hospitalisations are objective outcomes
Selective reporting (reporting bias)	Low risk	No evidence of selective reporting
Protection against contamination bias	High risk	Although nursing homes in the intervention and control groups were separate, some cross-contamination because of informal contacts between physicians may have occurred
Other bias	High risk	Short intervention period (6 months) and short follow-up (3 months)

Gernant 2016

Methods	Cluster-RT
Participants	656 home care participants (intervention n = 297, usual care n = 359) were available for this study
Interventions	The intervention began approximately 3 days after in-home health admission when a pharmacy technician completed telephonic medication reconciliation with the participant and/or caregiver. Then a trained pharmacist would consult with the participant or caregiver via telephone for an average of 30 min to complete a scheduled comprehensive medication therapy review to identify and resolve any medication-related problems. The pharmacist constructed a personal medication record and a medication-related action plan for the participant. The action plan was a participant-centred document that assisted participants, caregivers, and the pharmacist in the resolution of identified medication-related problems Control group: standard/usual care
Outcomes	The primary outcome of this study was participant-level, 60-day, all-cause ED utilisation. This outcome was defined as a dichotomous variable (i.e. the participant visited the ED 1 or more times following the intervention or they did not)
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Site and participant randomisation was a 2-step process. Firstly a simple random sample of 40 co-ordinating home healthcare centres, with a monthly census of ≥ 20 admitted participants, was selected among 419 care centres from a nationwide Home Health Agency (Amedisys, Inc, Baton Rouge, LA). Then, at each study site, using blocks of 7 participants, and constrained for equal allocation to study intervention or usual care groups
Allocation concealment (selection bias)	Low risk	Home Health Agency nurses were blinded to their participants' group assignment to prevent bias during the initial in-home admissions assessment
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Participants did not know to which group they were allocated
Incomplete outcome data (attrition bias) All outcomes	Low risk	All participants were accounted for.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not mentioned
Selective reporting (reporting bias)	Low risk	All outcomes were reported.

Gernant 2016 (*Continued*)

Protection against contamination bias	Low risk	Cluster-randomisation with a small chance of contamination
Other bias	Unclear risk	Unclear

Gurwitz 2014

Methods	RT, total study duration not provided
Participants	5077 hospital discharges: 2563 intervention discharges, 2514 control discharges Final sample: 1870 intervention, 1791 control Setting: large multispecialty group practice Diagnostic criteria: ≥ 65 years discharged from hospital to home
Interventions	Professional intervention Intervention: an automated system was developed to facilitate the flow of information to the medical group's primary care providers about individuals who were discharged to home from the hospital In addition to notifying providers about an individual's discharge, the system provided information about new drugs at the time of hospital discharge, warnings about selected drug-drug interactions, recommendations for consideration of dose changes and laboratory monitoring of high-risk medications, and alerts to the provider's support staff to schedule a post hospitalisation office visit within 1 week of discharge Control: care as usual
Outcomes	Whether discharged individuals had an office visit with a primary care physician in the 7-, 14-, and 30-day periods after hospital discharge was determined, as was whether a participant was rehospitalisation within 30 days. Information related to office visits and hospitalisations was ascertained from the medical group's electronic health record and from health plan data, which allowed for determination of whether a rehospitalisation had occurred at any hospital and not just the primary hospital that served individuals under the care of the medical group. Analysts blinded to intervention status determined these outcomes at least 6 months after completion of the study
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	A random number generator was used to assign a discharge to the intervention or control group
Allocation concealment (selection bias)	Low risk	Computer allocated discharges
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Automated system was used. Also participants were not aware of which group they were in

Gurwitz 2014 (*Continued*)

Incomplete outcome data (attrition bias) All outcomes	Low risk	Comparable rates of attrition in intervention and control groups
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Analysts blinded to intervention status determined the outcomes. (The trialist reviewing the data (JHG) was unaware of which type of unit the event had occurred on.)
Selective reporting (reporting bias)	Low risk	No evidence of selective reporting.
Protection against contamination bias	Unclear risk	The study is a cluster design and the authors stated the following, "Efforts were made to limit crossover of prescribers between intervention and control units, however, some prescribers worked simultaneously on both intervention and control units."
Other bias	Unclear risk	Unclear risk

Hawes 2014

Methods	RT 18 months
Participants	61 participants: 24 intervention, 37 control Unclear how many participants were analysed Setting: healthcare system's outpatient family medicine centre Diagnostic criteria: In the first year of the study, inclusion criteria had to be 1 of the following 3 criteria: • reason for admission was heart failure, COPD, hyperglycaemic crisis, stroke, or non-ST elevation myocardial infarction/unstable angina (NSTEM/UA) • > 3 hospitalisations in the past 5 years • ≥ 8 scheduled medication anticipated at discharge In the second year, the criteria were changed to the following: ≥ 8 scheduled medications anticipated at discharge
Interventions	Organisational. Participants in the intervention group were scheduled for a care transitions clinic visit with a clinical pharmacist approximately 72 h post discharge, and prior to the post-hospitalisation, primary care-provider visit. The visit involved performing a complete medication history, identifying and resolving medication discrepancies, creating a current medication list for both the medical record and the participant, and counselling on appropriate medication use. During these visits, the pharmacist identified discrepancies between the best possible medication discharge list and the discharge summary, and characterised medication discrepancies using predefined categories Study participants in the usual care group were scheduled to see their primary care provider for a post-hospitalisation visit with no interim pharmacist intervention. Medication discrepancies of study participants not attending care transitions visits were iden-

	tified and characterised by study personnel in the same manner as those in the intervention group Study personnel reviewed study participants' medical records to quantify 30-day ED visits and rehospitalisation at the study institution. All study participants received a phone call approximately 30 days after discharge to report hospitalisations or ED visits at outside institutions. Only hospitalisations and ED visits at the study institution were included for those participants who were not able to be contacted after 3 phone call attempts Both the intervention and control group received clinical pharmacy services for the family medicine inpatient service and outpatient family medicine clinic. Inpatient clinical pharmacists conducted rounds with the medical team daily, reviewed and monitored medications for effectiveness and safety, and made recommendations to the physician staff to optimise medications. Participants in both groups received this usual care from the inpatient pharmacist. The role of the inpatient pharmacist in the study was to collaborate with the inpatient medical team to create a BPMDL for all study participants just prior to discharge. The BPMDL was used to identify medication discrepancies, and it served as the gold standard list of medications that the participant should take after discharge. The BPMDL accounted for home medications, medication changes made during the hospitalisation, and medications that should be initiated or discontinued on discharge
Outcomes	The 3 prespecified primary outcomes of this study were a composite of the occurrence of a hospital admission or an ED visit within 30 days after hospital discharge and the resolution of medication discrepancies before the primary care provider visit. Secondary outcomes include the individual rates of rehospitalisation and ED visits within 30 days after discharge
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	For the first year of study, a random number generator was used to randomise participants. For the second year, block randomisation with a block size of 4 was used
Allocation concealment (selection bias)	Low risk	A computer was used to randomise
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Participants did not know they were receiving the intervention, however, pharmacists may have been aware that they were delivering the intervention
Incomplete outcome data (attrition bias) All outcomes	High risk	Half of the intervention participants did not participate in the clinic visit
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Hospital admissions and emergency room visits are objective outcomes

Hawes 2014 (*Continued*)

Selective reporting (reporting bias)	Low risk	There was no evidence of selective reporting.
Protection against contamination bias	Unclear risk	It cannot be determined if the control group was contaminated by the intervention
Other bias	Unclear risk	Small sample size. Also, recall bias may have operated as participants provided a self-report of hospitalisations and ED visits outside of the study institution. It is not clear what was the final analysis sample

Holland 2005

Methods	RT Setting: home visit study (primary care) Study duration: 6 months
Participants	872 participants in a home visit study. Researchers recruited patients from four general hospitals and six community hospitals if they were aged ≥ 80 years, admitted as an emergency, intended to be discharged to their own home or warden-controlled accommodation, and prescribed ≥ 2 drugs on discharge Exclusion criteria: participants received dialysis treatment and participation in an intensive discharge service on 1 site Age (years) (mean ± SD): intervention 85.4 (4); control 85.5 (4); not significant Sex female n (%): intervention 262 (61.1); control 272 (63.8); not tested for significance Country: UK Comorbidity: baseline diagnosis: cardiovascular (total): intervention 134 (31.2), control 144 (33.8); myocardial infarction/angina: intervention 57 (13.3), control 65 (15.3); heart failure: intervention 38 (8.9), control 34 (8.0); musculoskeletal (total): intervention 61 (14.2), control 65 (15.3); fracture: intervention 37 (8.6), control 40 (9.4); gastrointestinal (total): intervention 47 (11.0), control 54 (12.7); respiratory (total): intervention 48 (11.2), control 49 (11.5); COPD/asthma: intervention 15 (3.5), control 13 (3.1); lower respiratory tract infection: intervention 16 (3.7), control 22 (5.2); neurological: intervention 40 (9.3), control 25 (5.9); stroke/transient ischaemic attack: intervention 16 (3.7), control 14 (3.3); senility/dementia: intervention 16 (3.7), control 6 (1.4); genitourinary: intervention 17 (4.0), control 16 (3.8); cancer (total): intervention 15 (3.5), control 7 (1.6); other or unclassified: intervention 67 (15.6), Control 66 (15.5) Sociodemographic: not mentioned Ethnicity: not mentioned Participants recruited between October 2000 and December 2002
Interventions	Initial referral to a review pharmacist included a copy of the participant's discharge letter. Pharmacists arranged home visits at times when they could meet participants and carers. Pharmacists assessed participants' ability to self-medicate and drug adherence, and they completed a standardised visit form. Where appropriate, they educated the participant 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. Where a compliance aid was recommended, this was provided within the

	trial and a filling fee was paid to the local pharmacist. 1 follow-up visit occurred at 6-8 weeks after recruitment to reinforce the original advice Control participants received usual care.
Outcomes	The primary outcome was total number of emergency admissions to hospital over 6 months. Secondary outcomes included deaths, admissions to residential homes and nursing homes, and self-assessed QoL measured using the EQ-5D. Participants also rated their health on a visual analogue scale from 100 (perfect health) to 0 (worst imaginable health). The EQ-5D and visual analogue scales were collected at baseline, 3 months, and 6 months. Data were collected on emergency admissions from hospital episode statistics
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Third party telephone randomisation based on a computer-generated sequence in blocks of varying length. Randomisation appeared adequate
Allocation concealment (selection bias)	Low risk	Sequence was concealed based on what is noted above about sequence generation
Blinding of participants and personnel (performance bias) All outcomes	High risk	This was not done as stated in the manuscript, "Because of the nature of the intervention, no "placebo" could be provided. Participants were told after randomisation which group they were in."
Incomplete outcome data (attrition bias) All outcomes	Low risk	Follow-up of the main outcome (hospital admissions) was good-only 3% of participants withdrew or were lost to follow-up
Blinding of outcome assessment (detection bias) All outcomes	Low risk	This is less important for our purpose as we are looking at objective outcomes (hospitalisations, ED visits, and mortality)
Selective reporting (reporting bias)	Low risk	No evidence of selective reporting
Protection against contamination bias	Unclear risk	It can not be determined if the control group has been contaminated by intervention
Other bias	Low risk	There is no other bias.

Ibrahim 2013

Methods	RT Setting: community participants Follow up: 3 months
Participants	240 participants discharged to the community for the first time on oral anticoagulant warfarin (regardless of strength, gender, or age) There was no significant difference between the groups in terms of age, all participants 60.2 years ± 17.84 Sex of participants: male 160 (58.3%). There was no statistically significant difference found between the groups based on indication for anticoagulation, with atrial fibrillation representing the most common indication. All participants lived close to the participating medical centre and could access it easily Country: United Arab Emirates Comorbidity: atrial fibrillation: 82 (34.2%), valve replacement: 37(15.4%), CHF:32 (13.3%), peripheral artery disease: 8 (3.33%), left ventricular thrombus: 7 (2.91%), stroke: 9 (3.75%)
Interventions	Intervention (Group A) was the 'counselled' group, whereas, control (Group B) was the 'non-counselled' group After initial physician/pharmacist consultation in a standard care setting, 1 group was thoroughly counselled, defined by the following: • Once-a-week telephone consultation reviewing a series of pre-designed set of questions (same questions asked weekly) • 2 home visits per month per participant by either a nurse or a pharmacist (reviewing questions and basic information). Visits were 12-14 days apart, generally. • Any additional contact as requested by the participant in the intervention group. The other group received no follow-up consultation other than what was ordered by their own physician in a standard care setting. This group was asked only to visit the anticoagulation clinic twice a month for 3 months to evaluate international normalised ratio levels
Outcomes	Number of adverse events, emergency visits and inpatients admissions
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Randomisation is not described
Allocation concealment (selection bias)	Unclear risk	The first 240 participants discharged or prescribed for the first time warfarin (regardless of strength, gender, or age) were divided randomly and assigned a intervention or control group

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not fully described: separation of intervention and control groups is not exclusive
Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss of participants from the study
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not described how and who measured the outcomes
Selective reporting (reporting bias)	Low risk	The study reported the proposed outcome.
Protection against contamination bias	Unclear risk	It is not clear if the control group was contaminated by the intervention
Other bias	Unclear risk	Not applicable

Kaczorowski 2011

Methods	2-arm, community, cluster-randomised trial Study duration: 3 years 39 eligible communities were stratified, geographically defined according to municipal boundaries, by population size (3 strata) and geographical location (4 strata). An independent expert in cluster-randomised trials then used a random number generator to randomly allocate communities in each stratum to receive either CHAP or no intervention
Participants	39 communities (148,589 participants) initially and 145,441 participants after follow-up post intervention Setting: 39 eligible communities, geographically defined according to municipal boundaries, by population size (3 strata) and geographical location (4 strata); community-based Sex male (%): intervention communities 42.65 ± 1.19, control communities 42.92 ± 2.16 Country: Ontario, Canada Comorbidity: No. of prescription drugs in previous year: control communities: 7.25 (0.49), intervention communities: 6.98 (0.54) No. of comorbidity groups in previous 2 years: control communities: 7.31 (0.30), intervention communities: 7.17 (0.50) Charlson comorbidity index in previous 2 years: control communities: 0.57 (0.09), intervention communities: 0.58 (0.11) Diabetes (%): control communities: 22.16 (2.34), intervention communities: 21.20 (2.79) History of congestive heart failure (%): control communities: 12.19 (1.91), intervention communities: 12.45 (2.34) Rurality index: control communities 28.96 (13.60), intervention communities: 31.63 (14.09)

	Low-income status (%): control communities: 16.95 (8.55), intervention communities: 18.57 (11.33) Ethnicity: Not stated.
Interventions	Communities were randomised to receive CHAP (n = 20) or no intervention (n = 19) In CHAP communities, residents aged ≥ 65 were invited to attend volunteer-run cardiovascular risk assessment and education sessions held in community-based pharmacies over a 10-week period; automated blood pressure readings and self-reported risk factor data were collected and shared with participants and their family physicians and pharmacists In both intervention and control arms, residents received the usual health promotion and healthcare services available to all Ontarians under its publicly financed universal health insurance programme
Outcomes	Rates of hospital admission for acute myocardial infarction, CHF, and stroke in these 39 communities and the 2001 census population estimates for people aged ≥ 65 years and over for power calculations
Notes	A potential limitation of CHAP is the short duration of the intervention. The 10-week exposure to CHAP may be too short to affect hospital admission rates

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	The 39 eligible communities were stratified by size of the population ≥ 65 years (3 groups) and geographic location (4 groups) , forming seven substrata Communities within each stratum were randomly allocated to either the intervention (n = 20) or control arm of the study (n = 19) by an independent expert in cluster-randomised trials not associated with the study
Allocation concealment (selection bias)	Low risk	The independent expert in cluster-randomised trials was not associated with the study
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Although intervention community members (older adults, family physicians, volunteers, pharmacists) were clearly aware of their group assignment, the names of control communities were not publicised and control community members were not notified that the study was taking place

Kaczorowski 2011 (*Continued*)

Incomplete outcome data (attrition bias) All outcomes	Low risk	No attrition reported. Cluster-randomised trial of communities reporting rates of hospitalisation
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Though unlikely, community members' knowledge of the evaluation could influence outcomes, but hospitalisation rates were retrieved from a population-based administrative health dataset
Selective reporting (reporting bias)	Low risk	Data retrieved from routinely collected, population-based administrative health data
Protection against contamination bias	Unclear risk	It is hard to determine if the control group is contaminated with the intervention
Other bias	High risk	Short duration of the intervention may have had an impact on detection of outcomes such as hospital admissions. We considered other bias due to cluster randomisation

Korajkic 2011

Methods	RT Setting: ambulatory setting 9 months
Participants	70 participants Ambulatory setting Attendees at a heart failure outpatient clinic, > 18 years, had New York Heart Association class II, III or IV heart failure, stable signs and symptoms of heart failure, clinically euvolaemic, daily frusemide dose up to a maximum of 320 mg, treatment with other drugs such as beta-blockers, digoxin, vasodilators and spironolactone was permitted Participants were excluded if they were not on frusemide; were on a daily frusemide dose above 320 mg and/or thiazide diuretic; had baseline renal impairment (serum creatinine concentration > 200 µmol/L or on dialysis); had a severe psychiatric illness or moderate-severe dementia; life expectancy of < 3 months; severe hearing impairment or legal blindness; or had difficulty understanding and speaking English and did not have an interpreter or family member to assist. Other exclusions included scheduled cardiac surgery; heart transplant candidacy; inability to give informed consent; and no access to a telephone
Interventions	Pharmacist intervention focused on participants improving self-care, recognising symptoms of fluid retention, measuring weight daily and self-adjusting diuretic dose using frusemide Intervention group: participants assigned to the intervention group received usual care

	plus pharmacist intervention The intervention was provided to every participant in the intervention group and consisted of a 30-min educational session during the clinic appointment. The pharmacist intervention focused on participants improving self-care, recognising symptoms of fluid retention, measuring weight daily and self-adjusting diuretic dose using a flexible frusemide dose-adjustment regimen, and improving knowledge and understanding of heart failure and heart failure medications Usual care (control group): usual care was provided to all of the eligible participants by a cardiologist, heart failure nurse co-ordinators and a dietitian during the clinic appointment. Usual care consisted of assessment of clinical status and medications, education on daily weight measurement, diet, fluid and sodium management, and recognition of signs and symptoms of fluid retention and dehydration. In case of a sudden increase in weight of more than 1 kg/d for 2 d, participants were encouraged to contact the heart failure nurse co-ordinators for advice in consultation with the cardiologist to self-adjust their frusemide dose. The heart failure nurse co-ordinators followed up participants 48 h after a dose adjustment to assess if their weight had decreased and condition improved The key difference between the groups was that the control group called a heart failure nurse co-ordinator to discuss frusemide dose modification, while the intervention group adjusted the diuretic dose themselves
Outcomes	Hospital readmissions due to fluid overload: measured at 1st, 2nd and 3rd months
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Randomisation occurred after selection criteria had been observed. No description of the randomisation method/sequence generation was presented
Allocation concealment (selection bias)	Unclear risk	A significant number of heart failure participants were not good candidates for the intervention. Only 1 in 3 participants who met inclusion criteria remained eligible after application of exclusion criteria
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	It is unclear if participants were blinded to the intervention
Incomplete outcome data (attrition bias) All outcomes	Low risk	All participants completed the study.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Assessments and readmissions were evaluated and confirmed by an independent doctor blinded to the randomisation using

Korajkic 2011 (*Continued*)

		data from participants, hospital admissions records and medical records
Selective reporting (reporting bias)	Low risk	All outcomes were reported as mentioned at the start of the trial
Protection against contamination bias	Unclear risk	It can not be determined if the intervention group interacted with the control group
Other bias	Unclear risk	The intervention was delivered by the same pharmacist. It precludes study of other factors, such as pharmacist attitudes or behaviours that may have promoted delivery of the intervention and limit the generalisability of the intervention This study was conducted at a single institution, and the results may reflect local population characteristics and patterns of care

Krska 2001

Methods	RT Duration of study: 3 months
Participants	332 participants completed study (168 intervention and 164 control) Setting: general practice Diagnostic criteria: the inclusion criteria for participants were ≥ 65 years, regular request for ≥ 4 medicines via the computerised repeat prescribing system and ≥ 2 chronic diseases. Exclusion criteria were dementia and being considered by the GP to be unable to cope with the study Age (years) (mean ± SD): intervention 74.8 (6.2), control 75.2 (6.6) Sex female n (%): intervention 95 (56.5%), control 106 (64.6%) Country: UK Comorbidity: mean no. of chronic diseases: intervention 3.9 (1.4), control 3.8 (1.4), P = 0.968 Sociodemographics: nothing of note Ethnicity: not mentioned Date of study: not mentioned but paper received by journal on 23 December 1999
Interventions	1 intervention group Intervention group: a pharmaceutical care plan was drawn up for each intervention group participant, listing all potential and actual pharmaceutical care issues, together with the desired output(s), the action(s) planned to achieve the output(s) and the outcomes of any potential pharmaceutical care issues already resolved by the pharmacist. Copies of the plan were inserted in the participants' medical notes and given to their GP, who was asked to indicate their level of agreement with each pharmaceutical care issue identified and with the actions. The pharmacist then implemented all remaining agreed actions, assisted by other practice staff where appropriate Control participants were similarly interviewed and pharmaceutical care issues identified,

	although no pharmaceutical care plan was implemented. Participants were advised to consult any usual carers or health-care professionals in response to direct queries during interview
Outcomes	Number of hospital admissions
Notes	The pharmacists undertaking the medication review also administered the SF-36 questionnaire and identified all care issues. There is also potential for GPs receiving recommendations for some participants to increase their tendency to note similar issues in control participants. In some cases the care plan was not fully implemented by 3 months

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Using random number tables, 1 practice from each of the 6 resultant categories was selected and invited to participate. 1 practice refused and a further practice was randomly selected. Participants were randomly allocated to the intervention or control group
Allocation concealment (selection bias)	Unclear risk	Although a random number table was used to select practices, it was not clear whether participant assignment to intervention and control groups was concealed
Blinding of participants and personnel (performance bias) All outcomes	Low risk	This was adequate because pharmacists only treated intervention participants and did not know that the participants they interacted with were in a study. Also, participants did not appear to know whether they were receiving an intervention or not
Incomplete outcome data (attrition bias) All outcomes	Low risk	Equal numbers of participants in the control and intervention groups withdrew from the study. Around 14% to 15 % of the participants withdrew in each group
Blinding of outcome assessment (detection bias) All outcomes	Low risk	This is less important for our purpose as we are looking at objective outcomes (hospitalisations, ER visits, and mortality)
Selective reporting (reporting bias)	Low risk	There is no evidence that there was selective reporting of results
Protection against contamination bias	High risk	It can not be determined if the control group was contaminated with the intervention group

Krska 2001 (*Continued*)

Other bias	Unclear risk	In some cases, the care plan had not been fully implemented by the 3-month follow-up

Lapane 2011

Methods	Cluster-RT Study duration: 2 years
Participants	6523 participants Final sample: 1769 control, 1769 intervention Diagnostic criteria: not relevant as homes were the unit of analysis not individuals Age (years) (mean ± SD): average age of residents was not reported. At baseline 16% of the residents in both intervention and control homes were aged 65-74 years, 36% in intervention homes and 35% in usual care homes were 75-84 years, and 40% of the residents in the intervention homes and 36% in the usual care homes were ≥ 85 years. During the intervention period, 15% in both groups were 65-74 years, 39% were 75-84 years, and 39% were ≥ 85 years Sex, female n (%): at baseline, 72% of the residents in the intervention homes and 68% in the usual-care homes were female. During the intervention period, 74% of the residents in the intervention and usual-care homes were female Country: USA Comorbidity: (intervention, control), dementia (35.4, 43.4); Alzheimer's disease (12.7, 14.6), cancer (8.3, 12.1), diabetes mellitus (27.5, 31.0), cerebrovascular accident (22.2, 22.4), heart failure (26.5 , 28.5), coronary artery disease (18.6, 16.2), arrhythmia (15.8, 15.8), hypertension (64.9, 61.8), other cardiovascular disease (23.6, 28.0) Sociodemographics: nothing reported other than race Ethnicity: 18% in intervention group and 11% in usual care group were minority race at baseline. During the intervention period, 19% of both groups were minority race Date of study: 2003-2004
Interventions	Professional intervention The overarching idea was to use health information technology to engage consultant pharmacists and nursing staff to identify residents at risk for delirium and falls, implement proactive monitoring plans as appropriate, and provide reports to assist consultant pharmacists in conducting the medication regimen review Intervention: A Geriatric Risk Assessment MedGuide database for falls and delirium was integrated into the pharmacies' commercial pharmacy software system (Rescot LTCP System) for the intervention homes Control: usual care
Outcomes	Incidence of potential delirium, falls, hospitalisations potentially due to adverse drug events, and mortality
Notes	Residents in the intervention homes experienced fewer falls, less potential delirium, and death, but more hospitalisations than in the comparison homes. In new admissions, there appeared to be a trend toward lower mortality (adjusted hazard ratio 0.88, 95% CI 0.66 to 1.16) and a lower overall hospitalisation rate (adjusted hazard ratio 0.89, 95% CI 0.72 to 1.09) and a clear reduction in the rate of potential delirium (adjusted hazard

Lapane 2011 (*Continued*)

	ratio 0.42, 95% CI 0.35 to 0.52) in the intervention homes than the comparison homes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Cluster-randomisation
Incomplete outcome data (attrition bias) All outcomes	Low risk	All participants were reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated
Selective reporting (reporting bias)	Low risk	All outcomes were reported.
Protection against contamination bias	Low risk	It can not be determined if the intervention group was contaminated with the control group
Other bias	Unclear risk	There is no evidence of the presence of other bias. We considered other bias due to cluster randomisation

Lenaghan 2007

Methods	RT 6 months
Participants	136 participants registered with 1 general practice (1 participant from each group withdrew shortly after randomisation) Home-based > 80 years, living at home, taking ≥ 4 oral medications, and had ≥ 1 additional medicine-related risk factor Participants were excluded if they were resident in a care home or if there was documented use of an adherence aid Age: intervention 84.5 years, control 84.1 years (no SD supplied) Gender female: intervention 46 (67.6%), control 42 (63.6%) Country: UK Sociodemographics: living alone: intervention 44 (64.7%), control 43 (65.1%); social class (I, II, III): intervention 33 (48.5%), control 29 (43.9%); 9% of practice were aged over 80 years (twice the national average)

	Ethnicity: 98.5% of the local town population were white, compared to 90.9% for England
Interventions	Comparing home-based medication review with standard care The intervention: the pharmacist was asked to identify cases where adverse drug reactions or drug interactions may be occurring. This was noted using a tick box on the medication review form after detailed information had been gained from the participant regarding all over-the-counter and prescribed drugs The control group received standard care
Outcomes	• Non-elective hospital admissions during the 6-month follow-up period • Deaths • Admission to care homes • Number of drug items prescribed • Self-assessed QoL
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	No indication of random sequencing
Allocation concealment (selection bias)	Low risk	Randomisation was carried out by a third party and was stratified by whether the participant lived alone
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	It is unclear if participants were blinded to the intervention
Incomplete outcome data (attrition bias) All outcomes	Low risk	Attrition reported and reasons for attrition presented
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Outcome data on hospital admissions were provided by hospital episode statistics (not self-report) and are therefore unlikely to be biased
Selective reporting (reporting bias)	Low risk	Outcome data on hospital admissions were provided by hospital episode statistics (not self-report) and are therefore unlikely to be biased
Protection against contamination bias	Unclear risk	Unclear
Other bias	High risk	Research was carried out in 1 rural general practice with a single experienced review pharmacist, which has a bearing on the generalisability of the results

Lowrie 2012

Methods	Study design: a cluster-randomised design, this provides protection against contamination across trial groups when trial participants are managed within the same setting. Participants in practices in the UK were managed by all GPs within the practice; the control intervention was mediated by GPs, this precluded individual, participant-level randomisation Study duration: median follow-up was 4.7 years
Participants	2164 participants (174 practices) Setting: general practice Diagnostic criteria: consenting participants were eligible if aged ≥ 18 years and had left ventricular systolic dysfunction confirmed by cardiac imaging conducted at a local hospital (transthoracic echocardiography in 90% of cases). Participants did not have to have symptoms or signs of heart failure. Family doctors received a semi quantitative report of left ventricular systolic function (normal, mild, moderately or severely reduced) instead of ejection fraction Age (years) (mean ± SD): pharmacist intervention, 70.6 (10.3) and control 70.6 (10.1) Sex female n (%): pharmacist intervention 320 (29%), control 329 (31%) Country: UK Comorbidity: hypertension, myocardial infarction, pharmaceutical care issue, coronary artery bypass grafting, atrial fibrillation or flutter, diabetes mellitus, stroke, respiratory disease, asthma Sociodemographics: not mentioned Ethnicity: not mentioned Date of study: from 25 October 2004-6 September 2007
Interventions	1 intervention and 1 control Participants from practices assigned to the intervention were offered a 30-min appointment with a pharmacist. The main aim of this review was optimisation of medical treatment for left ventricular systolic dysfunction according to guidelines (supplementary material online). If there was agreement between the pharmacist and the participant 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. Family doctors provided usual care thereafter No instructions were given to family doctors in the usual care practices. The study pharmacists did not collect information on symptoms or examine the participants as this was not part of their professional training
Outcomes	• Death from any cause or hospital admission for heart failure (the primary outcome) • Death from any cause or hospital admission for a cardiovascular cause • The number of participants admitted to hospital for any reason, for a cardiovascular cause, and for heart failure • The number of deaths attributed to a non-cardiovascular cause
Notes	There was no difference in mortality or hospital admissions between the intervention and the control group. (Mortality from heart failure should be reported in the final analysis as this intervention was targeting heart failure management)
Risk of bias	

Lowrie 2012 (*Continued*)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation was generated by a computer
Allocation concealment (selection bias)	Low risk	Computer
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Cluster randomisation was undertaken
Incomplete outcome data (attrition bias) All outcomes	Low risk	All participants were reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated
Selective reporting (reporting bias)	Low risk	All outcomes were reported
Protection against contamination bias	Low risk	It can not be determined if the intervention group mixed with the control group
Other bias	Unclear risk	Unclear. We considered other bias due to cluster randomisation

Malet-Larrea 2016

Methods	Cluster-RT (pharmacies were the cluster unit of randomisation)
Participants	31; 17 intervention and 14 control, this was also the final sample that was analysed Setting: community pharmacists Diagnostic criteria: participants were ≥ 65, used ≥ 5 medications for ≥ 6 months, with the ability to complete the EuroQol 5D questionnaire
Interventions	Organisational IIntervention group: pharmacists allocated to the intervention group provided the medication with follow-up service according to national guidelines. The medication review with follow-up service started with a comprehensive interview undertaken in a private area of the pharmacy. The pharmacist collected relevant information about the participant's health problems, medicines used, clinical and biological parameters (gathered through medical records provided by the participant or measured in the pharmacy), medication use, lifestyle habits and concerns about diseases and medications. Pharmacists also assessed the level of control of health problems by using information referred by participants' and/or clinical and biological parameters, depending on the type of health problem (i.e. pain versus hyperlipidaemia) and classified every health problem as controlled, uncontrolled or unknown. After performing a comprehensive medication review, the pharmacist identified negative clinical outcomes related to medicines and

	drug-related problems. Subsequently, an action plan was agreed upon by the participant and the physician if required. This medication review with follow-up service was focused on both participants' outcomes and medication use process and required a commitment to follow-up The usual care consisted of dispensing medicines prescribed by physicians and advice on minor ailments
Outcomes	Medication-related hospital admission was the primary outcome of this sub analysis. Hospital admissions were recorded in participants' visits to the pharmacies and the medication related ones were identified through the expert panel after the fieldwork. Kappa values ranging from 0.61 to 1 were considered as an acceptable incidence rate ratio to measure the agreement among experts The cost of hospital admissions estimated by diagnosis-related group was a secondary outcome and the diagnosis-related groups were recorded after the fieldwork
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Pharmacies were randomised to the intervention or control group by an independent researcher
Allocation concealment (selection bias)	Low risk	An independent researcher performed randomisation using a computer-generated list of random numbers
Blinding of participants and personnel (performance bias) All outcomes	High risk	Neither the participants nor pharmacists were blinded.
Incomplete outcome data (attrition bias) All outcomes	Low risk	There was little attrition and comparable rates for intervention and control group
Blinding of outcome assessment (detection bias) All outcomes	Low risk	For the sub analysis, the expert panel was blind as to which group the participants belonged so whether a hospital admission was medication-related was not affected
Selective reporting (reporting bias)	Low risk	No evidence of selective reporting
Protection against contamination bias	Unclear risk	Although pharmacies were randomised to control and intervention groups, informal contact between pharmacists may have led to contamination
Other bias	Unclear risk	There is no evidence of other bias.

Malone 2000

Methods	A prospective, multisite RT Duration of study: 12 months
Participants	Of 1054 participants enrolled at the 9 Veterans Affairs clinics, 523 were randomised to the intervention and 531 to the control group. Of these, 950 participants completed 6-month follow-up questionnaires and 931 completed the study. Of participants completing the study, 447 were in the intervention group and 484 were in the control group Setting: Veterans Affairs clinics Interventions: clinical input by pharmacists Diagnostic criteria: participants were considered at high risk for drug-related problems if they met ≥ 3 of the following criteria: were taking ≥ 5, were taking ≥ 12 doses/d, had ≥ 3 chronic medical conditions, had ≥ 4 changes in their drug regimen over the past year, had a history of noncompliance with drug therapy, or were taking an agent that required therapeutic drug monitoring Age: (years) mean ± SD: 67 ± 10.1 Sex n (%): intervention group 21 (0.04%), control, 20 (0.04%) Country: USA Comorbidity: hypertension, angina, hyperlipidaemia, arthritis, diabetes and COPD Sociodemographics: not mentioned Ethnicity: not mentioned
Interventions	1 intervention and 1 control The intervention group was given a protocol to follow; the protocol indicated that each participant should have ≥ 3 visits with the clinical pharmacist during the study, but participants could be seen as frequently as deemed necessary to ensure appropriate care. Visits were to occur between or concurrent with appointments with the primary care provider or other physicians The control group followed the usual care with no specific protocol given to clinicians
Outcomes	Number of hospitalisations
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Participants were randomly assigned using a central computer
Allocation concealment (selection bias)	Low risk	Computer-based
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not possible
Incomplete outcome data (attrition bias) All outcomes	Low risk	Some participants did not complete the study and were reported in the study

Malone 2000 (*Continued*)

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear how it was done
Selective reporting (reporting bias)	Low risk	All outcomes were reported
Protection against contamination bias	Unclear risk	It is not possible to determine if the control group was contaminated with the intervention group
Other bias	Unclear risk	It is unclear if there are other biases.

Moertl 2009

Methods	Prospective, randomised study design Study duration: 2 years The major limitation of the study was selection bias because only participants who responded to a letter of invitation had the opportunity to take part in the study
Participants	96 participants took part in the study; 48 were randomised to the nurse group and 48 to the non-nurse group Setting: outpatient heart failure clinic Diagnostic criteria: participants who survived index hospitalisation were invited by letter to a visit for treatment optimisation at the outpatient heart failure unit. Among the participants who appeared at the ambulatory visit, those with a verified heart failure diagnosis and residing < 50 km from Vienna were eligible for the nurse intervention and therefore offered to participate in the present study. Baseline evaluation was performed by a cardiologist specialising in the management of heart failure. The ambulatory visit comprised a patient history, physical examination, electrocardiogram, a routine blood analysis, and, if necessary, an echocardiography. Furthermore, blood samples were taken for later analysis of natriuretic peptides. The participants were thoroughly informed about the disease of CHF and recommendations were made regarding medication, self-assessment of weight, blood pressure and pulse, and diet and exercise management The baseline demographic, clinical, and therapeutic characteristics were not statistically different between the nurse group and the non-nurse group Age (years) (mean ± SD): non-nurse, control (66 ± 13); nurse, intervention 70 ± 12 Country: Vienna, Austria Comorbidity: hypertension, diabetes, respiratory diseases Sociodemographics: not reported Ethnicity: Austrian (unclear if they were all white)
Interventions	1 intervention and 1 control. There were 48 participants in each group Intervention: home-based nurse care Participants in the nurse group were visited by a nurse specialised in caring for people with heart failure on the initial visit at the outpatient heart failure unit and then at their home 3, 6, 9, and 12 months after randomisation At home visits, the nurse checked and recorded weight, symptoms and signs of heart failure, heart rate and blood pressure, and organised and reviewed blood analyses on

	demand, especially of electrolytes and renal parameters. Furthermore, the nurse had to check for and, in co-ordination with the treating physician, implement guideline-based medication. Moreover, the nurse was in charge of individualised participant and caregiver education and enhancement of self-management. If the nurse noted any deterioration in the participant's status, she reported to the treating physician or advised the participant to visit the treating physician Control group received the usual care provided
Outcomes	Admission for heart failure at 12 months and 24 months Mortality at 12 months and 24 months
Notes	The major limitation of the study is selection bias because only participants who responded to a letter of invitation had the opportunity to take part in the study See notes to other relevant studies

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	It is unclear how the sequence generation was done.
Allocation concealment (selection bias)	High risk	The major limitation of the study was selection bias because only participants who responded to a letter of invitation had the opportunity to take part in the study
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	It is unclear if participants were blinded to the intervention
Incomplete outcome data (attrition bias) All outcomes	Low risk	There is no incomplete outcome data.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Independent data collector
Selective reporting (reporting bias)	Low risk	All outcomes were reported as mentioned at the start of the trial
Protection against contamination bias	Unclear risk	Unclear
Other bias	High risk	Small sample size

Murray 2004

Methods	RT with a 2 x 2 factorial design using physician and pharmacist interventions, which resulted in 4 groups of participants: physician intervention only, pharmacist intervention only, intervention by physician and pharmacist, and intervention by neither physician nor pharmacist (control) Study duration: 1 year
Participants	Total participants 712 with uncomplicated hypertension Control: (n = 171), pharmacist intervention: (n = 180), physician intervention: (n = 181), dual intervention: (n = 180) Setting: large, inner-city, academic, internal medicine practice affiliated with the Indiana University School of Medicine. The primary venues for this study were the general medicine practice and the Wishard Memorial Hospital outpatient pharmacy, which at the time of the study were located 1 floor apart in the Regenstrief Health Centre Eligibility for this study required that participants had evidence in their electronic medical records of hypertension as an active outpatient diagnosis or, in the absence of such a diagnosis, all of the following: ≥ 2 systolic blood pressure measurements of ≥ 140 mm Hg, ≥ 2 diastolic blood pressure measurements of ≥ 90 mm Hg, and a prescription for ≥ 1 antihypertensive agent. Qualifying antihypertensive agents were ace-converting enzyme inhibitors, b-blockers, calcium channel blockers, oral clonidine and topical patch, diuretics, and other less commonly prescribed drugs such as methyldopa and reserpine. Participants were excluded from taking part if they had evidence (diagnoses or test results) indicating the presence of a cardiovascular complication such as coronary artery disease, myocardial infarction, stroke, heart failure, or renal insufficiency Age mean ± SD: control: 54 ± 11, pharmacist intervention: 54 ± 11, physician intervention: 56 ± 11, dual intervention: 54 ± 11 Gender female n (%): control: 75 (44%), pharmacist intervention: 79 (44%), physician intervention: 78 (43%), dual intervention: 81 (45%) Country: USA Comorbidity: none stated Sociodemographics: potential participants who were able to communicate (could hear and speak English and understand instructions), had access to a working telephone, and were willing to provide written informed consent were enrolled Formal education, mean ± SD (years), control: 11 ± 3, pharmacist intervention: 10 ± 3, physician intervention: 11 ± 3, dual intervention: 11 ± 3 Married (%), control: 30, pharmacist intervention: 29, physician intervention: 28, dual intervention: 30 Number of people in household, mean ± SD , control: 2.3 ± 1.5, pharmacist intervention: 2.6 ± 1.7, physician intervention: 2.3 ± 1.4, dual intervention: 2.2 ± 1.2 Live alone (%), control: 32, pharmacist intervention: 28, physician intervention: 32, dual intervention: 30 Ethnicity: unknown; control: 57 (33%), pharmacist intervention: 61 (34%), physician intervention: 58 (32%), dual intervention: 58 (32%)
Interventions	Physician intervention The computer-based ordering system generated care suggestions for both intervention and control groups; however, the suggestions were displayed by the computer to physicians and/or pharmacists for participants randomised to the appropriate intervention groups. This allowed the researchers to assess the numbers and types of interventions that the control group was eligible to receive as well as those in the 3 intervention groups. For participants in the physician intervention group, all care suggestions based solely on

	earlier Regenstrief medical records system data were generated at the time that the encounter form was printed and were displayed at the end of the drug list. All hypertension care suggestions for intervention participants were displayed as "suggested orders" on physicians' workstations when they wrote orders after participant visits. This computer screen displayed the actual suggested order, possible actions for each order (order or omit), and a brief explanation of the rationale for the order. Physicians could list full guidelines and literature citations associated with the specific suggestions by using the workstation's 'help' key Pharmacist Intervention When any participant brought a new or refill prescription (written in any affiliated clinic, physician's office, or Wishard Hospital emergency department) to the Wishard outpatient pharmacy, a pharmacy technician entered the data into the Regenstrief medical records system pharmacy module. This was required for all prescriptions because it was the only way to generate and complete a financial transaction for prescriptions in the outpatient pharmacy. After entering prescription data, a high-speed printer created a label to affix to the participant's drug container. The technician who filled the prescription notified the pharmacist for all intervention participants. The labelled drug product was checked by a pharmacist who dispensed the agent to the participant and provided counselling. For this study the researchers created the pharmacist intervention recording system. This software programme was used by all Wishard pharmacists to document all pharmaceutical care interventions provided to any outpatient. For participants enrolled in this study only (regardless of study group), care suggestions generated by the Regenstrief medical records system or the outpatient workstations (in response to data entered by the physician, e.g. new antihypertensive prescriptions) were stored in the pharmacist intervention recording system. For participants randomised to receive care from an intervention pharmacist who had such care suggestions, the high-speed printer printed a note together with drug container labels directing the pharmacist to the pharmacist intervention recording system to display care suggestions that were identical to those viewed by intervention physicians Physician and pharmacist (dual) Intervention Control group: the control group did not receive any interventions by either physician nor pharmacist
Outcomes	The primary end point was generic health-related QoL. Secondary end points were symptom profile and side effects from antihypertensive drugs, number of emergency department visits and hospitalisations, blood pressure measurements, participant satisfaction with physicians and pharmacists, drug therapy compliance, and health care charges
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Participants were taken on a next-in-line basis - no random sequence, but sequentially allocated to either intervention or control. Physicians were randomly assigned to practices. There were no details of how randomisation was generated

Murray 2004 (*Continued*)

Allocation concealment (selection bias)	Low risk	Participating physicians and pharmacists were unaware of the study hypothesis
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Participating physicians and pharmacists were unaware of the study hypothesis. All research assistants and interviewers were blinded to group assignment
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	All reported
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Data extracted from Regenstrief medical records system records for ED visits, hospitalisations and mortality
Selective reporting (reporting bias)	Low risk	All selected outcomes were reported. Random audit (10%) of all paper records from intervention and control groups
Protection against contamination bias	Low risk	It is hard to determine if the control group was contaminated with the intervention group
Other bias	Unclear risk	Unclear. There is no evidence of other bias

Nabagiez 2013

Methods	RT Study duration: 13 months
Participants	701 participants Setting: home Diagnostic criteria: all participants discharged to home following coronary artery bypass graft procedure and/or valve repair or replacement and/or aneurysm repair, or other cardiac procedure Age (years) (mean ± SD): intervention group: 62.8 (10.6), control group: 63.2 (10.9) Sex female n (%): intervention group: 73 (21.5%), control group: 88 (24.4%) Country: USA Comorbidity n (%): diabetes mellitus: intervention 123 (34.0), control 111 (32.6); hypertension: intervention 268 (74.2), control 283 (83.2); dyslipidaemia: intervention 263 (72.8), control 274 (80.5); dialysis: intervention 8 (2.2), control 7 (2.0); cerebrovascular accident: intervention 15 (4.1), control 9 (2.6); COPD: intervention 44 (12.1), control 30 (8.8); peripheral vascular disease: intervention 29 (8.0); control 25 (7.3); previous myocardial infarction: intervention 146 (40.4), control 144 (42.3); CHF: intervention 51 (14.1), control 48 (14.1); arrhythmia: intervention 37 (10.2), control 39 (11.4) Sociodemographics: not stated Ethnicity: intervention group: 289 (84.4%) white, 53 (15.5%) non-white; control group:

	318 (88%) white, 43 (11.9%) non-white Date of study: August 2009-September 2011
Interventions	1 intervention group 340 participants, control 361 participants Hospital-employed, cardiothoracic physician assistants conducted home visits on post-discharge days 2 and 5, with occasional variation due to participant availability and Sundays, on which no house calls were made. The same hospital-based physician assistants responsible for perioperative and intraoperative care were assigned to make house calls. During a house call, the physician assistant performed a focused physical exam and reviewed the participant's medications. Adjustments were made to the participant's medications, and new medications were prescribed as necessary. The surgical wounds were examined carefully and all participant concerns were addressed. Prescriptions were written for antibiotics, blood work, or imaging studies when indicated. Arrangements were made if the participant needed to be evaluated as an inpatient. All findings were documented on the visit form Both groups were seen in the office on post-discharge weeks 2 and 4 The control group was seen at home by standard visiting nurses without any specialty training or expertise in caring for people with cardiac surgery
Outcomes	Hospital admissions/number of people admitted to hospital
Notes	Not sure of randomisation and these were hospital-based physician assistants working in homes

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Unclear from the document
Allocation concealment (selection bias)	Unclear risk	Unclear from the document
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Unclear from the document
Incomplete outcome data (attrition bias) All outcomes	High risk	19% of the participants in the intervention group refused to participate or failed to respond to requests to participate
Blinding of outcome assessment (detection bias) All outcomes	Low risk	This is less important for our purpose as we are looking at objective outcomes (hospitalisations, ED visits, and mortality)
Selective reporting (reporting bias)	Low risk	No evidence of this
Protection against contamination bias	Low risk	No contamination

Nabagiez 2013 (*Continued*)

Other bias	Unclear risk	Unclear. There is no evidence of other bias

Okamoto 2001

Methods	Prospective, randomised, comparative study Duration: 6 months
Participants	330 participants with mild-to-moderate essential hypertension Age, years (mean ± SD): intervention 61.95 ± 11.4, control 61.71 ± 11.3, P = 0.85 Sex female n (%): intervention 72 (44%), control 90 (54%) Country: USA, California No statistically significant differences were noted between the groups. Concurrent disease (number of participants) intervention 98, control 95, P = 0.74 Smoker (number of participants): intervention 15, control 9, P = 0.18 Alcohol consumer (number of participants): intervention 12, control 9, P = 0.47 Sociodemographics: not reported Ethnicity: not reported
Interventions	Hypertension care provided by either the pharmacist-managed hypertension clinic or physician-managed general medical clinics In the pharmacist-managed hypertension clinic, a clinical pharmacist managed the treatment of participants, who made up the experimental group. Physicians were contacted and provided consent for any therapeutic changes but were asked not to adjust drug therapy unless a lack of intervention would be dangerous for the participant In the physician-managed clinic, physicians managed the treatment of participants independently with no pharmacy intervention; this was the control group Participants randomly assigned to the pharmacist-managed hypertension clinic group were counselled by the clinical pharmacist. The pharmacist informed the participants that an effort would be made to decrease the number of drugs they took for hypertension or to alter their therapy by administering more appropriate or less expensive drugs to achieve similar or improved blood pressure control. The pharmacist determined the most appropriate antihypertensive regimen for the participant and ordered laboratory tests as needed. The pharmacist also provided education on nonpharmacologic ways to control blood pressure Control group: participants randomised to the physician-managed clinic group were referred back to their primary care provider for hypertension treatment. These participants received no intervention, and physicians treated them in the customary manner
Outcomes	Number of hospitalisations
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Randomisation, but no description of sequence generation

Okamoto 2001 (*Continued*)

Allocation concealment (selection bias)	Unclear risk	Not clear. The document does not state whether the allocation was concealed or not
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	It is unclear if participants were blinded to the intervention
Incomplete outcome data (attrition bias) All outcomes	Low risk	Attrition rates in both groups are comparable for various reasons
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Method of data collection is not clear.
Selective reporting (reporting bias)	Low risk	All outcomes were reported as mentioned at the start of the trial
Protection against contamination bias	Unclear risk	It is hard to determine if the intervention group was contaminated with the control group
Other bias	Unclear risk	It would have been more desirable to have only newly diagnosed participants, but the sample size was already small. Results cannot be extrapolated to other physician groups

Olesen 2014

Methods	RT Duration: not provided
Participants	630 participants, 315 intervention, 315 control. Final sample analysed 253 intervention, 264 control Setting: pharmaceutical care was provided at home Diagnostic criteria: participants aged ≥ 65 on 5 prescription medications taken without assistance
Interventions	Organisational Participants in the 'pharmaceutical care' group were visited at home by a pharmacist at the beginning of the project. The pharmacist examined the medicines list with regard to possible side-effects, interactions, and administration, then tried to make the regime less complex, informed the participants meanwhile about the drugs, listened to questions concerning the drugs, handed over information leaflets, and motivated adherence. Nine different pharmacists were involved and adhered to the Danish manual for pharmaceutical care: 'Medication Review - Managing Medicine Manual'. The aim of the 'Medication Review - Managing Medicine' is to prevent, identify, and resolve drug-related problems and to contribute to rational pharmacotherapy for participants and society

Olesen 2014 (*Continued*)

	Control participants were not provided any intervention.
Outcomes	The primary endpoint was treatment adherence assessed by a pill-count in all participants during 1 year. Only oral prescription drugs taken throughout the study period were included in the adherence calculation. In addition, a project nurse visited all participants initially, then at 6 and 12 months to photograph pills to be counted later by a 'counter pen' (a combination of a marker and a digital counter). The adherence rate (%) per drug was calculated as mean adherence rate during 1 year. We also calculated adherence rates for the intervals of 0-6 and 6-12 months. Secondary outcome measures included drug-related problems, hospitalisations and mortality measured during the intervention year and at 2-year follow-up
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Participants were randomly assigned to control and intervention groups
Allocation concealment (selection bias)	Unclear risk	No mention is made of allocation concealment.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Pharmacist was aware of whether the participant was in the intervention group
Incomplete outcome data (attrition bias) All outcomes	Low risk	Little differential attrition between intervention and control groups
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Hospitalisations and mortality are objective outcomes.
Selective reporting (reporting bias)	Low risk	No evidence of selective reporting
Protection against contamination bias	Low risk	Control group participants were not provided any pharmaceutical intervention
Other bias	Unclear risk	According to the study authors, control participants were not exposed to any intervention, but something was done and this was not specified

Pai 2009

Methods	Prospective, randomised, controlled, longitudinal, 2-year pilot study
Participants	104 participants, nonprofit university-affiliated dialysis clinic Participants > 18 years with end-stage renal disease who were undergoing a stable haemodialysis regimen for at least 3 months Age (yrs ± SD): intervention 56.3 ± 15, control 60.5 ± 14.7 Sex female n (%): intervention 22 (39), control 28 (60), P < 0.03 Country: USA, New Mexico Baseline clinical characteristics: length of time participant had been receiving haemodialysis (years): intervention 2.8 ± 1.8, control 2.4 ± 2.2 Number of drugs used: intervention 10 ± 4, control 10 ± 4 Cost of drugs (USD); intervention 430 ± 197, control 451 ± 267 Comorbidity: end-stage renal disease aetiology Diabetes mellitus n (%): intervention 22 (39), control 23 (49) Hypertension n (%): intervention 18 (32), control 12 (26) White n (%): intervention 13 (23), control 16 (34) Hispanic n (%): intervention 17 (30), control 15 (32) Native American n (%): intervention 13 (23), control 5 (11)
Interventions	Intervention group: effects of pharmaceutical care, consisting of 1-1, in-depth drug therapy reviews conducted by a clinical pharmacist, versus Control group: standard care, consisting of brief drug therapy reviews conducted by a nurse on several participant outcomes in ambulatory participants undergoing haemodialysis Participants assigned to pharmaceutical care had drug therapy reviews conducted by a nephrology-trained clinical pharmacist or 1 of 2 pharmacists completing postdoctoral training in nephrology pharmacotherapy. Types of drug-related problems were recorded and evaluated by using a previously described method. All drug-related problems were assigned to 10 possible categories: untreated indications, improper drug selection, sub therapeutic dosage, overdose, adverse drug reactions, drug interactions, failure to receive drugs, medical record discrepancy, inadequate education of participant or health care professional, and drug use without indication. The drug-related problems were further categorised into therapeutic drug classes, and the outcome related to the drug-related problem intervention was captured The standard care group served as the control group. The participants in the standard care group received periodic drug profile updates by dialysis nursing staff as mandated by the dialysis clinic policy and procedure. These are typically brief interactions in which participants are queried as to whether any drugs have changed since the last review
Outcomes	Mortality
Notes	The study experienced high attrition due to death, transplantation, or transfer to a different facility, with about 50% of participants remaining at the end of study The study also did not conduct an assessment of the relationship between drug-related problem resolution and hospitalisations, which could provide useful information as to whether targeted pharmaceutical care interventions would be helpful
Risk of bias	

Pai 2009 (*Continued*)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomly assigned, by dialysis shift but no description of sequence generation
Allocation concealment (selection bias)	Low risk	Randomisation was conducted by the clinic nurse manager, who had no affiliation with the study, by drawing the shift name from an opaque envelope and assigning the first 3 drawn shifts to pharmaceutical care and the remainder to standard care
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Blinding as far as participants and personnel were not communicating - different shifts
Incomplete outcome data (attrition bias) All outcomes	High risk	There was a high level of attrition due to death, transplantation or transfer to a different facility, with about 50% of participants remaining at the end of the study
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome data on hospital admissions were provided by hospital episode statistics (not self-report) and are therefore unlikely to be biased
Selective reporting (reporting bias)	Low risk	All outcomes were reported as mentioned at the start of the trial
Protection against contamination bias	Low risk	It can not be determined if the intervention group was contaminated with the control group
Other bias	Unclear risk	Unclear. It is unclear if there is other bias.

Roberts 2001

Methods	Cluster-RT Study duration: 12 months
Participants	3230 participants Setting: nursing homes Diagnostic criteria: none provided Age: participant characteristics not provided in terms of mean age, just percent of sample in intervention and control groups that were in particular age ranges Sex: participant characteristics not provided Country: Australia Comorbidity: not provided

	Ethnicity: participant characteristics not provided Date of study: unknown although paper was initially received for publication in May 2000
Interventions	1 intervention group The 12-month intervention involved 3 phases: introducing a new professional role to stakeholders with relationship building, nurse education, and medication review by pharmacists who had a postgraduate diploma in clinical pharmacy The clinical pharmacy service model introduced to each nursing home was supported with activities such as focus groups facilitated by a research nurse, written and telephone communication, and face-to-face professional contact between nursing home staff and clinical pharmacists on issues such as drug policy and specific resident problems, together with education and medication review. This was a multifaceted intervention directly targeting nursing homes. Most of the contact with GPs was indirect using the existing relationships between nursing homes and visiting GPs. A number of focus groups and personal interviews about the project were conducted with GPs Control nursing homes continued with usual care.
Outcomes	Mortality was collected at the end of the 12-month study.
Notes	No significant changes were observed in annual mortality rates or frequency of hospitalisations between intervention and control nursing home groups It is unclear from Table 5, which shows the mortality and hospitalisation data, how the study authors arrived at their figures or their conclusions. Therefore, we were unable to use the data to calculate hospitalisations

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Nursing homes were selected for the intervention treatment by random draws from a hat
Allocation concealment (selection bias)	Low risk	Not clear if this was done although the homes were independently assigned to the control or intervention groups. However, according to the EPOC criteria, the risk of bias for this study is low because units, in this case nursing homes, were assigned rather than individuals
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Unclear, although with the objective outcomes that we are interested in this is less of a concern (according to EPOC risk of bias criteria)
Incomplete outcome data (attrition bias) All outcomes	Low risk	Control and intervention groups did not appear to differ in terms of attrition

Roberts 2001 (*Continued*)

Blinding of outcome assessment (detection bias) All outcomes	Low risk	This is less important for our purpose as we are looking at objective outcomes (hospitalisations, ED visits, and mortality)
Selective reporting (reporting bias)	Low risk	No evidence of this
Protection against contamination bias	Low risk	There is indication to suggest that the intervention was contaminated by the control group
Other bias	Unclear risk	The limited duration of the study and size of the sample may have compromised the ability to detect an effect. We considered other bias due to cluster randomisation

Rytter 2010

Methods	RT Study duration: 26 weeks
Participants	148 intervention, 145 control Setting: primary care Age: median, intervention 84 years, control 83 years Sex female n (%): intervention 66%, control 66% Country: Denmark Diagnosis: cardiovascular disease: intervention 45 (30%), control 28 (19%); other intervention 103 (70%), control 117 (81%); P = 0.02 Sociodemographics: housing: living in private home intervention: 95%, control 97%; widow/widower: intervention 59%, control 57%; married: intervention 30%, control 29%; divorced/single: intervention 11%, control 14% Ethnicity: unclear, possibly white Danish Date of study: November 2003-June 2005
Interventions	1 intervention and 1 control The intervention follow-up consisted of 3 contacts. The main intervention was a joint home visit involving both the GP and the district nurse. It was conducted approximately 1 week after discharge and was guided by an agenda Control group: standard care
Outcomes	The primary outcome measures were hospital readmissions of any kind and the concordance between the GP's knowledge of the medical treatment and what the participant was actually taking
Notes	

Risk of bias

Rytter 2010 (*Continued*)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation was generated by a computer.
Allocation concealment (selection bias)	Low risk	Computer
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	This would be impossible
Incomplete outcome data (attrition bias) All outcomes	Low risk	All participants were reported
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Independent team
Selective reporting (reporting bias)	Low risk	All outcomes were reported
Protection against contamination bias	Low risk	There is no indication to suggest that the intervention was contaminated by the control group
Other bias	Unclear risk	It is unclear if there are other risks not accounted for.

Triller 2007

Methods	RT Study duration: 201 days (3-week intervention and 180 days of follow-up)
Participants	154 participants Setting: home Diagnostic criteria: participants had to have a primary or secondary diagnosis of heart failure and were referred to receive skilled nursing services Age (years) (mean ± SD): control: 78.1 (11.2), intervention: 81.3 (9.3), participants had to be ≥ 21 years Female n (%): control: 55 (72), intervention: 56 (73) Country: USA Comorbidity: heart failure Sociodemographics: the catchment area provided participants from urban, suburban, and rural environs and from across all socioeconomic classes. According to census data, 89% of the population of these 3 counties combined is white, and 87% of adults have a high school diploma. Median household income for the counties is approximately USD 47,000 (2003 data). Non-English-speaking participants were included if adequate translation services were available from family members or friends Ethnicity: unknown; it is difficult to ascertain the ethnicity from the information given control 68 (88%), intervention 75 (97%) Date of study: 1 July 2002 to end 2004

Interventions	1 intervention: pharmaceutical care services Pharmaceutical care services consisted of an initial comprehensive in-home medication assessment (concurrent with agency admission) and 2 follow-up visits (7-10 and 18-21 days later). The follow-up visits were contingent on the participant's continued receipt of visiting nurse services (i.e. participants discharged from the visiting nurse before 21 days would not receive all of the pharmacist's planned visits). Throughout the 3-week intervention period, the clinical pharmacist accessed and reviewed all pertinent physician notes and laboratory test values via the National Endowment for the Humanities data system and interacted with prescribers on behalf of the participants as necessary Control participants received the usual care provided by the visiting nurse association. Visiting nurse services (provided to both groups) included basic nursing care and a brief physical assessment and medical history
Outcomes	Hospitalisations and mortality were assessed during a 180 day follow-up period
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	This was adequate: "Patients provided informed consent for study participation and were randomised to receive usual care or usual care plus pharmaceutical care by means of a computer-generated random numbers table in blocks of four."
Allocation concealment (selection bias)	Low risk	This was adequate: "Once informed consent was received, the nurse obtained a baseline quality-of life assessment (using the SF-12) and then accessed a sealed envelope containing the group assignment from the intake office."
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Blinding or a lack of blinding was unlikely to affect the outcome because the usual care group received usual care from nurses whereas the intervention group received usual care plus the services of a pharmacist
Incomplete outcome data (attrition bias) All outcomes	Low risk	Attrition in both the intervention and control groups was comparable
Blinding of outcome assessment (detection bias) All outcomes	Low risk	This is of less concern in our case as all of our outcomes are objective (according to the EPOC risk of bias criteria)

Triller 2007 (*Continued*)

Selective reporting (reporting bias)	Low risk	No evidence of a problem
Protection against contamination bias	Low risk	There is no evidence of contamination between the intervention and the control groups
Other bias	High risk	Small sample may have produced low power to detect an effect. Poor pharmacist-prescriber communication may have reduced efficacy of intervention

Zermansky 2001

Methods	RT of clinical medication review by a pharmacist against normal general practice review Length of study: 12 months (study conducted: June 1999-June 2000)
Participants	Participants from general practices 1188 participants aged ≥ 65 or over who were receiving at least 1 repeat prescription and living in the community Age: mean (SD) intervention, 74 (6.6) control, 73 (6.4) Sex female n (%): intervention 339 (56%), control 325 (56%) Country: UK Comorbidity: not reported Sociodemographics: not reported Ethnicity: not reported
Interventions	1 intervention and 1 control; 601 participants in the intervention and 580 participants in the control group Intervention group: participants were invited to a consultation at which the pharmacist reviewed their medical conditions and current treatment according to a specific algorithm which includes history taking and data gathering, evaluation and implementation stages Control group: participants in the control group continued to receive normal care from their GP and primary healthcare staff. Participants were recalled for review of treatment by the GP according to normal custom in the practice
Outcomes	Hospital admission and mortality
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Randomisation was done by a computer.
Allocation concealment (selection bias)	Low risk	Practice based allocation.

Zermansky 2001 (*Continued*)

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	This would be impossible.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Some participants did not complete the study and were reported in the study
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No explanation given.
Selective reporting (reporting bias)	Low risk	All outcomes were reported.
Protection against contamination bias	Unclear risk	It is unclear if there was a contamination between the intervention and the control group
Other bias	Unclear risk	It is unclear to determine if there are other biases.

Zermansky 2006

Methods	An open randomised controlled trial of clinical medication review by a pharmacist of elderly care home residents against usual care Study duration: 6 months
Participants	661 participants (331 intervention group but only 315 received Intervention) and 330 participants in the control group Setting: aged care facilities in Leeds, UK (nursing, residential and mixed care homes for older people in Leeds, UK) Diagnostic criteria: residents aged ≥ 65, seeking to recruit all residents taking ≥ 1 repeat medicines Age (years) (mean ± SD): age mean (interquartile range), Intervention 85.3 (81 to 90) and control 84.9 (80 to 90) Sex male n (%): intervention 75 (22.7), control 79 (23.9) Country: UK Comorbidity: not stated Sociodemographics: not stated Ethnicity: not stated Date of study: not reported, but paper first published 12/8/2006
Interventions	1 intervention A clinical medication review was conducted by the study pharmacist within 28 days of randomisation. It comprised a review of the general practice clinical record and a consultation with the participant and carer The pharmacist formulated recommendations with the participant and carer and passed them on a written proforma to the GP for acceptance and implementation. GP acceptance was signified by ticking a box on the proforma

Zermansky 2006 (*Continued*)

	Control participants received usual GP care
Outcomes	The primary outcome measure was the number of changes in medication per participant. Secondary outcome measures were the following: • medication outcomes: number of repeat medicines per participant, cost of 28 days of repeat medicines per participant at end date, recorded medication reviews in the study period • clinical outcomes in 6 months: falls, number of GP consultations, Barthel Index, Standardised Mini-Mental State Examination, mortality, hospital admissions • hospitalisation in 6 months per participant and number of deaths
Notes	Randomisation was curtailed on 30 June 2003 when it became clear that the intended sample size was not achievable within the available timescale. Data were analysed on an intention-to-treat basis

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Participants were randomly sized blocks.
Allocation concealment (selection bias)	Unclear risk	This is not mentioned in the study.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	It is not clear if the participants were blinded to the intervention
Incomplete outcome data (attrition bias) All outcomes	Low risk	Some participants did not complete the study and were reported in the study
Blinding of outcome assessment (detection bias) All outcomes	Low risk	A nurse blind to the study assessed participants.
Selective reporting (reporting bias)	Low risk	All outcomes were reported.
Protection against contamination bias	Unclear risk	It is difficult to determine if the intervention group was contaminated by the control group
Other bias	Unclear risk	It is difficult to determine if there are other biases.

ADL: activities of daily living; **BPMDL**: best possible medication discharge list; **CI**: confidence interval; **CHAP**: Cardiovascular Health Awareness Program; **CHD**: coronary heart disease; **CHF**: congestive heart failure; **COPD**: chronic obstructive pulmonary disease; **ED**: emergency department; **EuroQoL-5D**: EuroQol Group Association ("The EuroQol Group") comprises a network of international, multilingual, multidisciplinary researchers; **EQ-5D**: a standardised instrument for use as a measure of health outcome;

GP: general practitioner; **ICU**: intensive care unit; **QoL**: quality of life; **RT**: randomised trial; **SD**: standard deviation; **SF-12**: Short Form-12; **SF-36**: Short Form-36; **STOPP**: Screening Tool of Older Persons Prescriptions; **START**: Screening Tool to Alert Doctors to Right Treatment

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Al-Arifi 2014	Irrelevant intervention
Alassaad 2014	Not primary care
Alicic 2016	Protocol of a study
Barker 2012	This study does not appear to be a primary care intervention
Barker 2016	Outcomes not relevant
Barnes 2014	Outcomes not relevant
Basheti 2016	Outcomes not relevant
Bell 2016	Not primary care
Benard-Laribiere 2015	Irrelevant intervention
Bhatt 2014	Study protocol
Billington 2015	Outcomes not relevant
Bonnet-Zamponi 2013	This was not a primary care intervention; it was done by geriatricians
Briggs 2015	Not primary care
Carrington 2013	Irrelevant intervention
Clyne 2013	Outcomes not relevant
Clyne 2015	Outcomes not relevant
Clyne 2016	Outcomes not relevant
Cowper 1998	Cost-effectiveness study that had data in a form not enabling data extraction
Desveaux 2016	Study protocol
Dhalla 2014	Outcomes not relevant

(*Continued*)

Elliott 2014	Study protocol
Forster 2015	Study protocol
Fredericks 2013	Irrelevant intervention
Furniss 2000	Study was for a pre-post design not included in the protocol
Geurts 2016	Outcomes not relevant
Gorgas 2012	This study did not occur in primary care.
Graffen 2004	Study was for a pre-post design not included in the protocol
Guthrie 2016	Outcomes not relevant
Hallsworth 2016	Outcomes not relevant
Hanlon 1996	This study did not occur in primary care.
Hugtenburg 2009	This is not a randomised trial (it is described as a controlled intervention study and there is no evidence of randomisation)
Huiskes 2014	Outcomes not relevant
Keane 2014	Not primary care
Knowlton 1994	Not possible to extract appropriate data
Lee 1996	This study was not a randomised trial.
Leendertse 2011	This study was not a randomised trial.
Leendertse 2013	This study was not a randomised trial.
Liu 2010	This study was a conference abstract only and did not address adverse drug reactions
Malin 2016	Outcomes not relevant
Mills 2001	This study is reported elsewhere (see Furniss 2000, also excluded)
Montero-Balosa 2016	Not a randomised trial
Moreno 2016	Not a randomised trial
Naunton 2003	This is a hospital intervention and not done in primary care. It appears that the study pharmacist is recruited from the hospital. As it says, the pharmacist complied with the Society of Hospital Pharmacist clinical pharmacy services. It is also published in a hospital journal

(*Continued*)

Neven 2016	Not primary care
Ni 2016	Not a randomised trial
Perula 2014	Outcomes not relevant
Phung 2013	Study protocol
Pinnock 2013	Irrelevant intervention
Przytula 2015	Study protocol
Safran 1993	This study was not a randomised trial
Saltzberg 2011	This study was not a randomised trial
Setter 2009	The outcomes reported are not appropriate for this study
Sinnott 2015	Outcomes not relevant
Stingl 2016	Study protocol
Sturgess 2003	Reported elsewhere (see Bernsten 2001)
Wolf 2015	Outcomes not relevant
Wooster 2016	Study protocol
Xin 2014	Not primary care
Yuan 2003	Complex study, which made data extraction not possible.

DATA AND ANALYSES

Comparison 1. Professional interventions versus standard care

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Number of hospital admissions	2	3889	Risk Ratio (M-H, Random, 95% CI)	1.24 [0.79, 1.96]
2 Number of people admitted to hospital	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
3 Number of emergency department visits	2	1067	Risk Ratio (M-H, Fixed, 95% CI)	0.71 [0.50, 1.02]
4 Mortality	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected

Comparison 2. Organisational interventions versus standard care

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Number of hospital admissions	11	6203	Risk Ratio (M-H, Random, 95% CI)	0.85 [0.71, 1.03]
2 Number of people admitted to hospital	13	152237	Risk Ratio (M-H, Random, 95% CI)	0.92 [0.86, 0.99]
3 Number of emergency department visits	5	1819	Risk Ratio (M-H, Random, 95% CI)	0.75 [0.49, 1.15]
4 Mortality	12	154962	Risk Ratio (M-H, Random, 95% CI)	0.94 [0.85, 1.03]

Analysis 1.1. Comparison 1 Professional interventions versus standard care, Outcome 1 Number of hospital admissions.

Review: Professional, structural and organisational interventions in primary care for reducing medication errors

Comparison: 1 Professional interventions versus standard care

Outcome: 1 Number of hospital admissions

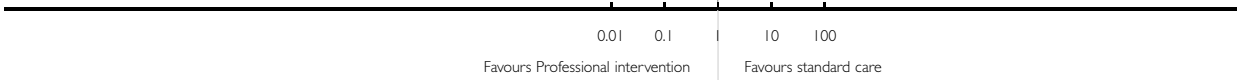
Study or subgroup	Professional intervention n/N	Standard/usual care n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Lapane 2011	39/1769	30/1769		93.4 %	1.30 [0.81, 2.08]
Murray 2004	2/180	3/171		6.6 %	0.63 [0.11, 3.74]
Total (95% CI)	**1949**	**1940**		**100.0 %**	**1.24 [0.79, 1.96]**

Total events: 41 (Professional intervention), 33 (Standard/usual care)

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.59$, df = 1 (P = 0.44); $I^2 = 0.0\%$

Test for overall effect: Z = 0.93 (P = 0.35)

Test for subgroup differences: Not applicable



Analysis 1.2. Comparison 1 Professional interventions versus standard care, Outcome 2 Number of people admitted to hospital.

Review: Professional, structural and organisational interventions in primary care for reducing medication errors

Comparison: 1 Professional interventions versus standard care

Outcome: 2 Number of people admitted to hospital

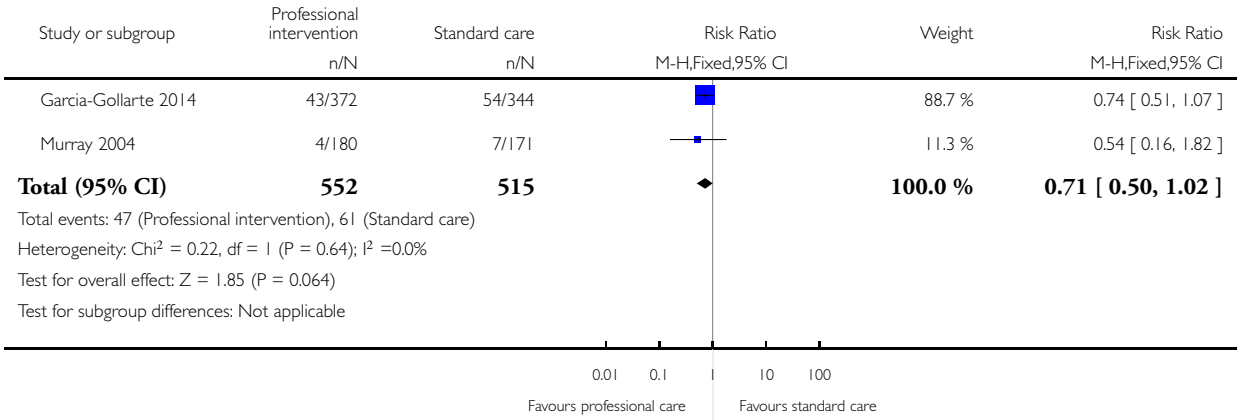
Study or subgroup	Professional intervention n/N	Standard Care n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
Gurwitz 2014	827/1870	802/1791		0.99 [0.92, 1.06]

Analysis 1.3. Comparison 1 Professional interventions versus standard care, Outcome 3 Number of emergency department visits.

Review: Professional, structural and organisational interventions in primary care for reducing medication errors

Comparison: 1 Professional interventions versus standard care

Outcome: 3 Number of emergency department visits

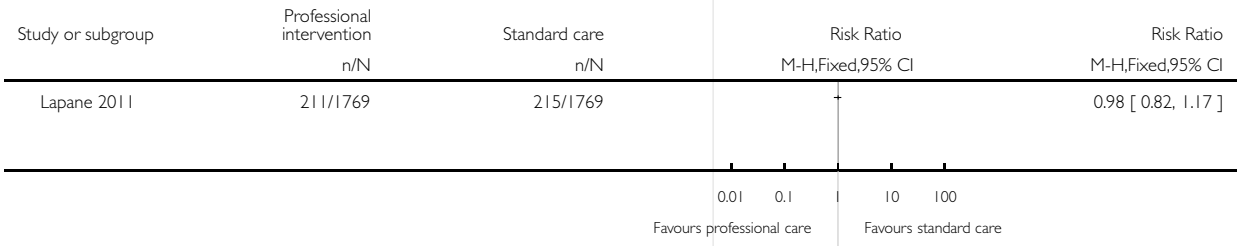


Analysis 1.4. Comparison 1 Professional interventions versus standard care, Outcome 4 Mortality.

Review: Professional, structural and organisational interventions in primary care for reducing medication errors

Comparison: 1 Professional interventions versus standard care

Outcome: 4 Mortality



Analysis 2.1. Comparison 2 Organisational interventions versus standard care, Outcome 1 Number of hospital admissions.

Review: Professional, structural and organisational interventions in primary care for reducing medication errors

Comparison: 2 Organisational interventions versus standard care

Outcome: 1 Number of hospital admissions

Study or subgroup	Organisational care n/N	Standard care n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Coleman 1999	45/78	29/49		11.6 %	0.97 [0.72, 1.32]
Holland 2005	234/429	178/426		15.2 %	1.31 [1.13, 1.50]
Ibrahim 2013	12/120	30/120		5.8 %	0.40 [0.22, 0.74]
Krska 2001	6/168	8/164		2.7 %	0.73 [0.26, 2.06]
Lenaghan 2007	20/68	21/66		7.3 %	0.92 [0.55, 1.54]
Lowrie 2012	107/1090	114/1074		12.8 %	0.92 [0.72, 1.19]
Malone 2000	276/447	300/484		15.9 %	1.00 [0.90, 1.10]
Moertl 2009	8/48	21/48		4.8 %	0.38 [0.19, 0.77]
Nabagiez 2013	42/340	59/361		10.1 %	0.76 [0.52, 1.09]
Okamoto 2001	0/164	4/166		0.4 %	0.11 [0.01, 2.07]
Rytter 2010	67/148	86/145		13.4 %	0.76 [0.61, 0.95]
Total (95% CI)	**3100**	**3103**		**100.0 %**	**0.85 [0.71, 1.03]**

Total events: 817 (Organisational care), 850 (Standard care)

Heterogeneity: $Tau^2 = 0.05$; $Chi^2 = 40.70$, df = 10 (P = 0.00001); $I^2 = 75\%$

Test for overall effect: Z = 1.70 (P = 0.090)

Test for subgroup differences: Not applicable

Analysis 2.2. Comparison 2 Organisational interventions versus standard care, Outcome 2 Number of people admitted to hospital.

Review: Professional, structural and organisational interventions in primary care for reducing medication errors

Comparison: 2 Organisational interventions versus standard care

Outcome: 2 Number of people admitted to hospital

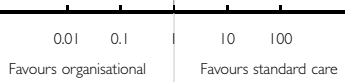
Study or subgroup	Organisational care n/N	Standard care n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Alvarez 2001	61/330	82/405		5.0 %	0.91 [0.68, 1.23]
Bernsten 2001	259/304	248/254		24.1 %	0.87 [0.83, 0.92]
Campins 2016	144/252	158/251		13.4 %	0.91 [0.79, 1.05]
Frankenthal 2014	80/160	73/146		7.7 %	1.00 [0.80, 1.25]
Hawes 2014	0/24	15/37		0.1 %	0.05 [0.00, 0.78]
Kaczorowski 2011	1951/69942	2274/75499		23.1 %	0.93 [0.87, 0.98]
Korajkic 2011	5/33	11/35		0.6 %	0.48 [0.19, 1.24]
Malet-Larrea 2016	31/688	52/715		2.6 %	0.62 [0.40, 0.95]
Nabagiez 2013	42/340	59/361		3.5 %	0.76 [0.52, 1.09]
Olesen 2014	77/253	73/264		5.9 %	1.10 [0.84, 1.44]
Triller 2007	39/77	32/77		3.9 %	1.22 [0.86, 1.72]
Zermansky 2001	110/579	92/550		6.5 %	1.14 [0.88, 1.46]
Zermansky 2006	47/331	52/330		3.6 %	0.90 [0.63, 1.30]
Total (95% CI)	**73313**	**78924**		**100.0 %**	**0.92 [0.86, 0.99]**

Total events: 2846 (Organisational care), 3221 (Standard care)

Heterogeneity: $Tau^2 = 0.01$; $Chi^2 = 22.45$, df = 12 (P = 0.03); $I^2 = 47\%$

Test for overall effect: Z = 2.10 (P = 0.036)

Test for subgroup differences: Not applicable



Analysis 2.3. Comparison 2 Organisational interventions versus standard care, Outcome 3 Number of emergency department visits.

Review: Professional, structural and organisational interventions in primary care for reducing medication errors

Comparison: 2 Organisational interventions versus standard care

Outcome: 3 Number of emergency department visits

Study or subgroup	Organisational care n/N	Standard care n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Alvarez 2001	70/330	80/405		29.1 %	1.07 [0.81, 1.43]
Coleman 1999	18/78	13/49		19.7 %	0.87 [0.47, 1.61]
Gernant 2016	72/297	90/359		29.6 %	0.97 [0.74, 1.27]
Hawes 2014	0/24	11/37		2.2 %	0.07 [0.00, 1.07]
Ibrahim 2013	11/120	33/120		19.3 %	0.33 [0.18, 0.63]
Total (95% CI)	**849**	**970**		**100.0 %**	**0.75 [0.49, 1.15]**

Total events: 171 (Organisational care), 227 (Standard care)

Heterogeneity: $Tau^2 = 0.14$; $Chi^2 = 14.93$, df = 4 (P = 0.005); $I^2 = 73\%$

Test for overall effect: Z = 1.32 (P = 0.19)

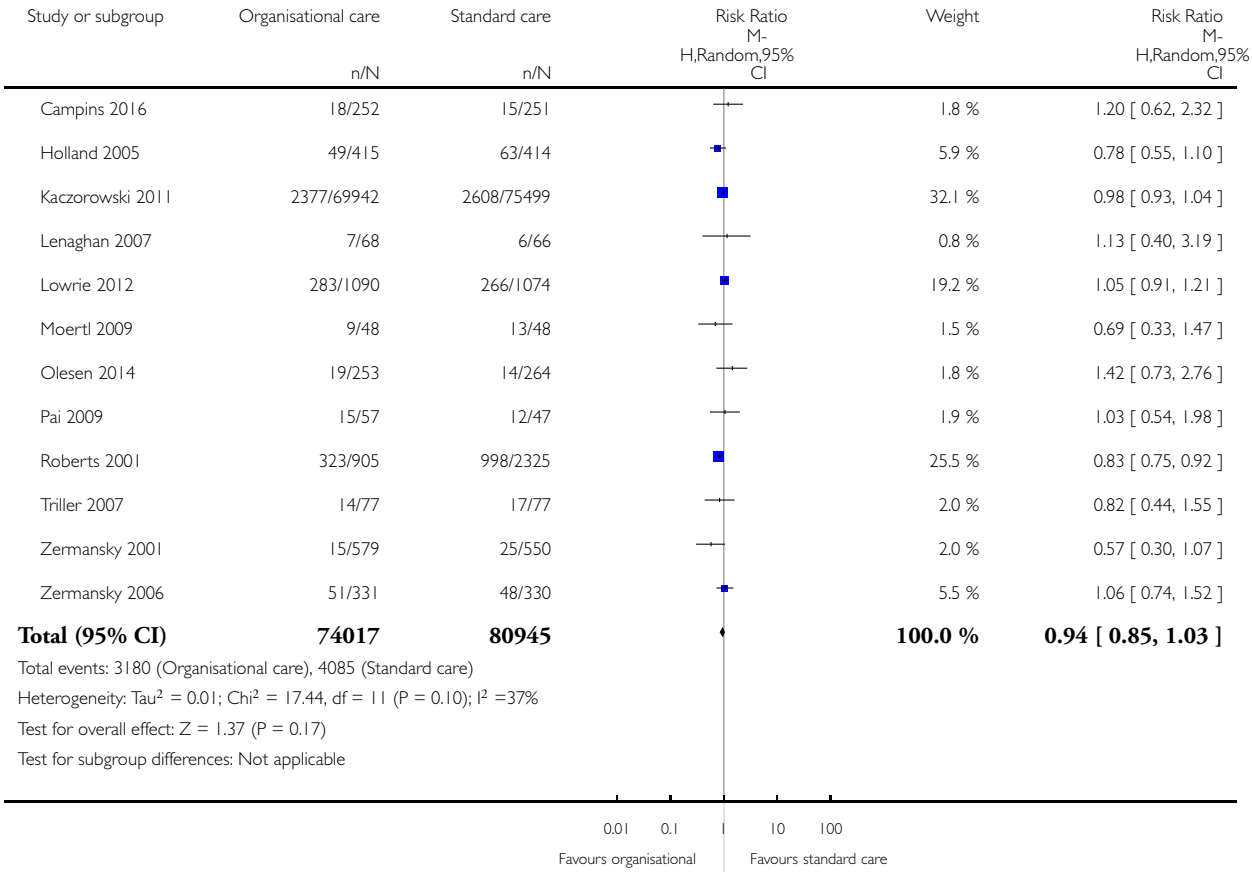
Test for subgroup differences: Not applicable

Analysis 2.4. Comparison 2 Organisational interventions versus standard care, Outcome 4 Mortality.

Review: Professional, structural and organisational interventions in primary care for reducing medication errors

Comparison: 2 Organisational interventions versus standard care

Outcome: 4 Mortality



ADDITIONAL TABLES

Table 1. Tentative description of interventions (part 1)

Study	Name	Theory	Materials	Procedures	Who provided intervention	Modes of delivery
Alvarez 2001	Pharmaceutical care	Pharmaceutical care is the provision of drug therapy	Pharmacies in the intervention group provided pharmaceutical	An Initial interview and assessment of the ther-	Pharmacists provided the intervention.	Individual and face-to-face

Table 1. Tentative description of interventions (part 1) (*Continued*)

		for the purpose of achieving outcomes that improve a person's quality of life	care, which consisted of offering the pharmaceutical care service to participants and to their corresponding GPs	apeutic plan was undertaken, registration of data during the subsequent visits to allow the identification of medication-related problems, and an intervention to solve the problem. The intervention involved proposing changes in the medication participants received, which had to be communicated to the patient's GP		
Bernsten 2001	Pharmaceutical care	Pharmaceutical care is the provision of drug therapy for the purpose of achieving outcomes that improve a person's quality of life, although little research has been conducted in community-based pharmaceutical care with elderly people	Training of pharmacists was done with a study manual. The manual contained an overview of the concept of pharmaceutical care and its provision to elderly people. No reference was provided for the study manual	The intervention group of pharmacists identified actual and potential drug-related problems using a structured approach. These pharmacists utilised a number of data sources in this assessment including the participant, the participant's GP, and pharmacy records. Following this assessment, pharmacists were instructed to formulate an intervention and monitoring plan	Community pharmacists were trained to provide the structured pharmaceutical care intervention. A study manual helped facilitate this process. It contained an overview of the concept of pharmaceutical care, its provision to elderly people, information on the therapeutic management of a number of disease states common in the elderly, together with other issues	Individual face-to-face

Table 1. Tentative description of interventions (part 1) (*Continued*)

					pertinent to drug therapy in the elderly	
Campins 2016	Drug evaluation and recommendation	Several instruments, criteria, and algorithms have been developed to enable more rational and appropriate use of medication, but limited evidence exists with regard to the outcomes that were investigated	The Good Palliative-Geriatric Practice algorithm Garfinkel 2007) and the STOPP/START criteria were used (O'Mahony 2015). Both of these tools assess the appropriate use of medication in older people	The intervention was composed of 3 phases. In the first phase, an experienced pharmacist evaluated all prescriptions using the GP-GP algorithm and based their decision about appropriateness on the STOPP/START criteria. In the second phase, the pharmacist discussed recommendations for each drug with the participant's physician in order to come up with a final list of recommendations. Finally, the recommendations were discussed with the participant and a final decision was agreed by physicians and participants	The intervention was delivered by a trained and experienced pharmacist. No details are provided concerning what is a "trained and experienced" pharmacist	Individual and face-to-face
Coleman 1999	Chronic care clinics	Chronic care clinics redesign the structure and content of primary care services through the delivery of scheduled visits de-	The chronic care clinics included an extended visit with the physician and nurse dedicated to planning chronic disease manage-	Frail older people were invited to participate in visits with the primary care team. During these visits, a shared treatment plan was	The team that provided the intervention consisted of the participant's physician, a team nurse, and a pharmacist. Physicians	The intervention was delivered individually and in groups in a face-to-face format

Table 1. Tentative description of interventions (part 1) (*Continued*)

		voted to chronic disease management. This mode of service delivery has the potential to improve outcomes for elderly people	ment, a pharmacist visit that emphasised reduction of polypharmacy and high-risk medications, and a patient self-management group	developed, a session was conducted with the pharmacist that addressed polypharmacy and medications associated with functional decline, patient self-management group sessions were conducted, and the provision of health status assessment information was provided to the practice team	and team nurses received training in population-based medicine and management strategies of geriatric syndromes. Team nurses received on-the-job coaching from study staff	
Frankenthal 2014	Medication review and drug recommendations	Potentially inappropriate prescriptions are prevalent in older people and are associated with adverse drug events. The STOPP/START criteria are designed to detect potentially inappropriate prescriptions in elderly people. However, little is known about the effects of an intervention involving the application of the STOPP/START criteria on clinical outcomes	The STOPP/START criteria were used to deliver the intervention (Gallagher 2008) . The STOPP criteria focus on avoiding the use of drugs that are potentially inappropriate for older people and the START criteria identify undertreatment or prescribing omissions in older people	Medication reviews were conducted by the study pharmacist for all residents. Recommendations made by the pharmacist were discussed with the chief physician. The physician then decided whether to accept these recommendations and implement prescribing changes	The intervention was conducted by the study pharmacist who applied the STOPP/START criteria during the medication review. The pharmacist also discussed the recommendations from the intervention with the chief physician, who decided whether to accept these recommendations and implement prescribing changes	Intervention was delivered individually and face-to-face.
Garcia-Gollarte 2014	Structured educational intervention	Inappropriate drug prescription is a	Educational material and references were given	The educational intervention included	A nursing home physician delivered the struc-	Face-to-face intervention delivered in

Table 1. Tentative description of interventions (part 1) (*Continued*)

		common problem in people living in nursing homes and is linked to adverse health outcomes. This study assessed the effect of an educational intervention directed to nursing home physicians in reducing inappropriate prescription and improving health outcomes and resource utilisation	to physicians and two 1-h workshops were used to review cases and promote practice changes. The STOPP/START criteria were reviewed with a random sample of 10 residents cared for by each physician (Gallagher 2008). The content of the educational intervention is provided in an appendix (Garcia-Gollarte 2014).	general aspects of prescription and drug use in geriatric patients, how to reduce the number of drugs, to perform a regular review of medications, to avoid inappropriate drug use, to discontinue drugs that do not show benefits, and to avoid under treatment with drugs that have shown benefits. It also discussed some drugs frequently related to adverse drug reactions in older people	tured educational intervention	a group and individual format
Gernant 2016	Medicine reconciliation and action plan	Emergency department overcrowding has been linked to increased mortality, costs, and length of stay. This study evaluated the effectiveness of a telephone-based, medicines-management service on reducing emergency department utilisation	Medication therapy management was provided to participants (APA 2008). A pharmacy technician completed telephonic medication reconciliation, after which a trained pharmacist consulted with the participant or caregiver via telephone to complete a scheduled, comprehensive medication therapy review to iden-	The intervention commenced with a pharmacy technician completing medication reconciliation with the participant over the telephone. Then, a pharmacist consulted with the participant by telephone for an average of 30 min to complete a comprehensive medication review to identify and resolve medication-related	A pharmacy technician delivered the initial medicine reconciliation with the participant. A trained pharmacist conducted the medication therapy review, constructed a personal medication record, and a medication-related action plan. The pharmacist also followed up with the participant's prescriber for resolution of	The intervention was conducted individually on the telephone

Table 1. Tentative description of interventions (part 1) (*Continued*)

			tify and resolve any medication-related problems. The pharmacist constructed a personal medication record and a medication-related action plan for the participant. The action plan was a participant-centred document that assisted participants, caregivers, and the pharmacist in the resolution of identified medication-related problems	problems. The pharmacist constructed a person medication-related action plan and followed-up with the participant's prescriber	problems that could not be resolved with the participant	
Gurwitz 2014	Automated system to facilitate flow of information and provide warnings, alerts, and recommendations	Transitions between the impatient and outpatient setting is a period of high risk for older adults. Most approaches to improving transitions require a substantial commitment of resources but automating these processes may improve the quality and safety of care	An automated system was used to facilitate the flow of information to the medical group's primary care providers about individuals who were discharged to home from the hospital (Field 2012).	An automated system was developed to facilitate the flow of information to the medical group's primary care providers. A computer interface linked the primary care provider's electronic health records to the hospital records, which provided information about admissions and discharges. The system also provided information about new drugs at discharge, warnings	The automated system delivered the intervention.	The intervention was delivered electronically.

Table 1. Tentative description of interventions (part 1) (*Continued*)

				about drug-drug interactions, recommendations about dose changes and laboratory monitoring of high-risk medications, and alerts to the provider's support staff to schedule a post-hospitalisation office visit within 1 week of discharge if not already scheduled		
Hawes 2014	Care transitions clinic visit	Medication errors related to hospital discharge result in rehospitalisations and emergency department visits, which may be reduced by pharmacist involvement during postdischarge transitions of care. This study evaluated the impact of a transitional care clinic visit conducted by a pharmacist	The Best Possible Medication Discharge List was used to identify medication discrepancies (Wong 2008). It served as the gold standard for the list of medications that the participant should take after discharge	Participants in the intervention group were scheduled for a care transitions clinic visit approximately 72 h after hospital discharge. The visit involved performing a complete medication history, identifying and resolving medication discrepancies, creating a current medication list, and counselling on appropriate medication use	Clinical pharmacists provided the intervention. They collaborated with the inpatient medical team to create the Best Possible Medication Discharge List	The intervention was delivered individually and face-to-face
Holland 2005	Pharmacist home visits	Older people often have trouble adhering to their medications. This study evaluated the effectiveness of a home-based medi-	A standardised visit form was used to record the home visit but no reference was provided	Pharmacists arranged home visits with the participant during which they assessed the participant's ability to self-medicate and drug adher-	Pharmacists conducted the home visits. Pharmacists held a postgraduate qualification in pharmacy practice or had recent contin-	The intervention was delivered individually and face-to-face

Table 1. Tentative description of interventions (part 1) (*Continued*)

		cation review on hospital admissions among elderly people		ence. They educated the participant, removed out-of-date drugs, reported drug reactions or interactions to the physician, and reported the need for a compliance aid	uing professional development in therapeutics. The pharmacists participated in a 2-day training course, which included lectures on adverse drug reactions, prescribing in elderly people, improving concordance, and communication skills	
Ibrahim 2013	Telephone consultation with home visits	Adherence to warfarin treatment and monitoring guidelines may be suboptimal among patients and staff. This study assessed the improvement in adherence to warfarin therapy with telephone and home visits	A predesigned set of questions was used in the telephone consultation, but no reference or any additional details were provided	The intervention group was counselled with once-a-week telephone consultations and 2 home visits per month by either a nurse or a pharmacist that dealt with warfarin use	A pharmacist or a nurse provided the home visits. The telephone consultation was conducted by a pharmacist	The intervention was delivered individually using a face-to-face format and telephone calls
Kaczorowski 2011	Cardiovascular risk assessment and education sessions	Strategies for managing blood pressure are essential as high blood pressure is the leading risk factor for death. The study authors evaluated the effectiveness of a community-based cardiovascular health promotion and disease prevention programme	The Cardiovascular Health Awareness Program was a standardised intervention that consisted of 10 weeks of cardiovascular risk assessment, blood pressure measurements, and education sessions (CHAP 2017).	The intervention consisted of 10 weeks of cardiovascular risk factor assessment and educational sessions. Volunteers were recruited to help participants measure their blood pressure and supported self-management by providing	Volunteers were recruited and trained to carry out the intervention. The volunteers were trained according to a standardised curriculum developed by a public health nurse and delivered by nurses working in the intervention community	The intervention was conducted individually in a face-to-face manner

Table 1. Tentative description of interventions (part 1) (*Continued*)

		in reducing morbidity		participants with their risk profile, risk-specific educational materials and information about access to local services. At the end of the 10-week programme and 6 months after the programme ended, the results were forwarded to family physicians who rank-ordered their participants by their most recent systolic blood pressure reading		
Korajkic 2011	Educational intervention with pharmacist	Few studies have examined a pharmacist's contribution to improving diuretic compliance and reducing rehospitalisation and health care use. This study aimed to determine the impact of a pharmacist-led intervention on patient-guided diuretic dose adjustment	The intervention group adjusted their diuretic dose using a flexible frusemide dose-adjustment guide that was provided in the paper	The intervention consisted of a 30-min educational session and focused on improving participant self-care, recognising symptoms of fluid retention, measuring weight daily, self-adjusting the diuretic dose and improving knowledge of heart failure and heart failure medications	A pharmacist provided the intervention. The frusemide dose-adjustment guide was developed in collaboration with cardiologists	Conducted individually in a face-to-face fashion.
Krska 2001	Pharmaceutical care plan	Regular medication reviews can reduce the risk of medication-related problems. This study aimed	Clinically-trained pharmacists completed a detailed profile for each participant using medi-	A pharmaceutical care plan was drawn up listing all pharmaceutical care issues together	The pharmacist performed the medication review. The participants' GP indicated their level	The mode of delivery was individual and face-to-face.

Table 1. Tentative description of interventions (part 1) (*Continued*)

		to evaluate the effect of a pharmacist-led medication review on pharmaceutical care issues and hospitalisations	cal notes and computer records. All participants were interviewed in their home about their use of and responses to medication and their use of health and social services. No references provided	with all the actions planned to achieve the outcomes of any pharmaceutical care issue. Copies of the plan were given to the GP who was asked to agree, after which the pharmacist implemented the plan	of agreement with each pharmaceutical care issue and with the actions taken	
Lapane 2011	Use of health information technology to identify people at risk for delirium and falls, implement monitoring plans, and provide reports to pharmacists	Falls and delirium pose the greatest threats to resident safety in nursing homes and contributes to further functional decline. Medication use is associated with greater risk of delirium and falls. Therefore, this study used health information technology to identify residents at risk for delirium and falls due to adverse drug events	A Geriatric Risk Assessment MedGuide was a database designed to identify medications that potentially contributed to delirium and fall risk (Tobias 1999). It also facilitated early recognition of signs and symptoms indicative of potential medication-related problems. Training was provided to nursing staff and pharmacists in how to use the reports generated by the Geriatric Risk Assessment MedGuide	Health information technology was used to identify residents at risk for delirium and falls, implement monitoring plans, and provide reports to pharmacists in conducting medication reviews. The consultant pharmacist shared the reports with the nurse contact at the facility and used the reports in their monthly drug review	The intervention was an automated system that provided reports to pharmacists and nurses, who were trained to use these reports. The training for nurses provided information regarding medications that cause, aggravate, or contribute to the risk of falls and delirium. The course also reviewed symptoms and signs of adverse medication effects and reinforced the importance of the early observation of symptoms and signs of adverse medication effects. Pharmacists were trained to provide a tar-	The intervention was delivered individually and face-to-face

Table 1. Tentative description of interventions (part 1) (*Continued*)

					geted drug review for all participants who experienced delirium and falls	
Lenaghan 2007	Home-based medication review	Home-based medication reviews are convenient for the patient and provide an opportunity to understand their medication-taking in their home environment. Therefore, this study looked at whether home-based medication reviews with elderly people could reduce hospital admissions	The intervention comprised 2 home visits by a community pharmacist who educated the participant/carer about their medicines, noted any pharmaceutical care issues and assessed the need for an adherence aid	At the home visit, the pharmacist educated the participant, removed out-of-date drugs, and assessed the need for an adherence aid. The pharmacist held regular meetings with the GP where changes to the participant's medications were discussed and amendments were implemented by the GP	A pharmacist with a post-graduate qualification in pharmacy practice conducted the home-based medication review. They had regular meetings with the lead GP. Possible changes to the participant's medication were discussed and agreed amendments were implemented by the GP	The intervention was delivered individually and face-to-face
Lowrie 2012	Pharmacist medication review	Although angiotensin-converting enzyme inhibitors and beta-blockers reduce morbidity and mortality in people with heart failure, these treatments are underused. Pharmacists may improve treatment through medication review. This study investigated whether a pharmacist intervention would re-	Pharmacists received training covering the aetiology, symptoms, and evidence-based management of heart failure. They also participated in monthly discussions of specific cases. The pharmacist used guidelines to optimise treatment for participants with left ventricular systolic dysfunction. All of	Participants were offered a 30-min appointment with the pharmacist If there was agreement between the pharmacist and the participant, and subsequently with the doctor, medications were initiated, discontinued, or modified by the pharmacist during 3-4 weekly or fortnightly consultations	The pharmacists, who delivered the medication review, had between 3 and 16 years of post-qualification experience, had experience delivering primary care-based medication review clinics for people receiving multiple-drug treatment and attended an in-house training day covering the aetiology, symptoms, and	The intervention was delivered individually and face-to-face

Table 1. Tentative description of interventions (part 1) (*Continued*)

		duce hospital admission and death for people with heart problems	these materials are available at onlinelibrary.wiley journal		evidence-based management of heart failure. An additional session covered the methods of the trial	
Malet-Larrea 2016	Pharmacist medication review	Aging and the use of polypharmacy are risk factors for drug-related problems and medication-related hospital admissions. Therefore, this study assessed the impact of a community pharmacist-led medication review on hospital admissions in older people	Pharmacists in the intervention group received a training course that covered the clinical management of older people and the medication review method. No reference was provided	The medication review consisted of the pharmacist collecting information about the participant's health problems, medication use, lifestyle habits, and concerns about diseases and medications. The pharmacist then identified negative clinical outcomes related to medicines and drug-related problems. Subsequently, an action plan was agreed upon which focused on participant outcomes and the medication use process	Pharmacists provided the medication review. They received a 3-day training course covering clinical management of elderly people, the medication review with follow-up method, communication with participants and doctors, study protocol and documentation forms	The intervention was delivered individually and face-to-face
Malone 2000	Pharmacist visits	Pharmacists have adopted pharmaceutical care, which is the provision of drug therapy to improve a person's quality of life, to reduce morbidity and mortality. Unlike previous studies that	Contacts between the pharmacist and participant were recorded on a data collection form, which contained the method of contact, time spent, medical problems ad-	The intervention participants received consultation and follow-up care from a clinical pharmacist	Pharmacists conducted the intervention. Most had a Doctor of Pharmacy degree and over 70% were either receiving or had completed postgraduate training	The intervention was delivered individually and face-to-face

Table 1. Tentative description of interventions (part 1) (*Continued*)

		did not focus on people who were most likely to benefit, this study examined veterans who were at high risk for a medication-related problem	dressed, drug-related problems addressed, and drug-related problems resolved. This form was not referenced			
Moertl 2009	Home-based nurse care	Home-based nurse care can reduce adverse events in people with chronic heart failure. High levels of natriuretic peptides in people with heart failure are predictors of death and hospitalisations. The study authors looked at whether high levels of these peptides can predict whether people with heart failure benefit from a home-based nurse intervention	The nurse checked for and, in co-ordination with the treating physician, implemented guideline-based medication (Remme 1997; Remme 2001).	At home visits, the nurse checked and recorded weight, recorded symptoms and signs of heart failure as well as heart rate and blood pressure, and organised and reviewed blood analyses on demand. The nurse also gave the patient education and self-management skills	Nurses who specialised in caring for people with heart failure provided the intervention	The intervention was delivered individually and face-to-face
Murray 2004	Computerised care suggestions	Hypertension is associated with cardiovascular morbidity and mortality, but is difficult to control. Guidelines on hypertension are complicated and can become outdated quickly, so this study inves-	This study used the pharmacist intervention recording system, which was used to document all pharmaceutical care interventions (Overhage 1999). This system gave the pharma-	The pharmacist intervention recording system was used by intervention pharmacists to receive care suggestions. The pharmacist could fill the prescription as written, discuss the suggestions with the	Pharmacists and physicians provided the intervention.	The intervention was delivered individually and face-to-face

Table 1. Tentative description of interventions (part 1) (*Continued*)

		tigated the benefits of evidence-based treatment for hypertension using a computerised system	cist care suggestions, which they could pass on to the physician The physician used an order writing workstation to write orders for drugs, tests, nursing activities, and consultations (McDonald 1999). The workstation gave the physician care suggestions for the treatment of hypertension	participant and encourage discussions between the participant and physician, or contact the ordering physician The physician intervention used an order-writing workstation to write orders for drugs, tests, nursing activities and consultations and display care suggestions. All hypertension care suggestions were displayed as suggested orders along with possible actions and a brief explanation of the rationale for the suggestion		
Nabagiez 2013	Home visits by physician assistants	Studies suggest that people who have undergone coronary artery bypass graft surgery benefit from a home intervention, but there are few studies of home visits by physicians or physician assistants. Therefore, this study examined the hospital readmissions of people who received home vis-	A physician assistant home care form/checklist was used to record all findings from the home visit. A copy of this form was provided in the paper	Cardiothoracic physician assistants conducted home visits during which they performed a physical examination and reviewed the participant's medications. Adjustments were made to the participant's medications and new medications were prescribed as needed. The	Physician assistants provided the intervention.	The intervention was delivered individually and face-to-face

Table 1. Tentative description of interventions (part 1) (*Continued*)

		its by physician assistants		surgical wounds were examined and participant concerns were addressed. Prescriptions were written for antibiotics, blood work, or imaging studies		
Okamoto 2001	Pharmacist-managed hypertension clinic	Hypertension can be controlled, but this study investigated whether it can be managed at a reasonable cost with minimal adverse effects by pharmacists	Sitting blood pressure was measured with a Datascope Accutorr automated sphygmomanometer (Datascope Corporation Montvale, NJ, USA). 2 readings were taken for each participant and the average of the 2 readings was recorded (Datascope Patient Monitoring 1996).	Participants were counselled by a pharmacist who told them that efforts would be made to decrease the number of antihypertensive drugs or alter their therapy by giving more appropriate or less expensive drugs to achieve similar or improved blood pressure control. The pharmacist determined the most appropriate antihypertensive regimen for each participant, ordered laboratory tests as needed, and provided education on non-pharmacological ways to control blood pressure	Clinical pharmacists provided the intervention.	The intervention was delivered individually and face-to-face
Olesen 2014	Pharmacist medication review	Pharmacists work with participants in designing, implement-	Pharmacists adhered to a manual to deliver the intervention (Medication Re-	Participants were visited at home by a pharmacist who examined the medicines	Pharmacists who had some practical experience or courses in medication review	The intervention was delivered individually. It was conducted by telephone and

Table 1. Tentative description of interventions (part 1) (*Continued*)

		ing and monitoring therapeutic plans, but elderly people may have problems with adhering to their medication. This study looked at treatment adherence, as well as hospitalisations and mortality, in elderly people who received a home visit by a pharmacist along with telephone follow-up	view-Managing Medicine Manual, Danmarks Apotekerforening, Pharmakon. Medicingennemgang 2004). This manual helps pharmacists identify and resolve drug-related problems (Danmarks 2004).	list with regard to side-effects, interactions and administration. The pharmacist tried to make the regime less complex, informed participants, and motivated adherence	provided the intervention	face-to-face
Pai 2009	Pharmacist medication review	People with end-stage renal disease take multiple drugs and experience multiple co morbidities, which places them at greater risk of drug-related problems. This paper looked at the effects of a pharmacist-led intervention on drug-related problems and hospitalisations in ambulatory patients undergoing haemodialysis	Drug-related problems were recorded, evaluated and assigned to 10 possible categories (Hepler 1990). The drug-related problems were also categorised into therapeutic drug classes and the outcome related to the drug-related problem intervention was captured	Participants assigned to pharmaceutical care had drug therapy reviews conducted by a nephrology-trained pharmacist. The pharmacist conducted a participant interview, generated a drug therapy profile, identified and addressed drug-related problems, and provided healthcare-provider and participant education. The pharmacist also provided consultative services that focused on optimising drug therapy	The clinical pharmacists who conducted the intervention were either nephrology-trained or completing postdoctoral training in nephrology pharmacotherapy	The intervention was delivered individually and face-to-face

Table 1. Tentative description of interventions (part 1) (*Continued*)

Roberts 2001	Medication review, nurse education, and development of professional relationships	Pharmacist-conducted medication reviews and nurse education about medication use may have an impact on drug use in nursing homes. This study looked at the effect of medication review and nurse education on mortality and hospitalisations in nursing homes	Problem-based educational sessions were provided to nurses and addressed basic geriatric pharmacology and some common problems in long-term care. No referenced documentation is provided for these sessions	The intervention introduced a new professional role to stakeholders with relationship building, nurse education, and a medication review by pharmacists. Professional contact between nursing home staff and pharmacists on issues such as drug policy and resident problems was conducted along with problem-based educational sessions for nurses. These sessions addressed geriatric pharmacology and problems in long-term care. The medication reviews highlighted adverse drug effects, ceasing or adding drugs, better use of specific drug therapy, non-drug interventions, and adverse effect and drug response monitoring	Clinical pharmacists delivered the intervention.	The intervention was delivered individually and in groups over the phone and face-to-face
Rytter 2010	Structured home visits by GP and nurse	Many hospital admissions are due to inappropriate medical treat-	The joint home visits were guided by an agenda. During the struc-	There was a joint home visit by the GP and district nurse approximately one	GPs and district nurses provided the intervention.	The intervention was delivered individually and face-to-face

Table 1. Tentative description of interventions (part 1) (*Continued*)

		ment, and the discharge of fragile elderly patients is associated with a high risk of readmission. This study examined whether home visits by GPs and district nurses reduced the risk of readmission of discharged elderly patients	tured home visit the agenda included checking the discharge letter for recommended follow-up, checking the need for adjustment of medication, checking if social and personal support was arranged, and checking the family's medicine cabinet. This agenda was provided in the article	week after discharge from the hospital. 2 more contacts were conducted by the GP in the GP's clinic or as a home visit. These visits included checking the discharge letter, checking the need for adjustment of medication, checking if social and personal support was arranged, and checking the family's medicine cabinet		
Triller 2007	Pharmacist medication reviews	Adverse drug events are frequently caused by cardiovascular drugs. Pharmacists can identify and resolve drug-related problems for people at home and reduce re-hospitalisation rates. This study investigated whether a pharmacist-led intervention could reduce re-hospitalisations and death in people with heart failure	Using a predefined checklist, the pharmacist tried to reduce the use of inappropriate mediations, encourage smoking cessation, suggest improvements in the participant's diet, and promote medication adherence, self-monitoring, and vaccination. The checklist is not provided in the paper	The pharmacist in the intervention group conducted an in-home medication assessment and 2 follow-up visits. This involved assessing and reviewing physician notes and laboratory test values and interacting with prescribers on behalf of the participants. The pharmacist catalogued all medications and interviewed the participant regarding medication use	A clinical pharmacist, who had over 20 years of combined experience as a hospital and community pharmacist and had received a doctor of pharmacy degree and completed a 1-year clinical residency in home care, provided the intervention	The intervention was delivered individually and face-to-face

Table 1. Tentative description of interventions (part 1) (*Continued*)

Zermansky 2001	Pharmacist medication review	Repeat prescribing is poorly managed in the UK, which puts people at risk. Pharmacists could review these prescriptions and reduce the pressure on GPs. This study tested whether pharmacists can review repeat prescriptions to reduce hospital admissions and deaths	The process for reviewing repeat prescriptions involved discussing each condition with the participant and asking about symptoms (Lowe 2000). If clinical or pathological monitoring was due, the pharmacist directed the participant to the practice nurse or doctor. Participants with new clinical problems were referred to the doctor	The pharmacists conducted a medication review during which they evaluated the therapeutic efficacy of each drug and the progress of the conditions being treated. Compliance, actual and potential adverse effects, interactions, and the participant's understanding of the condition and its treatment were considered. The outcome of the review was a decision about the continuation of the treatment	A pharmacist provided the medication review.	The intervention was delivered individually and face-to-face
Zermansky 2006	Pharmacist medication review	Elderly people take multiple medicines, which increases the risk of adverse drug events. Pharmacists can improve medicine management for elderly people in the community. In this study, the authors looked at whether a pharmacist-led review would reduce hospitalisations and deaths among elderly people in	The clinical medication review (Lowe 2000), which was conducted by the pharmacist, comprised a review of the GP clinical record, and a consultation with the participant and carer. The pharmacist made recommendations and passed them on a written proforma to the GP for acceptance and recommendation	The pharmacist conducted a medication review in which the pharmacist identified the drugs that were taken, identified the original indication for each drug, assessed adherence to medication, and identified unaddressed medical problems. They also considered the continuing need for each drug,	The study pharmacist provided the intervention.	The intervention was delivered individually and face-to-face

Table 1. Tentative description of interventions (part 1) (*Continued*)

		nursing homes		identified side effects, identified drug interactions or contraindications, and considered costs. Finally, the pharmacist implemented and documented any changes		

GP: general practitioner

Table 2. Tentative description of interventions (part 2)

Study	Location of intervention	When and how much of the intervention was delivered	Tailoring	Modifications	Adherence planning	Adherence assessment
Alvarez 2001	83 community pharmacies in the provinces of Asturias, Barcelona, Madrid and Biscay	The intervention was delivered once.	There was no tailoring made to the intervention.	Two additional seminars were given to the intervention group on real cases in order to approve the intervention	Not undertaken	Not undertaken
Bernsten 2001	Community pharmacies in 7 European countries; Denmark, Germany, The Netherlands, Northern Ireland (co-ordinating centre), Portugal, Republic of Ireland and Sweden. A minimum of 12 sites per country were chosen according to spe-	The intervention was delivered at least once according to the study manual. However, Each site was free to provide as much information as possible to the intervention group as per the study manual	A study manual describing the intervention was developed for all the participating countries. Each country translated the manual into their own language	Each country adapted the manual, translating and modifying sections where appropriate, according to differing national practices	Not undertaken	Not undertaken

Table 2. Tentative description of interventions (part 2) (*Continued*)

	cific criteria set within each participating country relating to the population of elderly people who visited the pharmacy, staffing levels within the pharmacy and working relationships with local GPs.					
Campins 2016	7 Primary Health care clinics in Mataró and Argentona	The intervention included 3 phases and the participants were followed up for 12 months. It is not clear if the intervention was repeated more than once	There was no tailoring made to the intervention.	There were no modifications made to the intervention during the study	Not undertaken	Not undertaken
Coleman 1999	9 primary care physician practices in Washington State. Clinics were allowed to select their target condition of focus: frail older adults or people with diabetes. The physicians were board certified in Family Practice and did not have formal training or certification in geriatric medicine.	The intervention was undertaken once. However there was variability in the frequency of one of its components	There was no tailoring made to the intervention.	There were no modifications made to the intervention during the study	A priori process of care measures for each of the geriatric syndromes were developed with decision rules for acceptable documentation by the study reviewers for the interventions	The chart abstraction of assessing the documentation for the interventions was performed by one member of the study team along with an additional reviewer blinded to knowledge of the study group and study hypothesis. The overall level of agreement between the 2 reviewers was acceptable based on published ranges

Table 2. Tentative description of interventions (part 2) (*Continued*)

						(kappas for geriatric syndrome process measures 0.75 to 0.85)
Frankenthal 2014	Chronic care geriatric facilities in Central Israel	The intervention was done once at 6 months and 12 months later	There was no tailoring made to the intervention.	There were no modifications made to the intervention during the study	Not undertaken	Not undertaken
Garcia-Gollarte 2014	A private organisation of 37 nursing homes in Spain	It is unclear how many times the intervention was given as the educator offered further on-demand advice on prescription for the next 6 months	There was no tailoring made to the intervention.	There was no modifications made to the intervention during the study	Not undertaken	Not undertaken
Gernant 2016	Home health patients within a medicare insured home health population in Canada	The intervention was undertaken at least once however, some participants received more than one phone call as additional telephone follow-up was provided as needed per the pharmacists' discretion during the first 30 days of the 60-day home healthcare episode.	Some participants received additional follow-up depending on their conditions	There were no modifications made to the intervention during the study	Not undertaken	Not undertaken
Gurwitz 2014	Large multispecialty group practice employing 265 physicians, including 66 primary care	Daily records generated by the computer system were examined	There was no tailoring made to the intervention.	There were no modifications made to the intervention during the study	Not undertaken	Not undertaken

Table 2. Tentative description of interventions (part 2) (*Continued*)

	providers caring for adults in the outpatient setting					
Hawes 2014	804-bed academic medical centre in North Carolina, USA	The intervention took place once.	There was no tailoring made to the intervention.	Only hospitalisations and ED visits at the study institution were included for those participants who were not able to be contacted after 3 phone call attempts	Not undertaken	Not undertaken
Holland 2005	Home-based medication review after discharge from acute or community hospitals in Norfolk and Suffolk, UK	The intervention was performed once.	It is possible that a small number of participants in both groups may have had their medication reviewed during the follow-up period by their GP or community pharmacist	There were no modifications made to the intervention during the study	Not undertaken. No data on adherence were collected.	Not undertaken
Ibrahim 2013	Telephone consultation with home visits	The intervention was performed once.	Any additional contact as requested by the participant in the intervention group was undertaken	There were no modifications made to the intervention during the study	Not undertaken	Not undertaken
Kaczorowski 2011	Community-based pharmacies in Canada	The intervention was performed once as planned.	The local lead organisations used several strategies to recruit volunteer peer health educators. These strategies included using the local lead organisation's ex-	When required, Cardiovascular Health Awareness Program support staff produced and mailed invitation letters on behalf of participating physi-	Feedback of results was given to primary healthcare providers	Evaluation data collected for the purpose of ongoing evaluation and quality improvement: 1. Success of different advertising/ invitation strate-

Table 2. Tentative description of interventions (part 2) (*Continued*)

			isting volunteer base, advertising in the local media, and giving presentations at local seniors' clubs.	cians (CHAP 2017).		gies 2. Attendance, consent, completed assessments 3. Nurse assessments, pharmacist consults, fax/call to family physician the same day Feedback to family physicians, pharmacists, and participants
Korajkic 2011	Outpatients clinic in Melbourne, Australia	The intervention was performed once as planned.	There was no tailoring made to the intervention.	There were no modifications made to the intervention during the study	There were written instructions on how to adjust the dose of frusemide per weight increase	Data on dosage adjustment of frusemide were collected and compared against the initial criteria
Krska 2001	General medical practices in the Grampian region of Scotland	The intervention was performed once as planned.	In the control group, when pharmacists considered a review to be serious and beneficial to the participants, an independent medical assessor decided on the need to withdraw the participants on clinical grounds	There were no modifications made to the intervention during the study	Any outstanding care issues in both groups were communicated to the participant's GP	Not undertaken
Lapane 2011	25 nursing homes serviced by 2 long-term care pharmacies in Northern Ireland	It is unclear the number of times the reports were generated and used by the pharmacists for every resident	The Geriatric Risk Assessment MedGuide database software for falls and delirium was integrated into the pharmacies' commercial pharmacy	It is unclear if there were any modifications to the interventions	The computer system did not capture if the recommendations done by the pharmacist were accepted	Not undertaken

Table 2. Tentative description of interventions (part 2) (*Continued*)

			software system (Rescot LTCP System) for the inter-vention homes (Tobias 1999).			
Lenaghan 2007	A GP setting in Norfolk, UK	It is unclear how many times the pharmacist and the GP met to discuss partic-ipant's care plan	A follow-up visit with the partici-pant occurred 6-8 weeks later to reinforce the original ad-vice, and assess whether there were any further pharmaceuti-cal care issues to address with the GP.	It is unclear if there were any modifications to the interventions	Not undertaken	Not undertaken
Lowrie 2012	The study was conducted within the NHS which provides free health care to the popula-tion of the UK. 27 primary care-based pharmacists em-ployed by the NHS to work with family doc-tors	It is unclear how many times the pharma-cist met the par-ticipant and the GP	If there was agreement be-tween the phar-macist and the participant dur-ing the consulta-tion and subse-quently with the fam-ily doctor, medi-cations were ini-tiated, discontin-ued, or modified by the pharma-cist during 3-4 subse-quent weekly or fortnightly con-sultations	It is unclear if there were any modifications to the interventions	Not undertaken	Not undertaken
Malet-Larrea 2016	The study was conducted in 178 commu-nity pharmacies in Spain	It is unclear how many times the intervention was undertaken	A specifically trained pharma-cist called a prac-tice change facil-ita-tor helped phar-macists of the in-tervention group	It is unclear if there were any modifications to the interventions	The prac-tice change facil-itator ensured fi-delity to the in-tervention and supported phar-macists of both	The experts were requested to an-swer individually for each case and the degree of agreement be-tween them was later established.

Table 2. Tentative description of interventions (part 2) (*Continued*)

			in the provision of the medication review with follow-up service, identifying barriers specific to each pharmacy and providing solutions		study groups on queries about documentation forms	Inter-rater reliability was measured using Fleiss's kappa
Malone 2000	9 Veterans Affairs medical centres in the USA	It is unclear how many times participants were seen by the pharmacist in the intervention group as the protocol indicated that each participant should have at least 3 visits with the clinical pharmacist during the study, but participants could be seen as frequently as deemed necessary to ensure appropriate care	To prevent contamination, some sites marked medical records of intervention and control participants to alert clinical pharmacists that participants were in the study. Other sites noted this distinction in electronic medical records One site distributed a list of participants enrolled in the study to all pharmacists providing primary care.	Clinical pharmacist intervention, however, occurred in one control participant; this participant was withdrawn from the study and his data were not included in the results	Each contact with the participant was recorded on a standard data collection form that contained information about the method of contact, estimated time spent with the participant, medical problems addressed, drug-related problems addressed, and drug-related problems resolved	Each month after enrolment the coordinating centre received electronic data on each participant's prescription drugs dispensed in the preceding month. When participants either completed the study or died, data on resource use from enrollment to termination were retrieved
Moertl 2009	Ambulatory patients participating in the Euro-Heart Failure Survey programme in Vienna	It is unclear how many times the nurse visited the intervention participants as more visits were made optional for participants	More frequent contacts such as visits or telephone calls between the nurse and the participants were optional in case the participant or the nurse considered them necessary	The nurse was in charge of individualised participant and caregiver education and enhancement of self-management. If the nurse noted any deterioration in the participant's status, she reported to the treating	Not undertaken	Not undertaken

Table 2. Tentative description of interventions (part 2) (*Continued*)

				physician or advised the participant to visit the treating physician		
Murray 2004	Academic primary care internal medicine practice in the USA	It is unclear how many times the intervention was undertaken	There was no tailoring made to the intervention.	There were no modifications made to the interventions.	Data necessary to generate care suggestions were derived from the computer programme. Treatment suggestions fell into 5 major categories	Not undertaken
Nabagiez 2013	Ambulatory patients discharged from a large 702-bed hospital in Staten University Hospital, USA	It is unclear how many times the physician visited each participant in the home after their discharge	There was no tailoring made to the intervention.	There were some modifications done to the intervention due to the participants not being available at the weekend. Participants were not seen directly after discharge as per the study protocol	All findings were documented on the intervention visit form.	It is unclear if this was undertaken.
Okamoto 2001	Managed care organisation in California, USA	It is unclear how many times participants were seen by the pharmacist in the intervention group as additional follow-up was organised by the pharmacists for some participants	Additional follow-up was organised by the pharmacists for some participants	The intervention was not modified.	Not undertaken	Not undertaken
Olesen 2014	Patients living at home in the municipality of Aarhus, Denmark	The intervention was performed at the intended follow-up.	Pharmacists could consult the project physician if they considered a participant's medication	The intervention was not modified.	Adherence to the medications were assessed by a pill-count in all participants during 1 year	Pill count was undertaken

Table 2. Tentative description of interventions (part 2) (*Continued*)

			problems to be life-threatening.			
Pai 2009	The study took place in a non-profit university-affiliated dialysis clinic in Albany, USA	It is unclear if all participants received the same number of follow-up visits by the pharmacist or the physician in the intervention group	It is unclear if there was any tailoring made to the intervention	The intervention was not modified.	Not undertaken	Not undertaken
Roberts 2001	52 nursing homes located in south-east Queensland and north-east New South Wales, Australia	There was variability in the number of educational sessions provided to staff in each nursing home as well as the number of visits by the intervention pharmacists	It is unclear if there was any tailoring made to the intervention	It is unclear if the intervention was modified.	Validation of prescription claim data with participants' medications profiles	To validate prescription claims data, a sample of 1328 cross-sectional medication profiles were collected for 8 nursing home clusters for control and intervention homes at post-intervention An audit, comparing original post-intervention medication data with the same data recollected up to 6 weeks later for a 6%, random sample, showed an overall reproducibility of 97% (range 92% to 100%)
Rytter 2010	Patients discharged from Glostrup Hospital, Denmark.	The intervention was performed as prescribed.	There was no tailoring made to the intervention.	There was no modification made to the intervention.	Not undertaken	Not undertaken
Triller 2007	Heart failure patients discharged from hospital in	The intervention was performed as prescribed.	The clinical pharmacist accessed and	There was no modification made to the	Not undertaken	Not undertaken

Table 2. Tentative description of interventions (part 2) (*Continued*)

	Albany, Scotland		reviewed all pertinent physician notes and laboratory test values via the National Endowment for the Humanities data system and interacted with prescribers on behalf of the participants, as necessary	intervention.		
Zermansky 2001	4 GPs in Leeds, UK	It is unclear how many times the pharmacist visited the participant	Immobile participants were visited at home. Non-attenders were invited once more by telephone	The study authors agreed with each practice the level of intervention that the pharmacist could make without seeking prior approval	It is unclear if this was undertaken.	It is unclear if this was undertaken.
Zermansky 2006	65 care homes for the elderly in Leeds, UK	It is unclear how many times the pharmacist reviewed each participant	There was no tailoring made to the intervention.	There was no modification made to the intervention.	Pharmacists filled in a proforma sheet including their recommendations	GP acceptance of the recommendations was signified by ticking a box on the proforma

ED: emergency department; GP: general practitioner; NHS: National Health Service

APPENDICES

Appendix 1. EPOC Taxonomy

Professional interventions

- Distribution of educational materials (distribution of published or printed recommendations for clinical care, including clinical practice guidelines, audiovisual materials and electronic publications; the materials may have been delivered personally or through mass mailings).
- Educational meetings (healthcare providers who have participated in conferences, lectures, workshops or traineeships)
- Local consensus processes (inclusion of participating providers in discussion to ensure that they agreed that the chosen clinical problem was important and the approach to managing the problem was appropriate).
- Educational outreach visits (use of a trained person who met with providers in their practice settings to give information with the intent of changing the provider's practice. The information given may have included feedback on the performance of the providers).
- Local opinion leaders (use of providers nominated by their colleagues as 'educationally influential'. The investigators must have explicitly stated that their colleagues identified the opinion leaders).
- Patient-mediated interventions (new clinical information (not previously available) collected directly from patients and given to the provider e.g. depression scores from an instrument).
- Audit and feedback (any summary of clinical performance of health care over a specified period of time. The summary may also have included recommendations for clinical action. The information may have been obtained from medical records, computerised databases, or observations from patients).

The following interventions are excluded

- Provision of new clinical information not directly reflecting provider performance which was collected from patients, e.g. scores on a depression instrument, abnormal test results. These interventions should be described as patient-mediated.
- Feedback of individual patients' health record information in an alternate format (e.g. computerised). These interventions should be described as organisational.
- Reminders (patient- or encounter-specific information, provided verbally, on paper or on a computer screen, which is designed or intended to prompt a health professional to recall information. This would usually be encountered through their general education; in the medical records or through interactions with peers, and so remind them to perform or avoid some action to aid individual patient care. Computer-aided decision support and drugs dosage are included).
- Marketing (use of personal interviewing, group discussion ('focus groups'), or a survey of targeted providers to identify barriers to change and subsequent design of an intervention that addresses identified barriers)
- Mass media (i. varied use of communication that reached great numbers of people including television, radio, newspapers, posters, leaflets, and booklets, alone or in conjunction with other interventions; ii. targeted at the population level)
- Other (other categories to be agreed in consultation with the EPOC editorial team)

Financial interventions

Provider

- Fee-for-service (provider has been paid for number and type of service delivered)
- Prepaid (no other description)
- Capitation (provider was paid a set amount per patient for providing specific care)
- Provider salaried service (provider received basic salary for providing specific care)
- Prospective payment (provider was paid a fixed amount for health care in advance)
- Provider incentives (provider received direct or indirect financial reward or benefit for doing specific action)
- Institution incentives (institution or group of providers received direct or indirect financial rewards or benefits for doing specific action)
- Provider grant/allowance (provider received direct or indirect financial reward or benefit not tied to specific action)

- Institution grant/allowance (institution or group of providers received direct or indirect financial reward or benefit not tied to specific action)
- Provider penalty (provider received direct or indirect financial penalty for inappropriate behaviour)
- Institution penalty (institution or group of providers received direct or indirect financial penalty for inappropriate behaviour)
- Formulary (added or removed from reimbursable available products)
- Other (other categories to be agreed in consultation with the EPOC editorial team)

Patient

- Premium (patient payment for health insurance. It is important to determine if the patient paid the entire premium, or if the patient's employer paid some of it. This includes different types of insurance plans).
- Co-payment (patient payment at the time of healthcare delivery in addition to health insurance, e.g. in many insurance plans that cover prescription medications, the patient may pay AUD 5 per prescription, with the rest covered by insurance).
- User fee (patient payment at the time of healthcare delivery)
- Patient incentives (patient received direct or indirect financial reward or benefit for doing or encouraging them to do specific action)
- Patient grant/allowance (patient received direct or indirect financial reward or benefit not tied to specific action)
- Patient penalty (patient received direct or indirect financial penalty for specified behaviour, e.g. reimbursement limits on prescriptions)
- Other (other categories to be agreed in consultation with the EPOC editorial team)

Organisational interventions

Provider-orientated

- Revision of professional roles (also known as 'professional substitution', 'boundary encroachment' and includes the shifting of roles among health professionals. For example, nurse midwives providing obstetrical care; pharmacists providing drug counselling that was formerly provided by nurses and physicians; nutritionists providing nursing care; physical therapists providing nursing care. Also includes expansion of role to include new tasks).
- Clinical multidisciplinary teams (creation of a new team of health professionals of different disciplines or additions of new members to the team who work together to care for patients)
- Formal integration of services (bringing together of services across sectors or teams or the organisation of services to bring all services together at one time also sometimes called 'seamless care')
- Skill mix changes (changes in numbers, types or qualifications of staff)
- Continuity of care (including one or many episodes of care for inpatients or outpatients)
- Arrangements for follow-up
- Case management (including co-ordination of assessment, treatment and arrangement for referrals)
- Satisfaction of providers with the conditions of work and the material and psychic rewards (e.g. interventions to 'boost morale')
- Communication and case discussion between distant health professionals (e.g. telephone links; telemedicine; there is a television/video link between specialist and remote nurse practitioners)
- Other (other categories to be agreed in consultation with the EPOC editorial team)

Patient-orientated

- Mail order pharmacies (e.g. compared to traditional pharmacies)
- Presence and functioning of adequate mechanisms for dealing with patients' suggestions and complaints
- Consumer participation in governance of healthcare organisation
- Other (other categories to be agreed in consultation with the EPOC editorial team)

Structural

- Changes to the setting/site of service delivery (e.g. moving a family planning service from a hospital to a school)
- Changes in physical structure, facilities and equipment (e.g. change of location of nursing stations, inclusion of equipment where technology in question is used in a wide range of problems and is not disease specific, for example an MRI scanner)
- Changes in medical records systems (e.g. changing from paper to computerised records, patient-tracking systems)
- Changes in scope and nature of benefits and services
- Presence and organisation of quality monitoring mechanisms
- Ownership, accreditation, and affiliation status of hospitals and other facilities
- Staff organisation
- Other (other categories to be agreed in consultation with the EPOC editorial team)

Regulatory interventions

Any intervention that aims to change health service delivery or costs by regulation or law. (These interventions may overlap with organisational and financial interventions).

- Changes in medical liability
- Management of patient complaints
- Peer review
- Licensure
- Other (other categories to be agreed in consultation with the EPOC editorial team)

Appendix 2. Search Strategies

MEDLINE

Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present Searched 4 October 2016

No.	Search terms	Results
1	*community pharmacy services/	2635
2	(prevent* adj2 medication error?).ti,ab.	436
3	(((medication or drug) adj2 event) and ((primary adj2 care) or ((family or general) adj (practice or practitioner?)))).ti,ab	46
4	("safety of medications" or prescribing safety or safe prescribing or (safely adj prescribing)).ti,ab	325
5	((structured adj2 (assessment? or care)) and drug?).ti,ab.	175
6	(changes adj4 prescription?).ti,ab.	568
7	(medication adherence/ or patient compliance/) and pharmacists/	634
8	(pharmacist? adj2 (driven or directed or managed)).ti.	243
9	or/1-8	4923

(*Continued*)

10	((adverse drug or adverse medication?) adj2 (admission? or readmission? or event or reduce? or prevent*)).ti,ab	1126
11	((medication related or drug related) adj2 (event? or adverse or admission? or readmission? or readmitted or admitted or problem?)).ti,ab	4316
12	((prevent* or reduce? or reducing or reduction or improve or lower or fewer) adj3 adverse drug).ti,ab	890
13	dt.fs. and ((readmission? or readmit*) adj4 (avoid* or fewer or improv* or less or lower or preventable or rate or rates or reduce? or reduction? or related or unnecessary or avoidable)).ti,ab	504
14	patient readmission/ and ((drug or prescription? or medication?) adj2 (error? or inappropriat* or problem? or related)).ti,ab	85
15	inappropriate prescribing/	1557
16	medication reconciliation/	580
17	community pharmacy services/	3350
18	(community pharmacy or community pharmacist?).ti.	1577
19	(exp drug therapy/ or (pharmaceutical? or prescrib* or prescription? or medication?).ti,ab,hw.) and (near miss or near misses or never event?).ti,ab	274
20	(changes adj3 (medication? or prescription? or prescribing)).ti,ab	2865
21	patient readmission/ and (preventing or preventable or prevent? or unnecessary or avoidable or reduce? or reducing or reduction? or fewer).ti	740
22	(self administration/ or medication adherence/) and medication errors/	239
23	medication errors/ and (prevent*.ti. or (preventable or avoidable).ab.)	931
24	(medication adherence and self care).ti,ab.	199
25	medication adherence.ti,ab. and (self care.ti,ab. or patient education.ti,ab,hw.)	848

(*Continued*)

26	(medication review and (community or home)).ti. or (medication review adj2 (community or home)).ab	48
27	(pharmacist? adj2 (driven or directed or managed)).ab.	390
28	decision support systems, clinical/ and ((drug? or medication?) adj3 (management or prevent* or adverse or event? or related)).ti,ab	284
29	or/10-28	17871
30	medication errors/	11484
31	(medication review or medication reconciliation).ti,ab. or clinical audit/	2574
32	exp *drug therapy/ and ((adverse and event?).ti. or (adverse drug event? or adverse medication*).ab.)	1070
33	((problem? or hospitali?ation? or mortality or morbidity or illness*) adj2 (drug related or drug induced)).ti,ab	1571
34	((error? or mistake? or wrong or adverse event? or near miss or near misses or never event? or incorrect* or inappropriat*) adj3 (drug? or dose or doses or dosage or dosing or pharmaceutical or medication? or prescription? or prescribing)).ti,ab	17195
35	(dispensing adj2 (error? or mistake? or wrong)).ti,ab.	262
36	(drug therapy/ or prescription drugs/ or drug prescriptions/ or pharmaceutical preparations/ or drug dosage calculations/ or drug repositioning/ or drug substitution/ or "off-label use"/ or "drug therapy, combination"/ or "drug therapy, computer-assisted"/ or polypharmacy/) and (mortality/ or (((preventable or avoidable or prescrib* or medication) adj2 (error? or event?)) or mistake? or wrong or incorrect* or inappropriat*).ti,ab.)	4290
37	or/30-36	29692
38	primary health care/ or general practice/ or family practice/ or general practice, dental/ or primary care nursing/	130955
39	((primary adj4 (care or healthcare)) or ((general or family) adj2 practice)).ti,ab	148502
40	(primary care or family medic* or general practice or family practi*).jn	8882

(*Continued*)

41	community medicine/ or community health nursing/ or community health services/ or community health centers/ or home care services/	79553
42	(community care or community healthcare).ti,ab.	4095
43	ambulatory care facilities/ or ambulatory care/	54315
44	((ambulatory or walk-in or neighbo?rhood or community) adj2 (clinic? or care centre or care centres or care center? or health* centre or health* centres or health* center?)).ti,ab	10784
45	maternal-child health centers/ or outpatient clinics, hospital/ or pain clinics/ or community mental health centers/	21343
46	nursing homes/ or intermediate care facilities/ or skilled nursing facilities/	34654
47	(nursing home? or care facility).ti,ab.	30670
48	or/38-47	398235
49	general practitioners/ or physicians, family/ or physicians, primary care/	22546
50	((general or family) adj2 (practitioner? or physician? or doctor?)).ti,ab	65949
51	nurse practitioners/ or physician assistants/	19913
52	(physician? assistant? or doctor? assistant? or physician? extender? or feldsher?).ti,ab. and (ambulatory or community or outpatient? or out-patient?).ti,ab,hw	672
53	(structured assessment? or structured care or case management).ti,ab	10118
54	nurses.ti. or (nurse? adj2 prescrib*).ti,ab.	57795
55	*pharmacists/	8741
56	pharmacist?.ti.	10013
57	or/49-56	174871
58	pharmacists/ or pharmacists' aides/ or pharmaceutical services/ or drug information services/ or clinical pharmacy information systems/	23085

(*Continued*)

59	medication review.ti,ab.	667
60	(pharmaceutical care or pharmacy or pharmacies or pharmacist? or prescriber? or prescribing or prescription? or drug therapy).ti	61398
61	((pharmacist? or prescription? or prescribing or medication?) adj3 (consult* or review* or service or services)).ab	6688
62	((medication? or prescrib* or pharmac*) adj2 (manage? or management or service? or system?)).ti,ab	18502
63	(drug? assess* or drug? audit? or drug? reconcil*).ti,ab.	387
64	(("drug therapy" or dosage? or dose? or medication? or prescription? or prescrib* or pharmacist? or pharmaceutical care) adj2 (managing or management or monitor*)).ti,ab	9624
65	((improv* or optimi?ing or optimi?e? or optimal*) and (dosing or dosage)).ti. or ((improv* or optimi?ing or optimi?e? or optimal*) adj2 (pharmaceutical care or pharmacy or prescrib* or prescript*)).ab	3363
66	((drug therapy or drug regime? or medication? or medicines or pharmacy or pharmacist? or pharmaceutical or prescrib* or prescription?) adj2 (audit* or monitor* or reconcil* or review?)).ti,ab	7239
67	drug utilization review/	3363
68	medication adherence/ or self administration/	21980
69	or/58-68	118774
70	((unexpected or return) adj2 (emergency adj2 (department? or room? or visit?))).ti,ab	62
71	(emergency adj3 (visit? or room? or clinic? or admission?) adj3 (reduc* or fewer or lower)).ti,ab	922
72	reduc* hospital admissions.ti,ab.	362
73	(readmission? adj3 (reduc* or fewer or lower)).ti,ab.	2124
74	((hospital admission? or (readmit* or readmission?)) adj3 (reduc* or fewer or lower)).ti,ab. or patient readmission/	13305

(*Continued*)

75	((preventable or avoidable) adj3 (admission? or readmission? or readmit*)).ti,ab	573
76	patient compliance.ti,ab.	7649
77	(adverse drug or adverse event?).ti,ab.	122534
78	(improve or improvement or improv* patient? or patient outcomes).ti,ab	1028191
79	(ambulatory or outpatient? or out-patient?).ti,ab,hw.	267824
80	or/70-79	1376183
81	(randomized controlled trial or controlled clinical trial).pt. or randomized.ab. or placebo.ab. or clinical trials as topic.sh. or randomly.ab. or trial.ti	1071692
82	exp animals/ not humans.sh.	4323394
83	81 not 82	988060
84	37 and (or/48,57)	4572
85	69 and (or/48,57) and 80	7995
86	or/9,29	19108
87	84 or 85 or 86	27506
88	(clinical decision and drug?).ti.	83
89	(collaborative and (drug? or medication?) and management).ti	45
90	((safe or safety) and ((medication? or drug?) adj management)).ti	26
91	((reduce or reducing or reduced or reduction) and ((medication? or prescrib*) adj2 (error? or mistake or adverse or event?))).ti	269
92	or/88-91	422
93	87 and 83	4692
94	92 or 93	5101

(*Continued*)

95	((prevent* or reduce or reducing) adj2 (medication error? or adverse drug or adverse medication)).ti,ab	1483
96	medication errors/ and (avoid* or intervention or prevent* or reducing or rate or improv* or quality).ti,ab,hw	5124
97	((medication? or drug or prescription?) adj (error? or mistake?) adj5 (avoid* or intervention? or prevent* or reducing or quality improv*)).ti,ab	1052
98	inappropriate prescribing/ and (avoid* or intervention or prevent* or reducing or rate or improv* or quality).ti,ab,hw	759
99	decision support systems, clinical/ and ((drug? or medication?) adj2 (management or adverse or event? or related)).ti,ab	241
100	((structured adj2 (assessment? or care)) and (drug? or medication?)).ti,ab	277
101	(structured assessment? or structured care or case management).ti,ab. and (drug therapy or medication? or pharmaco* therapy or prescription? or prescribing).ti,ab,hw	780
102	("safety of medications" or prescribing safety or safe prescribing or (safely adj prescribing)).ti,ab	325
103	((safe or safety or quality improv*) and ((medication? or drug?) adj management)).ti	31
104	(quality improv* adj10 ((medication? or drug?) adj management)).ab	8
105	(clinical decision and drug?).ti.	83
106	((clinical decision making or decision support) adj4 (prescribing or drug therap* or drug management or medication management or (managing adj2 (drug? or drug therapy or medication?)))).ti,ab	170
107	(collaborative and (drug? or medication?) and management).ti	45
108	medication reconciliation/	580
109	(drug? assess* or drug? audit? or drug? reconcil* or ((medication or drug or prescribing or prescription?) adj2 (reconciliation or review* or audit))).ti,ab	5413

(*Continued*)

110	((medication? or prescrib* or pharmac*) adj2 (manage? or management or service? or system?)).ti,ab	18502
111	(("drug therapy" or dosage? or dose? or medication? or prescription? or prescrib* or pharmacist? or pharmaceutical care) adj2 (managing or management or monitor*)).ti,ab	9624
112	drug utilization review/	3363
113	community pharmacy.ti. or (community adj (pharmacy or pharmacist? or pharmacies)).ab	4021
114	pharmacist?.ti. or (pharmacist? adj2 (collaborat* or driven or directed or led or managed or team*)).ab	10533
115	((pharmacist? or prescription? or prescribing or medication?) adj3 (consult* or review* or service or services)).ab	6688
116	patient readmission/ and (prescription? or drug therapy).ti,hw	179
117	patient readmission/ and (((adverse drug or adverse medication?) adj2 (event or related)) or ((medication related or drug related) adj2 (event? or problem?))).ti,ab	22
118	((drug related or medication related or adverse drug or adverse medication) adj5 (emergency department? or emergency unit? or emergency centre? or emergency center? or emergency room? or afterhours or after hours or (emergency adj2 (admission? or admitting)))).ti,ab	163
119	((drug related or medication related or adverse drug or adverse medication) adj5 (readmission? or readmitted or emergency visit or unexpected visit?)).ti,ab	51
120	(((hospital admission? or (readmit* or readmission?)) adj3 (reduc* or fewer or lower)) or ((avoidable or preventable or reduced or reducing) adj5 (admission? or readmission?))).ti,ab. and (drug or medication? or prescription?).ti,ab,hw	922
121	or/95-120	52001
122	community pharmacy services/	3350
123	primary health care/ or general practice/ or family practice/ or general practice, dental/ or primary care nursing/	130955
124	((primary adj2 care) or ((general or family) adj2 practice)).ti,ab	141092

(*Continued*)

125	(primary care or family medic* or general practice or family practi*).jn	8882
126	community medicine/ or community health nursing/ or community health services/ or community health centers/ or home care services/	79553
127	(community or ambulatory).ti,ab,hw.	556987
128	ambulatory care facilities/ or ambulatory care/	54315
129	((walk-in or neighbo?rhood) adj2 (clinic? or care centre or care centres or care center? or health* centre or health* centres or health* center?)).ti,ab	848
130	maternal-child health centers/ or outpatient clinics, hospital/ or pain clinics/ or community mental health centers/	21343
131	nursing homes/ or intermediate care facilities/ or skilled nursing facilities/	34654
132	((patient? adj2 (home or homes)) or home visit?).ti,ab.	14823
133	or/123-132	798316
134	general practitioners/ or physicians, family/ or physicians, primary care/	22546
135	((general or family) adj2 (practitioner? or physician? or doctor?)).ti,ab	65949
136	((primary care or family or general practice or community or home care) adj2 (nurse or nurses)).ti,ab	6697
137	or/134-136	82852
138	121 and (or/133,137)	13867
139	138 or 122	14799
140	(randomized controlled trial or controlled clinical trial).pt. or randomized.ab. or placebo.ab. or clinical trials as topic.sh. or randomly.ab. or trial.ti	1071692
141	exp animals/ not humans.sh.	4323394
142	140 not 141	988060

(*Continued*)

143	139 and 142	1916
144	94 or 143	5768
145	(pharmacist? and (adverse drug event? or adverse medication event?)).ti	23
146	(pharmacist? and adverse drug reaction?).ti.	58
147	(admission? and (adverse drug event? or adverse medication event? or adverse drug reaction?)).ti	101
148	(prevent$ and medication error?).ti.	224
149	(prevent$ and (adverse drug event? or adverse medication event? or adverse drug reaction?)).ti	214
150	or/145-149	597
151	83 and 150	32
152	144 or 151	5774

Embase

Embase 1974 to 2016 October 03
Searched 4 October 2016

No.	Search terms	Results
1	(((primary adj2 care) or general practi*) and (adverse drug? or adverse medication? or medication related or drug related or preventable drug? or preventable medication? or (avoidable and (drug? or medication? or pharmacother*)))).ti	101
2	((ambulatory or outpatient?) and (adverse drug? or adverse medication? or medication related or drug related or preventable drug? or preventable medication? or (avoidable and (drug? or medication? or pharmacother*)))).ti	158
3	or/1-2	257
4	((prevent* or reduce or reducing) adj2 (drug related or medication related or medication error? or adverse drug or adverse medication)).ti,ab	2780
5	*"drug use"/ and (adverse or readmission? or readmit* or emergency or problem or safety or safely or harm*).ti,ab	4163

(*Continued*)

6	((drug? or medication?) adj4 (emergency or readmission* or readmit* or (urgent adj2 (care or visit?)))).ti,ab	3206
7	*medication error/ and (avoid* or intervention or prevent* or reducing or rate or improv* or quality).ti,ab	3616
8	((medication? or drug or prescription?) adj (error? or mistake?) adj5 (avoid* or intervention? or prevent* or reducing or quality improv*)).ti,ab	1733
9	*inappropriate prescribing/ and (avoid* or intervention or prevent* or reducing or rate or quality improv*).ti,ab,hw	404
10	(*clinical decision making/ or *medical decision making/) and (drug? therapy or medication? management or prescribing or pharmaceutical care or adverse drug or adverse medication or medication related).ti,ab	286
11	((clinical decision making or decision support) adj4 (prescribing or drug therap* or drug management or medication management or (managing adj2 (drug? or drug therapy or medication?)))).ti,ab	198
12	((structured adj2 (assessment? or care)) and (drug? or medication?)).ti,ab	423
13	(case management and (drug therapy or medication? or pharmaco* therapy or prescription? or prescribing)).ti,ab	883
14	("safety of medications" or prescribing safety or safe prescribing or (safely adj prescribing)).ti,ab	554
15	((safe or safety or quality improv*) and ((medication? or drug?) adj2 management)).ti	87
16	(quality improv* adj10 ((medication? or drug?) adj management)).ab	15
17	(collaborative and (drug? or medication?) and management).ti	73
18	(computer assisted drug therapy/ or *drug therapy/ or *drug choice/ or *drug dose regimen/ or *pharmaceutical care/) and (((readmission? or readmit*) adj3 (patient? or rate or rates or reduce? or avoid* or prevent*)) or medication related or (emergency adj3 (vist? or admission? or admitt* or readmission? or readmit*)) or medication related or ((adverse or avoid* or drug or medication or prevent*) adj2 event?)).ti,ab	4260

(*Continued*)

19	*medication therapy management/	2813
20	(drug? assess* or drug? audit? or drug? reconcil* or ((medication or drug or prescribing or prescription?) adj2 (reconciliation or review* or audit))).ti,ab	9698
21	((medication? or prescrib* or pharmac*) adj2 (manage? or management or service? or system?)).ti,ab	30705
22	(("drug therapy" or dosage? or dose? or medication? or prescription? or prescrib* or pharmacist? or pharmaceutical care) adj2 (managing or management or monitor*)).ti,ab	14843
23	*"drug use"/ and (adverse or avoidable or emergency or preventable or readmission? or mortality).ti,ab	2412
24	(community adj (pharmacy or pharmacist? or pharmacies) adj5 (quality improv* or readmission? or readmitt* or mortalitly or (adverse adj2 (reduc* or prevent* or avoid*)))).ab	20
25	pharmacist?.ti. or (pharmacist? adj2 (collaborat* or driven or directed or led or managed or team*)).ab	21725
26	((pharmacist? or prescription? or prescribing or medication?) adj3 (consult* or review* or service or services)).ab	12144
27	*hospital readmission/ and (adverse drug or adverse medication or medication related or adverse event? or ((avoidable or preventable) adj2 (adverse or event?))).ti,ab	240
28	((drug related or medication related or adverse drug or adverse medication) adj5 (emergency department? or emergency unit? or emergency centre? or emergency center? or emergency room? or afterhours or after hours or (emergency adj2 (admission? or admitting)))).ti,ab	247
29	((drug related or medication related or adverse drug or adverse medication) adj5 (readmission? or readmitted or emergency visit or unexpected visit?)).ti,ab	87
30	((((hospital admission? or (readmit* or readmission?)) adj3 (reduc* or fewer or lower)) or ((avoidable or preventable or reduced or reducing) adj5 (admission? or readmission?))) and (drug? or medication? or prescription?)).ti,ab	1724
31	((problem? or hospitali?ation? or mortality or morbidity or illness*) adj2 (drug related or drug induced)).ti,ab	2687

(*Continued*)

32	*medication error/ and (reduc*.ti. or ((prevent* or avoid* or rate or rates or reduc* or fewer) adj3 (admission? or readmission? or emergency or prevent* or quality improv*)).ti,ab.)	2027
33	medication therapy management/ and (adverse or avoidable or emergency or preventable or readmission? or mortality).ti,ab	1596
34	*drug therapy/ and adverse event?.ti,ab.	2290
35	((*hospital readmission/ and dt.fs.) or (dt.fs. and (readmission? or readmit*)).ti,ab.) and (preventable or avoidable or adverse).ti,ab	392
36	(drug therapy/ or (pharmaceutical? or prescrib* or prescription? or medication?).ti,ab.) and (near miss or near misses or never event?).ti,ab	399
37	((appropriat* or inappropriate or unsafe) adj3 (medicine? or prescrib* or drug therap* or pharmacotherap*)).ti,ab	5847
38	or/4-37	94819
39	*primary health care/ or *primary medical care/ or *general practice/	97127
40	((primary adj2 care) or ((general or family) adj2 practice)).ti,ab	171036
41	(primary care or family medic* or general practice or family practi*).jn	10436
42	*community medicine/ or *community health nursing/ or *community care/ or *home care/	67132
43	(community or ambulatory).ti,ab.	514922
44	*outpatient/ or *outpatient care/ or *outpatient department/ or *community mental health center/	40935
45	((walk-in or neighbo?rhood) adj2 (clinic? or care centre or care centres or care center? or health* centre or health* centres or health* center?)).ti,ab	997
46	*nursing home/ or *residential home/	28324
47	((patient? adj2 (home or homes)) or home visit?).ti,ab.	20542

(*Continued*)

48	*general practitioner/	21735
49	((general or family) adj2 (practitioner? or physician? or doctor?)).ti,ab	82552
50	or/39-49	857629
51	(ecstasy or marijuana or methamphet* or illegal* or street drug? or cocaine? or cannabis or inject* drug or drug user?).ti,ab,hw	136236
52	((drug? or alcohol?) adj2 (abus* or addict* or dependence)).ti,ab,hw	165048
53	(placebo or "head to head").ti,ab.	251431
54	or/51-53	504531
55	multicenter study/	152623
56	controlled clinical trial/ or controlled study/ or randomized controlled trial/	5318787
57	randomi?ed.ti. or ((random* or control) adj3 (group? or cohort? or patient? or hospital* or department?)).ab. or (controlled adj2 (study or trial)).ti	894626
58	(random sampl* or random digit* or random effect* or random survey or random regression).ti,ab. not randomized controlled trial/	74604
59	(exp animals/ or exp invertebrate/ or animal experiment/ or animal model/ or animal tissue/ or animal cell/ or nonhuman/) and (human/ or normal human/ or human cell/)	18016161
60	(exp animals/ or exp invertebrate/ or animal experiment/ or animal model/ or animal tissue/ or animal cell/ or nonhuman/) not 59	5847628
61	(or/55-57) not (or/58,60)	3860921
62	medication safety.ti,ab.	1951
63	((optim* or evidence based or rational*) adj2 prescrib*).ti,ab	1711
64	hospitali?ation?.ti,ab.	181464

(*Continued*)

65	(emergency or urgent care or visit? or adverse or medication related or drug related or safely or safety or fewer or drug therapy or pharmacotherap* or improve? patient? outcome or readmission? or ((lower* or reduc*) adj2 admission?)).ti,ab,hw	2550209
66	*drug interaction/ and (prevent* or avoid* or reduc*).ti.	1132
67	(drug drug interaction? adj4 (reduc* or avoid* or prevent*)).ti,ab	382
68	or/62-67	2664679
69	((38 and 50 and 61 and 68) not 54) or 3	2877
70	(2013* or 2014* or 2015* or 2016*).dp,dd,yr,em.	29074507
71	69 and 70	2695

The Cochrane Library
Searched 4 October 2016

No.	Search terms	Results
#1	((prevent* or reduce or reducing) near/2 (medication error? or adverse drug or adverse medication)):ti,ab	61
#2	[mh "medication errors"] and (avoid* or intervention or prevent* or reducing or rate or improv* or quality):ti,ab,kw	250
#3	((medication? or drug or prescription?) near/1 (error? or mistake?) near/5 (avoid* or intervention? or prevent* or reducing or quality improv*)):ti,ab	2
#4	[mh "inappropriate prescribing"] and (avoid* or intervention or prevent* or reducing or rate or improv* or quality):ti,ab,kw	64
#5	[mh "decision support systems, clinical"] and ((drug? or medication?) near/2 (management or adverse or event? or related)):ti,ab	0
#6	((structured near/2 (assessment? or care)) and (drug? or medication?)):ti,ab	18
#7	(structured assessment? or structured care or case management):ti,ab and (drug therapy or medication? or pharmaco* therapy or prescription? or prescribing):ti,ab,kw	1074

(*Continued*)

#8	("safety of medications" or prescribing safety or safe prescribing or (safely next prescribing)):ti,ab	259
#9	((safe or safety or quality improv*) and ((medication? or drug?) near/1 management)):ti	0
#10	(quality improv* near/10 ((medication? or drug?) near/1 management)):ab	1
#11	(clinical decision and drug?):ti	0
#12	((clinical decision making or decision support) near/4 (prescribing or drug therap* or drug management or medication management or (managing near/2 (drug? or drug therapy or medication?)))):ti,ab	19
#13	(collaborative and (drug? or medication?) and management):ti	0
#14	[mh "medication reconciliation"]	40
#15	(drug? assess* or drug? audit? or drug? reconcil* or ((medication or drug or prescribing or prescription?) near/2 (reconciliation or review* or audit))):ti,ab	14511
#16	((medication? or prescrib* or pharmac*) near/2 (manage? or management or service? or system?)):ti,ab	626
#17	(("drug therapy" or dosage? or dose? or medication? or prescription? or prescrib* or pharmacist? or pharmaceutical care) near/2 (managing or management or monitor*)):ti,ab	222
#18	[mh "drug utilization review"]	134
#19	community pharmacy:ti or (community next pharmac*):ab	491
#20	pharmacist?:ti or (pharmacist? near/2 (collaborat* or driven or directed or led or managed or team*)):ab	268
#21	((pharmacist? or prescription? or prescribing or medication?) near/3 (consult* or review* or service or services)):ab	200
#22	[mh "patient readmission"] and (prescription? or drug therapy):ti,kw	59
#23	[mh "patient readmission"] and (((adverse drug or adverse medication?) near/2 (event or related)) or ((medication related or drug related) near/2 (event? or problem?))):ti,ab	4

(*Continued*)

#24	((drug related or medication related or adverse drug or adverse medication) near/5 (emergency department? or emergency unit? or emergency centre? or emergency center? or emergency room? or afterhours or after hours or (emergency near/2 (admission? or admitting))):ti,ab	3
#25	((drug related or medication related or adverse drug or adverse medication) near/5 (readmission? or readmitted or emergency visit or unexpected visit?)):ti,ab	8
#26	(((hospital admission? or (readmit* or readmission?)) near/3 (reduc* or fewer or lower)) or ((avoidable or preventable or reduced or reducing) near/5 (admission? or readmission?))): ti,ab and (drug or medication? or prescription?):ti,ab,kw	124
#27	{or #1-#26}	17390
#28	[mh "community pharmacy services"]	250
#29	[mh "primary health care"] or [mh "general practice"] or [mh "family practice"] or [mh "general practice, dental"] or [mh "primary care nursing"]	8243
#30	((primary near/2 care) or ((general or family) near/2 practice)):ti,ab	14278
#31	[mh "community medicine"] or [mh "community health nursing"] or [mh "community health services"] or [mh "community health centers"] or [mh "home care services"]	12860
#32	(community or ambulatory):ti,ab,kw	36494
#33	[mh "ambulatory care facilities"] or [mh "ambulatory care"]	5379
#34	((walk-in or neighbo?rhood) near/2 (clinic? or care centre or care centres or care center? or health* centre or health* centres or health* center?)):ti,ab	4
#35	[mh "maternal-child health centers"] or [mh "outpatient clinics, hospital"] or [mh "pain clinics"] or [mh "community mental health centers"]	842
#36	[mh "nursing homes"] or [mh "intermediate care facilities"] or [mh "skilled nursing facilities"]	1204
#37	((patient? near/2 (home or homes)) or home visit?):ti,ab	3045
#38	{or #29-#37}	61131

(*Continued*)

#39	[mh "general practitioners"] or [mh "physicians, family"] or [mh "physicians, primary care"]	747
#40	((general or family) near/2 (practitioner? or physician? or doctor?)):ti,ab	3101
#41	((primary care or family or general practice or community or home care) near/2 (nurse or nurses)):ti,ab	457
#42	{or #39-#41}	3950
#43	#27 and (#38 or #42)	2668
#44	#28 or #43	2719

CINAHL (EBSCO)
Searched 4 October 2016

No.	Search terms	Results
S1	MH Medication errors	8,902
S2	TI ((medication review or medication reconciliation)) OR AB ((medication review or medication reconciliation))	1,484
S3	MH "Drug Therapy+" AND (TI adverse event# OR AB adverse event#)	2,408
S4	TI (((problem# or hospitali#ation# or mortality or morbidity or illness*) N2 (drug related or drug induced))) OR AB (((problem# or hospitali#ation# or mortality or morbidity or illness*) N2 (drug related or drug induced)))	512
S5	TI (((error# or mistake# or wrong or adverse event# or near miss or near misses or never event# or incorrect* or inappropriat*) N3 (drug# or dose or doses or dosage or dosing or pharmaceutical or medication# or prescription# or prescribing))) OR AB (((error# or mistake# or wrong or adverse event# or near miss or near misses or never event# or incorrect* or inappropriat*) N3 (drug# or dose or doses or dosage or dosing or pharmaceutical or medication# or prescription# or prescribing)))	6,946
S6	TI ((dispensing N2 (error# or mistake# or wrong))) OR AB ((dispensing N2 (error# or mistake# or wrong)))	62

(*Continued*)

S7	((MH Mortality) AND (MH Drug therapy OR MH Prescriptions, Drug OR MH Drugs, Prescription OR MH Dosage Calculation OR MH Drugs, Off-Label OR MH "Drug Therapy, Combination" OR MH "Drug Therapy, Computer-Assisted" OR MH Polypharmacy)) OR (TI ((((preventable or avoidable or prescrib* or medication) N2 error#) or mistake# or wrong or incorrect* or inappropriat*)) OR AB ((((preventable or avoidable or prescrib* or medication) N2 error#) or mistake# or wrong or incorrect* or inappropriat*)))	20,695
S8	S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7	31,409
S9	MH Primary Health Care OR MH Family practice	43,304
S10	TI (((primary N4 (care or healthcare)) or ((General or family) N2 practice))) OR AB (((primary N4 (care or healthcare)) or ((General or family) N2 practice)))	47,581
S11	MH Community medicine OR MH community health nursing OR MH community health services OR MH community health centers OR MH home health care	49,837
S12	TI ((community care or community healthcare)) OR AB ((community care or community healthcare))	14,011
S13	MH Ambulatory Care Facilities OR MH Ambulatory Care	9,934
S14	TI (((ambulatory or walk-in or neighbo#rhood or community) N2 (clinic# or care centre or care centres or care center# or health* centre or health* centres or health* center#))) OR AB (((ambulatory or walk-in or neighbo#rhood or community) N2 (clinic# or care centre or care centres or care center# or health* centre or health* centres or health* center#)))	4,226
S15	MH Pain Clinics OR MH Nursing Homes OR MH Skilled Nursing Facilities	18,610
S16	TI ((nursing home# or care facility)) OR AB ((nursing home# or care facility))	22,849
S17	S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16	162,691
S18	MH Physicians, Family	9,090
S19	TI (((general or family) N2 (practitioner# or physician# or doctor#))) OR AB (((general or family) N2 (practitioner# or physician# or doctor#)))	12,972

(*Continued*)

S20	(MH nurse practitioners OR MH physician Assistants) AND (TI community OR AB community OR MW community)	834
S21	(TI ((physician# assistant# or doctor# assistant# or physician# extender# or feldsher#)) OR AB ((physician# assistant# or doctor# assistant# or physician# extender# or feldsher#))) AND ((TI community OR AB community OR MW community))	170
S22	S18 OR S19 OR S20 OR S21	20,115
S23	MH Pharmacists OR MH Pharmacy Technicians OR MH Drug Information Services OR MH Clinical Pharmacy Information Systems	6,238
S24	TI medication review OR AB medication review	1,119
S25	TI (pharmaceutical care or pharmacy or pharmacies or pharmacist# or prescriber# or prescribing or prescription# or drug therapy)	19,149
S26	AB ((pharmacist# or prescription# or prescribing or medication#) N3 (consult* or review* or service or services))	2,074
S27	TI (((medication# or prescrib* or pharmac*) N2 (manage# or management or service# or system#))) OR AB (((medication# or prescrib* or pharmac*) N2 (manage# or management or service# or system#)))	6,368
S28	TI ((drug# assess* or drug# audit# or drug# reconcil*)) OR AB ((drug# assess* or drug# audit# or drug# reconcil*))	2,283
S29	TI ((("drug therapy" or dosage# or dose# or medication# or prescription# or prescrib* or pharmacist# or pharmaceutical care) N2 (managing or management or monitor*))) OR AB ((("drug therapy" or dosage# or dose# or medication# or prescription# or prescrib* or pharmacist# or pharmaceutical care) N2 (managing or management or monitor*)))	3,702
S30	TI (((improv* or optimi#ing or optimi#e# or optimal*) and (dosing or dosage))) OR AB (((improv* or optimi#ing or optimi#e# or optimal*) N2 (pharmaceutical care or pharmacy or prescrib* or prescript*)))	846
S31	TI (((drug therapy or drug regime# or medication# or medicineS or pharmacy or pharmacist# or pharmaceutical or PRESCRIB* or prescription#) N2 (audit* or monitor* or reconcil* or review#))) OR AB (((drug therapy or drug regime#	3,183

(*Continued*)

	or medication# or medicineS or pharmacy or pharmacist# or pharmaceutical or PRESCRIB* or prescription#) N2 (audit* or monitor* or reconcil* or review#)))	
S32	MH Drug Utilization	4,070
S33	S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29 OR S30 OR S31 OR S32	35,911
S34	TI ((emergency N3 (visit# or room# or clinic# or admission#) N3 (reduc* or fewer or lower))) OR AB ((emergency N3 (visit# or room# or clinic# or admission#) N3 (reduc* or fewer or lower)))	412
S35	TI reduc* hospital admissions OR AB reduc* hospital admissions	552
S36	TI ((readmission# N3 (reduc* or fewer or lower))) OR AB ((readmission# N3 (reduc* or fewer or lower)))	989
S37	MH Readmission AND (TI (((hospital admission# or (readmit* or readmission#)) N3 (reduc* or fewer or lower))) OR AB (((hospital admission# or (readmit* or readmission#)) N3 (reduc* or fewer or lower))))	725
S38	S34 OR S35 OR S36 OR S37	1,902
S39	S8 and S17	2,345
S40	S8 and S22	464
S41	S33 and S17	4,462
S42	S33 and S22	945
S43	S33 and S38	102
S44	S39 OR S40 OR S41 OR S42 OR S43	6,625
S45	(MM "Clinical Trials+") OR (MH "Multicenter Studies")	23,509
S46	TI ("clinical study" or "clinical studies") or AB ("clinical study" or "clinical studies")	8,089
S47	TI random* or AB random*	130,238
S48	TI (control group or control groups OR control* experiment* or control* design or controlled study) OR AB (control group OR control groups or control* cohort* or controlled experiment* controlled design or controlled study)	58,722

(*Continued*)

S49	TI (cluster N2 trial* or cluster N2 study or cluster N2 group or cluster N2 groups or cluster N2 cohort or cluster N2 design or cluster N2 experiment*) OR AB (cluster N2 trial* or cluster N2 study or cluster N2 group or cluster N2 groups or cluster N2 cohort or cluster N2 design or cluster N2 experiment*)	2,286
S50	TI multicentre or multicenter or multi-centre or multi-center	25,954
S51	AB ((multicent* n2 design*) or (multicent* n2 study) or (multicent* n2 studies) or (multicent* n2 trial*)) or AB ((multi-cent* n2 design*) or (multi-cent* n2 study) or (multi-cent* n2 studies) or (multi-cent* n2 trial*))	8,384
S52	TI controlled AND TI (trial or trials or study or experiment* or intervention)	23,532
S53	S45 OR S46 OR S47 OR S48 OR S49 OR S50 OR S51 OR S52	192,373
S54	S44 and S53	835
S55	TI ((((medication or drug) N2 event) and ((primary N2 care) or ((family or general) N2 (practice or practitioner#))))) OR AB ((((medication or drug) N2 event) and ((primary N2 care) or ((family or general) N2 (practice or practitioner#)))))	58
S56	S54 OR S55	871
S57	S56 Limiters - Exclude MEDLINE records	116

Appendix 3. GRADE evidence profile: professional interventions compared to standard care for preventation of medication errors

Grade evidence profile: professional interventions compared to standard/usual care for prevention of medication errors			
Patient or population: adults receiving medication in primary care **Setting:** primary and community care **Intervention:** professional interventions (using health information technology to identify patients at risk or help to generate a care plan for patients) **Comparison:** standard/usual care			
Quality assessment	**Effect**	**Quality**	**Importance**

(*Continued*)

№ of participants/ studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Relative/ absolute (95% CI)		
Number of hospital admissions									
PI: 41/ 1949 (2. 1%) SC: 33/ 1940 (1. 7%) (2 studies)	Randomised trials	Not serious	Not serious	Not serious	Serious[a]	None	**Relative: RR 1.24** (0.79 to 1. 96) **Absolute: 4 more per 1000** (from 4 fewer to 16 more)	⊕⊕⊕◯ Moderate	Not Important
Number of people admitted to hospital									
PI: 827/ 1870 (44. 2%) SC: 802/ 1791 (44. 8%) (1 study)	Randomised trials	Not serious	Not serious	Not serious	Not serious	None	**Relative: RR 0.99** (0.92 to 1. 06) **Absolute: 5 fewer per 1000** (from 27 more to 36 fewer)	⊕⊕⊕⊕ High	Not Important
Number of emergency department visits									
PI: 47/552 (8.5%) SC: 61/ 515 (11. 8%) (2 studies)	Randomised trials	Serious[b]	Not serious	Not serious	Serious[a]	None	**Relative: RR 0.71** (0.50 to 1. 02) **Absolute: 33 fewer per 1000** (from 2 more to 59 fewer)	⊕⊕◯◯ Low	Important
Mortality									
PI: 211/ 1769 (11. 9%) SC:215/	Randomised trials	Serious[b]	Not serious	Not serious	Not serious	None	**Relative: RR 0.98** (0.82 to 1.	⊕⊕⊕◯ Moderate	Not Important

(*Continued*)

1769 (12.2%) (1 study)							17) **Absolute: 3 fewer per 1000** (from 21 more to 22 fewer)		

CI: confidence interval; **PI**: professional intervention; **RR:** risk ratio; **SC**: standard care
[a]We downgraded one level due to imprecision.
[b]We downgraded one level due to risk of bias (selection bias).

Appendix 4. GRADE evidence profile: organisational Interventions compared to standard care for prevention of medication errors

Organisational interventions compared to standard/usual care for prevention of medication errors
Patient or population: adults receiving medication in primary care **Setting:** primary care **Intervention:** organisational interventions (provision of pharmaceutical care, medication reviews, follow-up visits by a healthcare professional (e.g. pharmacist, nurse or physician) **Comparison:** standard/usual care
Quality assessment
№ of participants/ studies
Number of hospital admissions
OI: 817/3100 (26.4%) SC: 850/3103 (27.4%) (11 studies)
Number of people admitted to hospital
OI: 2846/73,313 (3.9%) SC: 3221/78,924 (4.1%) (13 studies)
Number of emergency departments visits
OI: 171/849 (20.1%) SC: 227/970 (23.4%) (5 studies)
Mortality

(*Continued*)

OI: 3180/74,017 (4.3%) SC: 4085/80,945 (5.0%) (12 studies)

CI: confidence interval; **OI**: organisational intervention; **RR:** risk ratio; **SC**: standard care
[a]We downgraded one level for unclear risk of bias (selection and attrition bias).
[b]We downgraded one level for inconsistency (high heterogeneity across studies).
[c]We downgraded one level for imprecision.
[d]We downgraded one level for high risk of bias (selection, performance and attrition bias).

HISTORY

Protocol first published: Issue 4, 2002

Review first published: Issue 10, 2017

Date	Event	Description
14 January 2013	New citation required and major changes	New authors list added and new contact author for this review is listed. Title changed from 'Interventions for reducing preventable drug-related hospital admissions or preventable drug-related morbidity in primary care'. The search strategy has been significantly revised from the original protocol

CONTRIBUTIONS OF AUTHORS

Anthony Avery, Hanan Khalil and Aziz Sheikh were involved in the conception of this review, the drafting of the initial protocol and providing critical feedback on drafts of the review.

Helen Chambers retrieved the studies and provided support with the searching.

Hanan Khalil, Helen Chambers and Brian Bell selected the studies for inclusion/exclusion and critically appraised the included studies.

Hanan Khalil undertook the analysis described in the review and wrote the review. Brian Bell helped with editing the review.

DECLARATIONS OF INTEREST

Hanan Khalil has no conflicts of interest to declare.

Brian Bell has no conflicts of interest to declare.

Helen Chambers has no conflicts of interest to declare.

Aziz Sheikh received a WHO grant addressing patient safety in primary care.

Tony Avery received BUPA Foundation funding in 2001 to 2002 on a much earlier version of this review (Smeaton 2002).

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- Monash University, Faculty of Medicine, Nursing and Health Sciences, School of Rural Health, Clayton, Vic 3168, Australia.

External sources

- No sources of support supplied

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

For the primary outcome, we included all the studies that reported on the number of hospital admissions and the number of participants admitted to hospitals. The two outcomes are different since some people can have more than one hospital admission.

We also included all the trials in the final meta-analysis, irrespective of their qualities. Removing them from the analysis would give rise to selective reporting.