BMJ Open

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Journal:	*BMJ Open*
Manuscript ID	bmjopen-2015-010003
Article Type:	Research
Date Submitted by the Author:	17-Sep-2015
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Primary Subject Heading:	Pharmacology and therapeutics
Secondary Subject Heading:	Pharmacology and therapeutics, Health services research
Keywords:	Quality in health care < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, Adverse events < THERAPEUTICS, Health & safety < HEALTH SERVICES ADMINISTRATION & MANAGEMENT

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

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Abstract count- 298

Number of tables- 2

Number of figures- 3

Keywords- Medication reconciliation, medication history, medication safety, medication review, medication errors, medication discrepancies, care transition, pharmacists, clinical pharmacists

Running head- Effect of pharmacy-led medication reconciliation programmes

Abstract

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

Design: Systematic review and meta-analysis

Data sources and study eligibility criteria: Electronic databases were searched in PubMed, MEDLINE, EMBASE, IPA, CINHAL and PsycINFO from inception to December, 2014. Included studies were all published studies in English that have compared the effectiveness of pharmacy-led medication reconciliation interventions to usual care, aimed at improving medication reconciliation programmes.

Analysis: Meta-analysis was done using random effects model, and subgroup analysis was conducted to determine the sources of heterogeneity.

Results: Seventeen studies involving 21,342 adult patients were included. Eight studies were RCTs, and eight non-RCTs, of which 5 studies employed a before-after study designs. Most studies target 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 substantial reduction of 67%, 28% and 19% in ADE-related hospital revisits (RR 0.33; 95%CI: 0.20-0.53), emergency department (ED) visits (RR 0.72; 95%CI: 0.57-0.92) and hospital readmissions (RR 0.81; 95%CI: 0.70-0.95), in the intervention group than the usual care respectively. The pooled data on mortality (RR 1.05; 95%CI: 0.95-1.16) and composite readmission and/or ED visit (RR 0.95; 95%CI: 0.90-1.00) 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 produced statistically significant results.

Conclusion: Pharmacy-led medication reconciliation programmes are effective at improving post-hospital healthcare utilization. This review supports the implementation of pharmacy-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 pharmacy-led medication reconciliation programs on clinical outcomes.
- In some of the clinical outcomes evaluated, there is substantial statistical heterogeneity and we couldn't identify the source of variation among the studies.
- The inclusion of non-controlled studies might affected the quality of evidence as seen by the high risk of bias in these groups of studies.

Introduction

The modern patient safety movement is dated back to the end of 1990's when the Institute of Medicine (USA) report described medication errors as common and contributing to over 7,000 deaths annually.[1] Approximately 230,000 medication-related admissions occurred each year in Australia.[2] More than half of the medication problems occur at care transitions,[3] and up to one third of these problems has the potential to cause harm.[4] Unintentional medication changes are common at care transitions,[4-9] and responsible for a huge utilization of healthcare resources.[10-14]

Preventing harm from medications remains a top patient safety priority at transitions in care, [15] and many healthcare organizations endorsed medication reconciliation as a safety strategy. Medication reconciliation as a National Patient Safety Goal (NPSG) was first adopted in 2005 by the Joint Commission.[16] Later, under the leadership of WHO, many safety programmes including medication reconciliation had been implemented across a range of countries.[17-19] Despite of these efforts, implementation of the service is a hospital wide challenge,[20] and there is no previous clinical evidence as to which member of the healthcare professional (s) or strategies should effectively perform medication reconciliation.[21] A number of medication reconciliation strategies were utilized for safe patient transitions: electronic reconciliation tools,[22-24] use of standardized forms,[25,26] collaborative models,[27, 28] patient engagement [29] and pharmacy-led. [30, 31]

The impact of medication reconciliation on clinical outcomes at hospital transitions were reported so far, however, two recently published systematic reviews[32, 33] have ascertained that the benefit as a patient safety strategy is not clear. Both studies have inconsistent findings in healthcare resource utilization. Unlike Mueller et al, [32] Kwan et al [33] did not report significant association between post-hospital healthcare utilization and medication discrepancies identified through medication reconciliation interventions. Both reviews

assessed broadly at the effect of medication reconciliation done by various strategies including the use of collaborative models. The aim of the present review is thus, to assess specifically the effectiveness of pharmacy-led medication reconciliation programmes compared to usual care on clinical outcomes at hospital transitions.

Methods

Data sources and searches

The study was conducted utilising PRISMA group (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines, [34] including the PRISMA check list 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, a comprehensive search was carried out involving the entire collections in the databases till December, 2014: PubMed/Medline (1946), Ovid/Medline (1946), International Pharmaceutical Abstracts (1970), Embase (1966), PsycINFO (1890), and CINHAL (1937) (Appendix A). The reference lists of review articles and eligible studies were hand-searched to identify articles that were not identified in the database search. Article search was performed by one reviewer (AM) with the support of a medical librarian. All studies identified for full text review and selected according to inclusion criteria were agreed by the second (AM) and third reviewer (JB).

Study selection

To be included in the selection, studies were required to present all of the following:

- Studies which reported medication reconciliation intervention primarily, and provide data on clinical endpoints [healthcare resource utilization, mortality, adverse drug event-related hospital visit].

- Studies which were published in English.
- The included interventions had to start in the hospital and must be performed primarily by pharmacy personnel with the aim of improving care transitions to and from a hospital.
- The intervention must be compared with a control group that received usual or standard care.

Along with duplicate references and irrelevant studies, the following types of studies were excluded:

- Other medication reconciliation practices or practices as part of a multicomponent intervention, 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 randomized controlled trials (RCTs), quasi-experimental studies with a control group, and before-and-after studies that evaluated pharmacy-led medication reconciliation programmes at hospital care transitions.

Data extraction

Data were extracted from full texts using a modified adapted Cochrane EPOC data collection checklist.[35] The following information was extracted from each included study: name of first author, year of publication, country and setting where the study 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 endpoints: healthcare utilization [readmission, ED visit and composite readmission and/or ED visit], mortality and ADE related hospital visits, compared with a usual care in the other arm and used at least 30 days of follow up. Studies were eligible for meta-analysis if such end point could be extractable. Data were processed in accordance with the Cochrane handbook. Together with 95% confidence intervals for each outcome, we derived the relative risk and weighted mean differences for dichotomous and continuous variables respectively.

After data were combined, the analyses were conducted with Cochrane Review Manager (RevMan) V5.3 software (Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014). We performed separate analyses for each outcome measured compared with usual care. The results were synthesized 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% confidence intervals (CI) were calculated. Because the analyses included medication reconciliation interventions with multiple components, designs and follow-up periods, we set a priori that might be associated with some variation in the outcomes between the studies. Methodological design factors (RCT and non-randomized studies) and outcome timing were considered, and thus, a subgroup analysis was performed using study design and duration of follow up when there were at least five studies per outcome. For studies that reported outcomes at different duration, the longer follow-up period was taken in the analysis, if there is no difference in the summary estimate. Otherwise, meta-analysis was done separately for the long and short duration in sub-groups. Statistical heterogeneity among studies was

assessed through calculating Tau^2, Chi-square (Q), I^2 and p-value. Sensitivity analysis was conducted to check the stability of summary estimates to outliers and the change in I^2 when any of the studies was withdrawn from the analysis. Publication bias was evaluated by inspection of funnel plot, Begg-Mazumdar and Egger's test using Comprehensive Meta-analysis, V3 (Biostat, Englewood, NJ, USA). In all analyses, p-value < 0.05 was considered as statistically significant.

Risk of bias of individual studies was assessed with EPOC risk of bias tool.[35] The main domains 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.

Results

Identification and selection of studies

A total of 2551 citations were identified from searches in the electronic databases and additional 59 records were found in reference lists of included studies. After removal of duplicate records, title and abstract screening were applied on 1832 publications. After title and abstract review, 1731 publications did not meet the inclusion criteria. The remaining 101 publications were obtained in full text and assessed for inclusion. Most full text articles were excluded due to reporting of a different outcome of interest (n=34) or medication reconciliation were not the primary intervention (n=11) (Appendix B). After applying all the inclusion criteria, we finally included 17 articles (Figure 1).

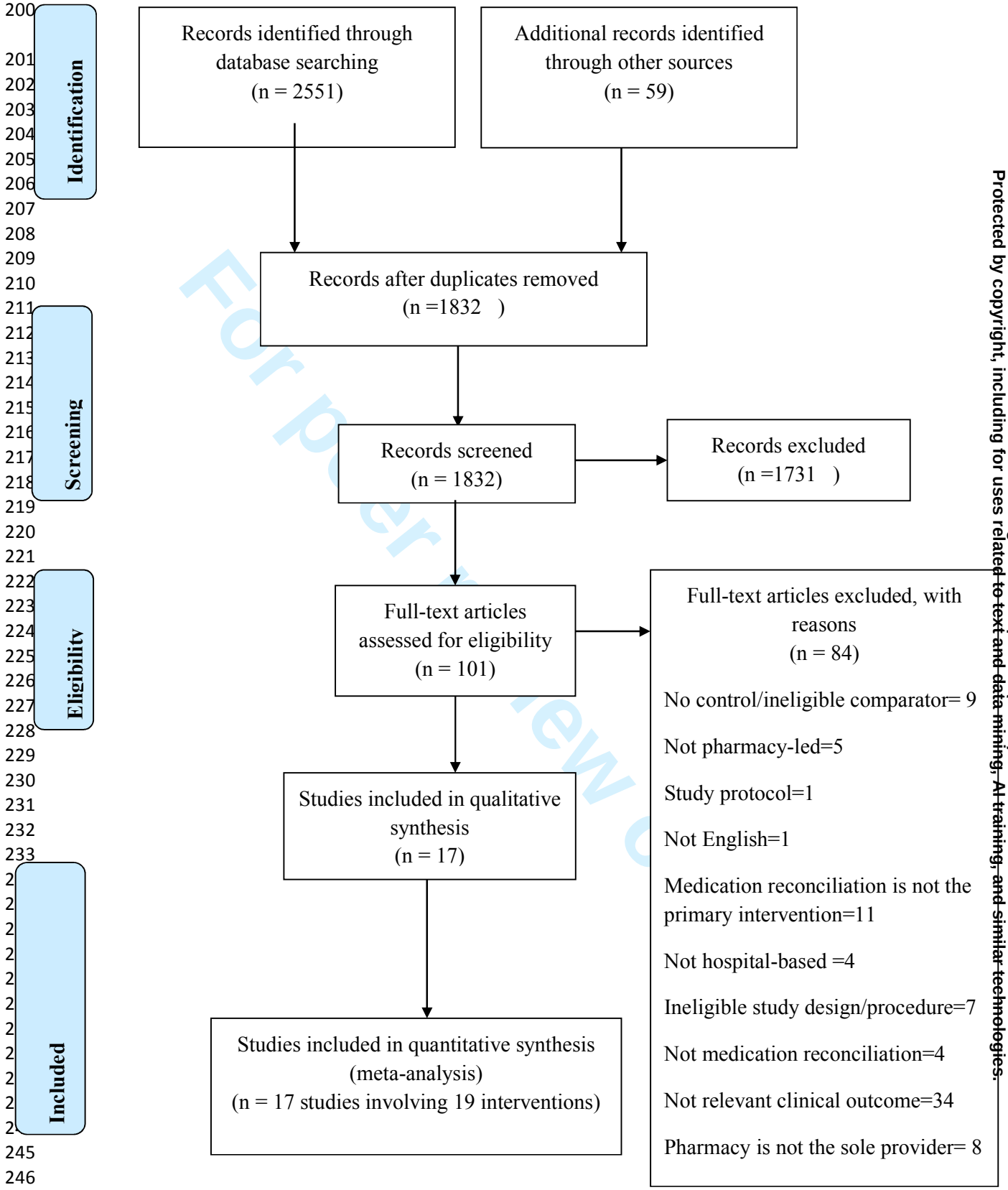


Figure 1 PRISMA flow diagram of the selection of eligible studies

Characteristics of included studies

The details of included studies are presented in table 1. They were randomized controlled trials (n=8, 47%), before-and-after studies (n= 6, 35%) and non-randomized controlled trials (n= 3, 18%). Majority of the studies, 11 were conducted in the US, [36-46] 3 were conducted in Sweden, [47-49] 2 in Ireland[50, 51] and 1 in Australia.[52] The studies were conducted between 2002 and 2014. Sample sizes ranged from 41 to 8,959 with a total of 21, 342 individuals. Only three studies were confined to multicentre.[39, 50, 52] All studies included adults of various ages. No studies in paediatrics were identified. Most studies reported outcomes up to 30 days of follow-up after selection of eligible patients; only six studies [38, 47-51] reported longer follow up of 3 month or more. Most studies recruited patients at high-risk of medication-related events excluding those with difficulty of communication, mental illness, and unable to be followed up. Besides, five studies focused on a specific patient population: heart failure patients, [45] chronic obstructive pulmonary disease (COPD) [37] and mixed.[38, 40, 49] Methodologically, a study by Anderegg et al [36] stratified patients in two groups: general population and high-risk patient groups. The high-risk group patients were defined in terms of receiving the anticoagulation therapy or were hospitalized for acute myocardial infarction, heart failure, pneumonia or COPD. Farris et al,[38] on the other hand, randomized the population into different levels of intervention (minimal and enhanced). Both interventions consisted of admission MedRec, patient education, discharge counselling and discharge medication list. Additionally, the enhanced group received telephone follow up and discharge care plan was communicated to primary physicians and community pharmacists. Studies compared comprehensive medication reconciliation programmes including telephone follow-up/home visit, [45, 49, 52] patient counselling[36, 39, 42, 46] or both.[38, 41, 43, 44, 47, 50, 51] After medication reconciliation, few studies [43, 47-50] conducted medication review as part of their interventional component. Moreover, interventions were initiated at different care transitions; most were

conducted at multiple transitions [36, 38-41, 43, 45, 47-52] and all studies targeting a single transition were carried out at the level of discharge.[37, 42, 44, 46] Results usually revealed a trend towards improvement in most of the end-points studied: percentage of patients with readmissions, ED visits, ADE-related hospital revisits (Table 1).

Table 1 Characteristics of included studies

Author, Year	Country, Setting	Study design	Intervention	Comparator	Target of intervention	Inclusion	Exclusion	Components of intervention	Follow-up Period	Relevant outcomes	Main results
Anderegg *et al*. 2014[36]	USA, single centre	Before-after	1664	1652	Admission, discharge	Age 18 years or older, discharge from internal medicine, family medicine, cardiology, or orthopedic 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 MeRrec, Discharge MedRec, patient education, medication calendar	30 days	Readmission, Readmission and/or ED visit	30 d readmission and/or ED visit (general population): NS In high-risk group, 30 d readmission : 12.3%(I) vs 17.8%(U) (p=0.042)
Bolas *et al.* 2004[51]	Ireland, single centre	RCT	81	81	In-patient stay, discharge, post discharge	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	Comprehensive medication history, discharge letter faxed to GP and community pharmacist, medicines record sheet, discharge	3 month	Readmission, hospital stay (following readmission)	Readmission rate: p>0.05; length of stay: p>0.05

								counselling, home visit/telephone call			
Eisenhower 2014[37]	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 d of discharge	Pharmacist MedRec at discharge, Medication reconciliation form, discharge summary	30 days	Readmission	Readmission rate, 16% (I) Vs 22.2% (U)
Farris *et al.* 2014[38]	USA, Single centre	RCT	Minimal=312 Enhanced= 311	313	Admission, in-patient stay, discharge	18 years or older, English or Spanish speaker, diagnosis of HPN, hyperlipidemia, 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	90 days	ADEs, readmission, ED visit, readmission and/or ED visit	16% experienced an AE, Health care utilization at 30 days and 90 days: NS
Gardella *et al.* 2012[39]	US, multicentre	Before-after	1624	7335	Pre-admission to post discharge	-	-	Preadmission medication list, patient education	60 days	ADE, ED visits and readmission	30 day readmission: 6%(I) vs 13.1% (U) [OR 2.34, 95%CI;1.87-2.94, p<0.001; 60 day readmission: 2.7% (I)

											vs 7.7%(U) [OR 3.02, 95%CI; 2.18-4.19, p<0.001]
Gillespie *et al.* 2009[47]	Sweden, single centre	RCT	182	186	Admission, in-patient 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	12 month	Readmissions, ED visits, mortality	Readmissions: 58.2%(I) vs 59.1%(U), OR 0.96 (0.64,1.46); ED visits per patient: 0.35 (I) vs 0.66 (U), OR 0.53 (0.37,0.75)
Hawes *et al.* 2014[40]	US, single centre	RCT	24	37	Discharge and post discharge	High risk patients [HF, COPD, hyperglycaemic crisis, stroke ,NSTEM, more than 3 hospitalizations in the past 5 yrs., 8 or more medications on discharge]	Age < 18 yrs, inability to communicate in English, unable to follow up (no transportation and telephone access),transfer to other facilities other than primary care, decisional impairment, incarceration	Post-discharge medication reconciliation	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 hospitalization or ED visit: 0 (I) vs 40.5% (C), p< 0.001
Hellstrom *et al.*	Sweden, single	Before-after	109	101	Admission,	Age 65 or	Staying during the	LIMM model,	3	Readmission	ED visit and readmission:

2011[48]	centre				in-patient stay, discharge	older, at least one regular medication	implementation period	admission and discharge MedRec, medication review and monitoring, quality control of discharge MedRec	month	and ED visit, ADE related hospital revisit	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[49]	Sweden, single centre	Before- after	1216	2758	Admission, inpatient stay	High risk patients[age ≥65 with any of HF, RF]	-	Admission MedRec, structured medication reviews, follow up at least two times a week	6 month	ED visits, hospital admissions and mortality	ED visit: 48.8% (I) vs 51.3% (U) (HR, 0.95,95%CI, 0.86-1.04); All ED visits, hospitalization or death: 58.9% (I) vs 61.2% (U) (HR,0.96;95%CI, 0.88-1.04) Mortality: 18.2% (I) vs 17.3%(U); p=0.55
Koehler *et al.* 2009[41]	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,	Primarily surgical procedure, life expectancy≤ 6 months, residence in long term care facility, refusal to participate, not enrolled within 72 hrs.	Targeted care bundle, medication reconciliation and education, follow up call, enhanced discharge form	60 days	Readmission and/or ED visits	30 d readmission/ED visits: 2/20 (I) vs 8/21(U) (p= 0.03); 60 d readmission/ED visits: 6/20(I) vs 9/21(U) (p= 0.52)

						phone contact					
Pal *et al.* 2013 [42]	US, single centre	NRCT	537	192	Discharge	Age 18 years or older, at least 10 regular medications	-	Patient counselling, pharmacist medication reconciliation, medication calendar	30 days	Readmission	30 d readmission: 16.8%(I) vs 26.0% (U), p=0.006 ADE prevented: 52.8%
Schnipper *et al*. 2006 [43]	US, single centre	RCT	92	84	In-patient stay, discharge, post discharge	Discharge to home, contacted 30 days after discharge, spoke English, cared for primary care physician/ internal medicine resident	-	Discharge medication reconciliation, telephone follow up, medication review, standard email template, patient counselling	30 days	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 utilization: 1% (I) vs 8%(U), p= 0.03
Scullin *et al.* 2007 [50]	Ireland, multicentre	RCT	371	391	Admission, in-patient stay, discharge	Age 65 or older, at least 4 regular medications, taking antidepressants,	Scheduled admissions and admissions from private nursing homes	Admission and discharge medication reconciliation, inpatient medication review and	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)

						previous admission in the last 6 months, taking IV antibiotics		counselling, follow up telephone call				
Stowasser *et al.* 2002 [52]	Australia, multicentre	RCT	113	127	Admission, discharge	Return to the community following discharge	Outpatients, discharge to hostel or nursing home, previous enrolment, unable to provide consent and follow up	Medication history confirmation with community health care professionals (telephone, faxing), 30 d post follow up	30 days	Mortality, readmission, ED visit	Mortality 30 d; 2/113 (I) vs 3/127 (U): NS Readmissions; 12/113(I) vs 17/127(U) ED visit per patient;7.54 (I) vs 9.94(U)
Walker *et al.* 2009 [44]	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,	Non English speaking, stay of 21 days or longer	Patient interviews, follow up plan, medication counselling, telephone follow up	30 days	Readmission, ED visit, readmission and/or ED visit	Readmission at 14 d: 12.6%(I) vs 11.5% (U), p=0.65; Readmission at 30 d: 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

						receiving a medication requiring therapeutic drug monitoring					
Warden *et al.* 2014 [45]	US, single centre	Before-after	35	115	Admission, in-patient stay, discharge	Age 18-85 years, systolic dysfunction (EF ≤40)	Diastolic dysfunction, valve replacement/left ventricular assist device	medication reconciliation, discharge instructions, follow up telephone call	30 days	Readmission	30 d all cause readmission:17%(I) vs 38% (U) [RR 0.45(0.21-0.96), p=0.02], 30 d HF related readmission: 6%(I) vs 18%(U)[RR 0.31(0.08-1.27), p=0.11]
Wilkinson *et al.* 2011 [46]	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	Refusal of pharmacist education, transfer to a skilled nursing facility, or discharge when the pharmacist was not available	Medication history at admission, during hospitalization and discharge, patient education upon discharge	30 days	Readmission	Readmission rate: 15.7% (I) vs 21.6% (U) [RR 0.728 (0.514-1.032), p =0.04]

literacy, having an absence of social support, prior hospitalization within the last 6 months

Abbreviations: MedRec: medication reconciliation; I: intervention; U: usual care; RCT: randomized controlled trials; GP: general practitioner; CAD: coronary artery disease; MI: myocardial infarction; COPD: chronic obstructive pulmonary disease; HF: heart failure; HPN: hypertension; RF: renal failure; EF: ejection fraction; NSEMI: non-ST segment elevation myocardial infarction; LIMM: Lund Integrated Medicines Management; LoS: length of stay; OR: odds ratio; RR: relative risk; CI: confidence interval

Risk of bias assessment

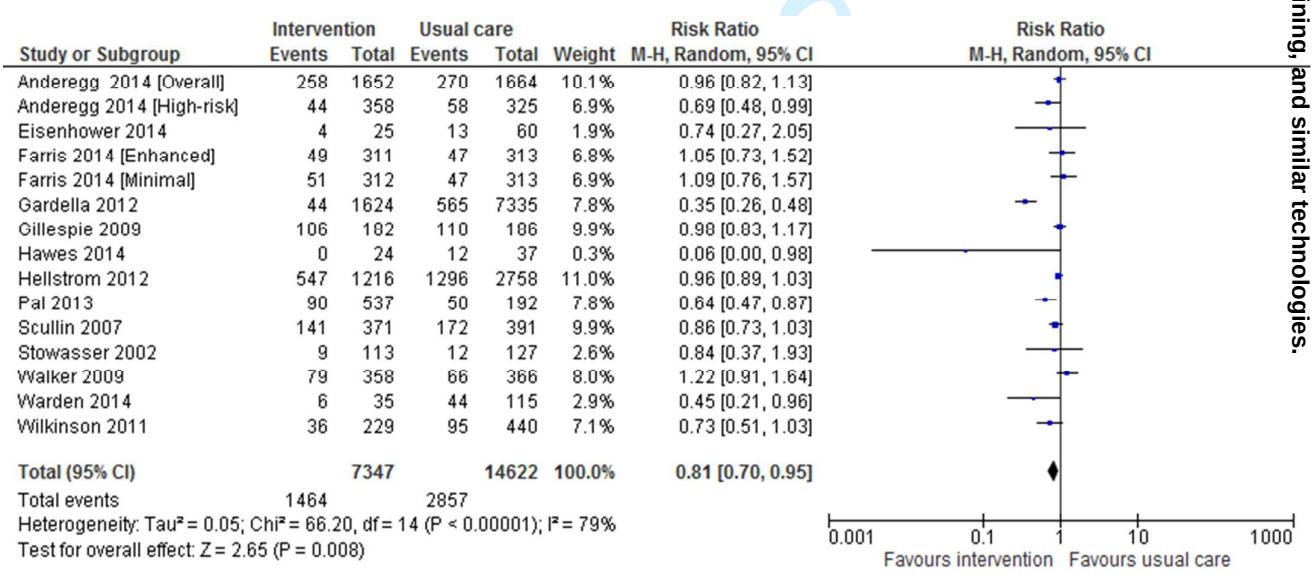
Patients included in the study were similar in the baseline characteristics except five studies [37, 39, 40, 46, 49] which were not clear or different in patient characteristics. However, in only three studies[44, 49, 52] that baseline clinical outcomes were reported or some form of adjustment analysis was performed. Eight out of 17 study reports[38, 40, 41, 43, 47, 50-52] provided enough details on randomization procedure to be judged as adequate. Among these studies, allocation concealment was fully described in all reports except one.[52] All but three studies [44, 46, 51], either care providers and outcome assessors were blinded or objective health outcomes were reported. Five studies [38, 42, 48, 49, 52] achieved more than 80% complete follow up. But, only a few studies examined the impact of losses to follow up or drop out. High risk of contamination was suspected in four studies.[36, 38, 42, 48] At least one of our outcomes of interest was selectively reported in four studies[37, 50-52] Overall, on a scale of 9, quality of randomized controlled trials falls within the range of 4 to 8 whereas for non-randomized controlled trial a lower range of 1 to 5 (Appendix C).

Effect of interventions

Of the 14 studies that reported data on all-cause readmissions, 13 were eligible for meta-analysis. One study[36] measured this outcome for a high-risk population separately; and another study[38] reported it for two different interventions. Thus, 15 interventions were meta-analysed. Eight studies reported this outcome at 30 days[36, 37, 40, 42, 44-46, 52] while three [47, 49, 50] reported long term data and two studies[38, 39] reported both. Seven studies[36, 39, 40, 42, 45, 46, 50] showed a significant reduction ($p<0.05$) in rehospitalizations although two of them had a very small sample size. [40, 45] The pooled RR (n=21,969 patients) across all studies was 0.81 (95% CI: 0.70-0.95). However, the results of these studies for this endpoint is substantially heterogenous (Figure 2A). With regards to all-cause emergency department (ED) contacts, 7 out of 8 studies[36, 38-40, 44, 47, 49] which measured ED visit as an outcome were pooled.

Considering studies that gave two data, 9 interventions were meta-analysed. The pooled analysis across all interventions showed some significance difference between the intervention and usual care (RR 0.72; 95% CI: 0.57-0.92) (Figure 2B). Evidence showed extreme heterogeneity, however, the findings were different when Gardella et al[39] was removed; no heterogeneity without affecting the significance (p=0.25; I^2=22%, RR 0.89; 95% CI 0.79-0.99). In 9 studies[36, 38, 40, 41, 43, 44, 47-49], which reported composite all-cause readmission and/or ED visit showed no difference in pooled analysis (RR 0.95; 95% CI: 0.90-1.00) (Figure 2C). Only 3 studies [39, 43, 48] were meta-analysed for ADE-related hospital revisits. One study[47] didn't give data in a suitable form. The pooled result showed a substantial reduction of 67% in hospital revisits (pooled RR 0.33; 95% CI: 0.20-0.53) when pharmacy-led medication reconciliation programmes were implemented (Figure 2D). Seven studies[38, 47-52] gave 8 separate data reporting all-cause mortality from 30 days to 12 months of follow up. However, mortality data from Bolas et al[51] and Farris et al[38] is not their outcome of interest and extracted from the reasons for exclusion of patients for their analysis. But, we included in our meta-analysis. Overall, there was no significance difference between the two groups in terms of all-cause mortality (RR 1.05; 95%CI: 0.95-1.16) (Figure 2E).

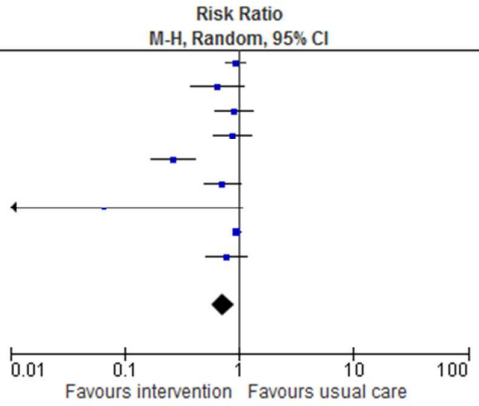
A



B

Study or Subgroup	Intervention Events	Intervention Total	Usual care Events	Usual care Total	Weight	Risk Ratio M-H, Random, 95% CI
Anderegg 2014 [Overall]	155	1652	168	1664	15.2%	0.93 [0.76, 1.14]
Anderegg 2014 [High-risk]	22	358	31	325	9.4%	0.64 [0.38, 1.09]
Farris 2014 [Enhanced]	41	311	46	313	11.8%	0.90 [0.61, 1.33]
Farris 2014 [Minimal]	40	312	46	313	11.8%	0.87 [0.59, 1.29]
Gardella 2012	20	1424	381	7199	10.8%	0.27 [0.17, 0.41]
Gillespie 2009	36	182	52	186	12.2%	0.71 [0.49, 1.03]
Hawes 2014	0	24	11	37	0.7%	0.07 [0.00, 1.07]
Hellstrom 2012	594	1216	1416	2758	16.9%	0.95 [0.89, 1.02]
Walker 2009	34	358	45	366	11.3%	0.77 [0.51, 1.18]
Total (95% CI)		**5837**		**13161**	**100.0%**	**0.72 [0.57, 0.92]**
Total events	942		2196			

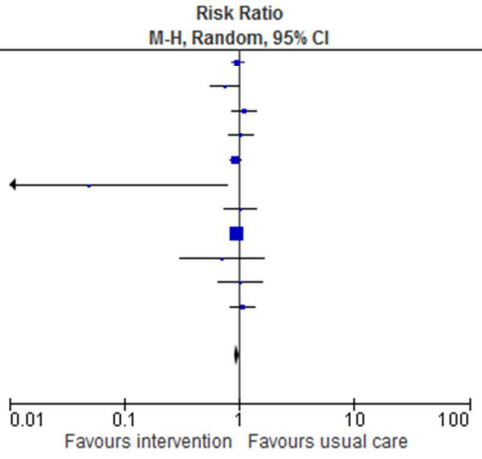
Heterogeneity: Tau² = 0.09; Chi² = 42.26, df = 8 (P < 0.00001); I² = 81%
Test for overall effect: Z = 2.63 (P = 0.009)



C

Study or Subgroup	Intervention Events	Intervention Total	Usual care Events	Usual care Total	Weight	Risk Ratio M-H, Random, 95% CI
Anderegg 2014 [Overall]	373	1652	389	1664	15.4%	0.97 [0.85, 1.09]
Anderegg 2014 [High-risk]	62	358	75	325	2.9%	0.75 [0.56, 1.01]
Farris 2014 [Enhanced]	97	311	88	313	4.5%	1.11 [0.87, 1.41]
Farris 2014 [Minimal]	90	312	88	313	4.2%	1.03 [0.80, 1.32]
Gillespie 2009	134	182	147	186	18.0%	0.93 [0.83, 1.04]
Hawes 2014	0	24	15	37	0.0%	0.05 [0.00, 0.78]
Hellstrom 2011	45	109	41	101	2.5%	1.02 [0.73, 1.41]
Hellstrom 2012	645	1216	1555	2758	46.2%	0.94 [0.88, 1.00]
Koehler 2009	6	20	9	21	0.4%	0.70 [0.30, 1.61]
Schnipper 2006	28	92	25	84	1.3%	1.02 [0.65, 1.61]
Walker 2009	98	358	94	366	4.5%	1.07 [0.84, 1.36]
Total (95% CI)		**4634**		**6168**	**100.0%**	**0.95 [0.90, 1.00]**
Total events	1578		2526			

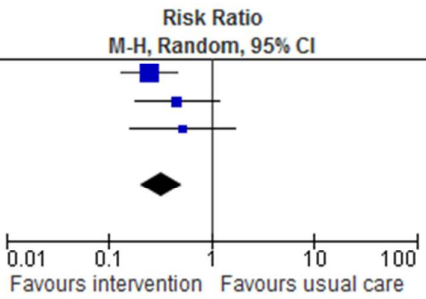
Heterogeneity: Tau² = 0.00; Chi² = 10.62, df = 10 (P = 0.39); I² = 6%
Test for overall effect: Z = 1.80 (P = 0.07)



D

Study or Subgroup	Intervention Events	Intervention Total	Usual care Events	Usual care Total	Weight	Risk Ratio M-H, Random, 95% CI
Gardella 2012	10	1624	183	7335	57.6%	0.25 [0.13, 0.47]
Hellstrom 2011	6	108	12	100	26.1%	0.46 [0.18, 1.19]
Schnipper 2006	4	92	7	84	16.3%	0.52 [0.16, 1.72]
Total (95% CI)		**1824**		**7519**	**100.0%**	**0.33 [0.20, 0.53]**
Total events	20		202			

Heterogeneity: Tau² = 0.00; Chi² = 1.99, df = 2 (P = 0.37); I² = 0%
Test for overall effect: Z = 4.53 (P < 0.00001)



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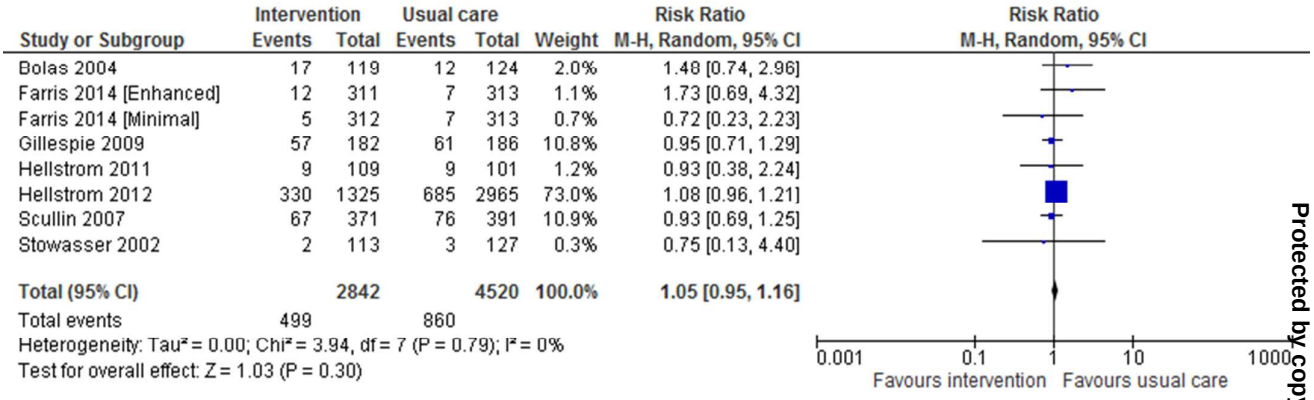


Figure 2 Forest plots of intervention effects on the proprortion of patients with all-cause readmission (A), emergency department visits (B), composite rate of readmissions and/or ED visits (C), ADE-related hospital revisits (D) and mortality (E). Pooled estimates (diamond) calculated by the Mantel-Haenszel random effects model. Horizontal bars and diamond widths represent 95% CIs. Anderegg et al[36] stratified patients in two groups: general population and high-risk patient groups. Farris et al[38] randomized the population into different levels of intervention (minimal and enhanced).

Other outcomes

Studies reporting other clinically important outcomes are summarized in table 2. Some studies[47-50] furnished information on the proportion of patients who didn't revisit the hospital. The intervention group in the 3 studies [47, 49, 50] showed a trend towards an increase in the number of patients who didn't revisit hospital for any causes, and the overall pooled analysis was statistically significant (RR 1.10; 95% CI: 1.03-1.17). There were no any 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.

Table 2 Other clinically relevant outcomes

Outcome	No of studies	No. of patients	RR	CI	WMD	CI
Patients who didn't revisit hospital	4	5314	1.10*	(1.03, 1.17)†		
Hospital stay (after readmission)	2	803			-0.57	(-5.32, 4.17)‡
Readmission per patient	3	1370			-0.12	(-0.24, 0.01)‡
ED visit per patient	2	4342			-0.15	(-0.53, 0.23)‡
Patients with ADE	3	1401	0.94	(0.75, 1.20)		

RR: risk ratio; CI: confidence interval; WMD: weighted mean difference

†p<0.01

‡p>0.05

*RR is > 1 when intervention increased the number of patients didn't revisit hospital (i.e. it showed success)

Sensitivity analysis

A one-on-one removal of studies in the meta-analysis didn't affect findings in all outcomes except for composite readmission/ED visit. A meta-analysis for composite readmission/ED visit showed that, when Faris et al [enhanced] [38] or Hawes et al[40] were removed, the result had a significant pooled summary estimate with similar risk ratio (RR 0.95; p=0.02 and 0.03 respectively).

Subgroup analysis

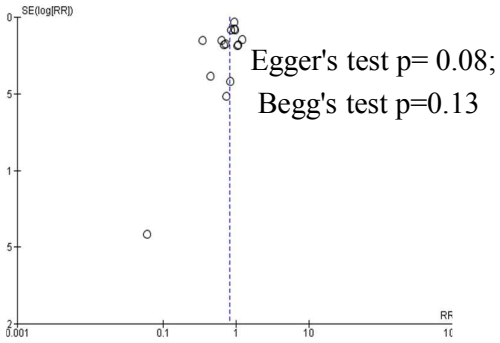
Subgroup analysis which compared studies that reported all-cause readmissions at earlier follow up period vs longer showed different patterns of effect: the effect of intervention was not statistically significant for longer follow up subgroups (RR 0.83, 95% CI 0.68, 1.06, p=0.14), whereas in earlier follow up subgroups, the effect was significant (RR 0.77, 95% CI

0.60, 0.98, p=0.03). However, there was no significance difference between these two subgroups. In addition, non-randomized studies showed a significant reduction in all-cause readmission (RR 0.74, 95%CI 0.58, 0.94, p=0.01) and all-cause ED visit (RR 0.68, 95%CI 0.48, 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-randomized studies (RR 0.95, 95% CI 0.90, 1.00, p=0.04); though there was no difference between the subgroups (Appendix D).

Publication bias

We examined the potential for publication bias by constructing the funnel plot and through statistical tests. There was some indication of asymmetry, particularly for all-cause ED visits in the funnel plots and therefore, there was some publication bias as evidenced by the Egger's (p=0.04) and Begg's test (p=0.01) in this outcome. Otherwise, we found no significant evidence of bias in the three outcomes reported 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 (Figure 3).

A



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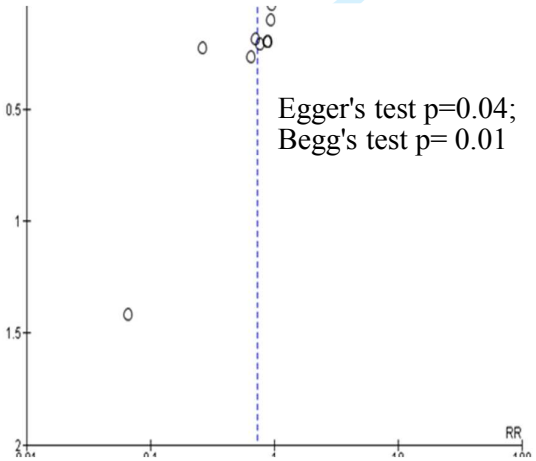

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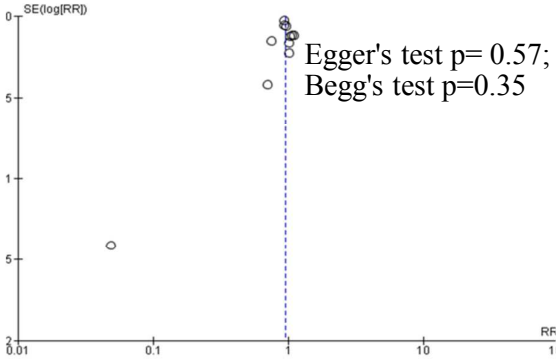

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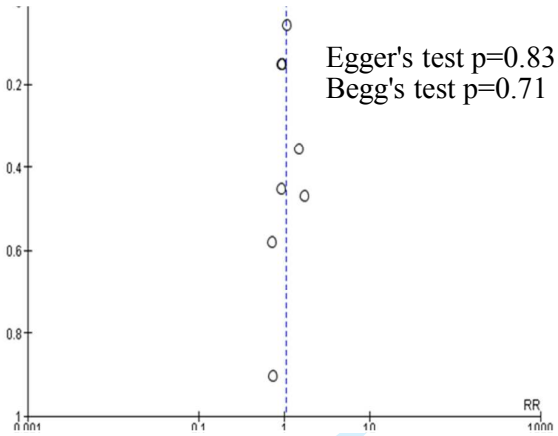

Figure 3 Funnel plots for the four outcomes for patients at hospital transitions. A) all-cause readmission B) all-cause ED visit C) composite readmission and/or ED visit D) all-cause mortality. The vertical line in the graphs corresponds to the pooled relative risk across studies.

Discussion

To our knowledge, this is the first meta-analysis that has investigated the effectiveness of pharmacy-led medication reconciliation programmes on clinical outcomes at hospital transitions. This review has shown better outcomes in favour of pharmacy-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*%).* But, pooled data on mortality and composite readmission/ED visit favoured neither the intervention nor the control. Patients allocated in the intervention group were not only readmitted or revisited hospital less frequently but also increased patients free of any events after hospital discharge (RR 1.10; 95% CI: 1.03-1.17).

No previous reviews have been conclusively and consistently shown effectiveness of medication reconciliation interventions; be it in the primary care,[53] long-term settings[54] or

hospital transitions.[32,33] Particularly, reviews from hospital-initiated medication reconciliation interventions searched the available literature on medication reconciliation strategies and impact on patient safety, and summarized the evidence that medication reconciliation alone was not strong enough to reduce post-discharge hospital utilization. [32, 33] It was thus, not clear to support the effectiveness of such interventions in the hospital environment. But, we believed that the influence of pharmacist's in healthcare utilization was diluted amongst those various medication reconciliation strategies, and thus, specifically assessing the effect of pharmacist in medication reconciliation is an important consideration.

Although Thomas et al [55] did not find a significant effect in reduction of readmissions due to medication-related problems; our review showed that pharmacist's influence in preventing ADE-related hospital revisits was more pronounced 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 that reported this outcome.[43, 48] Other studies also showed that medication discontinuity is the most common reason for discrepancy related ADE.[56, 57] Although Gillespie et al [47] wasn't 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 the control. Readmissions were frequent in earlier follow up periods. This is as opposed to a review by Kewan et al; [33] 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 for a relatively longer than 30 days. Therefore, it might be difficult to conclude as there wasn't a sustained benefit of the intervention; and this was supported by non-significance differences between the subgroups. Moreover, non-randomized 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. Nonetheless, it isn't surprising to observe such effects in quality improvement studies.

Some of the studies as part of their intervention consisted of intermingle components and difficult to ascertain the success to pharmacy-led intervention is due only because of 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 [58, 59] raised a debate as to the impact of medication reviews in general and pharmacy-led medication reviews in particular. In a review by Holland et al[58] where only 8 of the 32 included studies were of hospital-based and only 2 of these have extensive medical team involvement at hospital transitions, didn't support the evidence for pharmacy-led medication review. On the other hand, one of the issues rose in a Cochrane review [59] was that medication review has varied and wider meaning and didn't stand alone. Prior to medication review, it is medication reconciliation which practiced routinely at hospital transitions and thus, thinking of 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 equal effective as those with mixed interventions.

A number of recent studies have investigated medication reconciliation interventions at the level of real practice models or as in integrated management of medicines.[48-50] Medication reconciliation interventions are complex interventions targeting fragments of services across the entire care transitions. Medication reconciliation is thus, takes time and effort, but the outcome of safe patient transition is well worth it. This review further consolidates pharmacy-

led medication reconciliation programmes could contribute for quality transitions in combinations of those intervention components.

Limitation of the study

There are a number of limitations to this study. Firstly, most studies included high risk patients and, we did not confirm which patients were 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 hospitalization. Secondly, 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[60-63] to 35-71% during discharge.[5, 64, 65] Coleman et al [66] showed that patients with medication discrepancies have significantly high rate of readmission. Thus, if this value is extrapolated to clinical outcomes, there might have some variation among studies with respect to these outcomes at the different care transitions. Besides, few studies were carried out in hospitals where medication reconciliation has already been implemented in some defined areas. Therefore, future studies should evaluate specific areas suited to pharmacist services that would benefit the most. Thirdly, most of the studies were single centre evaluations. Considering success 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. Fourthly, 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 we 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 element of medication reconciliation can improve outcomes at hospital transitions.

We also noted in our work that only published studies were included. However, funnel plot asymmetry and statistical tests suggested 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 like Ulayar et al[67] published in non-English journals involving interventions for improving care transitions. In addition, research disseminated through grey literature, such as conference papers and unpublished reports, was not considered.

Conclusion

The results of this meta-analysis indicate that a pharmacy-led medication reconciliation programme at hospital transitions decreases ADE related hospital revisits, all-cause readmissions and ED visits. But, the effect on mortality and composite all-cause readmission/ED visit is inconclusive based on the current body of evidence, though improvements in 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 pharmacy-led medication reconciliation was beneficial at care transitions, we still need further research with robust, large randomized control trials of excellent quality to conform our conclusion. Overall, our findings support the implementation of pharmacy-led medication reconciliation programme that includes some components aimed at improving medication safety.

Acknowledgements

We would like to acknowledge Asres Berhan for his comments on the data analysis and interpretation, and statistical advice in using the meta-analysis software. We would also like to acknowledge Lorraine Evison for her invaluable contributions in the electronic database searching and abstract screening.

Contributors

ABM was responsible for the study conception and design under the supervision of JB. All literature searching, abstract screening, study and data extraction was undertaken by ABM with further confirmation from JB. ABM carried out the initial analysis, and drafted the first manuscript. JB and AM critically reviewed and revised the manuscript. All the authors have read and approved the final manuscript as submitted.

Funding

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests

None declared.

Data sharing statement

No additional data are available.

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66. Coleman EA, Smith JD, Raha D, et al. Posthospital medication discrepancies: prevalence and contributing factors. *Arch Intern Med* 2005;**165**:1842-7.

67. Sanchez Ulayar A, Gallardo Lopez S, Pons Llobet N, *et al*. Pharmaceutical intervention upon hospital discharge to strengthen understanding and adherence to pharmacological treatment. *Farm Hosp* 2012;**36**:118-23.

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	5
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	NA
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	5 and 6
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	5
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Appendix A
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	5 and 6
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	6
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	6
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	8
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	7
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2 for each meta-analysis.	7 and 8

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	8
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	7 and 8
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	8
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	10-19
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	20
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	20 and 21
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	21-24
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	25-27
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	24 and 25
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	27-29
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	30-31
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	31
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	32

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit: www.prisma-statement.org.

Appendix A

Electronic database Searches

Medline, IPA and PsychINFO

#	Searches	Results
1	((medic$ or drug$) adj2 discrepanc$).mp.	524
2	((medic$ or drug$) adj2 reconciliation$).mp.	1,193
3	((medic$ or drug$) adj2 histor$).mp.	75,175
4	((medic$ or drug$) adj2 list$).mp.	5, 023
5	(((medic$ adj2 chart$) or (medic$ adj2 record$)) adj2 assessment).mp.	125
6	((medic$ or drug$ or prescription$ or (medic$ adj2 chart$) or (medic$ adj2 record$)) adj2 review$).mp.	35,859
7	((medic$ or drug$) adj2 congruence$).mp.	20
8	((medic$ or drug$) adj2 management).mp.	37,424
9	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8	151,309
10	patient admission.mp. or Patient Admission/	20,054
11	patient discharge.mp. or Patient Discharge/	21,100
12	patient transfer.mp. or Patient Transfer/	6,658
13	Hospitalization/ or hospital transfer.mp.	81,536
14	"Continuity of Patient Care"/ or care transition.mp.	15,531
15	inpatients.mp. or Inpatients/	58,575
16	seamless care.mp.	154
17	continuum of care.mp.	3,103
18	"Delivery of Health Care, Integrated"/ or integrated health care.mp.	10,066
19	10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18	199,032
20	pharmac*.mp.	905,186
21	9 and 19 and 20	1,144
22	limit 21 to (abstracts and english language and humans)	1009

CINHAL

#	Searches	Results
S18	S14 AND S15 AND S16 Limiters-Peer Reviewed; English Language; Abstract Available	267
S17	S14 AND S15 AND S16	396
S16	S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13	306,305
S15	S1 OR S2 OR S3 OR S4 OR S5 OR S6	9,033
S14	"Pharmac*"	101,387
S13	(MH "Continuity of Patient Care+") OR "continu*"	187,044
S12	"seamless care"	104
S11	(MH "Inpatients")	55,914
S10	"emergency medic*"	29,880
S9	"transition of care"	143
S8	(MH "Transfer, Discharge")	3058
S7	(MH "Patient Admission") OR (MH "Hospitalization+") OR (MH "Patient Discharge+")	56,917
S6	"medication discrepancies"	45
S5	"medication discrepancy"	10
S4	"drug history"	122
S3	(MH "Medication Errors+")	8,626
S2	(MH "Medication History")	60
S1	(MH "Medication Reconciliation")	472

Embase

#	Searches	Results
24	#1.20 AND #1.21 AND #1.22 AND #1.23 [english]/lim AND [humans]/lim AND [abstracts]/lim	335
23	#1.15 OR #1.16 OR #1.17 OR #1.18 OR #1.19	375,805
22	#1.5 OR #1.6 OR #1.7 OR #1.8 OR #1.9 OR #1.10 OR #1.11 OR #1.12 OR #1.13 OR #1.14	454,467
21	#1.1 OR #1.2 OR #1.3 OR #1.4	4,019
20	pharmac*	3,875,936
19	'hospitalized patients'/exp OR 'hospitalized patients'	74,696
18	'inpatients'/exp OR 'inpatients'	108,750
17	'patient transfer'/exp OR 'patient transfer'	40,927
16	'patient discharge'/exp OR 'patient discharge'	96,003
15	'patient admission'/exp OR 'patient admission'	137,129
14	'medication'/exp OR medication AND record	179,120
13	'medication'/exp OR medication AND record AND systems	4,687

12	'medication'/exp OR medication AND record AND assessment	14,853
11	'medication'/exp OR medication AND record AND ('review'/exp OR review)	44,320
10	'medication'/exp OR medication AND chart AND ('review'/exp OR review)	9,372
9	medic* OR drug* AND list*	52,323
8	'medication'/exp OR medication AND ('history'/exp OR history)	91,985
7	'drug'/exp OR drug AND ('history'/exp OR history)	213,214
6	'drug'/exp OR drug AND ('history'/exp OR history) AND taking	9,182
5	'medication'/exp OR medication AND ('history'/exp OR history) AND taking	5389
4	'medication'/exp OR medication AND reconciliation AND errors	443
3	'medication'/exp OR medication AND ('history'/exp OR history) AND errors	570
2	'medication'/exp OR medication AND discrepancies	2464
1	'medication'/exp OR medication AND reconciliation	1453

PubMed

((((((medication reconciliation) OR medication discrepancies) OR medication history) OR ((medication AND (chart OR record) AND assessment)))) AND (((continuity of care) OR seamless care) OR ((hospital* OR inpatient* OR interface* OR discharge* OR admission*)))) AND pharmac* [640]

Appendix B

List of excluded full text papers and of the reasons for their exclusion

No control group/ ineligible comparator

Boso ribelles et al (2011). "Evaluation of a plan for cardiology medication reconciliation on admission, and patient information at discharge, in a teaching hospital." EJHP Practice 17(1)

Anderegg, S. V., et al. (2013). "Acceptance of recommendations by inpatient pharmacy case managers: unintended consequences of hospitalist and specialist care." Pharmacotherapy:The Journal of Human Pharmacology & Drug Therapy **33**(1): 11-21.

Cornu, P., et al. (2012). "Effect of medication reconciliation at hospital admission on medication discrepancies during hospitalization and at discharge for geriatric patients." Annals of Pharmacotherapy **46**(4): 484-494.

Hellstrom, L. M., et al. (2012). "Errors in medication history at hospital admission: prevalence and predicting factors." BMC Clin Pharmacol **12**: 9.

Lessard, S., et al. (2006). "Medication discrepancies affecting senior patients at hospital admission." Am J Health Syst Pharm **63**(8): 740-743.

Mergenhagen, K. A., et al. (2012). "Pharmacist- versus physician-initiated admission medication reconciliation: impact on adverse drug events." American Journal of Geriatric Pharmacotherapy **10**(4): 242-250.

Midlov, P., et al. (2012). "The effect of medication reconciliation in elderly patients at hospital discharge." International Journal of Clinical Pharmacy **34**(1): 113-119.

Quennery, S., et al. (2011). "Added value of pharmacist-acquired drug histories in an orthopaedic ward." Acta Clinica Belgica **66**(3): 196-199.

Reeder, T. A. and A. Mutnick (2008). "Pharmacist- versus physician-obtained medication histories." American Journal of Health-System Pharmacy **65**(9): 857-860.

Not Pharmacy-led medication reconciliation

Lalonde, L., et al. (2008). "Effectiveness of a medication discharge plan for transitions of care from hospital to outpatient settings." American Journal of Health-System Pharmacy **65**(15): 1451-1457.

Midlov, P., et al. (2008). "Medication report reduces number of medication errors when elderly patients are discharged from hospital." Pharmacy World & Science **30**(1): 92-98.

Schnipper, J. L., et al. (2009). "Effect of an electronic Medication reconciliation application and process redesign on potential adverse drug events a cluster-randomized trial." Archives of Internal Medicine **169**(8): 771-780.

Showalter, J. W., et al. (2011). "Effect of standardized electronic discharge instructions on post-discharge hospital utilization." J Gen Intern Med **26**(7): 718-723.

Zoni, A. C., et al. (2012). "The impact of medication reconciliation program at admission in an internal medicine department." European Journal of Internal Medicine **23**(8): 696-700.

Study Protocol

Salanitro, A. H., et al. (2013). "Rationale and design of the Multicenter Medication Reconciliation Quality Improvement Study (MARQUIS)." BMC Health Serv Res **13**: 230.

Not English

Sanchez Ulayar, A., et al. (2012). "Pharmaceutical intervention upon hospital discharge to strengthen understanding and adherence to pharmacological treatment." Farm Hosp **36**(3): 118-123.

Medication reconciliation is not the primary intervention

Nester TM et al (2002).” Effectiveness of a pharmacist acquired medication history in promoting patient safety”. Am J Health-Syst Pharm 59:2221-25.

Lisby M et al (2010). “The effect of systematic medication review in elderly patients admitted to an acute ward of Internal Medicine”. Basic & Clinical Pharmacology & Toxicology 106: 422–427.

Edwards, S. J., et al. (2014). "Outcomes assessment of a pharmacist-directed seamless care program in an ambulatory oncology clinic." Journal of Pharmacy Practice **27**(1): 46-52.

Fera T, Anderson C, Kanel KT, Ramusivich DL. Role of a care transition pharmacist in a primary care resource center. Am J Health Syst Pharm. 2014;71(18):1585-90.

Hutchison LJ, Mayzell GG, Bailey SC, Broyles JE. Impact of a discharge medication therapy management program in an extended care hospital. Consult Pharm 2014;29(1):33-8.

Marotti, S. B., et al. (2011). "A randomised controlled trial of pharmacist medication histories and supplementary prescribing on medication errors in postoperative medications." Anaesthesia and Intensive Care **39**(6): 1064-1070.

Nazareth, I., et al. (2001). "A pharmacy discharge plan for hospitalized elderly patients--a randomized controlled trial." Age & Ageing **30**(1): 33-40.

Sarangarm, P., et al. (2013). "Impact of pharmacist discharge medication therapy counselling and disease state education: Pharmacist Assisting at Routine Medical Discharge (project PhARMD)." American Journal of Medical Quality **28**(4): 292-300.

Spinewine, A., et al. (2007). "Effect of a collaborative approach on the quality of prescribing for geriatric inpatients: a randomized, controlled trial." J Am Geriatr Soc **55**(5): 658-665.

Szkiladz, A., et al. (2013). "Impact of pharmacy student and resident-led discharge counselling on heart failure patients." Journal of Pharmacy Practice **26**(6): 574-579.

Taber, D. J., et al. (2013). "Improved patient safety and outcomes with a comprehensive interdisciplinary improvement initiative in kidney transplant recipients." Am J Med Qual **28**(2): 103-112.

Not hospital based

Stewart S et al (1998). "Effects of a home-based intervention among patients with congestive heart failure discharged from acute hospital care". Arch Intern Med 158:1067-1072.

Boockvar, K. S., et al. (2006). "Medication reconciliation for reducing drug-discrepancy adverse events." American Journal of Geriatric Pharmacotherapy **4**(3): 236-243.

Kilcup, M., et al. (2013). "Postdischarge pharmacist medication reconciliation: impact on readmission rates and financial savings." J Am Pharm Assoc (2003) **53**(1): 78-84.

Stewart, A. L. and K. J. Lynch (2014). "Medication discrepancies despite pharmacist led medication reconciliation: the challenges of maintaining an accurate medication list in primary care." Pharm Pract (Granada) **12**(1): 360.

Ineligible study design/procedure

Carter, M. K., et al. (2006). "Pharmacist-acquired medication histories in a university hospital emergency department." American Journal of Health-System Pharmacy **63**(24): 2500-2503.

Karapinar-Carkit, F., et al. (2009). "Effect of medication reconciliation with and without patient counselling on the number of pharmaceutical interventions among patients discharged from the hospital." Annals of Pharmacotherapy **43**(6): 1001-1010.

Musgrave, C. R., et al. (2013). "Improving transplant patient safety through pharmacist discharge medication reconciliation." American Journal of Transplantation **13**(3): 796-801.

Mudge AM, Shakhovskoy R, Karrasch A. Quality of transitions in older medical patients with frequent readmissions: opportunities for improvement. Eur J Intern Med. 2013;24(8):779-83.

Sen S, Siemianowski L, Murphy M, McAllister SC. Implementation of a pharmacy technician-centered medication reconciliation program at an urban teaching medical center. Am J Health Syst Pharm. 2014;71(1):51-6.

Stitt, D. M., et al. (2011). "Medication discrepancies identified at time of hospital discharge in a geriatric population." American Journal of Geriatric Pharmacotherapy **9**(4): 234-240.

Unroe, K. T., et al. (2010). "Inpatient medication reconciliation at admission and discharge: A retrospective cohort study of age and other risk factors for medication discrepancies." American Journal of Geriatric Pharmacotherapy **8**(2): 115-126.

Not medication reconciliation intervention

Eijsbroek, H., et al. (2013). "Medication issues experienced by patients and carers after discharge from the intensive care unit." J Crit Care **28**(1): 46-50.

Hohmann, C., et al. (2013). "Adherence to hospital discharge medication in patients with ischemic stroke: a prospective, interventional 2-phase study." Stroke **44**(2): 522-524.

Hohmann, C., et al. (2014). "Providing systematic detailed information on medication upon hospital discharge as an important step towards improved transitional care." Journal of Clinical Pharmacy & Therapeutics **39**(3): 286-291.

Romero, C. M., et al. (2013). "Effects of the implementation of a preventive interventions program on the reduction of medication errors in critically ill adult patients." Journal of Critical Care **28**(4): 451-460.

Not relevant clinical outcome

Smith L et al (1997). "An investigation of hospital generated pharmaceutical care when patients are discharged home from hospital". Br J Clin Pharmacol 1997; 44: 163–165.

Michels R et al (2003). "Programme using pharmacy technicians to obtain medication histories." American Journal of Health-System Pharmacy 60: 1982-86.

Alassaad, A., et al. (2013). "Prescription and transcription errors in multidose-dispensed medications on discharge from hospital: an observational and interventional study." J Eval Clin Pract **19**(1): 185-191.

Basey AJ, Krska J, Kennedy TD, Mackridge AJ. Prescribing errors on admission to hospital and their potential impact: A mixed-methods study. BMJ Quality and Safety. 2014;23(1):17-25.

Becerra-Camargo, J., et al. (2013). "A multicentre, double-blind, randomised, controlled, parallel-group study of the effectiveness of a pharmacist-acquired medication history in an emergency department." BMC Health Services Research 13: 337.

Beckett, R. D., et al. (2012). "Effectiveness and feasibility of pharmacist-led admission medication reconciliation for geriatric patients." Journal of Pharmacy Practice 25(2): 136-141.

Benson, J. M. and G. Snow (2012). "Impact of medication reconciliation on medication error rates in community hospital cardiac care units." Hospital Pharmacy **47**(12): 927-932.

Bergkvist, A., et al. (2009). "Improved quality in the hospital discharge summary reduces medication errors--LIMM: Landskrona Integrated Medicines Management." European Journal of Clinical Pharmacology **65**(10): 1037-1046.

Brownlie K, Schneider C, Culliford R, Fox C, Boukouvalas A, Willan C, Maidment ID. Medication reconciliation by a pharmacy technician in a mental health assessment unit. Int J Clin Pharm 2014;36(2):303-9.

Buckley MS, Harinstein LM, Clark KB, Smithburger PL, Eckhardt DJ, Alexander E, et al. Impact of a clinical pharmacy admission medication reconciliation program on medication errors in "high-risk" patients. The Annals of pharmacotherapy. 2013;47(12):1599-610.

Chan, E. W., et al. (2010). "An intervention to encourage ambulance paramedics to bring patients' own medications to the ED: impact on medications brought in and prescribing errors." Emerg Med Australas **22**(2): 151-158.

Conklin, J. R., et al. (2014). "Care Transitions Service: A pharmacy-driven program for medication reconciliation through the continuum of care." American Journal of Health-System Pharmacy: 802-810.

Eggink, R. N., et al. (2010). "The effect of a clinical pharmacist discharge service on medication discrepancies in patients with heart failure." Pharmacy World & Science 32(6): 759-766.

Farley, T. M., et al. (2014). "Effect of clinical pharmacist intervention on medication discrepancies following hospital discharge." International Journal of Clinical Pharmacy 36(2): 430-437.

Fertleman, M., et al. (2005). "Improving medication management for patients: The effect of a pharmacist on post-admission ward rounds." Quality and Safety in Health Care 14(3): 207-211.

Grant, R. W., et al. (2003). "Improving Adherence and Reducing Medication Discrepancies in Patients with Diabetes." Ann Pharmacother **37**(7): 962-969.

Grimes, T. C., et al. (2014). "Collaborative pharmaceutical care in an Irish hospital: Uncontrolled before-after study." BMJ Quality and Safety 23(7): 574-583.

Hale, A. R., et al. (2013). "Perioperative medication management: expanding the role of the preadmission clinic pharmacist in a single centre, randomised controlled trial of collaborative prescribing." BMJ Open **3**(7).

Hayes, B. D., et al. (2007). "Pharmacist-conducted medication reconciliation in an emergency department." American Journal of Health-System Pharmacy **64**(16): 1720-1723.

Hick, H. L., et al. (2001). "The impact of the pharmacist on an elective general surgery pre-admission clinic." Pharmacy World & Science **23**(2): 65-69.

Ho, P. M., et al. (2014). "Multifaceted intervention to improve medication adherence and secondary prevention measures after acute coronary syndrome hospital discharge: a randomized clinical trial." JAMA Intern Med **174**(2): 186-193.

Kripalani, S., et al. (2012). "Effect of a pharmacist intervention on clinically important medication errors after hospital discharge: a randomized trial." Annals of Internal Medicine 157(1): 1-10.

Kwan, Y., et al. (2007). "Pharmacist medication assessments in a surgical preadmission clinic." Archives of Internal Medicine 167(10): 1034-1040.

Nickerson, A., et al. (2005). "Drug-therapy problems, inconsistencies and omissions identified during a medication reconciliation and seamless care service." Healthcare Quarterly 8 Spec No: 65-72.

Nielsen TR, Andersen SE, Rasmussen M, Honore PH. Clinical pharmacist service in the acute ward. Int J Clin Pharm. 2013;35(6):1137-51.

Magalhães GF, Santos GB, Rosa MB, Noblat Ld A. Medication Reconciliation in Patients Hospitalized in a Cardiology Unit. PLoS ONE 2014; 9(12): e115491. doi: 10.1371/journal.pone.0115491.

Mortimer, C., et al. (2011). "The impact of an aged care pharmacist in a department of emergency medicine." J Eval Clin Pract **17**(3): 478-485.

Peyton, L., et al. (2010). "Evaluation of medication reconciliation in an ambulatory setting before and after pharmacist intervention." J Am Pharm Assoc (2003) **50**(4): 490-495.

Rahman, M. H., et al. (2005). "An evaluation of pharmacist-written hospital discharge prescriptions on general surgical wards." International Journal of Pharmacy Practice **13**(3): 179-185.

Tompson, A. J., et al. (2012). "Utilizing community pharmacy dispensing records to disclose errors in hospital admission drug charts." International Journal of Clinical Pharmacology & Therapeutics **50**(9): 639-646.

Van den Bemt, P. M., et al. (2009). "Medication reconciliation performed by pharmacy technicians at the time of preoperative screening." Ann Pharmacother 43(5): 868-874.

Van den Bemt, P. M., et al. (2013). "Effect of medication reconciliation on unintentional medication discrepancies in acute hospital admissions of elderly adults: a multicenter study." J Am Geriatr Soc 61(8): 1262-1268.

Vasileff, H. M., et al. (2009). "The effect on medication errors of pharmacists charting medication in an emergency department." Pharmacy World & Science 31(3): 373-379.

Leguelinel-Blache G, Arnaud F, Bouvet S, Dubois F, Castelli C,Roux-Marson C, Ray V, Sottoe A, Kinowski J. Impact of admission medication reconciliation performed by clinical pharmacists on medication safety. Eur J Intern Med 2014; 25(9):808-14.

Pharmacy is not the sole provider

Poole DL et al (2006). "Medication reconciliation: a necessity in promoting a safe hospital discharge." Journal for Healthcare Quality **28**(3):12-19.

Coffey M et al (2009). "Implementation of admission medication reconciliation at two academic Health Sciences Centres: challenges and success factors." Healthcare Quarterly 12 Special Issue 2009

Dedhia, P., et al. (2009). "A quality improvement intervention to facilitate the transition of older adults from three hospitals back to their homes." Journal of the American Geriatrics Society **57**(9): 1540-1546.

Duggan, C., et al. (1998). "Reducing adverse prescribing discrepancies following hospital discharge." International Journal of Pharmacy Practice **6**(Jun): 77-82.

Henneman, E. A., et al. (2014). "An evaluation of a collaborative, safety focused, nurse-pharmacist intervention for improving the accuracy of the medication history." J Patient Saf **10**(2): 88-94.

Jack, B. W., et al. (2009). "A reengineered hospital discharge program to decrease rehospitalisation: a randomized trial." Annals of Internal Medicine **150**(3): 178-187.

Nassaralla, C. L., et al. (2007). "Implementation of a medication reconciliation process in an ambulatory internal medicine clinic." Qual Saf Health Care **16**(2): 90-94.

Setter, S. M., et al. (2009). "Effectiveness of a pharmacist-nurse intervention on resolving medication discrepancies for patients transitioning from hospital to home health care." American Journal of Health-System Pharmacy **66**(22): 2027-2031.

Appendix C

Summary of risk of bias assessment*

Study reference	Randomization	Allocation concealment	Similarity of baseline characteristics	Similarity of baseline outcomes	Incomplete outcome data	Assessors blind to outcome	Absence of contamination	Selective outcome reporting	Free of other biases	Total
Anderegg 2014	-	+	+	?	?	+	-	-	+	4
Bolas 2004	+	+	+	?	-	-	?	-	+	4
Eisenhower 2014	-	-	?	?	-	+	+	-	-	2
Farris 2014	+	+	+	?	+	+	-	+	+	7
Gardella 2012	-	-	?	?	?	+	+	+	-	3
Gillespie 2009	+	+	?	?	?	+	+	+	+	6
Hawes 2014	+	+	?	?	?	+	+	+	+	6
Hellstrom 2011	-	-	+	?	+	+	-	+	-	4
Hellstrom 2012	-	-	+	?	+	+	+	+	-	5
Koehler 2009	+	+	+	?	?	+	+	+	-	6
Pal 2013	-	-	+	?	+	+	-	+	-	4
Schnipper 2006	+	+	+	?	?	+	+	+	+	7
Scullin 2007	+	+	+	?	?	+	?	+	+	6
Stowasser 2002	+	?	+	+	+	+	+	-	+	8
Walker 2009	-	-	+	?	-	?	+	+	+	4
Warden 2014	-	-	+	?	?	+	+	+	+	5
Wilkinson 2011	-	-	?	?	?	-	?	+	-	1

Key: +: clear; -: unclear; ?: not done

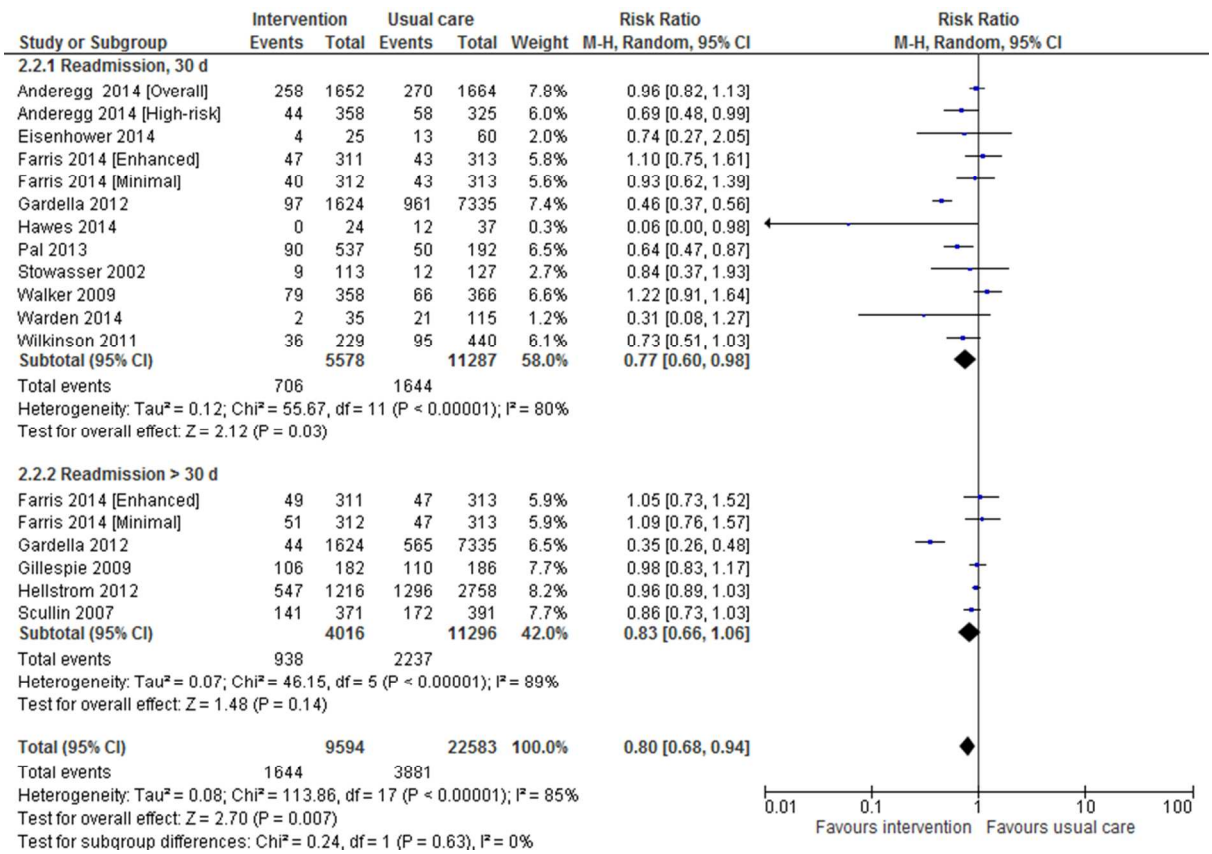
*EPOC risk of bias assessment; modified for non- controlled studies

Appendix D

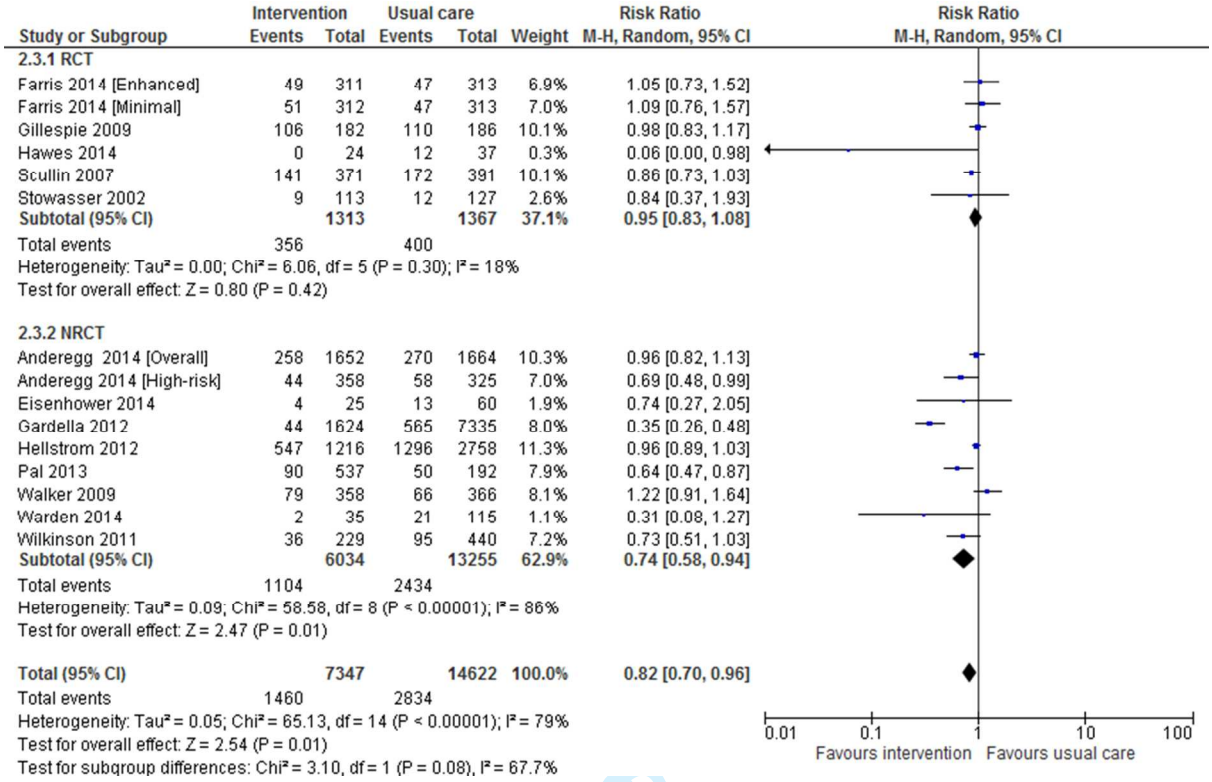
Subgroup analysis

4.1 All-cause Readmission

4.1.1 Subgroup analysis based on outcome timing

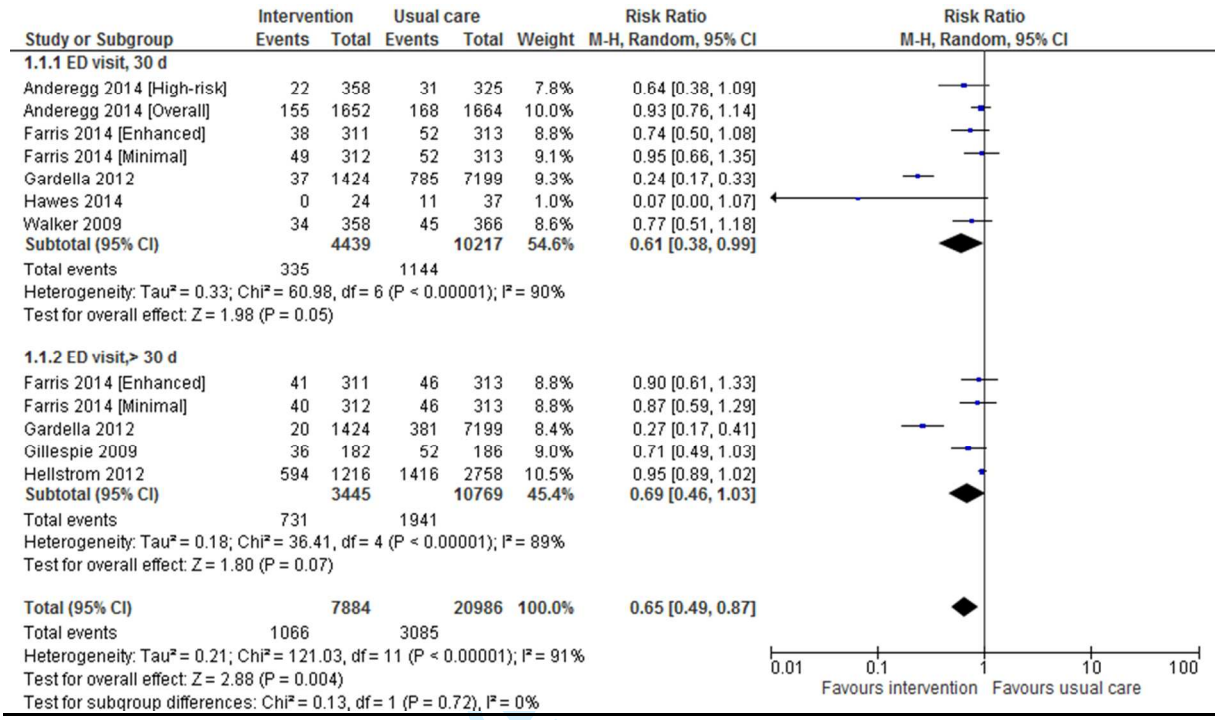


4.1.2 Subgroup analysis based on study design

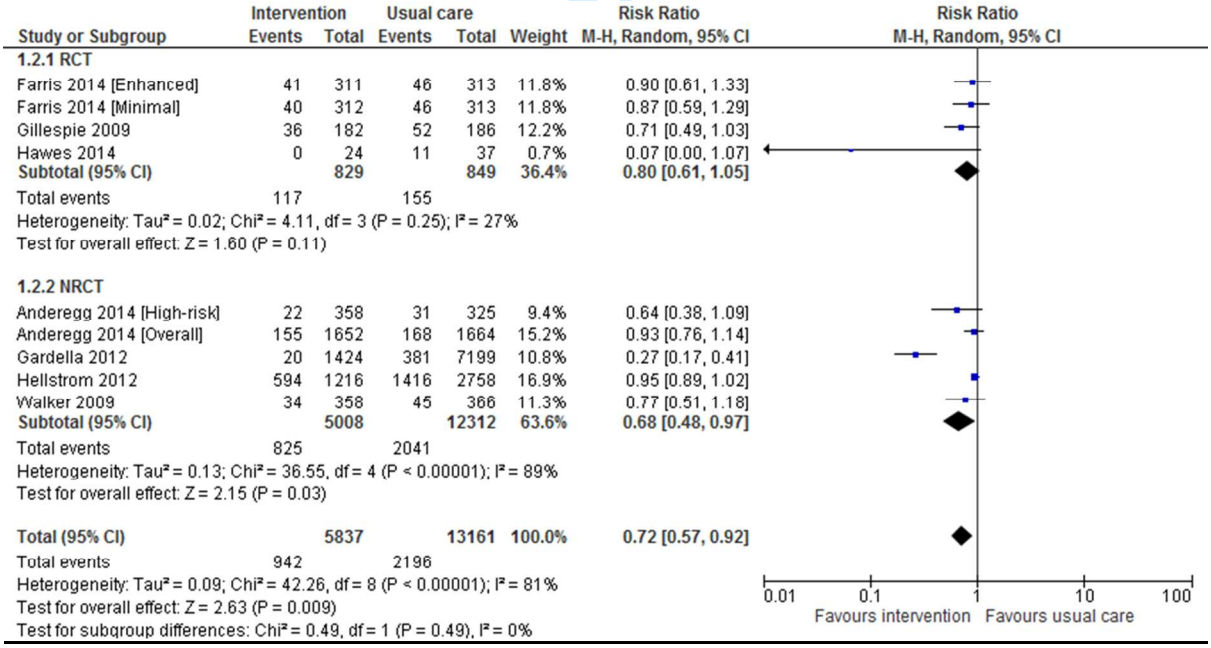


4.2 All-cause ED visits

4.2.1 Subgroup analysis based on outcome timing

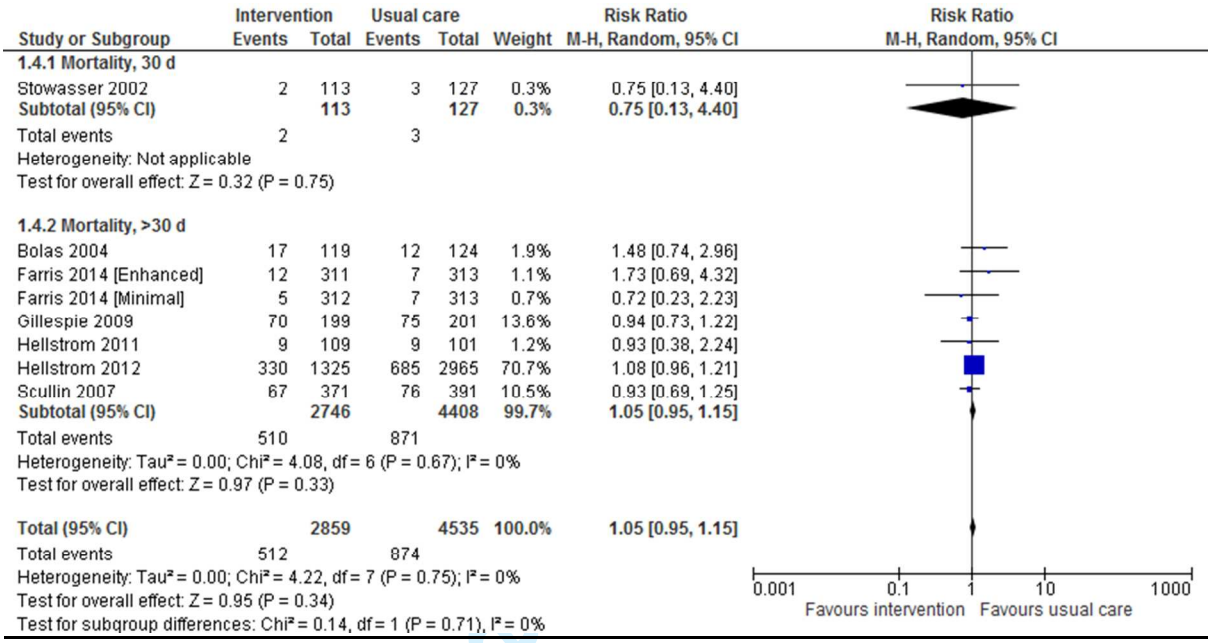


4.2.2 Subgroup analysis based on study design

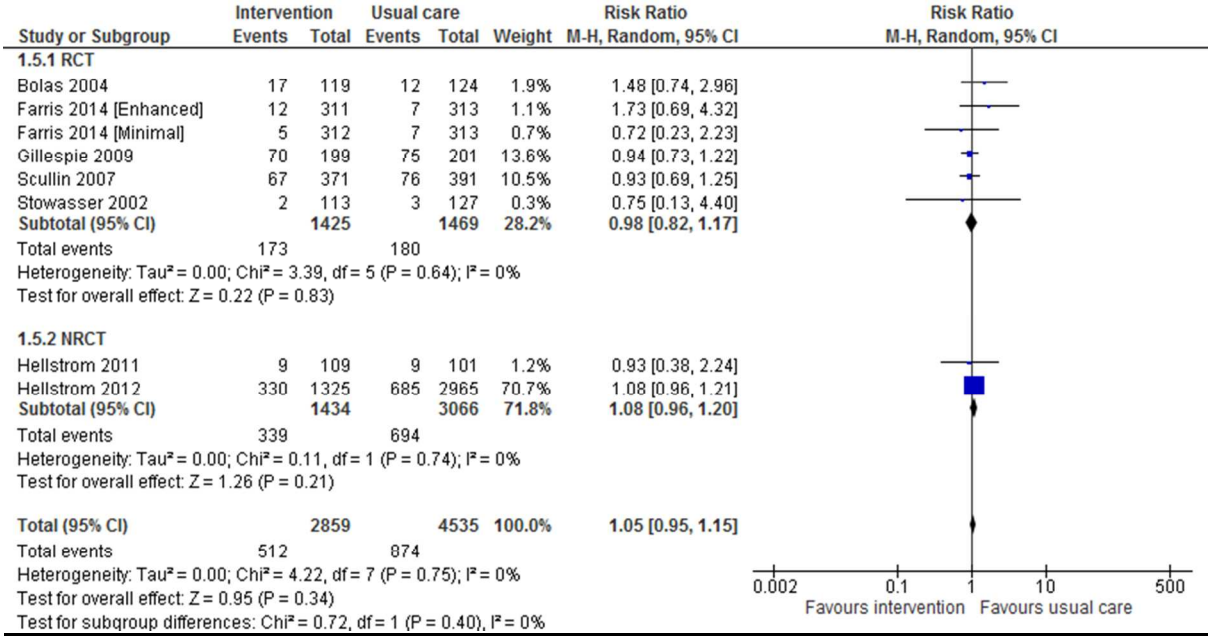


4.3 All-cause mortality

4.3.1 Subgroup analysis based on outcome timing

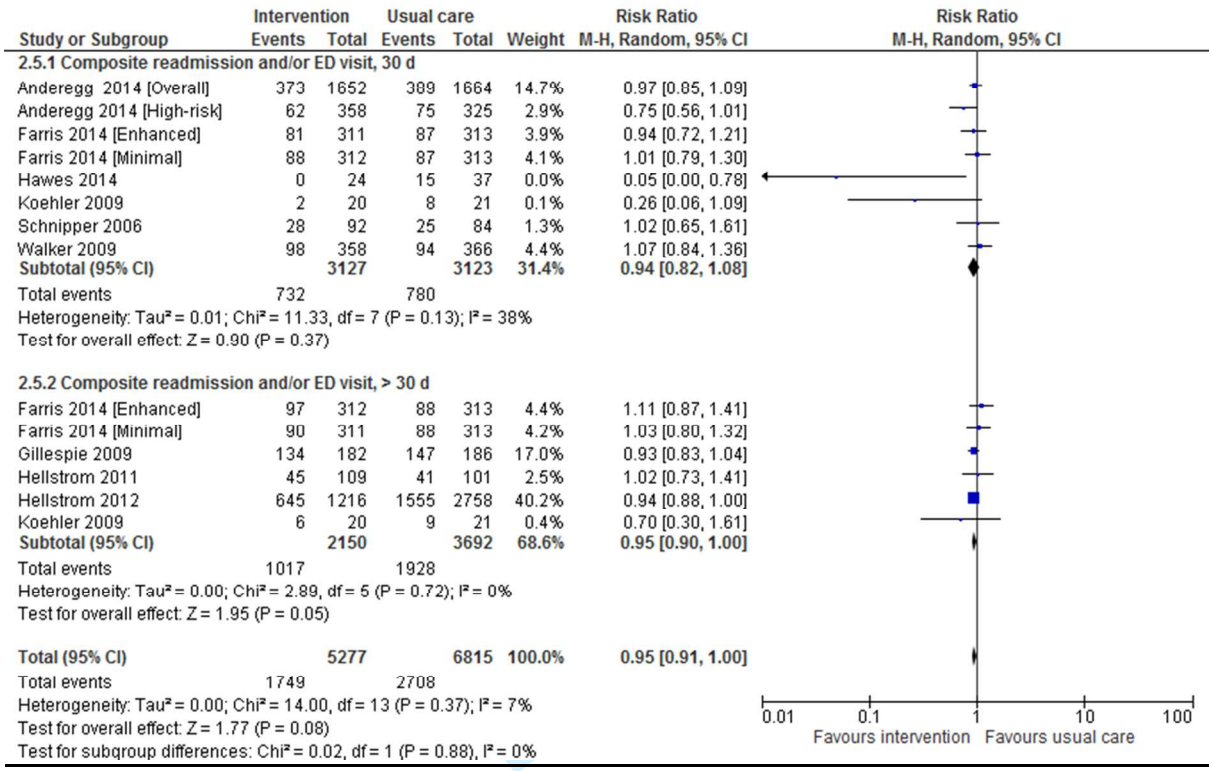


4.3.1 Subgroup analysis based on study design

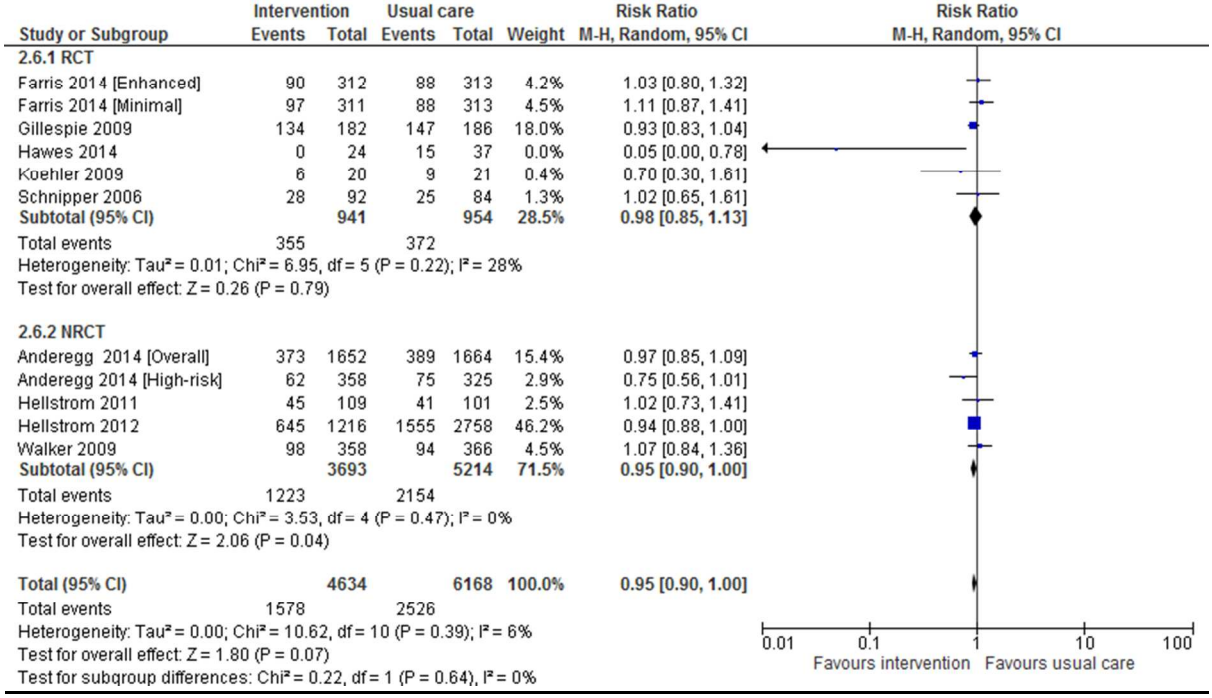


4.4 Composite readmission and/or ED admission

4.4.1 Subgroup analysis based on outcome timing



4.4.2 Subgroup analysis based on study design



BMJ Open

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

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2015-010003.R1
Article Type:	Research
Date Submitted by the Author:	26-Nov-2015
Complete List of Authors:	Mekonnen, Alemayehu; University of Sydney, Pharmacy; University of Gondar, School of Pharmacy McLachlan, Andrew; University of Sydney, Faculty of Pharmacy; Concord Repatriation General Hospital, Centre for Education and Research on Aging Brien, Jo-Anne; University of Sydney, Pharmacy; St vincents hospital, School of Medicine
Primary Subject Heading:	Pharmacology and therapeutics
Secondary Subject Heading:	Health services research, Medical management
Keywords:	Medication reconciliation, medication review, medication errors, medication discrepancies, pharmacists

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

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Abstract count- 292

Word count - 4171

Number of tables- 2

Number of figures- 2

Keywords- Medication reconciliation, medication history, medication safety, medication review, medication errors, medication discrepancies, care transition, pharmacists, clinical pharmacists

Running head- Effect of pharmacist-led medication reconciliation programmes

ABSTRACT

Objectives: Pharmacists play a role in providing medication reconciliation. However, data on effectiveness on patients' clinical outcomes appears 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 done using random effects model, and subgroup analysis was conducted to determine the sources of heterogeneity.

Results: Seventeen studies involving 21,342 adult patients were included. Eight studies were randomised controlled trials (RCTs). Most studies target 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 substantial reduction of 67%, 28% and 19% in adverse drug event-related hospital revisits (RR 0.33; 95% CI: 0.20-0.53), emergency department visits (RR 0.72; 95% CI: 0.57 -0.92) and hospital readmissions (RR 0.81; 95% CI: 0.70 - 0.95) in the intervention group than the usual care, respectively. The pooled data on mortality (RR 1.05; 95% CI: 0.95 - 1.16) and composite readmission and/or ED visit (RR 0.95; 95% CI: 0.90 - 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 utilization. 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 programs 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 affected 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 occurred at transitions in care, when patients move in, and out of, hospital or transferred to the care of other healthcare professional,[2] and up to one-third could have the potential to cause harm.[3] Unintentional medication changes are common at care transitions,[3-8] and are one of the reasons for a huge utilization of healthcare resources.[9-13] Medication reconciliation as a medication safety strategy has been championed by a number of healthcare organizations. 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] have been involved in endorsing this strategy across many countries.

Despite of 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 professional (s) or strategies effectively perform medication reconciliation.[19] A number of medication reconciliation strategies were utilized for safe patient transitions: electronic reconciliation tools,[20-22] use of standardised forms,[23, 24] collaborative models,[25, 26] patient engagement [27] and pharmacist-led. [28, 29]

The impact of medication reconciliation on clinical outcomes at hospital transitions were reported so far, 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 in healthcare resource utilization. Unlike Mueller et al, [30] Kwan et al [31] did not report significant association between post-hospital healthcare utilization and medication discrepancies identified through medication reconciliation interventions. Both reviews assessed broadly at the effect of medication reconciliation done by various strategies

including the use of collaborative models. The aim of the present review was thus, to assess specifically 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 PRISMA group (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) 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 the entire collections in the databases till December, 2014: PubMed/Medline (1946), Ovid/Medline (1946), International Pharmaceutical Abstracts (1970), Embase (1966), PsycINFO (1890), and CINHAL (1937) (Appendix A). The reference lists of review articles and included studies were hand-searched to identify 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 all of the following: studies which reported medication reconciliation intervention primarily, and provide data on any of these clinical endpoints [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 performed primarily by pharmacist, with the aim of improving care transitions to and from a hospital. The intervention must be 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 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 (e.g. nurse-led) or practices as part of a multicomponent intervention (e.g. 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 randomized 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 by the second (AM) and third reviewer (JB).

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 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 endpoints: healthcare utilization [readmission, ED visit and composite readmission and/or ED visit], mortality and ADE-related hospital visits, compared with a usual care in the other arm and used at least 30 days of follow-up. Studies were eligible for meta-analysis if such endpoint could be extractable. We analysed data in accordance with the Cochrane handbook.[34] Together with 95% confidence intervals 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) V5.3 software (Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014). We performed separate analyses for each outcome measured compared with usual care. We synthesized 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% confidence intervals (CI) were calculated. Because 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 done according to methodological design factors (RCT and non-randomised studies) and outcome timing (duration of follow-up). For studies that reported outcomes at 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 done separately for the long- and short-duration subgroups. We assessed statistical heterogeneity among studies through calculating Tau^2, Chi-square (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 was withdrawn from the analysis. We evaluated publication bias by inspection of funnel plot, Begg-Mazumdar and Egger's test using Comprehensive Meta-analysis, V3 (Biostat, Englewood, NJ, 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 done for each study. Studies with a 'clear data' on each of the domains were given a score of 1, and a study had been 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 additional 59 records were identified in reference lists of included studies. After removal of duplicate records, title and abstract screening were applied on 1832 publications. After title and abstract review, 1731 publications did not meet the inclusion criteria – the focus for the majority of studies were 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 medication

reconciliation was not the primary intervention (n=11) (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%). Majority of the studies were conducted in the US (eleven studies), [35-45] and the remainder were in Sweden (three studies), [46-48] Ireland (two studies) [49, 50] and Australia (one 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 ranged from 41 to 8,959 individuals. No studies in the 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 in 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] patient counselling [35, 38, 41, 45] or both telephone/home visit and patient counselling.[37, 40, 42, 43, 46, 49, 50]

After medication reconciliation, few studies [42, 46-49] additionally included a formal medication

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

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
Boles *et al.* 2004 [50]	Ireland, single centre	RCT	81	81	In-patient stay, discharge, post-discharge	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	Medication liaison service (comprehensive medication history, discharge letter faxed to GP and community	Standard clinical pharmacy service (not include discharge counselling	3 month	Readmission, hospital stay (following readmission)	Readmission rate: p>0.05; Length of stay: p>0.05

							declined	pharmacist, medicines record sheet, discharge counselling, home visit/telephone call)	and liaison service)			
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 d 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.* 2016[37]	USA, Single centre	RCT	Minimal=312 Enhanced=311	313	Admission, in-patient stay, discharge	18 years or older, English or Spanish speaker, diagnosis of HPN, hyperlipidemia, HF, CAD, MI, stroke, TIA, asthma, COPD or receiving	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	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, Health care utilization at 30 days and 90 days: NS

						oral anticoagulation		pharmacist				
Gardella *et al.* 2012 [38]	US, multicentre	Before-after	1624	7335	Pre-admission 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;1.87-2.94, p<0.001]; 60 day readmission: 2.7% (I) vs 7.7% (U) [OR 3.02, 95% CI; 2.18-4.19, p<0.001]
Gillespie *et al.* 2009 [46]	Sweden, single centre	RCT	182	186	Admission, in-patient 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 - 1.4]); ED visits per patient: 0.35 (I) vs 0.66 (U) [OR 0.53, 95% CI; 0.37 - 0.75]
Hawes *et al.* 2015 [39]	US, single centre	RCT	24	37	Discharge and post discharge	High risk patients [HF, COPD, hyperglycaemic crisis, stroke	Age < 18 yrs, inability to communicate in English, unable to follow up (no transportation and	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;

						,NSTEM, more than 3 hospitalizations in the past 5 yrs., 8 or more medications on discharge]	telephone access),transfer to other facilities other than primary care, decisional impairment, incarceration					Composite of hospitalization 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, in-patient stay, discharge	Age 65 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 with any of HF, RF]	NA	Admission MedRec, structured medication reviews, follow up at least two times a week	Usual care (no clinical pharmacists working in the wards)	6 month	ED visits, hospital admissions and mortality	ED visit: 48.8% (I) vs 51.3% (U) [HR 0.95, 95%CI:0.86-1.04]; All ED visits, hospitalization or death: 58.9% (I) vs 61.2% (U) [HR 0.96, 95% CI: 0.88-1.04] 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 hrs.	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 d readmission/ED visits: 2/20 (I) vs 8/21 (U) (p= 0.03); 60 d readmission/ED visits: 6/20 (I) vs 9/21 (U); p= 0.52
Pape *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 d 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	In-patient stay, discharge, post discharge	Discharge to home, contacted 30 days after discharge,	NA	Discharge medication reconciliation, telephone follow up, medication review,	Usual care (medication review by a pharmacist and discharge		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

						spoke English, cared for primary care physician/ internal medicine resident		standard email template, patient counselling	counselling by a nurse)			preventable medication related healthcare utilization: 1% (I) vs 8% (U), p= 0.03
Scullin *et al.* 2007 [49]	Ireland, multicentre	RCT	371	391	Admission, in-patient stay, discharge	Age 65 or older, at least 4 regular medications, taking antidepressants, previous admission in the last 6 months, taking IV 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.* 2008 [51]	Australia, multicentre	RCT	113	127	Admission, discharge	Return to the community following discharge	Outpatients, discharge to hostel or nursing home, previous enrolment, unable to provide consent and	Medication liaison service - medication history confirmation with community health care	Usual care (no medication liaison	30 days	Mortality, readmission, ED visit	Mortality, 30 d: 2/113 (I) vs 3/127 (U): NS Readmissions: 12/113 (I) vs 17/127 (U)

							follow up	professionals (telephone, faxing), 30 d post follow up	service)				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 d: 12.6% (I) vs 11.5% (U), p=0.65; Readmission, 30 d: 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, in-patient 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	Al- cause readmission, 30 day :17% (I) vs 38% (U) [RR 0.45, 95% CI:0.21-0.96, p=0.02], 30 d HF related readmission: 6%(I) vs 18% (U) [RR 0.31, 95% CI: 0.08-1.27, 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	Refusal of pharmacist education, transfer to a skilled nursing facility, or discharge when the pharmacist was not available	Medication history at admission, during hospitalization and discharge, patient education upon 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: 0.514-1.032, p =0.04]

social support, prior hospitalization within the last 6 months

ADE, adverse drug event; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; CI, confidence interval; 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; NSEMI, non-ST segment elevation myocardial infarction; NS, non-significant; OR, odds ratio; RCT, randomized controlled trials; RF, renal failure; RR, relative risk; TIA, transit ischemic attack; U, usual care.

Risk of bias assessment

Patients included in the study were similar in the baseline characteristics except five studies [36, 38, 39, 45, 48] which were not clear or different in patient characteristics. However, in only three studies[43, 48, 51] that baseline clinical outcomes were reported or some form of adjustment analysis was performed. Eight out of 17 studies [37, 39, 40, 42, 46, 49-51] provided enough details on randomization procedure to be judged as adequate. Among these studies, allocation concealment was fully described in all reports except one.[51] All but three studies, [43, 45, 50] either care providers and outcome assessors were blinded or objective health outcomes were reported. Five studies [37, 41, 47, 48, 51] achieved more than 80% complete follow-up. But, 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 randomized controlled trials falls within a range of 4 to 8, whereas for non-randomized controlled trials a lower range of 1 to 5 score was attained (Appendix C).

Effect of interventions

Of the 14 studies that reported data on all-cause readmissions, thirteen 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, fifteen 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 rehospitalizations 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 - 0.95). However, the results of these studies for this endpoint is substantially heterogenous (Figure 2A). With regards to all-cause emergency department (ED) contacts, seven out of 8 studies[35, 37-39, 43, 46, 48] which measured ED visit as an outcome were pooled.

Considering studies that gave two data, nine interventions were meta-analysed. The pooled analysis across all interventions showed some significance difference between the intervention and usual care (RR 0.72; 95% CI: 0.57 - 0.92) (Figure 2B). Evidence showed extreme heterogeneity in this outcome; however, the findings were different when Gardella et al [38] was removed; no heterogeneity without affecting the significance difference (p=0.25; I^2=22%, RR 0.89; 95% CI: 0.79 - 0.99). In nine studies [35, 37, 39, 40, 42, 43, 46-48] which reported composite all-cause readmission and/or ED visit showed no difference in pooled analysis (RR 0.95; 95% CI: 0.90 - 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 - 0.53) when pharmacist-led medication reconciliation programmes were implemented (Figure 2D). Seven studies [37, 46-51] gave 8 separate data for all-cause mortality that had been reported after 30 days to 12 months of follow-up. However, mortality data from Bolas et al [50] and Farris et al [37] was not their primary outcome of interest. But, we included in our meta-analysis. Overall, there was no significance difference between the two groups in terms of all-cause mortality (RR 1.05; 95% CI: 0.95 - 1.16) (Figure 2E).

Other outcomes

Studies reporting other clinically important outcomes are summarized 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 3 studies [46, 48, 49] showed a trend towards an increase in the number of patients who did not revisit hospital for any causes, and the overall pooled analysis was statistically significant (RR 1.10; 95% CI: 1.03 - 1.17). There were no any 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.

Table 2 Other clinically relevant outcomes

Outcome	No of studies	No. of patients	RR	CI	WMD	CI
Patients who did not revisit hospital	4	5314	1.10*	(1.03, 1.17)†		
Hospital stay (after readmission)	2	803			-0.57	(-5.32, 4.17)‡
Readmission per patient	3	1370			-0.12	(-0.24, 0.01)‡
ED visit per patient	2	4342			-0.15	(-0.53, 0.23)‡
Patients with ADE	3	1401	0.94	(0.75, 1.20)‡		

*RR is > 1 when the intervention increased the number of patients did not revisit hospital (i.e. it showed success)

†p<0.01

‡p>0.05

ADE, adverse drug event; ED, emergency department; RR, risk ratio; CI, confidence interval; WMD, weighted mean difference.

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 Faris et al [Enhanced] [37] or Hawes et al [39] were removed, the result showed a significant pooled summary estimate with similar risk ratio (RR 0.95; p=0.02 and 0.03, respectively).

Subgroup analysis

Subgroup analysis which compared studies that reported all-cause readmissions at earlier vs 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 - 1.06, p=0.14), whereas in earlier follow-up subgroups, the effect was significant (RR 0.77, 95% CI: 0.60 - 0.98, p=0.03). However, there was no significance difference between these two

subgroups. In addition, non-randomized studies showed a significant reduction in all-cause readmission (RR 0.74, 95% CI: 0.58 - 0.94, p=0.01) and all-cause ED visit (RR 0.68, 95% CI: 0.48 - 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-randomized studies (RR 0.95, 95% CI: 0.90 - 1.00, p=0.04); though there was no difference between the subgroups (Appendix D).

Publication bias

We examined the potential for publication bias by constructing the funnel plot and through statistical tests. There was some indication of asymmetry, particularly for all-cause ED visits in the funnel plots and therefore, there was some publication bias as evidenced by the Egger's (p=0.04) and Begg's test (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 (Appendix E).

DISCUSSION

To our knowledge, this is the first meta-analysis that has investigated 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*%).* But, pooled data on mortality and composite readmission/ED visit favoured neither the intervention nor the usual care. Patients allocated in the intervention group were not only readmitted or revisited hospital less

frequently but also increased patients free of any events after hospital discharge (RR 1.10; 95% CI: 1.03 - 1.17).

No previous reviews have been conclusively and consistently shown effectiveness of medication reconciliation interventions; be it in the 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 utilization. [30, 31] It was not clear to support the effectiveness of such interventions in the hospital environment. But, we believed that the influence of pharmacist's in healthcare utilization was diluted amongst 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 pharmacist's 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 that reported this outcome.[43, 47] Other studies also showed that medication discontinuity is the most common reason for discrepancy related ADE.[55, 56] Although 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 the control. Readmissions were frequent in earlier follow-up periods. This is as opposed to a review by Kewan et al; [31] 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 a relatively longer than 30 days. Therefore, it might be difficult to conclude as there was not a sustained benefit

of the intervention, and this was supported by non-significance differences between the subgroups. Moreover, non-randomized 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 intermingle components and difficult to ascertain the success to pharmacist-led intervention is due only because of 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. In a review by Holland et al [57] where only eight of the 32 included studies were of hospital-based and only two of these have 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 rose in a Cochrane review [58] was that medication review has varied and wider meaning and did not stand alone. Prior to medication review, it is medication reconciliation which practiced routinely at hospital transitions and thus, thinking of 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 equal effective as those with mixed interventions.

A number of recent studies have investigated medication reconciliation interventions at the level of real practice models or as in integrated management of medicines.[47-49] Medication

reconciliation interventions are complex interventions targeting fragments of services across the entire care transitions, and is thus, takes 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 for quality transitions in combinations of those multifaceted components.

Limitation of the study

There are a number of limitations to this study. Firstly, most studies included high-risk patients and, we did not confirm which patients were 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 hospitalization. Secondly, 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 rate of readmission. Thus, if this value is extrapolated to clinical outcomes, there might have 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 has already been implemented in some defined areas. Therefore, future studies should evaluate specific areas suited to pharmacist services that would benefit patients the most. Thirdly, most of the studies were single centre evaluations, and there were few studies with fewer patients. Considering success 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 Hellstrom et al [48] in the mortality forest plots were accounted for a large proportion of the studied subjects, yet these studies possessed low quality score.

Fourthly, 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 we 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 element of medication reconciliation can improve outcomes at hospital transitions.

We also noted in our work that only published studies were included. However, funnel plot asymmetry and statistical tests suggested 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 like Ulayar et al [66] published in non-English journals involving interventions for improving care transitions. In addition, research disseminated through 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. But, the effect on mortality and composite all-cause readmission/ED visit is inconclusive based on the current body of evidence, though improvements in 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 randomized control trials of excellent quality to conform our conclusion. Overall, our findings support the implementation of pharmacist-led medication reconciliation programme that includes some components aimed at improving medication safety.

Acknowledgements

We would like to acknowledge Asres Berhan for his comments on the data analysis and interpretation, and statistical advice in using the meta-analysis software. We would also like to acknowledge Lorraine Evison for her invaluable contributions in the electronic database searching and abstract screening.

Contributors

ABM was responsible for the study conception and design under the supervision of JB. All literature searching, abstract screening, study and data extraction was undertaken by ABM with further confirmation from JB. ABM carried out the initial analysis, and drafted the first manuscript. JB and AM critically reviewed and revised the manuscript. All the authors have read and approved the final manuscript as submitted.

Funding

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests

None declared.

Data sharing statement

No additional data are available.

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Figure legends

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

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 in two groups: general population and high-risk patients. Farris et al [37] randomised the population into different levels of intervention: minimal and enhanced.

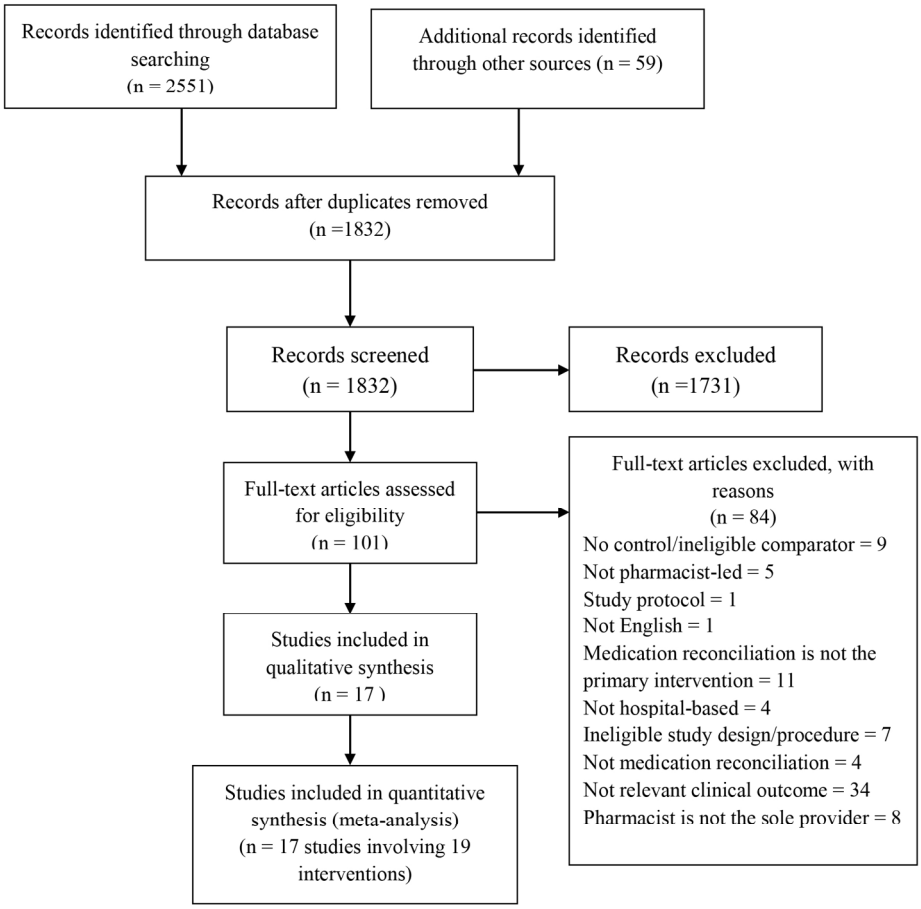

Figure 1 PRISMA flow diagram of the selection of eligible studies.
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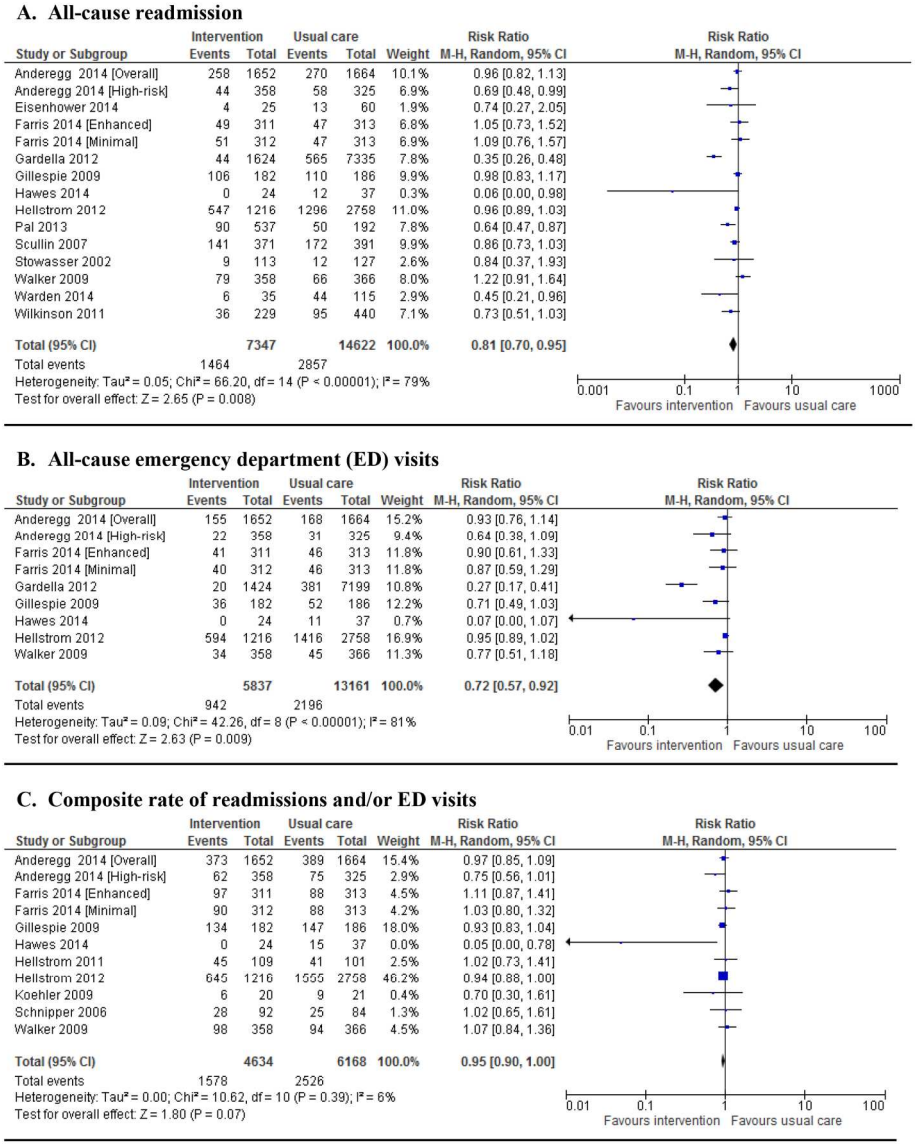

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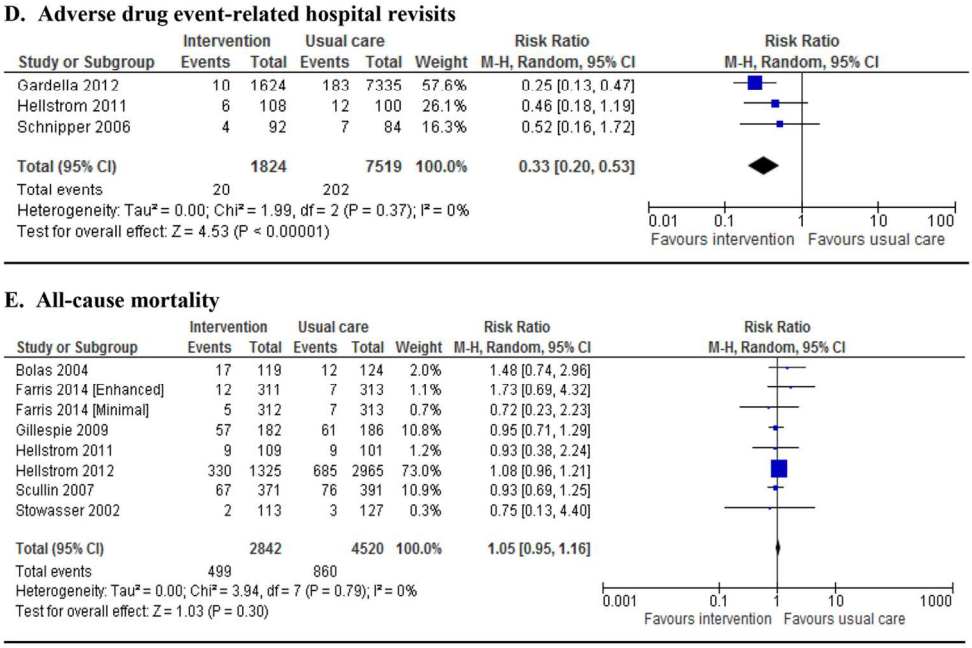


Figure 2 Forest plots of intervention effects on the proportion of patients with all-cause readmission (A), emergency department (ED) visits (B), composite rate of readmissions and/or ED visits (C), Adverse drug event-related hospital revisits (D) and mortality (E). Pooled estimates (diamond) calculated by the Mantel-Haenszel random effects model. Horizontal bars and diamond widths represent 95% CIs. Anderegg et al [35] stratified patients in two groups: general population and high-risk patients. Farris et al [37] randomised the population into different levels of intervention: minimal and enhanced.
119x81mm (300 x 300 DPI)

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2 and 3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	5
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	NA
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	5 and 6
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	5
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Appendix A
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	5 and 6
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	6
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	6
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	8
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	7
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2 for each meta-analysis.	7 and 8

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	8
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	7 and 8
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	8 and 9
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	9 - 19
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	Appendix C
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	20 - 22
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	20 - 22
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	20
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	22 and 23, Appendix D and E
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	23 - 25
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	26 and 27
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	27
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	28

PRISMA 2009 Checklist

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097.

Appendix A

Electronic database searches

Medline, IPA and PsychINFO

#	Searches	Results
1	((medic$ or drug$) adj2 discrepanc$).mp.	524
2	((medic$ or drug$) adj2 reconciliation$).mp.	1,193
3	((medic$ or drug$) adj2 histor$).mp.	75,175
4	((medic$ or drug$) adj2 list$).mp.	5, 023
5	(((medic$ adj2 chart$) or (medic$ adj2 record$)) adj2 assessment).mp.	125
6	((medic$ or drug$ or prescription$ or (medic$ adj2 chart$) or (medic$ adj2 record$)) adj2 review$).mp.	35,859
7	((medic$ or drug$) adj2 congruence$).mp.	20
8	((medic$ or drug$) adj2 management).mp.	37,424
9	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8	151,309
10	patient admission.mp. or Patient Admission/	20,054
11	patient discharge.mp. or Patient Discharge/	21,100
12	patient transfer.mp. or Patient Transfer/	6,658
13	Hospitalization/ or hospital transfer.mp.	81,536
14	"Continuity of Patient Care"/ or care transition.mp.	15,531
15	inpatients.mp. or Inpatients/	58,575
16	seamless care.mp.	154
17	continuum of care.mp.	3,103
18	"Delivery of Health Care, Integrated"/ or integrated health care.mp.	10,066
19	10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18	199,032
20	pharmac*.mp.	905,186
21	9 and 19 and 20	1,144
22	limit 21 to (abstracts and english language and humans)	1009

CINHAL

#	Searches	Results
S18	S14 AND S15 AND S16 Limiters-Peer Reviewed; English Language; Abstract Available	267
S17	S14 AND S15 AND S16	396
S16	S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13	306,305
S15	S1 OR S2 OR S3 OR S4 OR S5 OR S6	9,033
S14	"Pharmac*"	101,387
S13	(MH "Continuity of Patient Care+") OR "continu*"	187,044
S12	"seamless care"	104
S11	(MH "Inpatients")	55,914
S10	"emergency medic*"	29,880
S9	"transition of care"	143
S8	(MH "Transfer, Discharge")	3058
S7	(MH "Patient Admission") OR (MH "Hospitalization+") OR (MH "Patient Discharge+")	56,917
S6	"medication discrepancies"	45
S5	"medication discrepancy"	10
S4	"drug history"	122
S3	(MH "Medication Errors+")	8,626
S2	(MH "Medication History")	60
S1	(MH "Medication Reconciliation")	472

Embase

#	Searches	Results
24	#1.20 AND #1.21 AND #1.22 AND #1.23 [english]/lim AND [humans]/lim AND [abstracts]/lim	335
23	#1.15 OR #1.16 OR #1.17 OR #1.18 OR #1.19	375,805
22	#1.5 OR #1.6 OR #1.7 OR #1.8 OR #1.9 OR #1.10 OR #1.11 OR #1.12 OR #1.13 OR #1.14	454,467
21	#1.1 OR #1.2 OR #1.3 OR #1.4	4,019
20	pharmac*	3,875,936
19	'hospitalized patients'/exp OR 'hospitalized patients'	74,696
18	'inpatients'/exp OR 'inpatients'	108,750
17	'patient transfer'/exp OR 'patient transfer'	40,927
16	'patient discharge'/exp OR 'patient discharge'	96,003
15	'patient admission'/exp OR 'patient admission'	137,129

14	'medication'/exp OR medication AND record	179,120
13	'medication'/exp OR medication AND record AND systems	4,687
12	'medication'/exp OR medication AND record AND assessment	14,853
11	'medication'/exp OR medication AND record AND ('review'/exp OR review)	44,320
10	'medication'/exp OR medication AND chart AND ('review'/exp OR review)	9,372
9	medic* OR drug* AND list*	52,323
8	'medication'/exp OR medication AND ('history'/exp OR history)	91,985
7	'drug'/exp OR drug AND ('history'/exp OR history)	213,214
6	'drug'/exp OR drug AND ('history'/exp OR history) AND taking	9,182
5	'medication'/exp OR medication AND ('history'/exp OR history) AND taking	5389
4	'medication'/exp OR medication AND reconciliation AND errors	443
3	'medication'/exp OR medication AND ('history'/exp OR history) AND errors	570
2	'medication'/exp OR medication AND discrepancies	2464
1	'medication'/exp OR medication AND reconciliation	1453

PubMed

((((((medication reconciliation) OR medication discrepancies) OR medication history) OR ((medication AND (chart OR record) AND assessment)))) AND (((continuity of care) OR seamless care) OR ((hospital* OR inpatient* OR interface* OR discharge* OR admission*)))) AND pharmac* [640]

Appendix B

List of excluded full text papers and of the reasons for their exclusion

No control group/ ineligible comparator

Boso ribelles et al (2011). "Evaluation of a plan for cardiology medication reconciliation on admission, and patient information at discharge, in a teaching hospital." EJHP Practice 17(1)

Anderegg, S. V., et al. (2013). "Acceptance of recommendations by inpatient pharmacy case managers: unintended consequences of hospitalist and specialist care." Pharmacotherapy:The Journal of Human Pharmacology & Drug Therapy **33**(1): 11-21.

Cornu, P., et al. (2012). "Effect of medication reconciliation at hospital admission on medication discrepancies during hospitalization and at discharge for geriatric patients." Annals of Pharmacotherapy **46**(4): 484-494.

Hellstrom, L. M., et al. (2012). "Errors in medication history at hospital admission: prevalence and predicting factors." BMC Clin Pharmacol **12**: 9.

Lessard, S., et al. (2006). "Medication discrepancies affecting senior patients at hospital admission." Am J Health Syst Pharm **63**(8): 740-743.

Mergenhagen, K. A., et al. (2012). "Pharmacist- versus physician-initiated admission medication reconciliation: impact on adverse drug events." American Journal of Geriatric Pharmacotherapy **10**(4): 242-250.

Midlov, P., et al. (2012). "The effect of medication reconciliation in elderly patients at hospital discharge." International Journal of Clinical Pharmacy **34**(1): 113-119.

Quennery, S., et al. (2011). "Added value of pharmacist-acquired drug histories in an orthopaedic ward." Acta Clinica Belgica **66**(3): 196-199.

Reeder, T. A. and A. Mutnick (2008). "Pharmacist- versus physician-obtained medication histories." American Journal of Health-System Pharmacy **65**(9): 857-860.

Not Pharmacist-led medication reconciliation

Lalonde, L., et al. (2008). "Effectiveness of a medication discharge plan for transitions of care from hospital to outpatient settings." American Journal of Health-System Pharmacy **65**(15): 1451-1457.

Midlov, P., et al. (2008). "Medication report reduces number of medication errors when elderly patients are discharged from hospital." Pharmacy World & Science **30**(1): 92-98.

Schnipper, J. L., et al. (2009). "Effect of an electronic Medication reconciliation application and process redesign on potential adverse drug events a cluster-randomized trial." Archives of Internal Medicine **169**(8): 771-780.

Showalter, J. W., et al. (2011). "Effect of standardized electronic discharge instructions on post-discharge hospital utilization." J Gen Intern Med **26**(7): 718-723.

Zoni, A. C., et al. (2012). "The impact of medication reconciliation program at admission in an internal medicine department." European Journal of Internal Medicine **23**(8): 696-700.

Study Protocol

Salanitro, A. H., et al. (2013). "Rationale and design of the Multicenter Medication Reconciliation Quality Improvement Study (MARQUIS)." BMC Health Serv Res **13**: 230.

Not English

Sanchez Ulayar, A., et al. (2012). "Pharmaceutical intervention upon hospital discharge to strengthen understanding and adherence to pharmacological treatment." Farm Hosp **36**(3): 118-123.

Medication reconciliation is not the primary intervention

Nester TM et al (2002).” Effectiveness of a pharmacist acquired medication history in promoting patient safety”. Am J Health-Syst Pharm 59:2221-25.

Lisby M et al (2010). “The effect of systematic medication review in elderly patients admitted to an acute ward of Internal Medicine”. Basic & Clinical Pharmacology & Toxicology 106: 422–427.

Edwards, S. J., et al. (2014). "Outcomes assessment of a pharmacist-directed seamless care program in an ambulatory oncology clinic." Journal of Pharmacy Practice **27**(1): 46-52.

Fera T, Anderson C, Kanel KT, Ramusivich DL. Role of a care transition pharmacist in a primary care resource center. Am J Health Syst Pharm. 2014;71(18):1585-90.

Hutchison LJ, Mayzell GG, Bailey SC, Broyles JE. Impact of a discharge medication therapy management program in an extended care hospital. Consult Pharm 2014;29(1):33-8.

Marotti, S. B., et al. (2011). "A randomised controlled trial of pharmacist medication histories and supplementary prescribing on medication errors in postoperative medications." Anaesthesia and Intensive Care **39**(6): 1064-1070.

Nazareth, I., et al. (2001). "A pharmacy discharge plan for hospitalized elderly patients--a randomized controlled trial." Age & Ageing **30**(1): 33-40.

Sarangarm, P., et al. (2013). "Impact of pharmacist discharge medication therapy counselling and disease state education: Pharmacist Assisting at Routine Medical Discharge (project PhARMD)." American Journal of Medical Quality **28**(4): 292-300.

Spinewine, A., et al. (2007). "Effect of a collaborative approach on the quality of prescribing for geriatric inpatients: a randomized, controlled trial." J Am Geriatr Soc **55**(5): 658-665.

Szkiladz, A., et al. (2013). "Impact of pharmacy student and resident-led discharge counselling on heart failure patients." Journal of Pharmacy Practice **26**(6): 574-579.

Taber, D. J., et al. (2013). "Improved patient safety and outcomes with a comprehensive interdisciplinary improvement initiative in kidney transplant recipients." Am J Med Qual **28**(2): 103-112.

Not hospital based

Stewart S et al (1998). "Effects of a home-based intervention among patients with congestive heart failure discharged from acute hospital care". Arch Intern Med 158:1067-1072.

Boockvar, K. S., et al. (2006). "Medication reconciliation for reducing drug-discrepancy adverse events." American Journal of Geriatric Pharmacotherapy **4**(3): 236-243.

Kilcup, M., et al. (2013). "Postdischarge pharmacist medication reconciliation: impact on readmission rates and financial savings." J Am Pharm Assoc (2003) **53**(1): 78-84.

Stewart, A. L. and K. J. Lynch (2014). "Medication discrepancies despite pharmacist led medication reconciliation: the challenges of maintaining an accurate medication list in primary care." Pharm Pract (Granada) **12**(1): 360.

Ineligible study design/procedure

Carter, M. K., et al. (2006). "Pharmacist-acquired medication histories in a university hospital emergency department." American Journal of Health-System Pharmacy **63**(24): 2500-2503.

Karapinar-Carkit, F., et al. (2009). "Effect of medication reconciliation with and without patient counselling on the number of pharmaceutical interventions among patients discharged from the hospital." Annals of Pharmacotherapy **43**(6): 1001-1010.

Musgrave, C. R., et al. (2013). "Improving transplant patient safety through pharmacist discharge medication reconciliation." American Journal of Transplantation **13**(3): 796-801.

Mudge AM, Shakhovskoy R, Karrasch A. Quality of transitions in older medical patients with frequent readmissions: opportunities for improvement. Eur J Intern Med. 2013;24(8):779-83.

Sen S, Siemianowski L, Murphy M, McAllister SC. Implementation of a pharmacy technician-centered medication reconciliation program at an urban teaching medical center. Am J Health Syst Pharm. 2014;71(1):51-6.

Stitt, D. M., et al. (2011). "Medication discrepancies identified at time of hospital discharge in a geriatric population." American Journal of Geriatric Pharmacotherapy **9**(4): 234-240.

Unroe, K. T., et al. (2010). "Inpatient medication reconciliation at admission and discharge: A retrospective cohort study of age and other risk factors for medication discrepancies." American Journal of Geriatric Pharmacotherapy **8**(2): 115-126.

Not medication reconciliation intervention

Eijsbroek, H., et al. (2013). "Medication issues experienced by patients and carers after discharge from the intensive care unit." J Crit Care **28**(1): 46-50.

Hohmann, C., et al. (2013). "Adherence to hospital discharge medication in patients with ischemic stroke: a prospective, interventional 2-phase study." Stroke **44**(2): 522-524.

Hohmann, C., et al. (2014). "Providing systematic detailed information on medication upon hospital discharge as an important step towards improved transitional care." Journal of Clinical Pharmacy & Therapeutics **39**(3): 286-291.

Romero, C. M., et al. (2013). "Effects of the implementation of a preventive interventions program on the reduction of medication errors in critically ill adult patients." Journal of Critical Care **28**(4): 451-460.

Not relevant clinical outcome

Smith L et al (1997). "An investigation of hospital generated pharmaceutical care when patients are discharged home from hospital". Br J Clin Pharmacol 1997; 44: 163–165.

Michels R et al (2003). "Programme using pharmacy technicians to obtain medication histories." American Journal of Health-System Pharmacy 60: 1982-86.

Alassaad, A., et al. (2013). "Prescription and transcription errors in multidose-dispensed medications on discharge from hospital: an observational and interventional study." J Eval Clin Pract **19**(1): 185-191.

Basey AJ, Krska J, Kennedy TD, Mackridge AJ. Prescribing errors on admission to hospital and their potential impact: A mixed-methods study. BMJ Quality and Safety. 2014;23(1):17-25.

Becerra-Camargo, J., et al. (2013). "A multicentre, double-blind, randomised, controlled, parallel-group study of the effectiveness of a pharmacist-acquired medication history in an emergency department." BMC Health Services Research 13: 337.

Beckett, R. D., et al. (2012). "Effectiveness and feasibility of pharmacist-led admission medication reconciliation for geriatric patients." Journal of Pharmacy Practice 25(2): 136-141.

Benson, J. M. and G. Snow (2012). "Impact of medication reconciliation on medication error rates in community hospital cardiac care units." Hospital Pharmacy **47**(12): 927-932.

Bergkvist, A., et al. (2009). "Improved quality in the hospital discharge summary reduces medication errors--LIMM: Landskrona Integrated Medicines Management." European Journal of Clinical Pharmacology **65**(10): 1037-1046.

Brownlie K, Schneider C, Culliford R, Fox C, Boukouvalas A, Willan C, Maidment ID. Medication reconciliation by a pharmacy technician in a mental health assessment unit. Int J Clin Pharm 2014;36(2):303-9.

Buckley MS, Harinstein LM, Clark KB, Smithburger PL, Eckhardt DJ, Alexander E, et al. Impact of a clinical pharmacy admission medication reconciliation program on medication errors in "high-risk" patients. The Annals of pharmacotherapy. 2013;47(12):1599-610.

Chan, E. W., et al. (2010). "An intervention to encourage ambulance paramedics to bring patients' own medications to the ED: impact on medications brought in and prescribing errors." Emerg Med Australas **22**(2): 151-158.

Conklin, J. R., et al. (2014). "Care Transitions Service: A pharmacy-driven program for medication reconciliation through the continuum of care." American Journal of Health-System Pharmacy: 802-810.

Eggink, R. N., et al. (2010). "The effect of a clinical pharmacist discharge service on medication discrepancies in patients with heart failure." Pharmacy World & Science 32(6): 759-766.

Farley, T. M., et al. (2014). "Effect of clinical pharmacist intervention on medication discrepancies following hospital discharge." International Journal of Clinical Pharmacy 36(2): 430-437.

Fertleman, M., et al. (2005). "Improving medication management for patients: The effect of a pharmacist on post-admission ward rounds." Quality and Safety in Health Care 14(3): 207-211.

Grant, R. W., et al. (2003). "Improving Adherence and Reducing Medication Discrepancies in Patients with Diabetes." Ann Pharmacother **37**(7): 962-969.

Grimes, T. C., et al. (2014). "Collaborative pharmaceutical care in an Irish hospital: Uncontrolled before-after study." BMJ Quality and Safety 23(7): 574-583.

Hale, A. R., et al. (2013). "Perioperative medication management: expanding the role of the preadmission clinic pharmacist in a single centre, randomised controlled trial of collaborative prescribing." BMJ Open **3**(7).

Hayes, B. D., et al. (2007). "Pharmacist-conducted medication reconciliation in an emergency department." American Journal of Health-System Pharmacy **64**(16): 1720-1723.

Hick, H. L., et al. (2001). "The impact of the pharmacist on an elective general surgery pre-admission clinic." Pharmacy World & Science **23**(2): 65-69.

Ho, P. M., et al. (2014). "Multifaceted intervention to improve medication adherence and secondary prevention measures after acute coronary syndrome hospital discharge: a randomized clinical trial." JAMA Intern Med **174**(2): 186-193.

Kripalani, S., et al. (2012). "Effect of a pharmacist intervention on clinically important medication errors after hospital discharge: a randomized trial." Annals of Internal Medicine 157(1): 1-10.

Kwan, Y., et al. (2007). "Pharmacist medication assessments in a surgical preadmission clinic." Archives of Internal Medicine 167(10): 1034-1040.

Nickerson, A., et al. (2005). "Drug-therapy problems, inconsistencies and omissions identified during a medication reconciliation and seamless care service." Healthcare Quarterly 8 Spec No: 65-72.

Nielsen TR, Andersen SE, Rasmussen M, Honore PH. Clinical pharmacist service in the acute ward. Int J Clin Pharm. 2013;35(6):1137-51.

Magalhães GF, Santos GB, Rosa MB, Noblat Ld A. Medication Reconciliation in Patients Hospitalized in a Cardiology Unit. PLoS ONE 2014; 9(12): e115491. doi: 10.1371/journal.pone.0115491.

Mortimer, C., et al. (2011). "The impact of an aged care pharmacist in a department of emergency medicine." J Eval Clin Pract **17**(3): 478-485.

Peyton, L., et al. (2010). "Evaluation of medication reconciliation in an ambulatory setting before and after pharmacist intervention." J Am Pharm Assoc (2003) **50**(4): 490-495.

Rahman, M. H., et al. (2005). "An evaluation of pharmacist-written hospital discharge prescriptions on general surgical wards." International Journal of Pharmacy Practice **13**(3): 179-185.

Tompson, A. J., et al. (2012). "Utilizing community pharmacy dispensing records to disclose errors in hospital admission drug charts." International Journal of Clinical Pharmacology & Therapeutics **50**(9): 639-646.

Van den Bemt, P. M., et al. (2009). "Medication reconciliation performed by pharmacy technicians at the time of preoperative screening." Ann Pharmacother 43(5): 868-874.

Van den Bemt, P. M., et al. (2013). "Effect of medication reconciliation on unintentional medication discrepancies in acute hospital admissions of elderly adults: a multicenter study." J Am Geriatr Soc 61(8): 1262-1268.

Vasileff, H. M., et al. (2009). "The effect on medication errors of pharmacists charting medication in an emergency department." Pharmacy World & Science 31(3): 373-379.

Leguelinel-Blache G, Arnaud F, Bouvet S, Dubois F, Castelli C,Roux-Marson C, Ray V, Sottoe A, Kinowski J. Impact of admission medication reconciliation performed by clinical pharmacists on medication safety. Eur J Intern Med 2014; 25(9):808-14.

Pharmacist is not the sole provider

Poole DL et al (2006). "Medication reconciliation: a necessity in promoting a safe hospital discharge." Journal for Healthcare Quality **28**(3):12-19.

Coffey M et al (2009). "Implementation of admission medication reconciliation at two academic Health Sciences Centres: challenges and success factors." Healthcare Quarterly 12 Special Issue 2009

Dedhia, P., et al. (2009). "A quality improvement intervention to facilitate the transition of older adults from three hospitals back to their homes." Journal of the American Geriatrics Society **57**(9): 1540-1546.

Duggan, C., et al. (1998). "Reducing adverse prescribing discrepancies following hospital discharge." International Journal of Pharmacy Practice **6**(Jun): 77-82.

Henneman, E. A., et al. (2014). "An evaluation of a collaborative, safety focused, nurse-pharmacist intervention for improving the accuracy of the medication history." J Patient Saf **10**(2): 88-94.

Jack, B. W., et al. (2009). "A reengineered hospital discharge program to decrease rehospitalisation: a randomized trial." Annals of Internal Medicine **150**(3): 178-187.

Nassaralla, C. L., et al. (2007). "Implementation of a medication reconciliation process in an ambulatory internal medicine clinic." Qual Saf Health Care **16**(2): 90-94.

Setter, S. M., et al. (2009). "Effectiveness of a pharmacist-nurse intervention on resolving medication discrepancies for patients transitioning from hospital to home health care." American Journal of Health-System Pharmacy **66**(22): 2027-2031.

Appendix C

Summary of risk of bias assessment*

Study reference	Randomization	Allocation concealment	Similarity of baseline characteristics	Similarity of baseline outcomes	Incomplete outcome data	Assessors blind to outcome	Absence of contamination	Selective outcome reporting	Free of other biases	Total†
Anderegg 2014	-	+	+	?	?	+	-	-	+	4
Bolas 2004	+	+	+	?	-	-	?	-	+	4
Eisenhower 2014	-	-	?	?	-	+	+	-	-	2
Farris 2014	+	+	+	?	+	+	-	+	+	7
Gardella 2012	-	-	?	?	?	+	+	+	-	3
Gillespie 2009	+	+	?	?	?	+	+	+	+	6
Hawes 2014	+	+	?	?	?	+	+	+	+	6
Hellstrom 2011	-	-	+	?	+	+	-	+	-	4
Hellstrom 2012	-	-	+	?	+	+	+	+	-	5
Koehler 2009	+	+	+	?	?	+	+	+	-	6
Pal 2013	-	-	+	?	+	+	-	+	-	4
Schnipper 2006	+	+	+	?	?	+	+	+	+	7
Scullin 2007	+	+	+	?	?	+	?	+	+	6
Stowasser 2002	+	?	+	+	+	+	+	-	+	8
Walker 2009	-	-	+	?	-	?	+	+	+	4
Warden 2014	-	-	+	?	?	+	+	+	+	5
Wilkinson 2011	-	-	?	?	?	-	?	+	-	1

Key: +, clear; -, not done; ?, unclear.

*EPOC risk of bias assessment; modified for non-controlled studies.

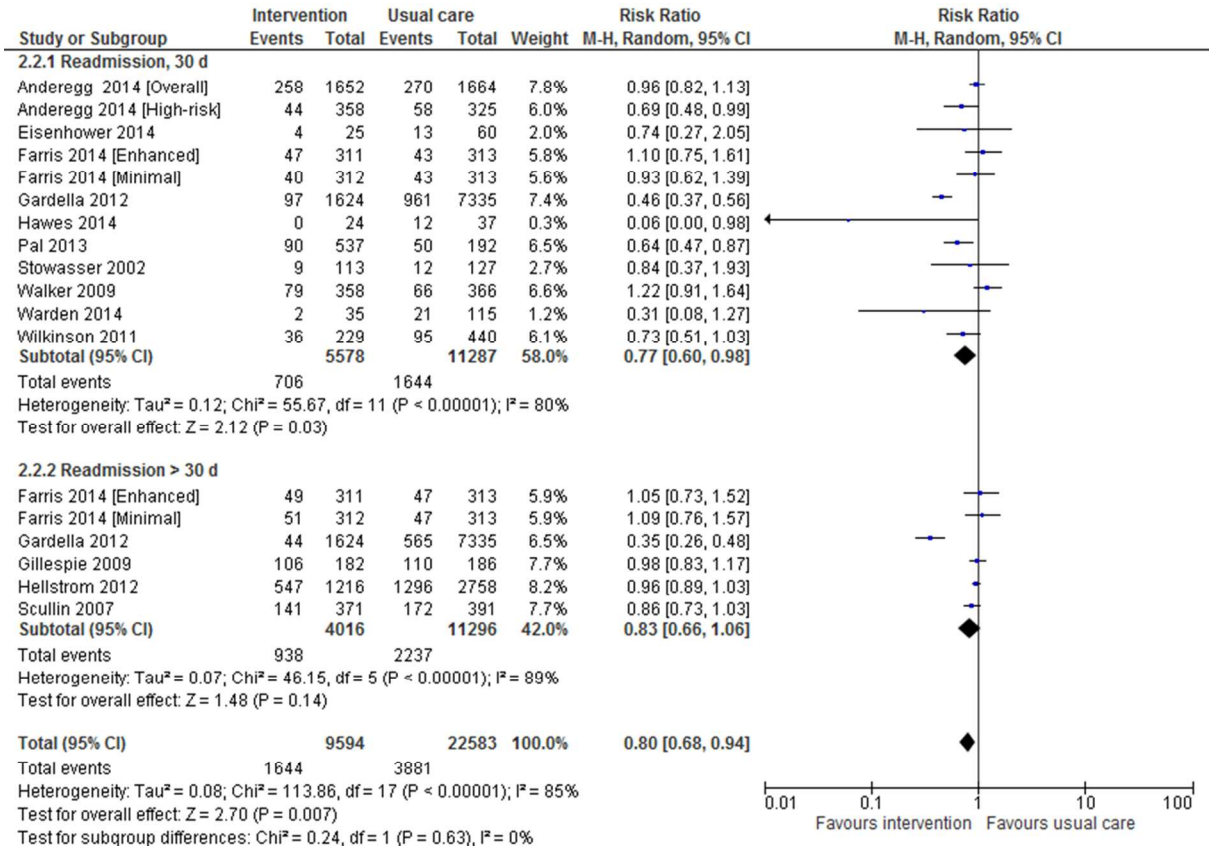
†Studies with a 'clear data' on each of the domains were given a score of 1.

Appendix D

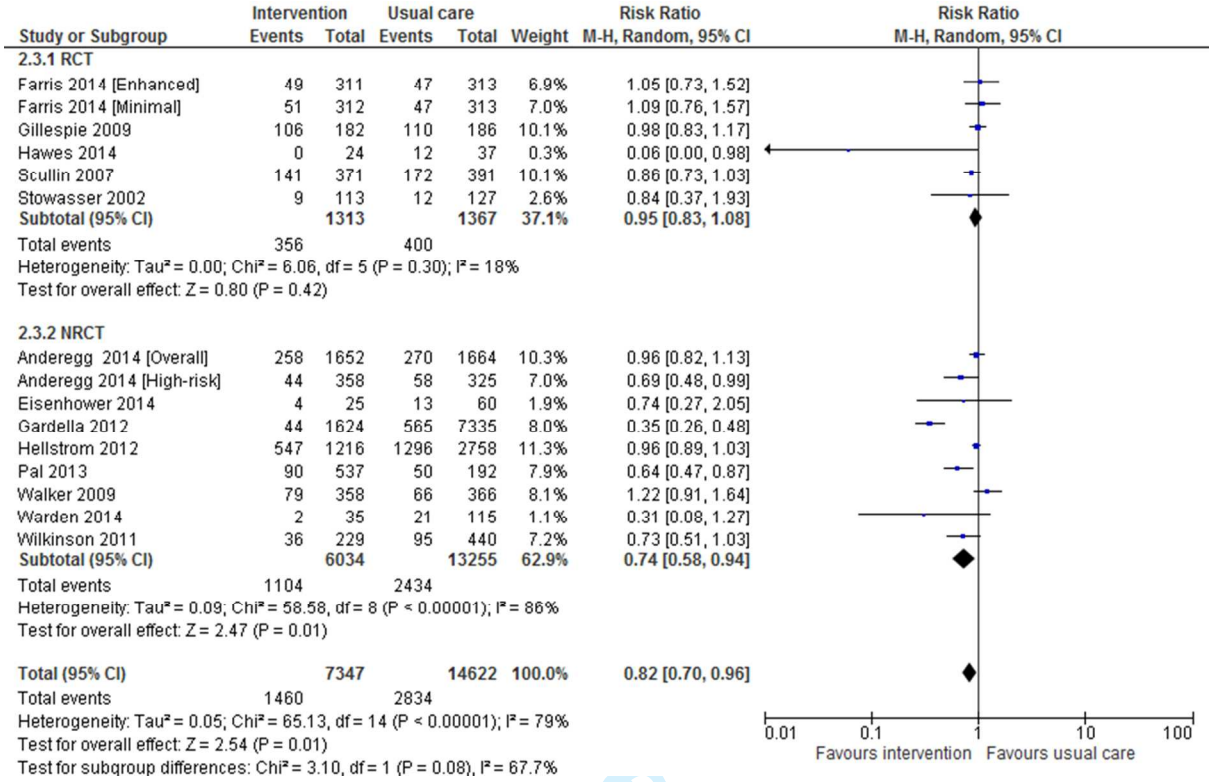
Subgroup analysis

4.1 **All-cause Readmission**

4.1.1 Subgroup analysis based on outcome timing

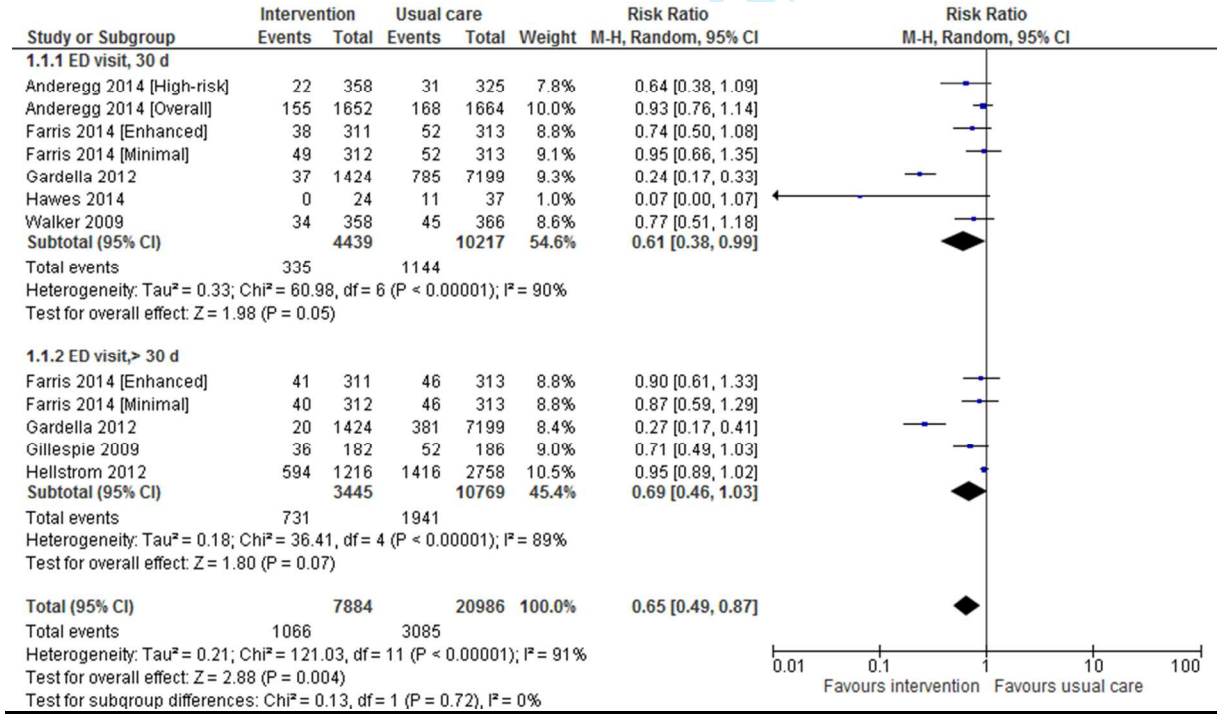


4.1.2 Subgroup analysis based on study design

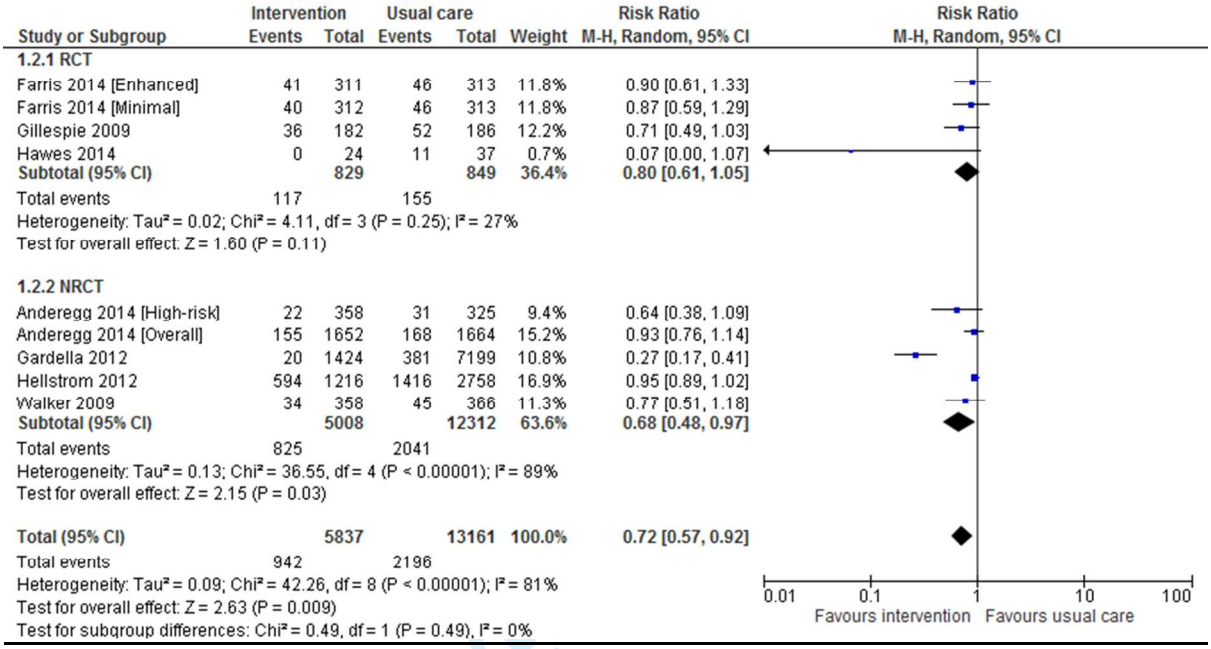


4.2 **All-cause ED visits**

4.2.1 Subgroup analysis based on outcome timing

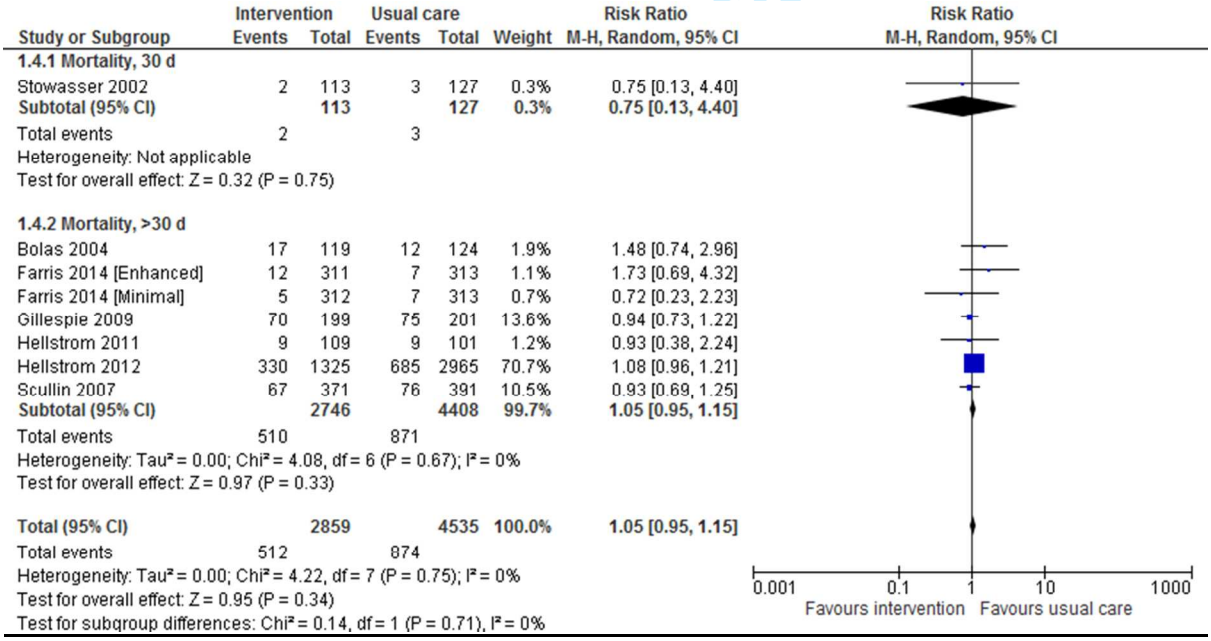


4.2.2 Subgroup analysis based on study design

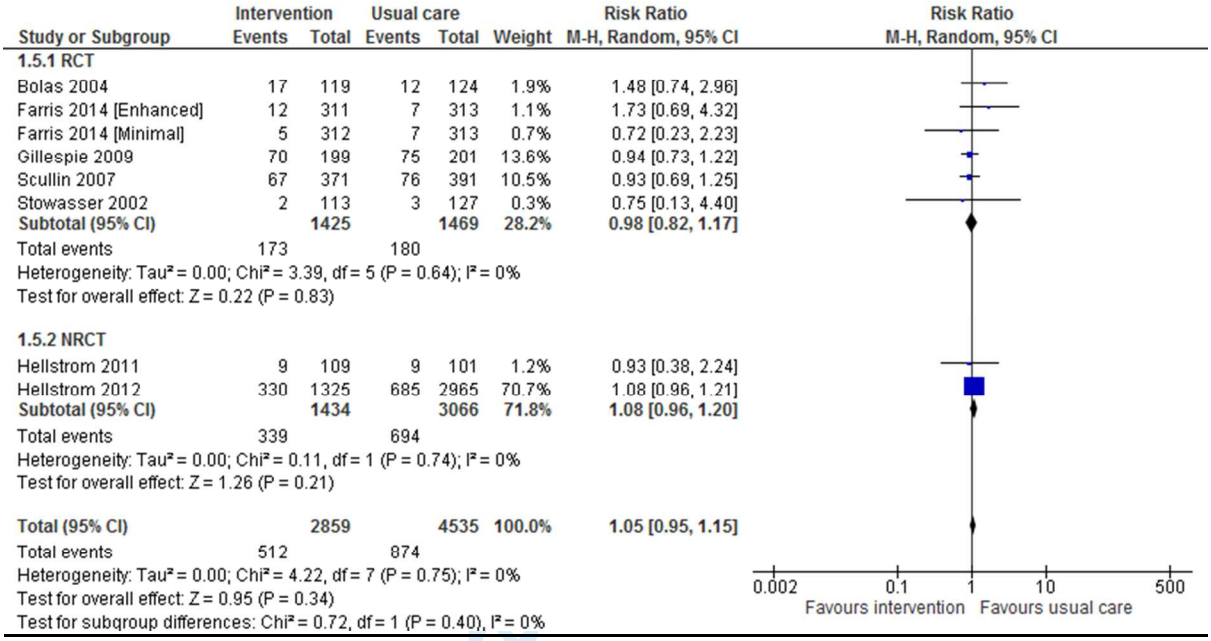


4.3 **All-cause mortality**

4.3.1 Subgroup analysis based on outcome timing

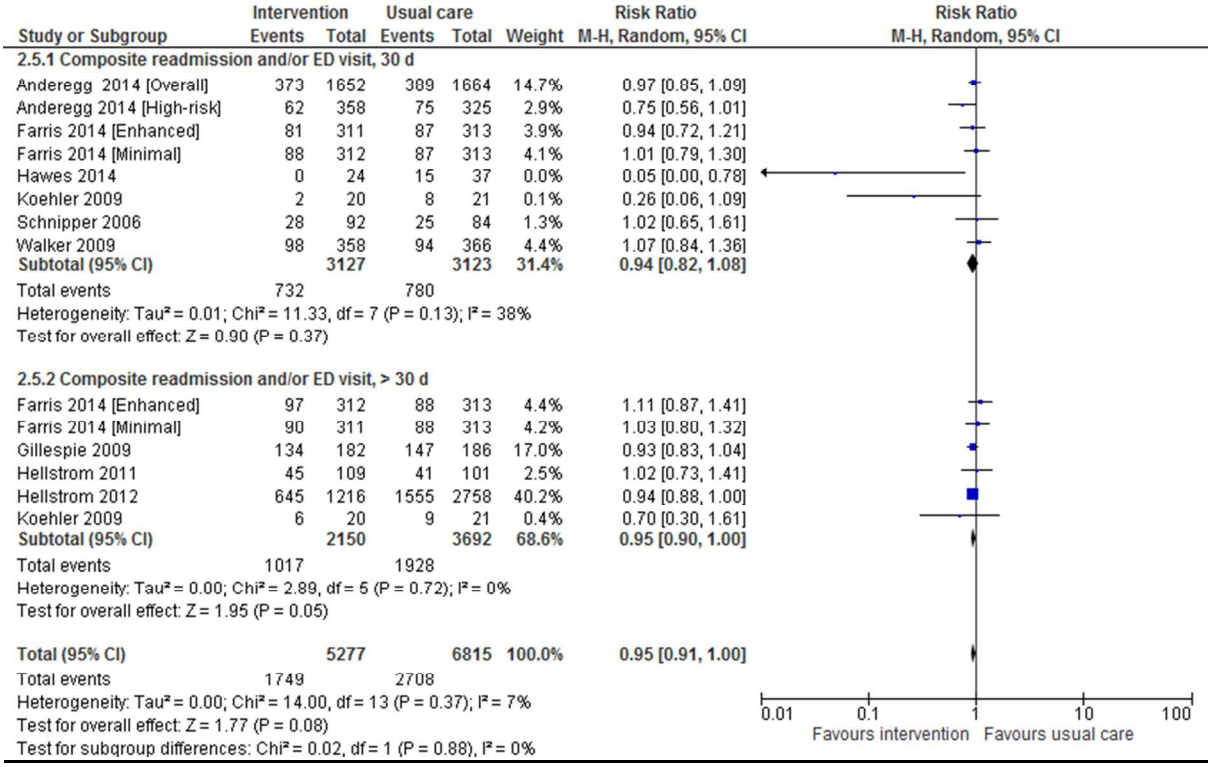


4.3.1 Subgroup analysis based on study design

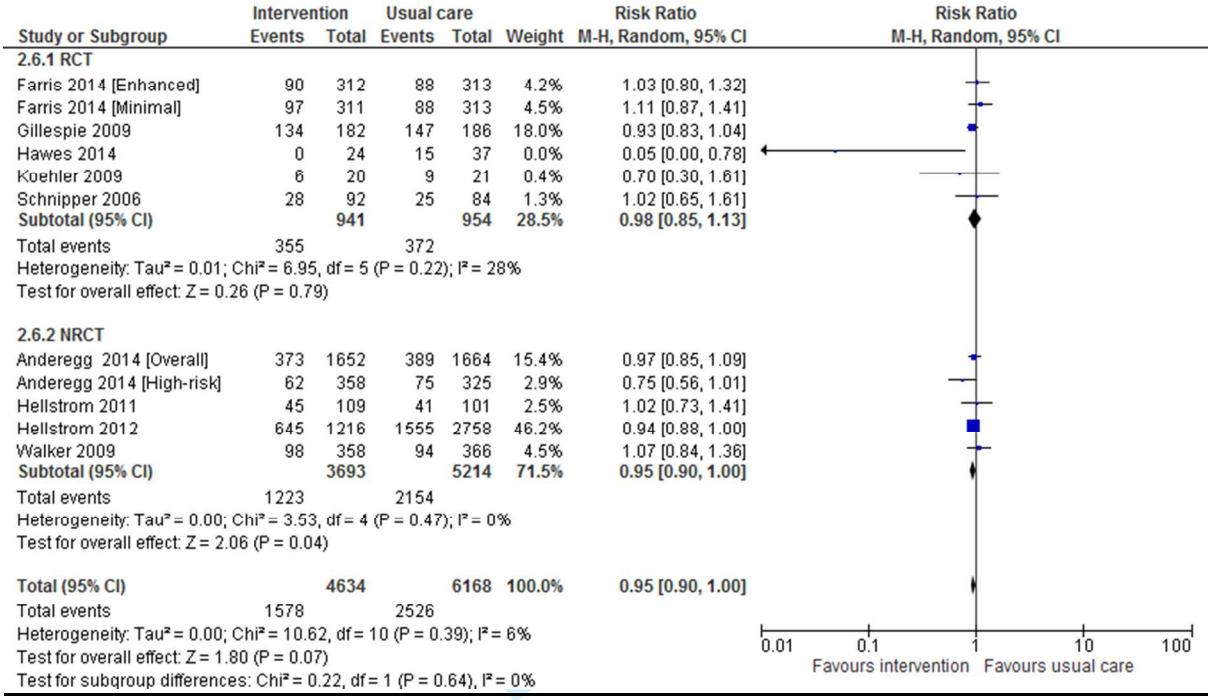


4.4 **Composite readmission and/or ED visit**

4.4.1 Subgroup analysis based on outcome timing



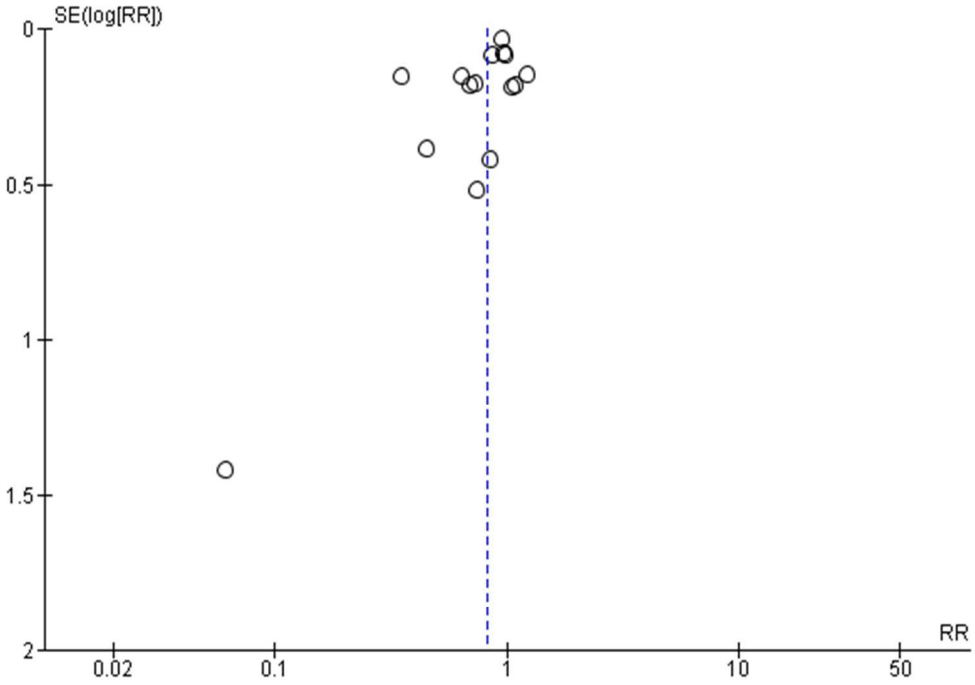
4.4.2 Subgroup analysis based on study design



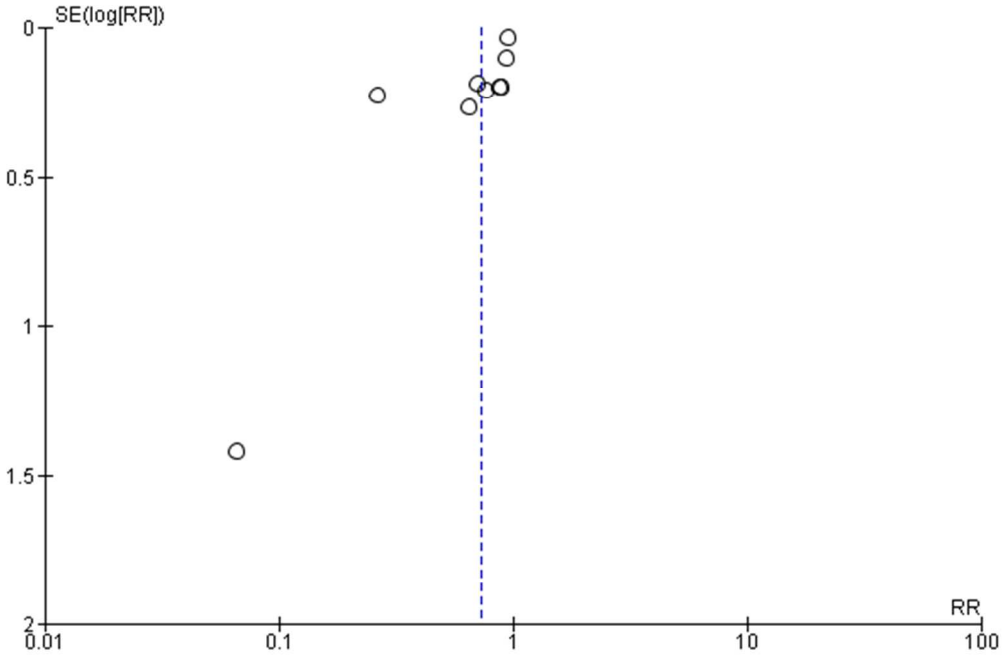
Appendix E

Funnel Plots

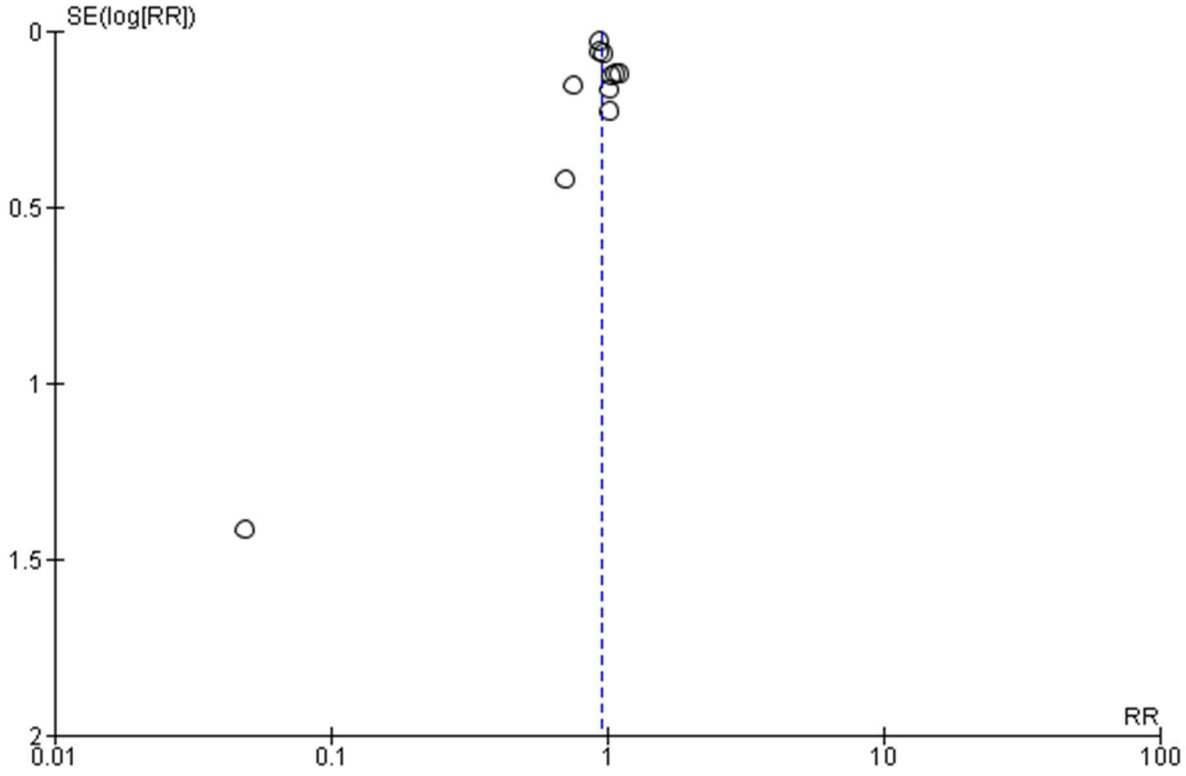
A. All-cause readmission Egger's test, p= 0.08; Begg's test, p=0.13



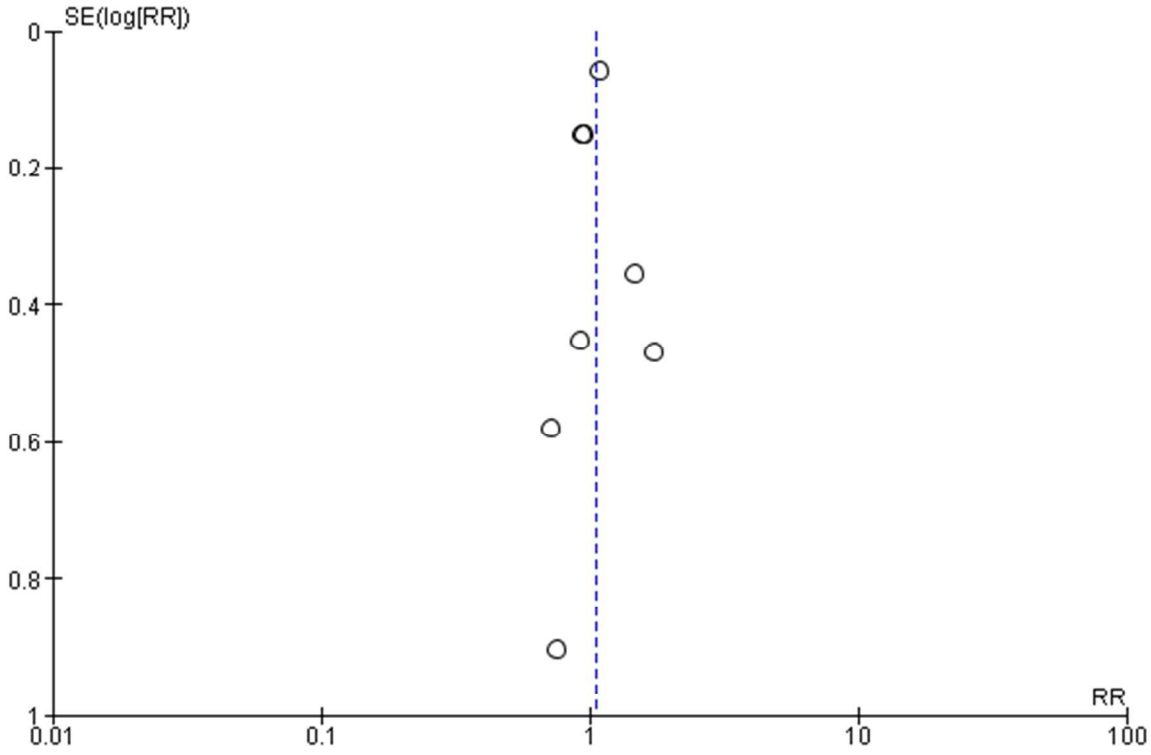
B. All-cause ED visit Egger's test, p= 0.04; Begg's test, p=0.01



C. **Composite readmission and/or ED visit** Egger's test, p= 0.57; Begg's test, p=0.35



D. **All-cause mortality** Egger's test p=0.83; Begg's test p=0.71



Funnel plots for the four outcomes for patients at hospital transitions. A) all-cause readmission B) all-cause ED visit C) composite readmission and/or ED visit D) all-cause mortality. The vertical line in the graphs corresponds to the pooled relative risk across studies.