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Effectiveness of pharmacist-led medication reconciliation programmes on clinical outcomes at hospital transitions: a systematic review and meta-analysis

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ABSTRACT

Objectives: Pharmacists play a role in providing medication reconciliation. However, data on effectiveness on patients' clinical outcomes appear inconclusive. Thus, the aim of this study was to systematically investigate the effect of pharmacist-led medication reconciliation programmes on clinical outcomes at hospital transitions.

Design: Systematic review and meta-analysis.

Methods: We searched PubMed, MEDLINE, EMBASE, IPA, CINHAL and PsycINFO from inception to December 2014. Included studies were all published studies in English that compared the effectiveness of pharmacist-led medication reconciliation interventions to usual care, aimed at improving medication reconciliation programmes. Meta-analysis was carried out using a random effects model, and subgroup analysis was conducted to determine the sources of heterogeneity.

Results: 17 studies involving 21 342 adult patients were included. Eight studies were randomised controlled trials (RCTs). Most studies targeted multiple transitions and compared comprehensive medication reconciliation programmes including telephone follow-up/home visit, patient counselling or both, during the first 30 days of follow-up. The pooled relative risks showed a more substantial reduction of 67%, 28% and 19% in adverse drug event-related hospital revisits (RR 0.33; 95% CI 0.20 to 0.53), emergency department (ED) visits (RR 0.72; 95% CI 0.57 to 0.92) and hospital readmissions (RR 0.81; 95% CI 0.70 to 0.95) in the intervention group than in the usual care group, respectively. The pooled data on mortality (RR 1.05; 95% CI 0.95 to 1.16) and composite readmission and/or ED visit (RR 0.95; 95% CI 0.90 to 1.00) did not differ among the groups. There was significant heterogeneity in the results related to readmissions and ED visits, however. Subgroup analyses based on study design and outcome timing did not show statistically significant results.

Conclusion: Pharmacist-led medication reconciliation programmes are effective at improving post-hospital healthcare utilisation. This review supports the implementation of pharmacist-led medication reconciliation programmes that include some component aimed at improving medication safety.

Strengths and limitations of this study

- This is the first systematic review investigating the effect of pharmacist-led medication reconciliation programmes on clinical outcomes.
- In some of the clinical outcomes evaluated, there is substantial statistical heterogeneity and we could not identify the source of variation among the studies.
- The inclusion of non-controlled studies might affect the quality of evidence as seen by the high risk of bias in these groups of studies.

INTRODUCTION

Medication reconciliation has been recognised as a major intervention tackling the burden of medication discrepancies and subsequent patient harm at care transitions.[1] Unjustifiable medication discrepancies are responsible for more than half of the medication errors occurring at transitions in care, when patients move in and out of hospital or get transferred to the care of other healthcare professionals,[2] and up to one-third could have the potential to cause harm.[3] Incidence of unintentional medication changes is common at care transitions,[3–8] and is one of the reasons for a huge utilisation of healthcare resources.[9–13] Medication reconciliation as a medication safety strategy has been championed by a number of healthcare organisations. It was first adopted in 2005 as a National Patient Safety Goal (NPSG) by the Joint Commission[14] and, later, the WHO and collaborators[15–17] involved themselves in endorsing this strategy across many countries.

Despite these efforts, implementation of a medication reconciliation service is a hospital-wide challenge,[18] and there is no previous clinical evidence as to which member of the healthcare profession(s) or which strategies effectively perform medication reconciliation.[19] A number of medication reconciliation strategies have been utilised for safe patient transitions: use of electronic reconciliation tools,[20–22] standardised forms[23 24] and collaborative models,[25 26] as well as patient engagement[27] and pharmacist-led approaches.[28 29]

The impact of medication reconciliation on clinical outcomes at hospital transitions has been reported, however, two recently published systematic reviews[30 31] have ascertained that the benefit as a patient safety strategy is not clear. Both studies have inconsistent findings on healthcare resource utilisation. Unlike Mueller *et al*,[30] Kwan *et al*[31] did not report significant association between post-hospital healthcare utilisation and medication discrepancies identified through medication reconciliation interventions. Both reviews broadly assessed the effect of medication reconciliation produced by various strategies, including the use of collaborative models. The aim of the present review was, thus, to specifically assess the effectiveness of pharmacist-led medication reconciliation programmes on clinical outcomes during the transition to and from hospital settings.

METHODS

Data sources and searches

The study was conducted utilising Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) group guidelines,[32] including the PRISMA checklist, to ensure inclusion of relevant information. An initial limited search of articles was undertaken and the search strategy was broadened after analysis of the text words contained in the title, abstract and index terms. 'Medication reconciliation', 'medication discrepancies', 'medication errors', 'medication history' and 'pharmac*', were the main Medicine Subject Headings (MeSH) and text word terms in the electronic searches. Then, we carried out a comprehensive search involving all the collections in the databases until December 2014: PubMed/MEDLINE (1946), Ovid/MEDLINE (1946), International Pharmaceutical Abstracts (1970), EMBASE (1966), PsycINFO (1890) and CINHAL (1937) (see online supplementary appendix A). The reference lists of review articles and included studies were manually searched to locate articles that were not identified in the database search. Article search was performed by one reviewer (ABM) with the support of a medical librarian.

Study selection

To be included in the selection, studies were required to present the following: papers that reported medication reconciliation intervention primarily and that provide data on any of these clinical end points (all-cause readmission, emergency department (ED) visits, composite rate of readmission and/or ED visits, mortality, adverse drug event (ADE)-related hospital visit). We adopted the definition of 'medication reconciliation' utilised by the Institute for Healthcare Improvement: 'the process of identifying the most accurate list of a patient's current medicines including the name, dosage, frequency and route—and comparing them to the current list in use, recognising and documenting any discrepancies, thus resulting in a complete list of medications'.[1] Included studies had to be original peer-reviewed research articles that were published in English. The included interventions had to start in the hospital and be performed primarily by a pharmacist, with the aim of improving care transitions to and from a hospital. The intervention had to have been compared with another group that received usual or standard care. 'Usual or standard care' was defined as any care where targeted medication reconciliation was not undertaken as an intervention, or where, if an intervention was conducted, it was not provided by a pharmacist. Along with duplicate references, and other studies that did not satisfy the inclusion criteria and were not medication reconciliation studies, we excluded the following types of studies: other medication reconciliation practices (eg, nurse-led) or practices as part of a multicomponent intervention (eg, medication therapy management), case studies, systematic reviews, qualitative outcomes and non-research articles. Abstracts from conferences and full-texts without raw data available for retrieval were not considered. Therefore, the studies selected for inclusion and exclusion assessment were randomised controlled trials (RCTs), quasi-experimental studies with a control group, and before-and-after studies that evaluated pharmacist-led medication reconciliation programmes at hospital transitions. The titles and abstracts were screened by one author (ABM), and studies identified for full-text review and selected according to inclusion criteria were agreed on by the second (AJM) and third reviewer (JEB).

Data extraction

One review author (ABM) was responsible for data extraction from full-texts, using a modified adopted Cochrane EPOC data collection checklist,[33] including quality assessment of studies. The following information was extracted from each included study: name of first author, year of publication, country and setting where the study was conducted, study design, sample size, target of intervention, patient characteristics, components of intervention, and relevant outcomes and results. If insufficient details were reported, study authors were contacted for further information.

Outcomes and statistical analysis

Our analysis included studies that reported at least one of these end points: healthcare utilisation (readmission, ED visit and composite readmission, and/or ED visit),

mortality and ADE-related hospital visits, compared with usual care in the other arm; and using at least 30 days of follow-up. Studies were eligible for meta-analysis if such end point could be extractable. We analysed data in accordance with the Cochrane handbook.[34] Together with 95% CIs for each outcome, we derived the relative risk and weighted mean differences for dichotomous and continuous variables, respectively.

After we combined data, the analyses were conducted with Cochrane Review Manager (RevMan) V.5.3 software (Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014). We performed separate analyses for each outcome measured compared with usual care. We synthesised the results by constructing a forest plot using a random effects model for each of the outcomes. We analysed intention-to-treat data whenever available. The Mantel-Haenszel risk ratio (RR) summary estimate was determined for outcome measures of dichotomous variables and the weighted mean difference was calculated for continuous data variables. To confirm the reliability of the summary estimate, 95% CIs were calculated. Since the analyses included medication reconciliation interventions with multiple components, different designs and follow-up periods, we set a priori that might be associated with some variation in the outcomes between the studies. When there were at least five studies per outcome, subgroup analyses were carried out according to methodological design factors (RCT and non-randomised studies) and outcome timing (duration of follow-up). For studies that reported outcomes at a different duration, the longer follow-up period was taken in the analysis, if there was no difference in the summary estimate. Otherwise, meta-analysis was performed separately for the long-duration and short-duration subgroups. We assessed statistical heterogeneity among studies through calculating τ^2, χ^2 (Q), I^2 and p value. We conducted sensitivity analysis to check the stability of summary estimates to outliers and the change in I^2 when any of the studies were withdrawn from the analysis. We evaluated publication bias by inspection of funnel plot, and Begg-Mazumdar and Egger's test using Comprehensive Meta-analysis, V.3 (Biostat, Englewood, New Jersey, USA). In all analyses, p value <0.05 was considered as statistically significant.

We assessed the risk of bias of individual studies with EPOC risk of bias tool.[33] The main domains considered were random sequence generation, allocation concealment, blinding of outcome assessment, attrition and reporting biases. We also determined whether groups were balanced at baseline in terms of characteristics and outcomes. Included studies were evaluated for each domain and a quality scoring was then calculated for each study. Studies with 'clear data' on each of the domains were given a score of 1, and studies were assigned a point score out of the maximum of 9 (9 domains were included in the risk of bias assessment).

RESULTS

Identification and selection of studies

We identified a total of 2551 citations from searches in the electronic databases and 59 additional records were identified in reference lists of included studies. After removal of duplicate records, title and abstract screening was applied on 1832 publications. After title and abstract review, 1731 publications did not meet the inclusion criteria—the focus for the majority of studies was not related to medication reconciliation interventions. The remaining 101 publications were obtained in full-text and assessed for inclusion. Most full-text articles were excluded either due to reporting of a different outcome of interest (n=34) or because medication reconciliation was not the primary intervention (n=11) (see online supplementary appendix B). After applying all the inclusion criteria, we finally included 17 articles (figure 1).

Characteristics of included studies

Major characteristics of the included studies are presented in table 1. They were randomised controlled trials (n=8, 47%), before-and-after studies (n= 6, 35%) and non-randomised controlled trials (n= 3, 18%). The majority of the studies were conducted in the USA (11 studies),[35–45] and the remainder were in Sweden (3 studies),[46–48] Ireland (2 studies)[49 50] and Australia (1 study).[51] The studies had been conducted between 2002 and 2014. The included studies involved a total of 21 342 adult patients of various ages with sample sizes ranging from 41 to 8959 individuals. No studies in paediatrics were identified. Only three studies were confined to multicentre.[38 49 51] Most studies reported outcomes up to 30 days of follow-up after selection of eligible patients; only six studies[37 46–50] reported longer follow-up of 3-month or more. Interventions were initiated at different care transitions; most were conducted at multiple transitions,[35 37–40 42 44 46–51] and all studies targeting a single transition intervention were carried out at hospital discharge.[36 41 43 45]

Most studies recruited high-risk patients (including elderly patients, patients with multiple medications and patients at risk of medication-related events). Five studies[36 37 39 44 48] focused on a specific patient population, mainly patients with heart failure and chronic obstructive pulmonary disease (COPD). Methodologically, one study[35] stratified patients into two groups: general population and high-risk patients, and another study[37] randomised the population into two levels of intervention: minimal and enhanced.

Some studies compared comprehensive medication reconciliation programmes, for example, multifaceted interventions including telephone follow-up and/or home visit,[44 48 51] and patient counselling,[35 38 41 45] or both telephone/home visit and patient counselling.[37 40 42 43 46 49 50] After medication reconciliation, a few studies[42 46–49] additionally included a formal medication review. Comparator groups in the

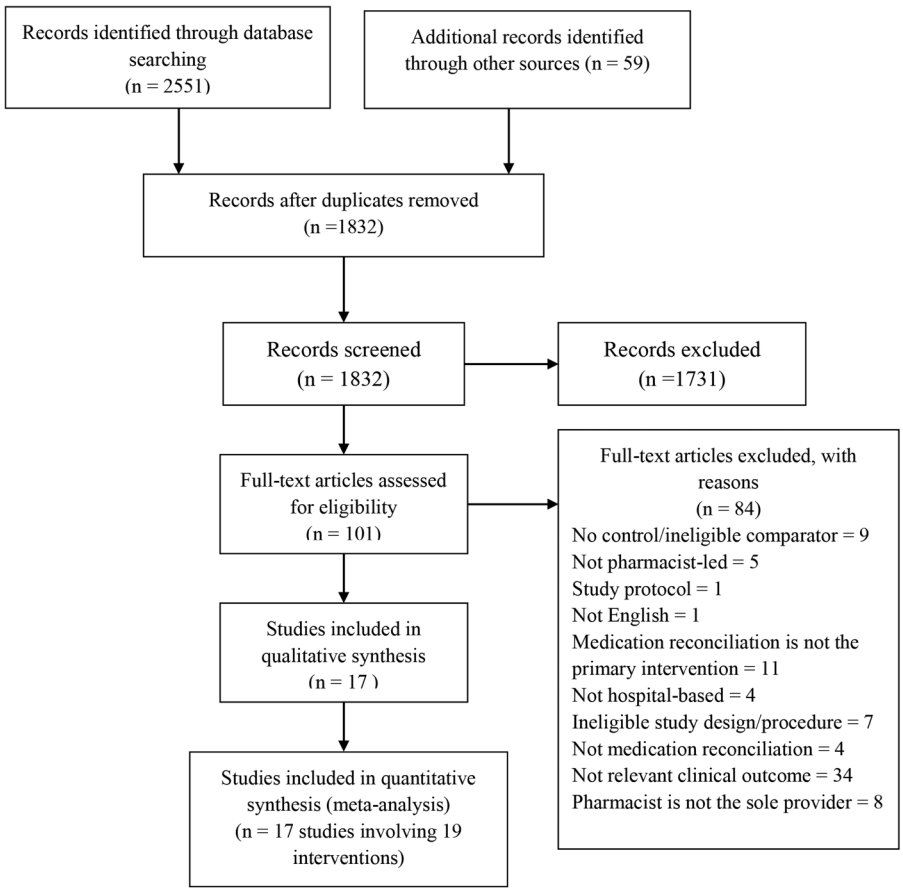

Figure 1 PRISMA flow diagram of the selection of eligible studies.

included studies were varied, and most studies compared medication reconciliation interventions with a usual care group that did not receive pharmacist-led intervention.

Risk of bias assessment

Patients included in the study were similar in baseline characteristics except in five studies,[36 38 39 45 48] which were not clear or different in patient characteristics. However, in only three studies[43 48 51] were baseline clinical outcomes reported or was some form of adjustment analysis performed. Eight out of 17 studies[37 39 40 42 46 49–51] provided enough details on randomisation procedure to be judged as adequate. Among these studies, allocation concealment was fully described in all reports except one.[51] In all but three studies[43 45 50] had care providers and outcome assessors been blinded or objective health outcomes reported. Five studies[37 41 47 48 51] achieved more than 80% complete follow-up. However, only a few studies examined the impact of losses to follow-up or drop-out. High-risk of contamination was suspected in four studies.[35 37 41 47] At least one of our outcomes of interest was selectively reported in four studies.[36 49–51] Overall, on a scale of 9, quality of randomised controlled trials falls within a range of 4–8, whereas for non-randomised controlled trials a lower range of 1–5 score was attained (see online supplementary appendix C).

Effect of interventions

Of the 14 studies that reported data on all-cause readmissions, 13 were eligible for meta-analysis. One study[35] measured this outcome for a high-risk population separately; and another study[37] reported it for two different interventions. Thus, 15 interventions were meta-analysed. Eight studies reported this outcome at 30 days,[35 36 39 41 43–45 51] while three[46 48 49] reported long-term data and two studies[37 38] reported both. Seven studies[35 38 39 41 44 45 49] showed a significant reduction ($p<0.05$) in rehospitalisations although two[39 44] of them had a very small sample size. The pooled RR (n=21 969 patients) across all studies was 0.81 (95% CI 0.70 to 0.95). However, the results of these studies for this end point are substantially heterogeneous (figure 2A). With regard to all-cause emergency department (ED) contacts, seven of eight studies[35 37–39 43 46 48] that measured ED visit as an outcome were pooled. Considering studies that gave two sets of data, nine interventions were meta-analysed. The pooled analysis across all interventions showed some significant difference between the intervention and usual care (RR 0.72; 95% CI 0.57 to 0.92; figure 2B). Evidence showed extreme heterogeneity in this outcome; however, the findings were different when the study by Gardella *et al*[38] was removed; there was no heterogeneity without affecting the significance difference ($p=0.25$; $I^2=22\%$, RR 0.89; 95% CI 0.79 to 0.99).

Table 1 Characteristics of included studies

Author, Year	Country, Setting	Study design	Intervention	Comparator	Target of intervention	Inclusion	Exclusion	Components of intervention	Comparator	Follow-up Period	Relevant outcomes	Main results
Anderegg *et al* 2014[35]	USA, single centre	Before–after	1664	1652	Admission, discharge	Age 18 years or older, discharge from internal medicine, family medicine, cardiology, or orthopaedic surgery medical	Mental illness/ alcohol or drug use; discharge to a rehabilitation unit/ long-term care facility, readmission for chemotherapy/ radiation therapy/ rehabilitation therapy	Admission MedRec, Discharge MedRec, patient education, medication calendar	Control group (admission MedRec as needed)	30 days	Readmission, Readmission and/or ED visit	30-day readmission and/or ED visit (general population): NS; 30-day readmission (high-risk): 12.3% (I) vs 17.8% (U), p=0.042
Bolas *et al* 2004[50]	Ireland, single centre	RCT	81	81	Inpatient stay, discharge, postdischarge	Age 55 years or older, at least 3 regular medications	Transfer to another hospital or nursing home, unable to communicate, mental illness or alcohol-related admission, follow-up was declined	Medication liaison service (comprehensive medication history, discharge letter faxed to GP and community pharmacist, medicines record sheet, discharge counselling, home visit/telephone call)	Standard clinical pharmacy service (not include discharge counselling and liaison service)	3 month	Readmission, hospital stay (following readmission)	Readmission rate: p>0.05; Length of stay: p>0.05
Eisenhower 2014[36]	US, single centre	Before–after	25	60	Discharge	Age 65 years or older, with history of COPD	Left the hospital without medical advice, death within 30 days of discharge	MedRec at discharge, Medication reconciliation form, discharge summary	Usual care (pharmacist was not present during baseline data collection)	30 days	Readmission	Readmission rate: 16% (I) vs 22.2% (U)
Farris *et al* 2014 [37]	USA, Single centre	RCT	Minimal=312 Enhanced=311	313	Admission, inpatient stay, discharge	18 years or older, English or Spanish speaker, diagnosis of HPN, hyperlipidaemia, HF, CAD, MI, stroke, TIA, asthma, COPD or receiving oral anticoagulation	Admission to psychiatry, surgery or haematology/ oncology service, could not use a telephone, had life expectancy <6 months, had dementia or cognitive impairment	Admission MedRec, patient education during inpatient stay, discharge counselling, discharge medication list, telephone call, care plan faxed to primary care physician/ community pharmacist	Usual care (admission MedRec, nurse-led discharge counselling and medication list)	90 days	ADEs, readmission, ED visit, readmission and/or ED visit	16% experienced an AE, Healthcare utilisation at 30 days and 90 days: NS

Continued

Table 1 Continued

Author, Year	Country, Setting	Study design	Intervention	Comparator	Target of intervention	Inclusion	Exclusion	Components of intervention	Comparator	Follow-up Period	Relevant outcomes	Main results
Gardella *et al* 2012[38]	US, multicentre	Before–after	1624	7335	Preadmission to post discharge	NA	NA	Preadmission medication list, patient education	Historical control group (preadmission medication list gathered by nurse)	60 days	ADE, ED visits and readmission	30-day readmission: 6% (I) vs 13.1% (U) (OR 2.34, 95% CI 1.87 to 2.94, p<0.001); 60-day readmission: 2.7% (I) vs 7.7% (U) (OR 3.02, 95% CI 2.18 to 4.19, p<0.001)
Gillespie *et al* 2009[46]	Sweden, single centre	RCT	182	186	Admission, inpatient stay and discharge	Age 80 or older	Previous admission during the study period	Admission MedRec, discharge counselling, medication review, faxing discharge summary to primary care physicians, telephone follow-up at 2 months	Usual care (without pharmacist involvement)	12 month	Readmissions, ED visits, mortality	Readmissions: 58.2% (I) vs 59.1% (U) (OR 0.96, 95% CI 0.64 to 1.4); ED visits per patient: 0.35 (I) vs 0.66 (U) (OR 0.53, 95% CI 0.37 to 0.75)
Hawes *et al* 2014[39]	US, single centre	RCT	24	37	Discharge and post discharge	High-risk patients (HF, COPD, hyperglycaemic crisis, stroke ,NSTEM, more than 3 hospitalisations in the past 5 years., 8 or more medications on discharge)	Age <18 years, inability to communicate in English, unable to follow-up (no transportation and no telephone access), transfer to facilities other than primary care, decisional impairment, incarceration	Post discharge medication reconciliation	Usual care (with no pharmacist intervention)	30 days	Readmission, ED visit, readmission and /or ED visit	ED visit: 0 (I) vs 29.7% (U), p=0.004; Readmission: 0 (I) vs 32.4% (U), p=0.002; Composite of hospitalisation or ED visit: 0 (I) vs 40.5% (C), p<0.001
Hellstrom *et al* 2011[47]	Sweden, single centre	Before–after	109	101	Admission, inpatient stay, discharge	Age 65 years or older, at least one regular medication	Staying during the implementation period	LIMM model, admission and discharge MedRec, medication review and monitoring, quality control of discharge MedRec	Standard care (no formal MedRec by clinical pharmacists)	3 month	Readmission and ED visit, ADE-related hospital visit	ED visit and readmission: 45/108 (I) vs 41/100 (U) Mortality, 3 month: 9/108 (I) vs 9/100 (U) ADE-related revisit: 6/108 (I) vs 12/100 (U)
Hellstrom *et al* 2012[48]	Sweden, single centre	Before–after	1216	2758	Admission, inpatient stay	High-risk patients (age ≥65 years with any of HF, RF)	NA	Admission MedRec, structured medication reviews,	Usual care (no clinical pharmacists	6 month	ED visits, hospital	ED visit: 48.8% (I) vs 51.3% (U) (HR 0.95, 95% CI 0.86 to 1.04);

Continued

Table 1 Continued

Author, Year	Country, Setting	Study design	Intervention	Comparator	Target of intervention	Inclusion	Exclusion	Components of intervention	Comparator	Follow-up Period	Relevant outcomes	Main results
								follow-up at least two times a week	working in the wards)		admissions and mortality	All ED visits, hospitalisation or death: 58.9% (I) vs 61.2% (U) (HR 0.96, 95% CI 0.88 to 1.04) Mortality: 18.2% (I) vs 17.3% (U), p=0.55
Koehler *et al* 2009[40]	US, single centre	RCT	20	21	Admission, discharge and post discharge	Age 70 years or older, ≥5 medications, ≥3 chronic comorbid conditions, assisted living, English language, phone contact	Primarily surgical procedure, life expectancy ≤6 months, residence in long-term care facility, refusal to participate, not enrolled within 72 h.	Targeted care bundle, medication reconciliation and education, follow-up call, enhanced discharge form	Usual care (nurse and care coordination staff providing care)	60 days	Readmission and/or ED visits	30 days readmission/ ED visits: 2/20 (I) vs 8/ 21 (U), p= 0.03; 60days readmission/ ED visits: 6/20 (I) vs 9/ 21 (U), p= 0.52
Pal *et al* 2013[41]	US, single centre	NRCT	537	192	Discharge	Age 18 years or older, at least 10 regular medications	NA	Patient counselling, pharmacist medication reconciliation, medication calendar	Usual care (without discharge review by pharmacist)	30 days	Readmission	30 days readmission: 16.8% (I) vs 26.0% (U), p=0.006 ADE prevented: 52.8%
Schnipper *et al* 2006[42]	US, single centre	RCT	92	84	Inpatient stay, discharge, post discharge	Discharge to home, contacted 30 days after discharge, spoke English, cared for primary care physician/internal medicine resident	NA	Discharge medication reconciliation, telephone follow-up, medication review, standard email template, patient counselling	Usual care (medication review by a pharmacist and discharge counselling by a nurse)		ADEs-related hospital visit, readmission and/or ED visit	Preventable ADE: 1% (I) vs 11% (U), p=0.01; ED visit/readmission: 30% (I) vs 30% (U), p>0.99; preventable medication-related healthcare utilisation: 1% (I) vs 8% (U), p= 0.03
Scullin *et al* 2007[49]	Ireland, multicentre	RCT	371	391	Admission, inpatient stay, discharge	Age 65 years or older, at least 4 regular medications, taking antidepressants, previous admission in the past 6 months, taking intravenous antibiotics	Scheduled admissions and admissions from private nursing homes	Integrated medicines management service admission and discharge MedRec, inpatient medication review and counselling, telephone follow-up	Usual care (did not receive integrated medicines management service)	12 month	Length of hospital stay, readmission	LoS reduced by 2 days for intervention vs usual care, p=0.003 Readmissions per patient: 0.8 (I) vs 1 (U)
Stowasser *et al* 2002[51]	Australia, multicentre	RCT	113	127	Admission, discharge	Return to the community following discharge	Outpatients, discharge to hostel or nursing home,	Medication liaison service—medication history confirmation	Usual care (no medication liaison service)	30 days	Mortality, readmission, ED visit	Mortality, 30 days: 2/ 113 (I) vs 3/127 (U): NS

Continued

Table 1 Continued

Author, Year	Country, Setting	Study design	Intervention	Comparator	Target of intervention	Inclusion	Exclusion	Components of intervention	Comparator	Follow-up Period	Relevant outcomes	Main results
							previous enrolment, unable to provide consent and follow-up	with community healthcare professionals (telephone, faxing), 30 days post follow-up				Readmissions: 12/113 (I) vs 17/127 (U) ED visit per patient: 7.54 (I) vs 9.94 (U)
Walker *et al* 2009[43]	US, single centre	NRCT	138	366	Discharge, post discharge	Age 18 years or older, 5 or more regular medications, receiving 1 or more targeted medications, having 2 or more therapy modification, unable to manage their medication, receiving a medication requiring therapeutic drug monitoring	Non-English speaking, stay of 21 days or longer	Patient interviews, follow-up plan, medication counselling, telephone follow-up	Usual care (nurse-led service)	30 days	Readmission, ED visit, readmission and/or ED visit	Readmission, 14 days: 12.6% (I) vs 11.5% (U), p=0.65; Readmission, 30 days: 22.1% (I) vs 18.0% (U), p=0.17; Readmissions and/or ED visits: 27.4% (I) vs 25.7% (U), p= 0.61
Warden *et al* 2014[44]	US, single centre	Before–after	35	115	Admission, inpatient stay, discharge	Age 18–85 years, systolic dysfunction (EF ≤40)	Diastolic dysfunction, valve replacement/left ventricular assist device	Medication reconciliation (admission and discharge), discharge instructions, telephone follow-up	Historical control group (physicians—admission MedRec; nurses-discharge counselling)	30 days	Readmission	All cause readmission, 30-day :17% (I) vs 38% (U) (RR 0.45, 95% CI 0.21 to 0.96, p=0.02), 30 days HF-related readmission: 6%(I) vs 18% (U) (RR 0.31, 95% CI 0.08 to 1.27, p=0.11)
Wilkinson *et al* 2011[45]	US, single centre	NRCT	229	440	Discharge	Age 18 years or older, English speaking, patients with depression, receiving high-risk medications and polypharmacy, poor health literacy, having an absence of social support, prior hospitalisation within the past 6 months	Refusal of pharmacist education, transfer to a skilled nursing facility, or discharge when the pharmacist was not available	Medication history at admission, during hospitalisation and discharge, patient education on discharge	Control group (pharmacists not provide medication counselling at discharge)	30 days	Readmission	Readmission rate: 15.7% (I) vs 21.6% (U) (RR 0.728, 95% CI 0.514 to 1.032, p =0.04)

ADE, adverse drug event; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; D, days; ED, emergency department; EF, ejection fraction; GP, general practitioner; HF, heart failure; HPN, hypertension; I, intervention; IV, intravenous; LIMM, Lund Integrated Medicines Management; LoS, length of stay; MedRec, medication reconciliation; MI, myocardial infarction; NA, not available; NS, non-significant; NSEMI, non-ST segment elevation myocardial infarction; RCT, randomised controlled trials; RF, renal failure; RR, relative risk; TIA, transit ischaemic attack; U, usual care.

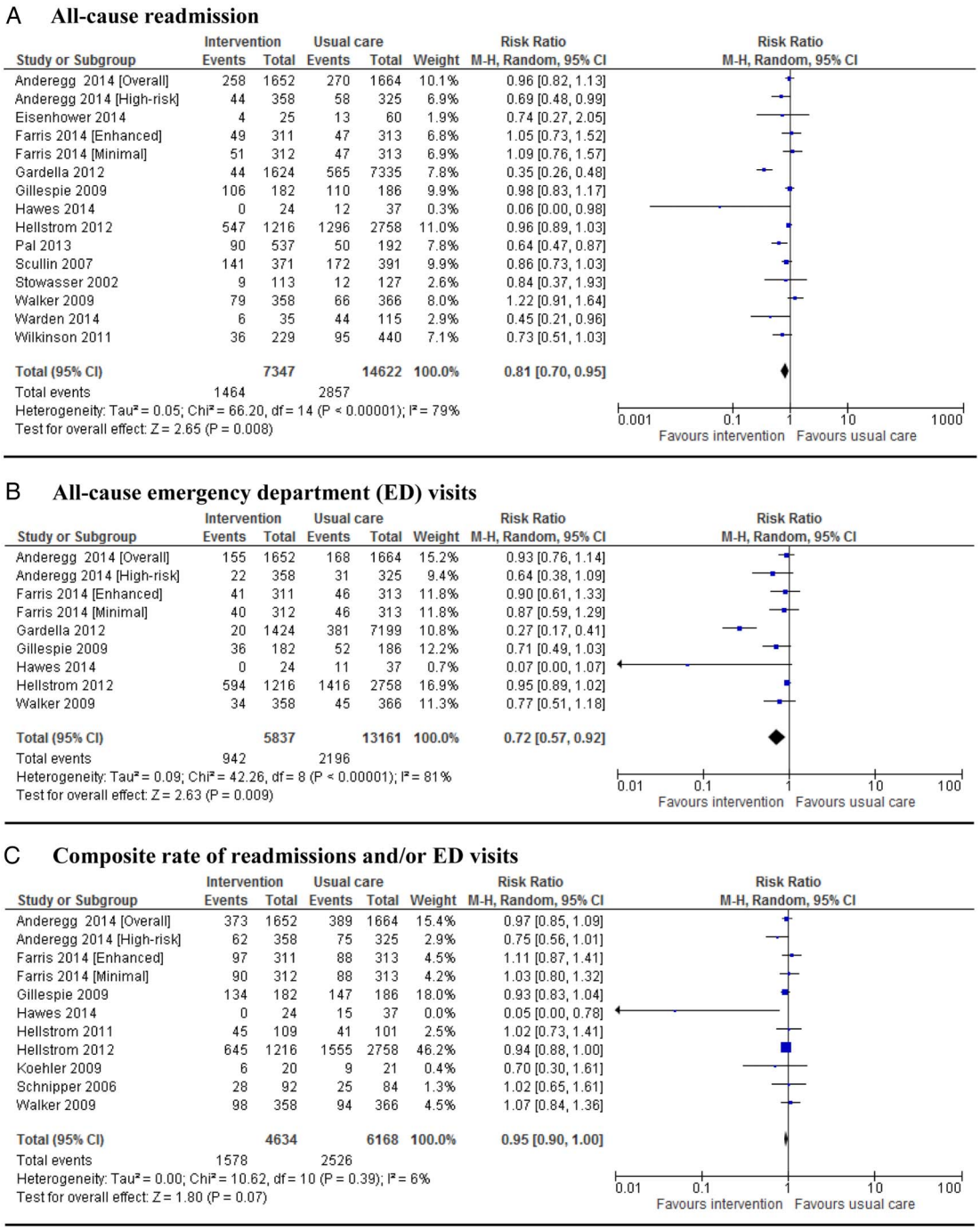

Figure 2 Forest plots of intervention effects on the proportion of patients with all-cause readmission (A), emergency department (ED) visits (B), composite rate of readmissions and/or ED visits (C), adverse drug event-related hospital revisits (D) and mortality (E). Pooled estimates (diamond) calculated by the Mantel-Haenszel random effects model. Horizontal bars and diamond widths represent 95% CIs. Anderegg *et al*[35] stratified patients into two groups: general population and high-risk patients. Farris *et al*[37] randomised the population into different levels of intervention: minimal and enhanced.

Nine studies[35 37 39 40 42 43 46–48] that reported composite all-cause readmission and/or ED visit showed no difference in pooled analysis (RR 0.95; 95% CI 0.90 to 1.00 figure 2C). Only three studies[38 42 47] were meta-analysed for ADE-related hospital revisits. One study[46] did not give data in a suitable form. The pooled result showed a substantial reduction of 67% in hospital revisits (pooled RR 0.33; 95% CI 0.20 to 0.53) when pharmacist-led medication reconciliation programmes were implemented (figure 2D). Seven studies[37 46–51] gave eight separate sets of data for all-cause mortality that had been reported after 30 days to 12 months of follow-up. However, information on mortality from Bolas *et al*[50] and Farris *et al*[37] was not their primary outcome of interest; nevertheless, we included it in our meta-analysis. Overall, there was no significance difference

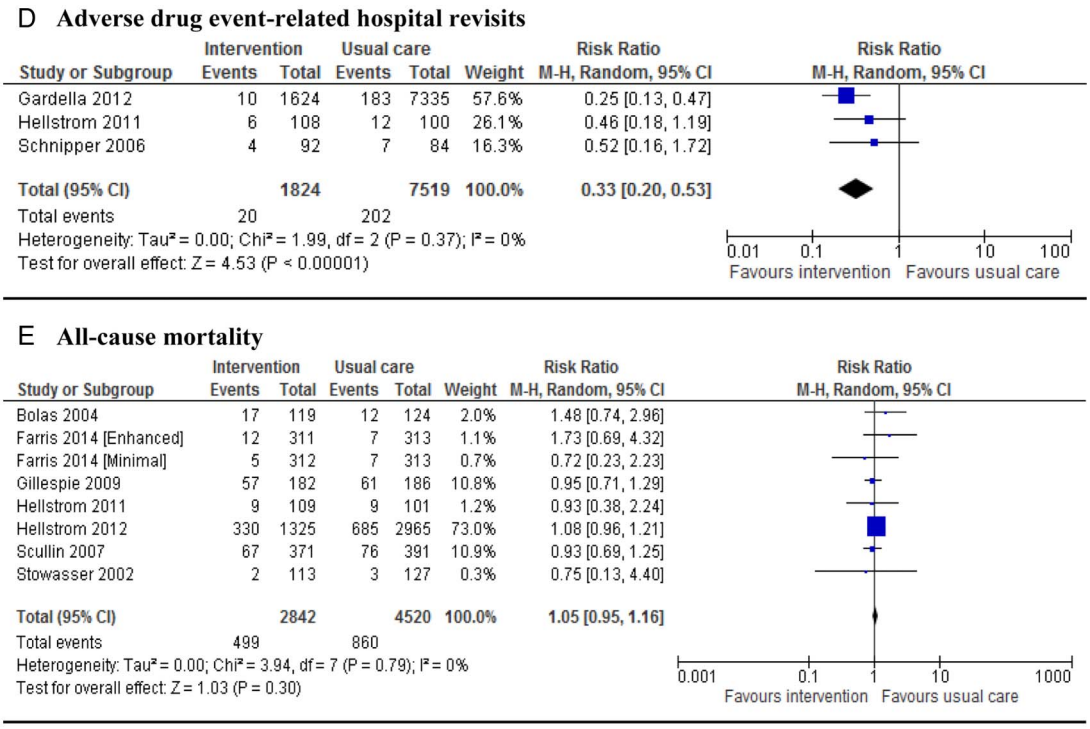

Figure 2 Continued.

between the two groups in terms of all-cause mortality (RR 1.05; 95% CI 0.95 to 1.16) (figure 2E).

Other outcomes

Studies reporting other clinically important outcomes are summarised in table 2. Some studies[46–49] furnished information on the proportion of patients who did not revisit the hospital. The intervention group in the three studies[46 48 49] showed a trend towards an increase in the number of patients who did not revisit the hospital for any causes, and the overall pooled analysis was statistically significant (RR 1.10; 95% CI 1.03 to 1.17). There were no significance differences between the intervention and usual care in terms of other relevant clinical outcomes: length of stay after readmission, readmission per patient, ED visit per patient and proportion of patients with ADEs.

Sensitivity analysis

A one-on-one removal of studies in the meta-analysis did not affect findings in all outcomes except for composite readmission and/or ED visit. A meta-analysis for composite readmission/ED visit showed that only when the study by Faris *et al* (Enhanced)[37] or Hawes *et al*[39] was removed did the result show a significant pooled summary estimate with similar risk ratio (RR 0.95; p=0.02 and 0.03, respectively).

Subgroup analysis

Subgroup analysis comparing studies that reported all-cause readmissions at earlier versus longer follow-up period showed different patterns of effect: the effect of intervention was not statistically significant for longer follow-up subgroups (RR 0.83, 95% CI 0.68 to 1.06, p=0.14), whereas in earlier follow-up subgroups, the

Table 2 Other clinically relevant outcomes

Outcome	Number of studies	Number of patients	RR	CI	WMD	CI
Patients who did not revisit hospital	4	5314	1.10*	(1.03 to 1.17)†		
Hospital stay (after readmission)	2	803			−0.57	(−5.32 to 4.17)‡
Readmission per patient	3	1370			−0.12	(−0.24 to 0.01)‡
ED visit per patient	2	4342			−0.15	(−0.53 to 0.23)‡
Patients with ADE	3	1401	0.94	(0.75 to 1.20)‡		

*RR is >1 when the intervention increased the number of patients who did not revisit the hospital (ie, it showed success).
†p<0.01.
‡p>0.05.
ADE, adverse drug event; ED, emergency department; RR, risk ratio; WMD, weighted mean difference.

effect was significant (RR 0.77, 95% CI 0.60 to 0.98, p=0.03). However, there was no significant difference between these two subgroups. In addition, non-randomised studies showed a significant reduction in all-cause readmission (RR 0.74, 95% CI 0.58 to 0.94, p=0.01) and all-cause ED visit (RR 0.68, 95% CI 0.48 to 0.97, p=0.03), but there was no difference in terms of study design with these outcomes. As opposed to what has been observed in the entire analysis, the composite outcome seemed to have a slight significant reduction in non-randomised studies (RR 0.95, 95% CI 0.90 to 1.00, p=0.04); though there was no difference between the subgroups (see online supplementary appendix D).

Publication bias

We examined the potential for publication bias by constructing a funnel plot and through statistical tests. There was some indication of asymmetry—particularly for all-cause ED visits—in the funnel plot and, therefore, there was some publication bias, as evidenced by the Egger's (p=0.04) and Begg's tests (p=0.01) in this outcome. We did not find any significant evidence of bias in the other outcomes, as shown by Egger's test value of 0.08 for all-cause readmission, 0.57 for composite readmission/ED visit and 0.83 for all-cause mortality; this was further supported by Begg's test p value of 0.13, 0.35 and 0.71, respectively (see online supplementary appendix E).

DISCUSSION

To the best of our knowledge, this is the first meta-analysis to investigate the effectiveness of pharmacist-led medication reconciliation programmes on clinical outcomes at hospital transitions. This review has shown better outcomes in favour of pharmacist-led interventions. We found a substantial reduction in the rate of all-cause readmissions (19%), all-cause ED visits (28%) and ADE-related hospital revisits (67%). However, pooled data on mortality and composite readmission/ED visit favoured neither the intervention nor the usual care. Not only were patients allocated to the intervention group readmitted or not only did they revisit the hospital less frequently, but patients free of any events after hospital discharge also increased (RR 1.10; 95% CI 1.03 to 1.17).

No previous reviews have conclusively and consistently shown effectiveness of medication reconciliation interventions, be it in primary care,[52] long-term settings[53] or hospital transitions.[30 31] Particularly, reviews from hospital-initiated medication reconciliation interventions searched the available literature on medication reconciliation strategies and impact on patient safety, and summarised the evidence that medication reconciliation alone was not strong enough to reduce post discharge hospital utilisation.[30 31] It was not clear to support the effectiveness of such interventions in the hospital setting. However, we believe that the influence of pharmacist's in healthcare utilisation was diluted among those various medication reconciliation strategies and, thus, specifically assessing the effect of pharmacist in medication reconciliation is an important consideration.

Although Thomas *et al*[54] did not find a significant effect in reduction of readmissions due to medication-related problems, our review showed that pharmacists' influence in preventing ADE-related hospital revisits was more impactful than any of the outcomes measured. This might be because medication reconciliation picks patients with discontinued medication more powerfully, where this is the case for studies reporting this outcome.[43 47] Other studies also showed that medication discontinuity is the most common reason for discrepancy-related ADE.[55 56] Although the study by Gillespie *et al*[46] was not included in the meta-analysis of this outcome, it showed a much higher reduction of 80% in medication-related readmissions in the intervention group than in the control group. Readmissions were frequent in earlier follow-up periods. This is as opposed to a review by Kwan *et al*,[31] where harm due to medication discrepancies occurred only some months after discharge. However, for most studies, the duration of follow-up was short; only one-third of interventions followed patients for longer than 30 days. Therefore, it might be difficult to come to a conclusion, as there was no sustained benefit from the intervention, and this was supported by non-significant differences between the subgroups. Moreover, non-randomised studies showed a slight significant reduction in all-cause ED visit and readmission and composite outcome, but there was no difference in terms of study design with these outcomes. Otherwise, pooled estimates showed consistent results in all of these three outcomes, regardless of the study design and duration of follow-up. However, care should be taken in interpreting the results as some of the influence of observational studies on the success of outcome was clear, and their heterogeneity should be taken into consideration.

Some of the studies, as part of their intervention, consisted of intermingled components, and the difficulty in ascertaining the success of pharmacist-led intervention is due only to medication reconciliation. After medication reconciliation, for example, medication review as intervention component was added in some studies. Previous systematic reviews that focused on medication review[57 58] raised a debate as to the impact of medication reviews in general, and pharmacist-led medication reviews in particular. A review by Holland *et al*,[57] where only 8 of the 32 included studies were hospital-based and only 2 of these had extensive medical team involvement at hospital transitions, did not support the evidence for pharmacist-led medication review. On the other hand, one of the issues raised in a Cochrane review[58] was that medication review had varied and wider meaning, and did not stand alone. Prior to medication review, it is medication reconciliation that is practiced routinely at hospital transitions and, thus, considering medication

review without ensuring the most accurate list of a patient's current medications would be theoretical. This would strengthen our anticipation that interventions with medication reconciliation might be as equally effective as those with mixed interventions.

A number of recent studies have investigated medication reconciliation interventions at the level of real practice models or in integrated management of medicines.[47–49] Medication reconciliation interventions are complex interventions targeting fragments of services across the entire spectrum of care transitions, and thus take time and effort, but the outcome of safe patient transition is well worth it. This review further consolidates pharmacist-led medication reconciliation programmes might contribute to quality transitions in combinations of those multifaceted components.

Limitation of the study

There are a number of limitations to this study. First, most studies included high-risk patients, and we did not confirm which patients benefited most from such interventions. Various definitions pertaining to high-risk were employed, including patients with specific disease state, polypharmacy, older age and patients at risk of hospitalisation. Second, interventions target different transitions; we could not take into account this effect in our meta-analysis. For instance, previous prospective studies showed varied results on the rate of medication discrepancies from 30–55% during admission,[59–62] to 35–71% during discharge.[4 63 64] Coleman *et al*[65] showed that patients with medication discrepancies have significantly high rates of readmission. Thus, if this value is extrapolated to clinical outcomes, there might be some variation among studies with respect to these outcomes at the different care transitions. Additionally, few studies were carried out in hospitals where medication reconciliation had already been implemented in some defined areas. Therefore, future studies should evaluate specific areas suited to pharmacist services that would benefit patients the most. Third, most of the studies were single centre evaluations, and there were a few studies with a small number of patients. Considering the success rates within small single centre studies raises an issue about bias. Our included studies were not free of bias and most possessed moderate quality, which leaves the findings open to criticism—for example, Gardella *et al*,[38] in the ADE-related hospital visit, and Hellström *et al*,[48] in the mortality forest plots, accounted for a large proportion of the studied subjects, yet these studies possessed low quality score. Fourth, the lack of homogeneity in the data from this meta-analysis confirms the complexity of medication reconciliation and warrants further investigation. We attempted to investigate the sources of variation between studies, but were unable to explain much of it. We were also unable to assess interactions between medication reconciliation and components of interventions. For example, integrated care models may be particularly effective for improving care for some of the interventions, but not for other types, and a pooled analysis would not identify such interactions. Despite these limitations, our meta-analyses showed that interventions that contain one or more elements of medication reconciliation can improve outcomes at hospital transitions.

We also note that only published studies were included in our work. However, the funnel plot asymmetry and statistical tests suggest that the impact of bias was less likely to have a significant effect on the findings. Only articles published in English were assessed for this review. Potentially, there may have been studies, such as that by Sánchez Ulayar *et al*,[66] published in non-English journals, involving interventions for improving care transitions. In addition, research disseminated through the grey literature, such as conference papers and unpublished reports, was not considered.

CONCLUSION

The results of this meta-analysis indicate that a pharmacist-led medication reconciliation programme at hospital transitions decreases ADE-related hospital revisits, all-cause readmissions and ED visits. However, the effect on mortality and composite all-cause readmission/ED visit is inconclusive based on the current body of evidence, though improvements in the majority of studies were demonstrated. Future research is needed to assess whether improvements in such outcomes can be achieved with this programme and to determine what/which components of the intervention are necessary to improve clinical outcomes. Although our results showed that pharmacist-led medication reconciliation was beneficial at care transitions, we still need further research with robust, large randomised control trials of excellent quality to conform our conclusion. Overall, our findings support the implementation of a pharmacist-led medication reconciliation programme that includes some components aimed at improving medication safety.

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