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META-ANALYSIS

Do pharmacist-led medication reviews in hospitals help reduce hospital readmissions? A systematic review and meta-analysis

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Keywords clinical pharmacy, medication reconciliation, medication review, meta-analysis, pharmacists, systematic review

AIMS

The aim of this meta-analysis is to examine the impact of in-hospital pharmacist-led medication reviews in paediatric and adult patients.

METHODS

Relevant studies were identified from the Medline and Cochrane Library databases. Studies were included if they met the following criteria (without any language or date restrictions): design: randomized controlled trial; intervention: in-hospital pharmacist-led medication review (experimental group) *vs.* usual care (control group); participants: paediatric or adult population. The primary outcome was all-cause readmissions and/or emergency department (ED) visits at different time points. The secondary outcomes were all-cause readmissions, all-cause ED visits, drug-related readmissions, mortality, length of hospital stay, adherence and quality of life. We calculated the relative risk (RR) or mean differences (MD) with 95% confidence intervals (CIs) for each study. We used fixed and/or random effects models. Heterogeneity was assessed using the I^2 statistic.

RESULTS

We systematically reviewed 19 randomized controlled trials (4805 participants). The readmission rates did not differ between the experimental group and the control group (RR = 0.97, 95% CI 0.89; 1.05, $p = 0.470$). The secondary outcomes did not differ between the two groups, except for in drug-related readmissions, which were lower in the experimental group (RR = 0.25, 95% CI 0.14; 0.45, $p < 0.001$), and all-cause ED visits (RR = 0.70, 95% CI 0.59; 0.85 $p = 0.001$).

CONCLUSION

The low-quality evidence in this analysis suggests an impact of pharmacist-led medication reviews on drug-related readmissions and all-cause ED visits. Few studies reported on adherence and quality of life. More high-quality randomized clinical trials are needed to assess the impact of pharmacist-led medication reviews on patient-relevant outcomes, including adherence and quality of life.

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WHAT IS ALREADY KNOWN ABOUT THIS SUBJECT

- Pharmacist-led medication reconciliation interventions are an effective strategy to reduce medication discrepancies, and have a greater impact when conducted at either hospital admission or discharge. However, pharmacist-led medication reviews at hospital settings programmes have not shown great interest in the use of post-hospital healthcare.

WHAT THIS STUDY ADDS

- In this article, we further explore the clinical impact of pharmacist-led medication review at the hospital setting. We show that pharmacist-led medication reviews have an impact on drug-related readmission, all-cause ED visits and adherence. We also show the quality and strength of evidence from these studies is low.

Introduction

Early hospital readmission of patients discharged from hospital are a public health problem. The ENEIS 2 study reported that the number of hospital admissions caused by preventable serious adverse drug events (ADEs) represented 1.3% of hospital admissions in France in 2009 [1]. Medication reviews are considered a key element in improving the quality of prescriptions and in preventing ADEs among hospitalized patients [2]. A medication review is 'a structured, critical examination of a patient's medicines with the objective of reaching an agreement with the patient about treatment, optimising the impact of medicines, minimising the number of medication-related problems and reducing waste' [3]. When performed by pharmacists, this process is called a pharmacist-led medication review. Pharmacist-led medication reviews have been widely introduced in hospitals based on three types of interventions: (i) prescription review (type 1), (ii) adherence review (AR) (type 2) and (iii) clinical medication review (CMR) (type 3).

However, the impact of in-hospital pharmacist-led medication reviews has not been clearly demonstrated. To our knowledge, four meta-analyses have studied the impact of hospital pharmacist-led medication reviews [4–7], but they did not explore several outcomes of clinical importance (i.e., all-cause readmission, emergency department visits, drug-related readmissions, all-cause mortality, length of hospital stay, adherence and quality of life). Moreover, they varied in terms of the location of the intervention (hospital and community settings) [5, 6]. The primary outcomes also varied, including reducing drug-related problems, adverse drug reactions, and hospital readmissions and improving the appropriateness of medications. No studies to date have been sufficiently broad to test whether this type of intervention can reduce mortality, and although many studies have measured quality of life, this is rarely a primary outcome. Furthermore, the various analyses did not take into account the different timing of endpoints used to calculate the hospital readmission rates [4–7]. Indeed, such studies usually considered hospital readmissions at various time points (i.e., 30 days, 60 days, 6 months or 1 year) a common outcome. This could be very problematic, as the causes of readmissions may strongly differ according to these time points. Finally, some meta-analyses have included randomized controlled trials (RCTs) and non-RCTs [4].

The aim of the present review is to evaluate the impact of in-hospital pharmacist-led medication reviews on clinical outcomes at different time points.

Methods

Searching strategy

This meta-analysis was based on the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) criteria [8]. To identify relevant studies, we reviewed the following databases: Medline (from January 1990 to December 2015) and the Cochrane Library (from January 1990 to December 2015). A specific search strategy was developed based on a broad range of indexed terms and medical subject headings (*i.e.*, medication reconciliation, medication therapy management, pharmaceutical services, drug therapy, drug utilization, patient education as topic, medication adherence, medication errors, patient medication knowledge, hospital, patient discharge, emergency medical services, hospitalization, ambulatory care, pharmacies, pharmacists and pharmacy). The algorithm used is listed in Appendices S1 and S2. Furthermore, the ProQuest dissertations and theses full-text database was used to identify unpublished dissertations. The references of the included studies were examined to search for additional trials.

Selecting studies

Studies were included if they met the following criteria: design: RCT; intervention: pharmacist-led medication review in a hospital (experimental group) *vs*. usual care (control group); participants: adult or paediatric participants; outcomes: evaluation of the selected outcomes based on a validated measure; and language: French or English. Because prescription review (type 1) is usually considered a component of pharmacists' routine practice in dispensing medications, this service was considered the usual care or control group.

The interventions had to be principally delivered by a pharmacist. The pharmacist-led medication reviews were categorized by type based on objective descriptions (see Table 1).

Manuscripts that met the following criteria were excluded: reports of qualitative data only, user-satisfaction surveys, conference presentations, opinion pieces, letters, non-RCTs, and interventions delivered principally by a community pharmacist. Interventions that were delivered by combinations of health professionals (e.g., physicians, nurses) in which the pharmacist was only partly involved were also excluded.

Outcome measures

The primary outcome was all-cause readmissions and/or ED visits, i.e., the number of hospitalized patients regardless of

Table 1

Description of the types of medication review led by pharmacists

Type	Name of service	Definition/Objective	Possible intervention provided
1	Prescription review	Definition: addresses issues related to patient prescriptions or medications. Objective: to address the technical issues related to a patient's prescriptions such as anomalies or changed items.	✓ Drug interactions ✓ Side effects ✓ Dosage ✓ Drug availability
2	Adherence review	Definition: a comprehensive and systematic evaluation of patient's understanding of and adherence to prescribed medication treatment. Objective: to improve understanding and adherence to prescribed medication treatment: identify and address factors linked to non-adherent behaviours as well as minimize pharmaceutical waste.	✓ Medication review of drug adherence ✓ Therapeutic education ○ Therapeutic goals ○ Management of adverse events
3	Clinical medication review	Definition: a systematic and patient-centred clinical assessment of all medicines currently taken by a patient. Objective: to identify, resolve and prevent medication-related problems as well as optimize the effectiveness of medication treatment.	✓ Medication reconciliation ✓ Treatment review (dosages, drug interactions, side effects and therapeutic objectives, etc.) ✓ Pharmaceutical interventions ✓ Multidisciplinary revision of drug prescriptions ✓ Medication liaison service ▪ Comprehensive medication history, ▪ Discharge letter faxed to general practitioner and community pharmacist, ▪ Discharge counselling

the cause of hospitalization and the number of non-hospitalized patients who visited an emergency department. The secondary outcomes were all-cause readmissions (the number of hospitalized patients regardless of the cause of hospitalization), all-cause ED visits (the number of non-hospitalized patients who visited an emergency department), drug-related readmissions, all-cause mortality, length of hospital stay, adherence and quality of life.

Selection of studies and data extraction

Two authors (PR and SH) screened the titles and abstracts of the database records, retrieved full texts to assess their eligibility and independently checked the full-text records for eligibility. Disagreements were resolved by consensus. The manuscripts of the studies were then independently reviewed by two of the authors (PR and SH). The following data were independently extracted into a standard electronic form: first author name, date of publication, country, design, sample size, number of patients, mean age, type of pharmacist-led medication review, follow-up after discharge, readmission rate collection, intervention details, all-cause readmissions and/or ED visits, all-cause readmissions, all-cause ED visits, drug-related readmissions, all-cause mortality, length of hospital stay, adherence and quality of life. We developed a data extraction form (based on the Cochrane Consumers and Communication Review Group's data extraction template), pilot-tested it on ten randomly-selected included studies, and refined it accordingly [9]. Data extraction was performed based on the intention-to-treat (ITT) principle. For all events, we considered the shortest available follow-up period because the impact of pharmacist-led medication reviews is probably the most substantial during the first 30 days following discharge. After this period, external factors can become predominant, and readmissions could thus be more influenced by these external factors than by pharmacist-led medication reviews. Any discrepancies were resolved by consensus with a third reviewer (LB).

Assessing the methodological quality of included studies

The methodological quality of the included studies was assessed independently by two authors (PR and SH). Any discrepancies were resolved by consensus with a third reviewer (LB). We used indicators of internal validity from the Cochrane Risk of Bias Tool [10]. The risk of selection bias was assessed at the study level (sequence generation, allocation sequence concealment), the risk of performance bias at the comparison level (i.e., blinding of participants and personnel), and the risk of detection bias as well as attrition bias at the outcome level (blinding of outcome assessors, handling of incomplete outcome data). The studies' risk of bias was then qualified as low, unclear or high.

Statistical analysis

All-cause readmissions and/or ED visit rates, all-cause readmission rates, all-cause ED visit rates, drug-related readmission rates and all-cause mortality rates were analysed using relative risks (RRs), defined as the ratio of the probability of an event occurring between two groups.

The mean length of hospital stay was analysed using the mean difference (MD) with 95% confidence intervals (CIs) for each study. We used fixed effects [11] and random effects

models [12], which account for the between-study heterogeneity by weighting studies similarly. Heterogeneity was assessed using the I^2 statistic, which represents the percentage of variance due to between-study factors rather than to sampling error [13]. We considered values of $I^2 > 50\%$ as indicative of large heterogeneity [14]. We used funnel plots (i.e., plots of effect estimates against sample size) to estimate the risk of bias: an asymmetry in these plots may indicate publication bias in the meta-analysis [15]. The robustness of the findings was investigated using the following sensitivity analyses when possible: (i) the use of random effects methods, (ii) risk of bias [10], (iii) follow-up after discharge, (iv) medication reconciliation, (v) treatment review, (vi) medication service liaison, (vii) full MR and (viii) CMR or AR. Analyses were performed with RevMan software version 5.3.

Results

Search results and study characteristics

In total, 303 titles were identified in the MEDLINE and Cochrane Library databases and in the search for additional references. After removing duplicates, 239 studies were identified. After reading the titles and abstracts, 159 studies were excluded according to the inclusion and exclusion criteria. After reading the full studies, we selected 19 randomized controlled studies. Details on the article locations and the studies included/excluded from the systematic review are shown in Figure 1. The characteristics of the included studies are presented in Table 1.

One of the studies was conducted in a paediatric population [16], and the others were conducted with adults. The average age of the adults was between 58.6 and 87.6 years, with the proportion of men ranging from 23% to over 70% (see Table 2).

All interventions were performed by a hospital pharmacist working directly in the care units ($n = 19$); 15 studies concerned clinical medication review (CMR, type 3) and four concerned adherence review (AR, type 2) ($n = 4$). In the studies assessing CMRs, the pharmacists delivered various interventions: medication reconciliation ($n = 9$), treatment review ($n = 9$) and medication liaison services ($n = 9$). Nine studies included a follow-up after hospital discharge (five for CMR and four for AR).

Methodological quality of included studies

Table 3 summarizes the assessments of the risk of bias. All 19 trials were at high risk of performance bias because the nature

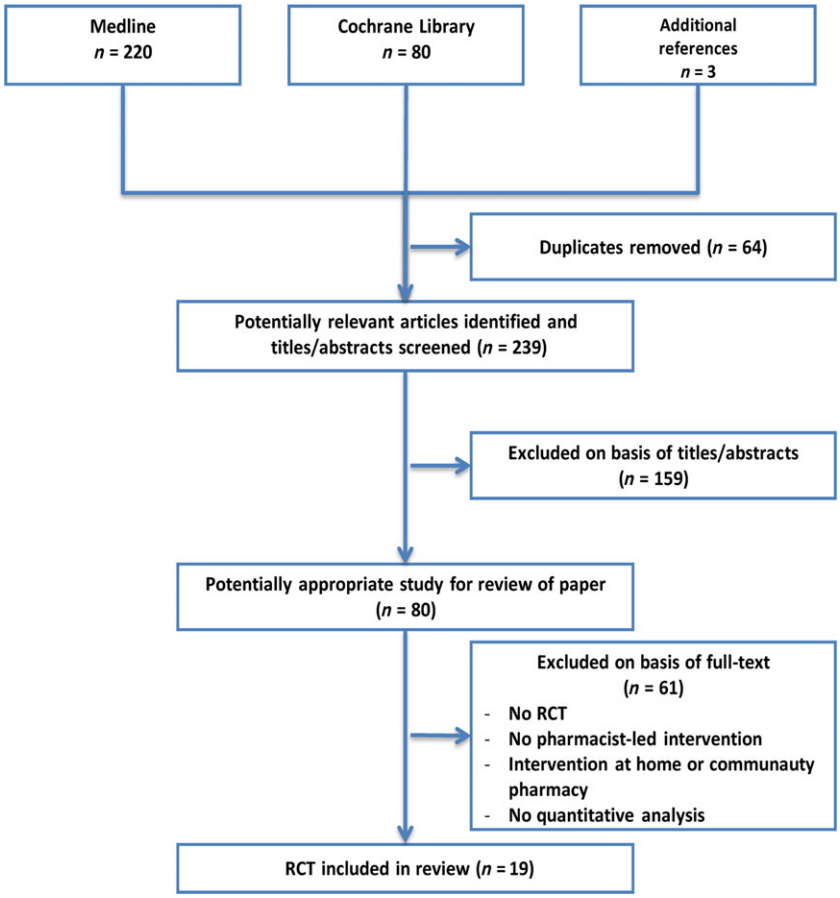

Figure 1
Systematic review inclusion and exclusion flowchart

Table 2

Characteristics of included studies

Study author	Country	Design	No. of patients	Mean age, years	% male	Type of medication review	Follow-up after discharge	Outcomes	Results	Readmission rates collection	Intervention[a]
Bladh [42]	Sweden	RCT	345	82	39%	CMR	No	Quality of life (EQ-5D) Quality of life (HRQoL) Length of stay	I = C I = C I = C		Medication service liaison Multidisciplinary revision of drug prescriptions
Bolas [43]	Ireland	RCT	162	74	50%	CMR	No	Readmission Length of stay	I = C I = C	3 months	Medication service liaison
Farris [17]	USA	RCT	945	61		CMR	Yes	Readmission	I = C	30 days	Minimal and enhanced group: – Medication reconciliation, Medication service liaison (minus faxed care plan) Enhanced group: – Telephone call 3–5 days post-discharge, – Care plan faxed to primary care physician/community pharmacist
Frankenthal [44]	Israel	RCT	306	>65	35%	CMR	No	Readmission Quality of life (SF-12)	I = C I = C	12 months	Treatment review Multidisciplinary revision of drug prescriptions
Gillespie [28]	Sweden	RCT	400	86.4	23%	CMR	Yes	Readmission Length of stay	I = C I = C	12 months	Medication reconciliation Treatment review Medication service liaison Telephone follow-up during 2 months. If patient is re-admitted to the hospital, can be reinstated once into the interventional group
Jarab [33]	UK	RCT	127	62.5	40%	AR	No	Quality of life (SGRQ) Adherence	I = C I > C		Medication review of drug adherence Motivational interviewing Drug action plan Therapeutic education programme for smokers Medication service liaison
Koehler [29]	USA	RCT	41	78	25%	CMR	Yes	Readmission Readmission	I > C I = C	30 days 2 months	Medication reconciliation Treatment review Medication service liaison Telephone follow-up to 5–7 days
Lipton [26]	USA	RCT	706	74.6		CMR	Yes	Adherence Readmission	I > C I = C	3 months	Medication reconciliation Treatment review Medication service liaison Telephone follow-up at 2–4 weeks and 2, 3 and 6 months.
Lisby [20]	Denmark	RCT	99	≥70	70%	CMR	No	Length of stay Readmission	I = C I = C	3 months	Medication reconciliation Treatment review Pharmaceutical intervention on drug pharmacology

(*continues*)

Table 2

(Continued)

Study author	Country	Design	No. of patients	Mean age, years	% male	Type of medication review	Follow-up after discharge	Outcomes	Results	Readmission rates collection	Intervention[a]
Lisby [21]	Denmark	RCT	108	80.5		CMR	No	Length of stay	I = C		Medication reconciliation Treatment review
McMullin [45]	USA	RCT	259	>61	36%	CMR	No	Readmission	I = C	30 days	Prescription review Pharmaceutical intervention on antibiotics
Morgado [22]	Portugal	RCT	197	59	45%	AR	No	Adherence	I > C		Medication review of drug adherence motivational interviewing Drug action plan Therapeutic education
Nazareth [18]	UK	RCT	362	84	38%	AR	Yes	Readmission Readmission	I = C I = C	3 months 6 months	Medication review of drug adherence Drug action plan Therapeutic education Medication service liaison Pharmacist community follow-up at home with therapeutic education and review of drug action plan
Sadik [23]	UK	RCT	221	58.6	45%	CMR	No	Readmission Quality of life (MLHFQ) Quality of life (SF-36)	I > C I > C I = C	12 months	Treatment review Multidisciplinary revision of drug prescriptions Medication service liaison
Schnipper [19]	USA	RCT	178	59.2	34%	AR	Yes	Readmission Adherence	I = C I = C	30 days	Medication review of drug adherence Therapeutic education Telephone follow-up to 3–5 days
Scullin [27]	North Ireland	RCT	762	71.3	55%	CMR	No	Length of stay Readmission	I > C I > C	30 days (and each month until 12 months)	Medication reconciliation Medication service liaison
Spinewine [24]	Belgium	RCT	186	82.4	28%	CMR	No	Readmission	I = C	12 months	Medication reconciliation Medication service liaison
Stowasser [25]	Australia	RCT				CMR	No	Readmission Length of stay	I = C I = C	30 days	Medication liaison service Medication history confirmation with community healthcare professionals (telephone, faxing)
Zhang [16]	China	RCT	150	< 18	43%	CMR	Yes	Length of stay Adherence Readmission	I > C I > C I = C	14 days	Treatment review Multidisciplinary revision of drug prescriptions Telephone follow-up to 3–4 days

[a]Results based on significant findings reported in the individual study. I > C, intervention is significantly better than control; I = C, no significant difference between intervention and control; C > I, control is significantly better than intervention. AR, adherence review; CMR, clinical medication review; SF-12, Short-form [12] health survey; MLHFQ, Minnesota Living With Heart Failure Questionnaire; SF-36, Short-form [13] health survey; SGRQ, St. George's respiratory questionnaire; EQ-5D, EuroQol-5D; HRQoL, Health-related quality of life.

Table 3

Risk of bias regarding outcomes of the studies included in the systematic review

	Random sequence generation	Allocation concealment	Blinding: participants, personnel	Blinding: outcomes	Incomplete outcome assessment	Selective reporting	Other	Global risk
Bladh [42]	Unclear	Low	High	Unclear	Low	High		**High risk of bias**
Bolas [43]	Low	Low	High	High	High	High	Low	**High risk of bias**
Farris [17]	Low	Low	High	Low	Low	Low	Low	**Low risk of bias**
Frankenthal [44]	Low	Low	High	Low	Low	Low	Unclear	**Unclear risk of bias**
Gillepsie [28]	Low	Low	High	Low	Low	Low	High	**High risk of bias**
Jarab [33]	Low	Low	High	Low	Low	Low	Unclear	**Unclear risk of bias**
Koehler [29]	Low	Low	High	Low	Low	Unclear	High	**High risk of bias**
Lipton [26]	Low	High	High	Low	Low	Low	High	**High risk of bias**
Lisby [20]	Low	Unclear	High	Low	Low	High	Unclear	**High risk of bias**
Lisby [21]	Unclear	Unclear	High	Unclear	Low	Low	High	**High risk of bias**
McMullin [45]	Low	Low	High	High	Low	Low	Low	**High risk of bias**
Morgado [22]	High	Unclear	High	Low	Low	Low	Unclear	**High risk of bias**
Nazareth [18]	Low	Low	High	Low	Low	Low	Low	**Low risk of bias**
Sadik [23]	Low	Unclear	High	Low	Low	Low	Unclear	**Unclear risk of bias**
Scullin [27]	Low	High	High	Low	High	Low	High	**High risk of bias**
Schnipper [19]	Low	Low	High	Low	Low	Low	Low	**Low risk of bias**
Spinewine [24]	High	Unclear	High	Low	Low	Low	High	**High risk of bias**
Stowasser [25]	Low	Unclear	High	Low	Low	Low	Low	**Unclear risk of bias**
Zhang [16]	Low	Low	High	Low	Low	High	Unclear	**High risk of bias**

of the intervention meant that the personnel and participants could not be blinded, and thus performance bias was not included in the calculation of global risk. Three out of 19 RCTs were classified as good quality [17–19]. The allocation concealment procedures of six studies was unclear [20–25], and two studies were considered at high risk of bias [26, 27]. There was a high risk of other bias assessed in six trials, including a possible contamination bias with the same pharmacists caring for both the control and intervention groups, a lack of power to detect changes in admission rates, and the recruitment of only half of the eligible patients into the trial [21, 24, 26–29].

All-cause readmission and/or ED visits

We identified 13 studies that compared the effects of pharmacist-led medication reviews (n = 2385) to those of usual care (n = 2420) on rates of all-cause readmissions and/or ED visits. There were no significant differences between the two groups (RR = 0.97, 95% CI 0.90; 1.05, P = 0.44, I^2 = 0%) (see Figure 2). Moreover, there were no significant differences between all-cause readmission and/or ED visits at 30 days (RR = 0.98, 95% CI 0.86; 1.12, P = 0.80, I^2 = 0%) or between 2 months and 12 months (RR = 0.96, 95% CI 0.87; 1.05, P = 0.38, I^2 = 22%) after hospital discharge. The associated funnel plot was symmetrical (Appendix S3). Moreover, we did not find any significant differences in the sensitivity analyses (see Table 4). The sensitivity analysis did not show significant differences between the studies assessing full medication reviews (medication reconciliation, treatment review, medication liaison service and telephone follow-up) and those without full medication review. Only one study, which almost reached significance (0.26 [0.06; 1.09]) in this outcome, included a full medication review and the readmission rate at 30 days [29]. However, these results concerned only 41 patients, and the effects of sampling may thus be important.

All-cause readmission

We identified 12 studies that compared the effects of pharmacist-led medication reviews (n = 2331) to usual care (n = 2382) on all-cause readmission rate. There were no significant differences between the two groups (RR = 0.98, 95% CI 0.90; 1.06, P = 0.59, I^2 = 0%) (see Figure 3). Moreover, there were no significant differences between all-cause readmissions 30 days (RR = 0.95, 95% CI 0.80; 1.13, P = 0.56, I^2 = 0%) or 2 months to 12 months (RR = 0.99, 95% CI 0.90; 1.09, P = 0.83, I^2 = 0%) after hospital discharge. The associated funnel plot was symmetrical (Appendix S3).

All-cause emergency department visits

We identified four studies that compared the effects of pharmacist-led medication reviews (n = 951) to those of usual care (n = 951) on all-cause ED visit rates. There was a significant difference between the two groups (RR = 0.70, 95% CI 0.59; 0.85 P = 0.0002, I^2 = 39%) (see Figure 3).

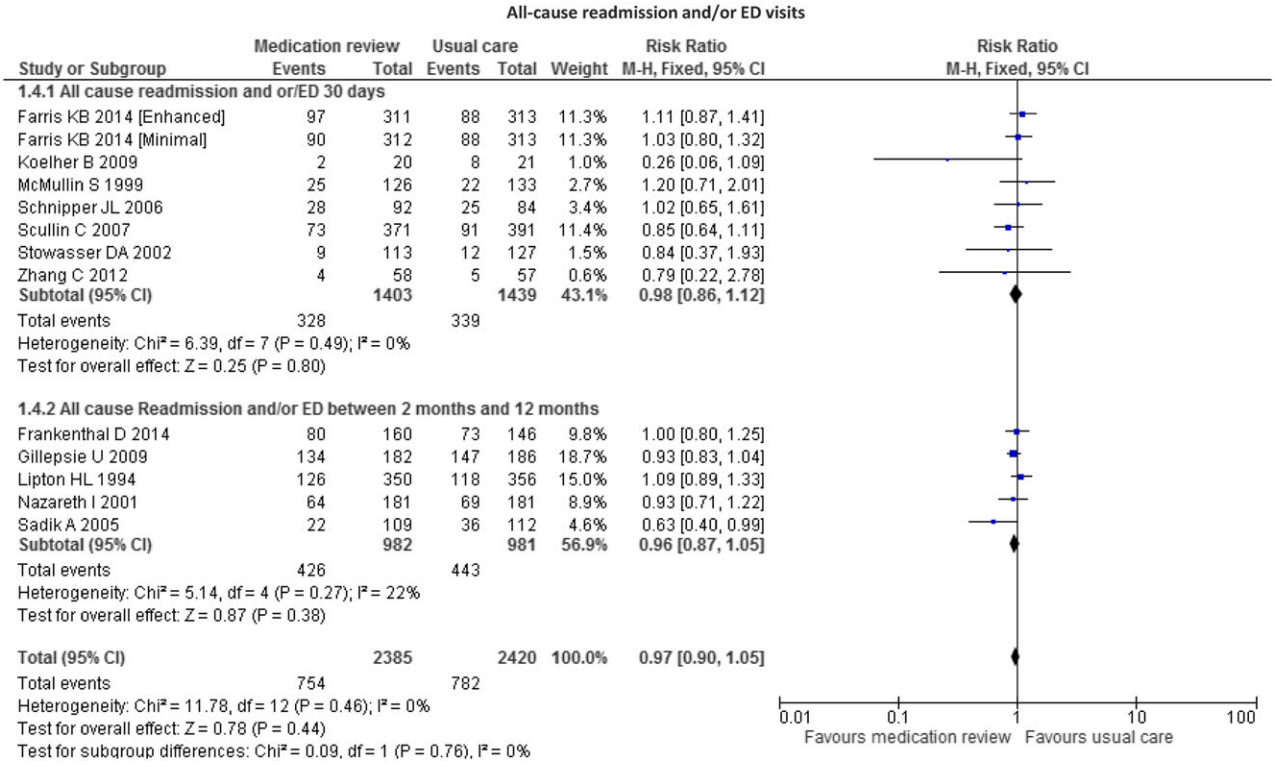

Figure 2

Forest plot of the effect of medication review on 30 days' all-cause readmissions and/or ED visits and all cause readmission and/or ED visits between 2 months and 12 months after hospital discharge

Table 4

Sensitivity analysis of primary outcome (all-cause readmission and/or ED visits) and secondary outcome (length of hospital stay)

	All-cause readmission and/or ED visits				Length of hospital stay			
	No. of patients (no. of trials)	Relative risk (95% CI)	*P*-value of overall effect	I^2-value of heterogeneity (%)	No. of patients (no. of trials)	MD (95% CI)	*P*-value of overall effect	I^2-value of heterogeneity (%)
Random vs. Fixed effects								
Random effects	4805 (12)	0.97 (0.90, 1.05)	0.44	0	1887 (6)	−0.0.6 (−0.23, 0.11)	0.50	65
Fixed effects	4805 (12)	0.97 (0.90, 1.04)	0.33	0	1887 (6)	−0.08 (−0.17, −0.01)	0.09	65
Level quality								
High quality [17–19]	1787 (3)	1.03 (0.89; 1.18)	0.70	0	—	—	—	—
Low and unclear quality	3018 (9)	0.94 (0.86; 1.03)	0.18	0	1887 (6)	−0.0.6 (−0.23, 0.11)	0.50	65
Medication reconciliation								
Yes [20, 21, 24, 26–29]	1877 (4)	0.95 (0.85; 1.05)	0.31	47	1337 (4)	−0.03 (−0.24; 0.19)	0.81	66
No	2928 (8)	0.99 (0.89. 1.11)	0.89	36	550 (2)	−0.14 (−0.57; 0.29)	0.54	81
Treatment review								
Yes [16, 20, 23, 26, 28, 44, 45]	1975 (6)	1.98 (0.88; 1.08)	0.62	16	617 (3)	−0.07 (−0.38; 0.25)	0.67	70
No	2830 (6)	0.96 (0.85; 1.09)	0.55	0	1270 (3)	−0.06 (−0.29; 0.18)	0.64	70
Medication service liaison								
Yes [17, 18, 23–27, 29, 33, 42]	2956 (6)	0.95 (0.85; 1.07)	0.41	42	—	—	—	—
No	1849 (6)	0.99 (0.89; 1.10)	0.84	0	—	—	—	—
Full medication review								
Yes [26, 28, 29]	1115 (3)	0.96 (0.77; 1.21)	0.75	69	—	—	—	—
No	3690 (9)	0.96 (0.87; 1.07)	0.49	0	—	—	—	—
Inpatient only vs. with follow up								
Inpatient without follow up	1788 (5)	0.90 (0.77, 1.05)	0.16	14	—	—	—	—
Inpatient with follow up [16–19, 26, 28, 29]	3017 (7)	1.00 (0.92, 1.10)	0.98	0	—	—	—	—
Clinical medication review [16, 17, 20, 21, 23–29, 42–45]	4267 (10)	0.97 (0.89; 1.06)	0.50	14	1887 (6)	−0.06 (−0.23, 0.11)	0.50	65
Adherence review [18, 19, 22, 33]	538 (2)	0.95 (0.76; 1.20)	0.69	0	—	—	—	—

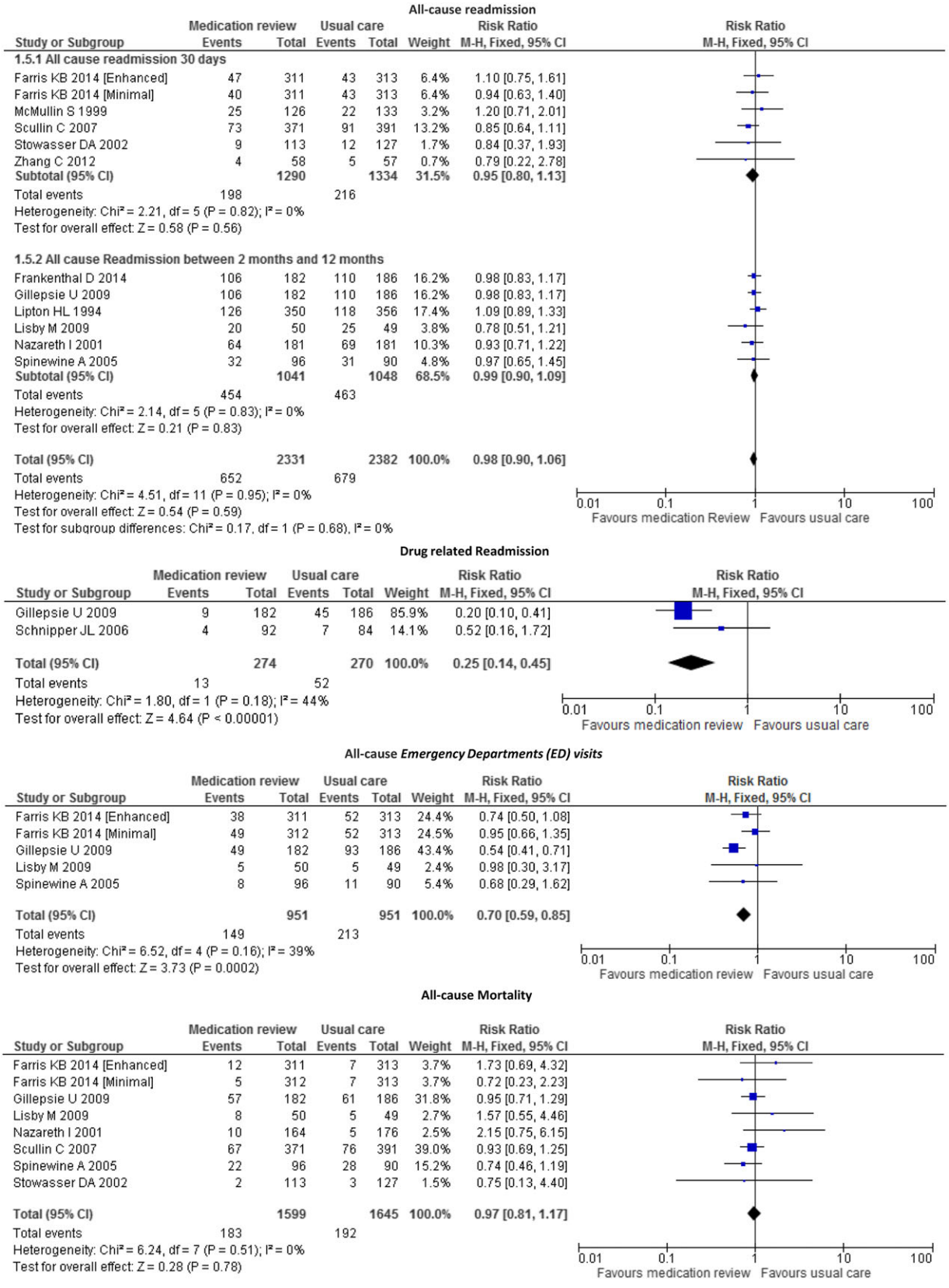

Figure 3

Forest plot of the effect of medication review on 30 days' all-cause readmissions, all-cause readmission between 2 months and 12 months after hospital discharge, all-cause ED visits, drug-related readmission and all-cause mortality

Drug-related readmissions

We identified two studies that compared the effects of pharmacist-led medication review (n = 274) to usual care (n = 270) on drug-related readmission rates. There was a significant difference between the two groups (RR = 0.25, 95% CI 0.14; 0.45, $P < 0.0001$, $I^2 = 44\%$) (see Figure 3).

All-cause mortality

We identified seven studies that compared the effects of pharmacist-led medication review (n = 1599) to usual care (n = 1645) on all-cause mortality rate. There was no significant difference between the two groups (RR = 0.97, 95% CI 0.81; 1.17, $P = 0.86$, $I^2 = 0\%$) (see Figure 3).

Length of hospital stay

We identified six studies comparing the effects of pharmacist-led medication review (n = 931) to usual care (n = 956) on length of hospital stay. There was no significant difference between the two groups (MD −0.45 days, 95% CI −1.73; 0.82, P = 0.48, I^2 = 58%) (see Figure 4). Moreover, we did not find any significant differences in the sensitivity analyses (see Table 4).

Adherence and quality of life

Formal pooling was not possible for the adherence and quality of life variables due to the small number of studies and the diversity of assessments used. Nevertheless, qualitative reviews of the results were performed in terms of the number of studies showing a significant positive effect, a nonsignificant positive effect, no or negative effect. Five studies reported adherence to medications as an outcome of their research (see Table 5). The majority of the studies (n = 80%) reported a significant improvement in adherence to medication as a result of the pharmacist-led medication review. Patients' quality of life was measured in four studies, and one study with CMR as the intervention reported a significant impact on one of the two scales of quality of life used [23].

Discussion

Our study found no significant reductions in the rate of all-cause readmissions and/or ED visits due to pharmacist-led medication reviews in hospitals. However, pharmacist-led medication reviews were associated with a decrease in the number of ED visits and drug-related readmissions. One primary component of the pharmacist-led medication review is pharmacist-led medication reconciliation. To our knowledge, only one meta-analysis has investigated the effectiveness of pharmacist-led medication reconciliation programmes on clinical outcomes in hospital transitions and found a substantial reduction in the rate of all-cause readmissions (19%), all-cause ED visits (28%) and ADE-related hospital revisits (67%) [30]. However, that meta-analysis, conducted by Mekonnen *et al.*, included not only RCTs but also before/after studies and non-RCTs. The inclusion of non-RCTs in meta-analyses is not recommended because it decreases the level of evidence of the meta-analysis [31]. Our meta-analysis did not show any significant reductions in the rate of all-cause readmissions (RR = 0.98, 95% CI 0.90; 1.06, P = 0.59). This difference in our findings from those of Mekonnen *et al.* may be due to a study by Hawes et *al.* [32], which included a pharmacist-led medication reconciliation

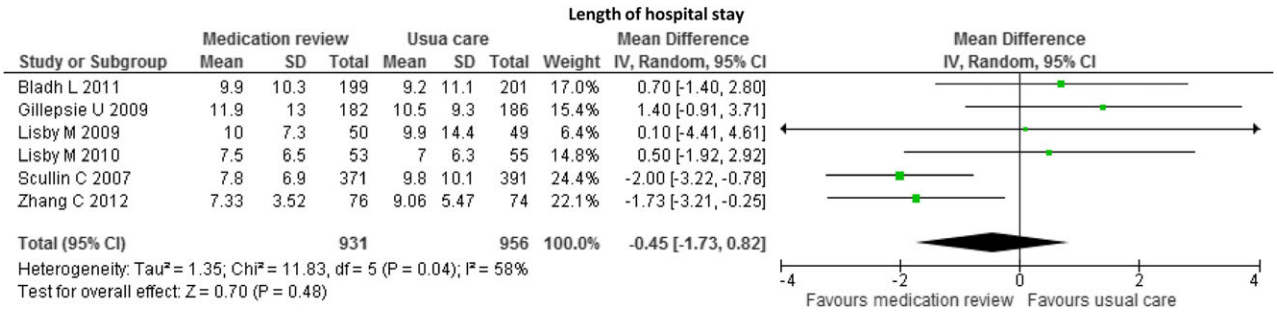

Figure 4

Forest plot of the effect of medication review on the length of hospital stay

Table 5

Summary of reported findings on adherence and quality of life outcomes

Outcomes	Number of trials	Favours medication review	Favours usual care	No significant differences between groups	Study reported both[a] significant and non-significant differences
Adherence	5	4	—	1	—
Quality of life	4	0	—	3	1[b]

[a]Outcomes were measured using two different methods, for example self-reported adherence and medication refill.
[b]Analysis using the MLHFQ but not SF-36 showed a significant impact.

after discharge at home that did not meet our inclusion criteria. The rate of all-cause readmissions and/or ED visits was significantly different at 30 days (0% *vs.* 40.5%, $P < 0.001$). Moreover, our results are comparable to most pharmacist-led medication review or pharmacist-led medication reconciliation meta-analyses that have studied the rate of readmissions [4–7].

To our knowledge, the various pharmacist-led medication review or pharmacist-led medication reconciliation meta-analyses that examined all-cause readmission rates pooled the different results and did not study the effect of the time points used in the calculation of readmission rates. Our meta-analysis identified no differences when including only the studies that investigated the all-cause readmission rates and all-cause readmission and/or ED visits within 30 days.

However, pharmacist-led medication reviews significantly reduced all-cause ED visits (RR = 0.70; 95% CI 0.59; 0.85, $P = 0.0002$) using the 30-day and the 12-month endpoint.

It is difficult to study the impact of medication reviews alone because the process is affected by the patient's overall care and many intervening factors. Moreover, the interventions differ depending on the studies. For example, the interventions of Scullin *et al.* [27] and Spinewine *et al.* [24] consist of a medication reconciliation and medication service liaison. Other studies [16–19, 26, 28, 29] have included, for example, a follow-up post-discharge by telephone or by a community pharmacist for a more or less lengthy period of time. The sensitivity analyses showed no significant differences depending on the presence or absence of medication reconciliation, treatment review, follow-up post-discharge or medication service liaison.

This systematic review on in-hospital pharmacist-led medication reviews did not identify an effect on the length of hospital admission (−0.50 (CI) −0.20, 0.10, $P = 0.49$). Another related meta-analysis also did not identify an effect on the length of hospital stay (−0.04 days (−1.63; 1.55), $P = 0.96$). This can be explained by the incomplete medication reviews performed in the interventions. Indeed, the overall results are conflicting, with two trials providing significant results on the length of hospital stay in favour of the intervention [16, 27]. It should be noted that the study by Zhang *et al.* [16] included a paediatric population and that Scullin *et al.* [27] integrated medication reconciliation into their intervention.

One RCT study has been conducted with children [16], whereas most studies have been conducted in patients over 65 years of age. It is currently difficult to review whether medication reviews have an impact on all-cause readmissions in the paediatric population, although it is likely that it has an impact on the length of hospital stay [32].

Our study found that clinical medication reviews [16, 26] and adherence reviews [22, 33] had an impact on adherence. Adherence was measured by several scales, such as the Morisky scale [34], the method of Williford and Johnson [35], or by asking patients whether they had taken each medication exactly as prescribed during the previous day and on how many days during the previous week [19]. Our study did not find a clear impact of pharmacist-led medication review on quality of life. Indeed, only one study found an impact on patient's quality of life. This may be due to the range of assessments used: the SF-12 [36], SF-36 [37], EQ-5D [38], MLHFQ [39], HRQL [40] or SGRQ [41] specific to chronic obstructive pulmonary disease. The variety of the scales used does not enable us to confirm the utility of pharmacist-led clinical services as an activity to improve patient's quality of life.

Limitations of the study

There are a number of limitations to this study. The first is the small number of subjects that were included in some studies, which may raise concerns about the study sampling. Moreover, many studies were single centre, which raises the issue of replicability. It is necessary to cautiously interpret the impact of pharmacist reviews on all-cause ED visits and drug-related readmissions because we found few studies that examined these endpoints. These results were based on only four and two studies, respectively.

Only articles published in English or French were assessed in this review. There may have been studies published in non-English language journals that involved interventions for improving care transitions. In addition, research disseminated in the grey literature, such as conference papers and unpublished reports, was not considered. This may have resulted in an over-representation of studies with statistically significant findings, an inflation of effect size estimates, and less precise effect size estimates than meta-analyses including grey literature.

Conclusion

The impact of pharmacist-led medication reviews on all-cause readmissions is not clear, but these clinical pharmacist services have a significant impact on all-cause ED visits and drug-related readmissions. However, the latter two results are based on only four and two studies, respectively. The impact of medication reviews on the length of hospital stay and adherence remains unclear. Based on the results of this meta-analysis and other meta-analyses, it seems very unlikely, as might be expected, that medication reviews have an impact on mortality. However, the impact on patient quality of life may be more in question; indeed, the variety of the assessments used did not enable us to determine any effects.

It is important to consider the timing of endpoints when studying readmission rates in future investigations. Indeed, medication reviews appeared to impact early hospital readmissions, i.e., at 30 days post-discharge. The majority of studies investigated the elderly; it is important to demonstrate whether medication reviews can affect the paediatric population. Finally, the global quality of the studies is low, and, to our knowledge, there are no randomized controlled trials involving a large number of subjects; this type of study is necessary to demonstrate a significant impact on readmission rates after hospital discharge. Indeed, to demonstrate a reduction of at least 6% in readmission rates, future trials should include over 1400 subjects. An RCT with a large number of subjects using a standardized medication review in populations at risk for drug-related readmission is necessary.

Competing Interests

All authors have completed the Unified Competing Interest form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare no support from any organization for the submitted work; no financial relationships with any organizations that might have an interest in the submitted work in the previous 3 years; and no other relationships or activities that could appear to have influenced the submitted work.

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Supporting Information

Additional Supporting Information may be found in the online version of this article at the publisher's web-site:

http://onlinelibrary.wiley.com/doi/10.1111/bcp.13085/suppinfo.

Appendix S1 Medline search strategy
Appendix S2 Cochrane Library search strategy
Appendix S3 All-cause readmission and/or ED visits; All-cause readmission