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

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Effectiveness of pharmacy-led medication reconciliation programmes on clinical 1 2 outcomes at hospital transitions: A systematic review and meta-analysis 3 Alemayehu B. Mekonnen<sup>1</sup>, Andrew J. McLachlan<sup>1,2</sup>, 4 Jo-anne E. Brien<sup>1,3</sup> 5 <sup>1</sup>Faculty of Pharmacy, University of Sydney, Sydney, Australia 6 <sup>2</sup>Centre for Education and Research on Ageing, Concord Hospital, Sydney, Australia 7 <sup>3</sup>School of Medicine, St Vincent's Hospital, Sydney, Australia 8 9 10 Corresponding author: Alemayehu B. Mekonnen 11 Faculty of Pharmacy, The University of Sydney 12 A 15 Pharmacy and Bank building, NSW 2006 Tel: +61 2 9351 2363 13 Fax: +61 2 9351 4391 14 Email: aber5592@uni.sydney.edu.au 15 Abstract count- 298 16 Number of tables- 2 17 18 Number of figures- 3 Keywords- Medication reconciliation, medication history, medication safety, medication 19 review, medication errors, medication discrepancies, care transition, pharmacists, clinical 20 21 pharmacists 22 Running head- Effect of pharmacy-led medication reconciliation programmes 23 24 25

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#### 26 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

32 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

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analyses based on study design and outcome timing did not produced statistically significant 50 51 results. Conclusion: Pharmacy-led medication reconciliation programmes are effective at improving 52 post-hospital healthcare utilization. This review supports the implementation of pharmacy-led 53 54 medication reconciliation programmes that include some component aimed at improving 55 medication safety. 56 Strengths and limitations of this study 57 This is the first systematic review investigating the effect of pharmacy-led medication 58 59 reconciliation programs on clinical outcomes. In some of the clinical outcomes evaluated, there is substantial statistical 60 heterogeneity and we couldn't identify the source of variation among the studies. 61 The inclusion of non-controlled studies might affected the quality of evidence as seen 62 by the high risk of bias in these groups of studies. 63 64 65 66 67 68 69 70 71 72 73 74

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### 75 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.<sup>1</sup> Approximately 230,000 medication-related admissions occurred each year in Australia.<sup>2</sup> More than half of the medication problems occur at care transitions,<sup>3</sup> and up to one third of these problems has the potential to cause harm.<sup>4</sup> Unintentional medication changes are common at care transitions,<sup>4-9</sup> and responsible for a huge utilization of healthcare resources.<sup>10-14</sup>

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

The impact of medication reconciliation on clinical outcomes at hospital transitions were reported so far, however, two recently published systematic reviews<sup>32, 33</sup> 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, <sup>32</sup> Kwan et al <sup>33</sup> did not report significant association between post-hospital healthcare utilization and medication discrepancies identified through medication reconciliation interventions. Both reviews

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100 assessed broadly at the effect of medication reconciliation done by various strategies 101 including the use of collaborative models. The aim of the present review is thus, to assess 102 specifically the effectiveness of pharmacy-led medication reconciliation programmes 103 compared to usual care on clinical outcomes at hospital transitions.

104 Methods

105 Data sources and searches

The study was conducted utilising PRISMA group (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines, <sup>34</sup> 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). 

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- 120 Study selection
- 121 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].

125	- Studies which were published in English.
126	- The included interventions had to start in the hospital and must be performed
127	primarily by pharmacy personnel with the aim of improving care transitions to and
128	from a hospital.
129	- The intervention must be compared with a control group that received usual or
130	standard care.
131	Along with duplicate references and irrelevant studies, the following types of studies were
132	excluded:
133	- Other medication reconciliation practices or practices as part of a multicomponent
134	intervention, case studies, systematic reviews, qualitative outcomes, and non-research
135	articles.
136	- Abstracts from conferences and full texts without raw data available for retrieval were
137	not considered.
138	Therefore, the studies selected for inclusion and exclusion assessment were randomized
139	controlled trials (RCTs), quasi-experimental studies with a control group, and before-and-
140	after studies that evaluated pharmacy-led medication reconciliation programmes at hospital
141	care transitions.
142	Data extraction
143	Data were extracted from full texts using a modified adapted Cochrane EPOC data collection
144	checklist. <sup>35</sup> The following information was extracted from each included study: name of first
145	author, year of publication, country and setting where the study conducted, study design,
146	sample size, target of intervention, patient characteristics, components of intervention and
147	relevant outcomes and results. If insufficient details were reported, study authors were
148	contacted for further information.
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#### 150 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<sup>2</sup>, Chi-square (Q), I<sup>2</sup> and p-value. Sensitivity analysis was conducted to check the stability of summary estimates to outliers and the change in I<sup>2</sup> 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 Metaanalysis, V3 (Biostat, Englewood, NJ, USA). In all analyses, p-value < 0.05 was considered as statistically significant.

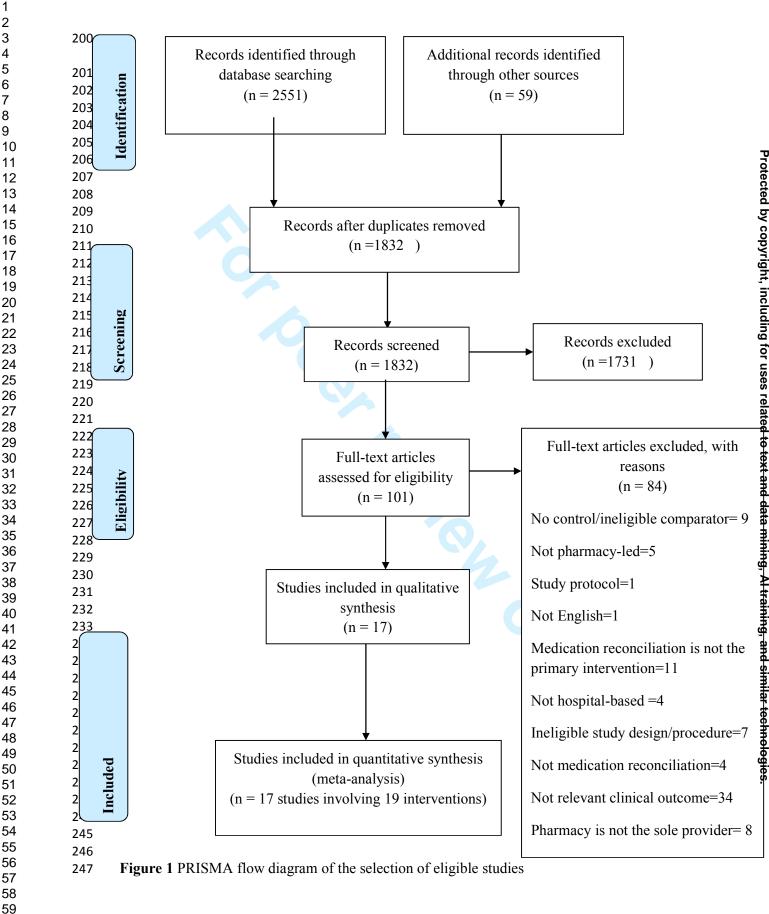
181 Risk of bias of individual studies was assessed with EPOC risk of bias tool.<sup>35</sup> The main 182 domains were random sequence generation, allocation concealment, blinding of outcome 183 assessment, attrition and reporting biases. We also determined whether groups were balanced 184 at baseline in terms of characteristics and outcomes.

**Results** 

#### 186 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). 

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#### 248 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, <sup>36-46</sup> 3 were conducted in Sweden, <sup>47-49</sup> 2 in Ireland<sup>50, 51</sup> and 1 in Australia.<sup>52</sup> 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.<sup>39, 50, 52</sup> 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 <sup>38, 47-51</sup> 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, <sup>45</sup> chronic obstructive pulmonary disease (COPD) <sup>37</sup> and mixed.<sup>38, 40, 49</sup> Methodologically, a study by Anderegg et al <sup>36</sup> 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,<sup>38</sup> 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 <sup>43, 47-50</sup> conducted medication review as part of their interventional component. Moreover, interventions were initiated at different care transitions; most were 

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273	conducted at multiple transitions <sup>36, 38-41, 43, 45, 47-52</sup> and all studies targeting a single transition
274	were carried out at the level of discharge. <sup>37, 42, 44, 46</sup> Results usually revealed a trend towards
275	improvement in most of the end-points studied: percentage of patients with readmissions, ED
276	visits, ADE-related hospital revisits (Table 1).
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# 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	Main results
Anderegg et al.	USA, single centre	Before-after	1664	1652	Admission,	Age 18 years	Mental illness /alcohol	Admission MeRrec,	30 days	Readmission,	30 d readmission and/or ED
2014 <sup>36</sup>					discharge	or older,	or drug use; discharge	Discharge MedRec,		Readmission	visit (general population): N
						discharge from	to a rehabilitation unit/	patient education,		and/or ED visit	In high-risk group, 30 d
						internal	long-term care	medication calendar			readmission : 12.3%(I) vs
					20,	medicine,	facility, readmission				17.8%(U) (p=0.042)
						family	for chemotherapy/				
						medicine,	radiation therapy/				
						cardiology, or	rehabilitation therapy				
						orthopedic					
						surgery					
						medical					
Bolas <i>et al.</i>	Ireland, single	RCT	81	81	In-patient	Age 55 years or	Transfer to another	Comprehensive	3	Readmission,	Readmission rate: p>0.05;
2004 <sup>51</sup>	centre				stay,	older, at least 3	hospital or nursing	medication history,	month	hospital stay	length of stay: p>0.05
					discharge,	regular	home, unable to	discharge letter faxed		(following	
					post discharge	medications	communicate, mental	to GP and		readmission)	
					F		illness or alcohol	community		)	
							related admission,	pharmacist,			
							follow up was	medicines record			
							declined	sheet, discharge			
							decimed	sheet, discharge			
						12					

1 2												
3 4												
5									counselling, home			
6 7									visit/telephone call			
8	Eisenhower	US, single centre	Before -after	25	60	Discharge	Age 65 years or	Left the hospital	Pharmacist MedRec	30 days	Readmission	Readmission rate, 16% (I) Vs
9 10	2014 <sup>37</sup>						older, with	without medical	at discharge,			22.2% (U)
11							history of	advice, death within	Medication			
12 13							COPD	30 d of discharge	reconciliation form,			
14									discharge summary			
15 16	Farris et al.	USA, Single centre	RCT	Minimal=312	313	Admission,	18 years or	Admission to	Admission MedRec,	90 days	ADEs,	16% experienced an AE,
17	2014 <sup>38</sup>			Enhanced=		in-patient	older, English	psychiatry, surgery or	patient education		readmission,	Health care utilization at 30
18 19				311		stay,	or Spanish	haematology/oncology	during inpatient stay,		ED visit,	days and 90 days: NS
20						discharge	speaker,	service, could	discharge		readmission	
21 22							diagnosis of	not use a telephone,	counselling,		and/or ED visit	
23							HPN,	had life expectancy <6	discharge medication			
24 25							hyperlipidemia,	months, had dementia	list, telephone call,			
26 27							HF, CAD, MI,	or cognitive	care plan faxed to			
28							stroke, TIA,	impairment	primary care			
29 30							asthma, COPD		physician/community			
31							or receiving		pharmacist			
32 33							oral					
34				1/04	7225	D 1 ' '	anticoagulation		<b>N</b> 1 1 1	60.1		
35 36	Gardella <i>et al.</i> 2012 <sup>39</sup>	US, multicentre	Before-after	1624	7335	Pre-admission	-	-	Preadmission	60 days	ADE, ED	30 day readmission: 6%(I) vs
37	20125					to post			medication list,		visits and	13.1% (U) [OR 2.34,
38 39						discharge			patient education		readmission	95%CI;1.87-2.94, p<0.001;
40												60 day readmission: 2.7% (I)
41 42												
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10	Gillespie <i>et al.</i> 2009 <sup>47</sup>	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,	12 month	Readmissions, ED visits, mortality	vs 7.7%(U) [OR 3.02, 95%CI; 2.18-4.19, p<0.001] Readmissions: 58.2%(I) vs 59.1%(U), OR 0.96 (0.64,1.46);
12 13									medication review,			ED visits per patient: 0.35 (I)
14 15									faxing discharge			vs 0.66 (U), OR 0.53
16 17									summary to primary care physicians,			(0.37,0.75)
18									telephone follow up			
19 20									at 2 months			
21	Hawes et al.	US, single centre	RCT	24	37	Discharge and	High risk	Age < 18 yrs, inability	Post-discharge	30 days	Readmission,	ED visit: 0 (I) vs 29.7%(U),
22 23	2014 <sup>40</sup>					post discharge	patients [ HF,	to communicate in	medication		ED visit,	p=0.004;
24 25							COPD,	English, unable to	reconciliation		readmission	Readmission: 0 (I) vs 32.4%
25 26							hyperglycaemic	follow up ( no			and /or ED visit	(U), p=0.002;
27 28							crisis, stroke	transportation and				composite of hospitalization or
20 29							,NSTEM, more	telephone				ED visit: 0 (I) vs 40.5% (C),
30 31							than 3	access), transfer to				p< 0.001
32							hospitalizations	other facilities other				
33 34							in the past 5	than primary care,				
35							yrs., 8 or more	decisional impairment,				
36 37							medications on	incarceration				
38							discharge]					
39 40	Hellstrom et al.	Sweden, single	Before-after	109	101	Admission,	Age 65 or	Staying during the	LIMM model,	3	Readmission	ED visit and readmission:
41												
42 43							14					
44												
45 46			ເຂຍເດີດເດເມເວລ		renieween	w.ehito://b	mionenvami	pape(sits/shout/s	น่สตรีเมธยานหมา	ייבים הא נ	רוטופר	
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1 2												
3 4 5	2011 <sup>48</sup>	contro				in-patient	older at least	implementation period	admission and	month	and ED visit,	45/108 (I) vs 41/100(U)
6	2011	centre					older, at least	implementation period		month		
7						stay,	one regular		discharge MedRec,		ADE related	Mortality, 3 month: 9/108 (I)
8 9						discharge	medication		medication review		hospital revisit	vs 9/100 (U)
10									and monitoring,			ADE related revisit: 6/108 (I)
11									quality control of			vs 12/100 (U)
12 13									discharge MedRec			
14	Hellstrom et al.	Sweden, single	Before- after	1216	2758	Admission,	High risk	-	Admission MedRec,	6	ED visits,	ED visit: 48.8% (I) vs 51.3%
15 16	201249	centre				inpatient stay	patients[ age		structured	month	hospital	(U) (HR, 0.95,95%CI, 0.86-
17							$\geq$ 65 with any of		medication reviews,		admissions and	1.04);
18 19							HF, RF]		follow up at least two		mortality	All ED visits, hospitalization
20									times a week			or death: 58.9% (I) vs 61.2%
21												(U) (HR,0.96;95%CI, 0.88-
22 23												1.04)
24												Mortality: 18.2% (I) vs
25 26												17.3%(U); p=0.55
27	Koehler et al.	US, single centre	RCT	20	21	Admission,	age 70 years or	Primarily surgical	Targeted care	60 days	Readmission	30 d readmission/ED visits:
28 29	200941					discharge and	older, $\geq 5$	procedure, life	bundle, medication		and/or ED	2/20 (I) vs 8/21(U) ( p= 0.03);
30						post discharge	medications, $\geq 3$	expectancy≤ 6	reconciliation and		visits	60 d readmission/ED visits:
31 32							chronic	months, residence in	education, follow up			6/20(I) vs 9/21(U) ( p= 0.52)
33							comorbid	long term care facility,	call, enhanced			
34 35							conditions,	refusal to participate,	discharge form			
36							assisted living,	not enrolled within 72				
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P       Pal et al. 2013 <sup>al</sup> US, single centre       NRCT       537       192       Discharge       Age 18 years or       -       Palentounseling       30 day       Readmission: 16.8%(1) valice         P       et al. 2013 <sup>al</sup> US, single centre       NRCT       537       192       Discharge       Age 18 years or       -       Palentounseling       30 day       Readmission: 16.8%(1) valice         P       et al. 2013 <sup>al</sup> US, single centre       NRCT       537       192       NRCT       Age 18 years or       -       Palentounseling       Palentounseling       30 day       Readmission: 16.8%(1) valice         P       et al. 2014 <sup>al</sup> US, single centre       NRCT       537       192       NRCT       -       -       Palentounseling       Palentounseling       ADE provented: 52.8%         P       schnipper et al.       US, single centre       RCT       92       84       In-patient       Discharge       -       Discharge       Discharge       Palentounseling       ADE provented: 52.8%       -       -       -       ADE provented: 52.8%       -       -       -       -       -       -       -       -       -       -       -       -       -       -       -       -       -
7       Pail et al. 2013       US, single centre       NC 1       3.7       192       Discharge       Age is years of -       Pattern counseling, 30 days       Readmission       So dreadmission       So dreadmission       So days       Readmission       ADE prevented: 52.8%         10       regular       medications       reconciliation,       medication calendar       medication calendar       medication       Readmission       So days       ADEs related       Preventable ADE: 1% (1) vs         15       2006 43       50       stay,       home,       medication       reconciliation,       readmission       ED visit/readmission: 30%(1) (P)         16       2006 43       stay,       home,       contacted 30       reconciliation,       readmission       ED visit/readmission: 30%(1)         18       soch 43       stay,       post discharge       contacted 30       age after       redefterior encoc
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10       nedication       nedication       ADE prevented: \$2.8%         11       nedication       nedication       reconciliation,       nedication calendar         12       schnipper et al.       US, single centre       RCT       92       84       In-patient       Discharge to       nedication calendar       nedication       nedication         14       Schnipper et al.       US, single centre       RCT       92       84       In-patient       Discharge to       -       Discharge       30 days       ADEs related       Preventable ADE: 1% (1) vs         15       2006 43       -       medication       nedication       nedication       nedication       in patient       in patient       Discharge       or catetd 30       reconciliation,       readmission       20%(1) (vp<0.9);
11 12 13redicationsreconciliation,14 14 15Schnipper et al.US, single centreRCT9284In-patientDischarge to 15 16Discharge to 16Discharge to 16
13       Schnipper et al.       US, single centre       RCT       92       84       In-patient       Discharge to       Discharge       30 days       ADEs related       Preventable ADE: 1% (1) vs         16       2006 43       -       Discharge to       -       medication calendar       hospital visit,       11% (U), p=0.01;         17       -       -       -       -       medication       reconciliation,       -       readmission       20%(1) (p>0.99);         18       -       -       -       -       discharge,       contacted 30       medication review,       -       readmission: 30%(1) (p>0.99);       vs 30%(U) (p>0.90;
14       Schnipper et al.       US, single centre       RCT       92       84       In-patient       Discharge to       Discharge to       Discharge to       30 days       ADEs related       Preventable ADE: 1% (1) vs         16       2006 43
16
17discharge,contacted 30reconciliation,readmissionED visit/readmission: 30%(I)18post dischargedays aftertelephone follow up,and/or ED visitvs 30%(U) (p>0.99);20discharge,medication review,preventable medication related21spoke English,standard emailhealthcare utilization: 1% (I)23cared fortemplate, patientvs 8%(U), p= 0.03
1919and of ED visitvs 50%(0) (p>0.55),20discharge,medication review,preventable medication related21spoke English,standard emailhealthcare utilization: 1% (I)23cared fortemplate, patientvs 8%(U), p= 0.03
20discharge,medication review,preventable medication related21spoke English,standard emailhealthcare utilization: 1% (I)22cared fortemplate, patientvs 8%(U), p= 0.03
2223cared fortemplate, patientvs 8%(U), p= 0.03
cared for template, patient vs 8%(U), p= 0.03
24 primary care counselling
26 physician/
27 28
29 medicine
30 resident 31
32 Scullin <i>et al.</i> Ireland, multicentre RCT 371 391 Admission, Age 65 or Scheduled admissions Admission and 12 Length of LoS reduced by 2 days for
<ul> <li>33 2007 <sup>50</sup></li> <li>34 in-patient older, at least 4 and admissions from discharge month hospital stay, intervention vs usual care,</li> </ul>
35 stay, regular private nursing homes medication readmission p=0.003
36dischargemedications,reconciliation,Readmissions per patient:0.837
37inpatient medication(I) vs 1(U)38
antidepressants, review and
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1													
2													
3 4													
5							previous		counselling, follow				
6 7							admission in		up telephone call				
8							the last 6						
9							months, taking						
10 11							IV antibiotics						
12	Stowasser et al.	Australia,	RCT	113	127	Admission,	Return to the	Outpatients, discharge	Medication history	30 days	Mortality,	Mortality 30 d; 2/113 (I) vs	
13 14	2002 52	multicentre				discharge	community	to hostel or nursing	confirmation with	2	readmission,	3/127 (U): NS	
15						C	following	home, previous	community health		ED visit	Readmissions; 12/113(I) vs	
16 17							discharge	enrolment, unable to	care professionals (			17/127(U)	
18							uisenuige	provide consent and	telephone, faxing),			ED visit per patient;7.54 (I) vs	
19								follow up	30 d post follow up			9.94(U)	
20 21	Walker <i>et al</i> .	US, single centre	NRCT	138	366	Discharge,	age 18 years or	Non English speaking,		30 days	Readmission,	Readmission at 14 d: 12.6%(I)	
22	2009 <sup>44</sup>	03, single centre	NKC I	156	500	-				50 days	,		
23 24 25	2009					post discharge	older, 5 or	stay of 21 days or	follow up plan,		ED visit,	vs 11.5% (U), p=0.65;	
25							more regular	longer	medication		readmission	Readmission at 30 d: 22.1%(I)	
26 27							medications,		counselling,		and/or ED visit	vs 18.0%(U), p = 0.17;	
28							receiving 1 or		telephone follow up			Readmissions and/or ED	
29							more targeted					visits: 27.4% (I) vs 25.7% (U),	
30 31							medications,					p= 0.61	
32							having 2 or						
33 34							more therapy						
35							modification,						
36 37							unable to						
37							manage their						
39							medication,						
40 41													
42							17						
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2 3												
4												
5							receiving a					
6 7							medication					
8							requiring					
9 10							therapeutic					
11							drug					
12							monitoring					
13 14	Warden et al.	US, single centre	Before-after	35	115	Admission,	Age 18-85	Diastolic dysfunction,	medication	30 days	Readmission	30 d all cause
15 16	2014 45					in-patient	years, systolic	valve replacement/left	reconciliation,			readmission:17%(I) vs 38%
17						stay,	dysfunction	ventricular assist	discharge			(U) [RR 0.45(0.21-0.96),
18						discharge	(EF ≤40)	device	instructions, follow			p=0.02],
19 20									up telephone call			30 d HF related readmission:
21												6%(I) vs 18%(U)[RR
22 23												0.31(0.08-1.27), p=0.11]
24	Wilkinson et al.	US, single centre	NRCT	229	440	Discharge	Age 18 years or	Refusal of	Medication history at	30 days	Readmission	Readmission rate: 15.7% (I)
24 25 26	2011 46						older , English	pharmacist education,	admission, during			vs 21.6% (U) [RR 0.728
27							speaking,	transfer to a skilled	hospitalization and			(0.514-1.032), p =0.04]
28 29							patients with	nursing facility, or	discharge, patient			
30							depression,	discharge when the	education upon			
31 32							receiving	pharmacist	discharge			
33							high-risk	was not available				
34 35							medications					
36							and					
37 38							polypharmacy,					
39							poor health					
40_ 41												
41							18					
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4 5	literacy,
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7	having an
8	absence of
9 10	social support,
11	prior
12	prior hospitalization within the last
13	
14 15	
16	6 months
17	Abbreviations: MedRec: medication reconciliation; I: intervention; U: usual care; RCT: randomized controlled trials; GP: general practitioner;
18	
19 20	CAD: coronary artery disease; MI: myocardial infarction; COPD: chronic obstructive pulmonary disease; HF: heart failure; HPN: hypertension;
20	
22	RF: renal failure; EF: ejection fraction; NSEMI: non-ST segment elevation myocardial infarction; LIMM: Lund Integrated Medicines
23	Management; LoS: length of stay; OR: odds ratio; RR: relative risk; CI: confidence interval
24 25	Wanagement, Los. length of stay, OK. odds fatto, KK. felative fisk, Cf. confidence interval
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#### 297 Risk of bias assessment

Patients included in the study were similar in the baseline characteristics except five studies <sup>37, 39, 40, 46, 49</sup> which were not clear or different in patient characteristics. However, in only three studies<sup>44, 49, 52</sup> that baseline clinical outcomes were reported or some form of adjustment analysis was performed. Eight out of 17 study reports<sup>38, 40, 41, 43, 47, 50-52</sup> provided enough details on randomization procedure to be judged as adequate. Among these studies, allocation concealment was fully described in all reports except one.<sup>52</sup> All but three studies <sup>44, 46, 51</sup>, either care providers and outcome assessors were blinded or objective health outcomes were reported. Five studies <sup>38, 42, 48, 49, 52</sup> 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.<sup>36, 38, 42, 48</sup> At least one of our outcomes of interest was selectively reported in four studies<sup>37, 50-52</sup> 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).

#### 311 Effect of interventions

Of the 14 studies that reported data on all-cause readmissions, 13 were eligible for metaanalysis. One study<sup>36</sup> measured this outcome for a high-risk population separately; and another study<sup>38</sup> reported it for two different interventions. Thus, 15 interventions were meta-analysed. Eight studies reported this outcome at 30 days<sup>36, 37, 40, 42, 44-46, 52</sup> while three <sup>47, 49, 50</sup> reported long term data and two studies<sup>38, 39</sup> reported both. Seven studies<sup>36, 39, 40, 42, 45, 46, 50</sup> 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<sup>36, 38-40, 44, 47, 49</sup> which measured ED visit as an outcome were pooled. 

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322	Considering studies that gave two data, 9 interventions were meta-analysed. The pooled
323	analysis across all interventions showed some significance difference between the
324	intervention and usual care (RR 0.72; 95% CI: 0.57-0.92) (Figure 2B). Evidence showed
325	extreme heterogeneity, however, the findings were different when Gardella et al <sup>39</sup> was
326	removed; no heterogeneity without affecting the significance (p=0.25; $I^2$ =22%, RR 0.89; 95%
327	CI 0.79-0.99). In 9 studies <sup>36, 38, 40, 41, 43, 44, 47-49</sup> , which reported composite all-cause
328	readmission and/or ED visit showed no difference in pooled analysis (RR 0.95; 95% CI:
329	0.90-1.00) (Figure 2C). Only 3 studies <sup>39, 43, 48</sup> were meta-analysed for ADE-related hospital
330	revisits. One study <sup>47</sup> didn't give data in a suitable form. The pooled result showed a
331	substantial reduction of 67% in hospital revisits (pooled RR 0.33; 95% CI: 0.20-0.53) when
332	pharmacy-led medication reconciliation programmes were implemented (Figure 2D). Seven
333	studies <sup>38, 47-52</sup> gave 8 separate data reporting all-cause mortality from 30 days to 12 months of
334	follow up. However, mortality data from Bolas et al <sup>51</sup> and Farris et al <sup>38</sup> is not their outcome of
335	interest and extracted from the reasons for exclusion of patients for their analysis. But, we
336	included in our meta-analysis. Overall, there was no significance difference between the two
337	groups in terms of all-cause mortality (RR 1.05; 95%CI: 0.95-1.16) (Figure 2E).

A

	Internet	41	Henel			Disk Datis	Diels Detie	
	Interver		Usual			Risk Ratio	Risk Ratio	ġ
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI	
Anderegg 2014 (Overall)	258	1652	270	1664	10.1%	0.96 [0.82, 1.13]	<b>†</b>	-
Anderegg 2014 [High-risk]	44	358	58	325	6.9%	0.69 [0.48, 0.99]		1
Eisenhower 2014	4	25	13	60	1.9%	0.74 [0.27, 2.05]		-
Farris 2014 [Enhanced]	49	311	47	313	6.8%	1.05 [0.73, 1.52]	+	
Farris 2014 (Minimal)	51	312	47	313	6.9%	1.09 [0.76, 1.57]	+	
Gardella 2012	44	1624	565	7335	7.8%	0.35 [0.26, 0.48]	-	;
Gillespie 2009	106	182	110	186	9.9%	0.98 [0.83, 1.17]	+	
Hawes 2014	0	24	12	37	0.3%	0.06 [0.00, 0.98]		
Hellstrom 2012	547	1216	1296	2758	11.0%	0.96 [0.89, 1.03]	+	9
Pal 2013	90	537	50	192	7.8%	0.64 [0.47, 0.87]		
Scullin 2007	141	371	172	391	9.9%	0.86 [0.73, 1.03]	-	ġ
Stowasser 2002	9	113	12	127	2.6%	0.84 [0.37, 1.93]		2
/Valker 2009	79	358	66	366	8.0%	1.22 [0.91, 1.64]	-	
Warden 2014	6	35	44	115	2.9%	0.45 [0.21, 0.96]		
Wilkinson 2011	36	229	95	440	7.1%	0.73 [0.51, 1.03]	-	
Total (95% CI)		7347		14622	100.0%	0.81 [0.70, 0.95]	•	
Total events	1464		2857					
Heterogeneity: Tau <sup>2</sup> = 0.05; C	hi <sup>2</sup> = 66.2	20, df = 1	14 (P < 0.	00001);	I <sup>2</sup> = 79%		0.001 0.1 1 10	1000
Test for overall effect: Z = 2.6	5 (P = 0.0	08)					Favours intervention Favours usual care	1000
							Favours intervention Favours usual care	

#### B

	Interver	ntion	Usual	care		Risk Ratio		Risk Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI		M-H, Random, 95% Cl	
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: Tau <sup>2</sup> = 0.09; (	Chi <sup>2</sup> = 42.2	26, df = 1	B (P < 0.0	0001); P	²= 81%		L		- 100
Test for overall effect: Z = 2.6	3 (P = 0.0	09)					0.01	0.1 1 10 Favours intervention Favours usual care	100
								avours intervention i avours usual care	

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	Intervention	usual	care		<b>Risk Ratio</b>	Risk Ratio	
Study or Subgroup	Events To	tal Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI	
Anderegg 2014 [Overall]	373 16	52 389	1664	15.4%	0.97 [0.85, 1.09]	+	
Anderegg 2014 [High-risk]	62 3	158 75	325	2.9%	0.75 [0.56, 1.01]		
Farris 2014 [Enhanced]	97 3	11 88	313	4.5%	1.11 [0.87, 1.41]	+-	
Farris 2014 (Minimal)	90 3	12 88	313	4.2%	1.03 [0.80, 1.32]	+	
Gillespie 2009	134 1	82 147	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 1	09 41	101	2.5%	1.02 [0.73, 1.41]	+	
Hellstrom 2012	645 12	16 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 3	58 94	366	4.5%	1.07 [0.84, 1.36]	+	
Total (95% CI)	46	34	6168	100.0%	0.95 [0.90, 1.00]		
Total events	1578	2526					
Heterogeneity: Tau <sup>2</sup> = 0.00;	Chi <sup>2</sup> = 10.62, d	lf = 10 (P = 0	.39); l² =	= 6%		0.01 0.1 1 10	1(
Test for overall effect: Z = 1.8	80 (P = 0.07)					Favours intervention Favours usual care	10
						Favours intervention Favours usual care	

D							
	Interver	tion	Usual o	care		<b>Risk Ratio</b>	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	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: Tau <sup>2</sup> =	0.00; Chi	<sup>2</sup> = 1.99	, df = 2 (P	= 0.37	); I <sup>2</sup> = 0%		0.01 0.1 1 10 10
Test for overall effect:	Z= 4.53 (	P < 0.00	0001)				Favours intervention Favours usual care

346

E

	Interver	tion	Usual	care		<b>Risk Ratio</b>	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
Bolas 2004	17	119	12	124	2.0%	1.48 [0.74, 2.96]	+
Farris 2014 [Enhanced]	12	311	7	313	1.1%	1.73 [0.69, 4.32]	
Farris 2014 [Minimal]	5	312	7	313	0.7%	0.72 [0.23, 2.23]	
Gillespie 2009	57	182	61	186	10.8%	0.95 [0.71, 1.29]	+
Hellstrom 2011	9	109	9	101	1.2%	0.93 [0.38, 2.24]	
Hellstrom 2012	330	1325	685	2965	73.0%	1.08 [0.96, 1.21]	
Scullin 2007	67	371	76	391	10.9%	0.93 [0.69, 1.25]	+
Stowasser 2002	2	113	3	127	0.3%	0.75 [0.13, 4.40]	
Total (95% CI)		2842		4520	100.0%	1.05 [0.95, 1.16]	•
Total events	499		860				
Heterogeneity: Tau <sup>2</sup> = 0.00	); Chi <sup>z</sup> = 3	.94, df=	7 (P = 0	.79); I <sup>z</sup> =	= 0%		
Test for overall effect: Z = 1	1.03 (P = 0	).30)					0.001 0.1 1 10 1000 Favours intervention Favours usual care

**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<sup>36</sup> stratified patients in two groups: general population and high-risk patient groups. Farris et al<sup>38</sup> randomized the population into different levels of intervention (minimal and enhanced).

355 Other outcomes

Studies reporting other clinically important outcomes are summarized in table 2. Some studies<sup>47-50</sup> furnished information on the proportion of patients who didn't revisit the hospital. The intervention group in the 3 studies <sup>47, 49, 50</sup> 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.

367							
Outcome		No of	No. of	RR	CI	WMD	CI
		studies	patients				
Patients w	who didn't revisit hospital	4	5314	1.10*	(1.03, 1.17)*		
Hospital s	stay (after readmission)	2	803			-0.57	(-5.32, 4.17)‡
Readmiss	sion per patient	3	1370			-0.12	(-0.24, 0.01)‡
ED visit p	per patient	2	4342			-0.15	(-0.53, 0.23)‡
Patients w	with ADE	3	1401	0.94	(0.75, 1.20)		
368 R	R: risk ratio; CI: confidence	ce interva	l; WMD: we	eighted m	ean difference		
369 †1	p<0.01						
	P 0.01						
	p>0.05						
370 ‡] 371 *R		n increase	ed the numbe	er of patie	ents didn't revisit	hospital (i.e	. it
370 ‡j 371 *R 372 sł 373	p>0.05 RR is > 1 when intervention howed success)	n increase	ed the numbe	er of patie	ents didn't revisit	hospital (i.e	. it
370       ‡]         371       *R         372       sh         373       373         374       Set	p>0.05 RR is > 1 when intervention howed success)			G			
370       ‡]         371       *R         372       sh         373       373         374       Se         375       A	p>0.05 RR is > 1 when intervention howed success) <b>Sensitivity analysis</b> A one-on-one removal of s	tudies in	the meta-an	alysis dic	In't affect finding	gs in all out	comes
370       ‡1         371       *R         372       sh         373       373         374       Se         375       A         376       ex	p>0.05 RR is > 1 when intervention howed success) Sensitivity analysis A one-on-one removal of so xcept for composite readn	tudies in nission/El	the meta-an D visit. A n	alysis dic neta-analy	dn't affect finding ysis for composit	gs in all out e readmissio	comes on/ED
370       ‡1         371       *R         372       sh         373       373         374       So         375       A         376       e2         377       vi	p>0.05 RR is > 1 when intervention howed success) <b>Gensitivity analysis</b> A one-on-one removal of so xcept for composite readn isit showed that, when Far	tudies in nission/El ris et al [	the meta-an D visit. A n enhanced] <sup>3</sup>	alysis dic neta-analy <sup>8</sup> or Haw	dn't affect finding ysis for composit es et al <sup>40</sup> were re	gs in all out re readmission removed, the	comes on/ED result
370       ‡1         371       *R         372       sh         373       373         374       So         375       A         376       en         377       vi	p>0.05 RR is > 1 when intervention howed success) Sensitivity analysis A one-on-one removal of so xcept for composite readn	tudies in nission/El ris et al [	the meta-an D visit. A n enhanced] <sup>3</sup>	alysis dic neta-analy <sup>8</sup> or Haw	dn't affect finding ysis for composit es et al <sup>40</sup> were re	gs in all out re readmission removed, the	comes on/ED result
370       ‡]         371       *R         372       sh         373       373         374       Sa         375       A         376       ex         377       vi         378       ha	p>0.05 RR is > 1 when intervention howed success) <b>Gensitivity analysis</b> A one-on-one removal of so xcept for composite readn isit showed that, when Far	tudies in nission/El ris et al [	the meta-an D visit. A n enhanced] <sup>3</sup>	alysis dic neta-analy <sup>8</sup> or Haw	dn't affect finding ysis for composit es et al <sup>40</sup> were re	gs in all out re readmission removed, the	comes on/ED result
370       ‡1         371       *R         372       sh         373       373         374       So         375       A         376       ex         377       vi         378       ha         379       re	p>0.05 RR is > 1 when intervention howed success) <b>Gensitivity analysis</b> A one-on-one removal of so xcept for composite readn isit showed that, when Fan ad a significant pooled sur	tudies in nission/El ris et al [	the meta-an D visit. A n enhanced] <sup>3</sup>	alysis dic neta-analy <sup>8</sup> or Haw	dn't affect finding ysis for composit es et al <sup>40</sup> were re	gs in all out re readmission removed, the	comes on/ED result
<ul> <li>370 ‡]</li> <li>371 *R</li> <li>372 sł</li> <li>373</li> <li>374 S</li> <li>375 A</li> <li>376 ez</li> <li>377 vi</li> <li>378 ha</li> <li>379 re</li> <li>380 Si</li> </ul>	p>0.05 RR is > 1 when intervention howed success) <b>Gensitivity analysis</b> A one-on-one removal of so xcept for composite readn isit showed that, when Fan ad a significant pooled sur espectively).	tudies in nission/El ris et al [ nmary es	the meta-an D visit. A n enhanced] <sup>3</sup> timate with	alysis dic neta-analy <sup>8</sup> or Haw similar ri	In't affect finding ysis for composit es et al <sup>40</sup> were re sk ratio (RR 0.95	gs in all out e readmission emoved, the s; p=0.02 and	comes on/ED result d 0.03
370       ‡1         371       *R         372       sh         373       374         375       A         376       e2         377       vi         378       ha         379       re         380       Si         381       Si	p>0.05 RR is > 1 when intervention howed success) <b>Gensitivity analysis</b> A one-on-one removal of so xcept for composite readn isit showed that, when Fan ad a significant pooled sur espectively).	tudies in nission/El ris et al [ nmary es compared	the meta-an D visit. A n enhanced] <sup>3</sup> timate with	alysis dic neta-analy <sup>8</sup> or Haw similar ri t reporte	In't affect finding ysis for composit es et al <sup>40</sup> were re sk ratio (RR 0.95 d all-cause readr	gs in all out e readmissio emoved, the c; p=0.02 and nissions at	comes on/ED result d 0.03 earlier
370       ‡1         371       *R         372       sh         373       374         375       A         376       e2         377       vi         378       ha         379       re         380       Si         381       Si         382       fc	p>0.05 RR is > 1 when intervention howed success) <b>Gensitivity analysis</b> A one-on-one removal of so xcept for composite readn isit showed that, when Fan ad a significant pooled sur espectively). <b>Subgroup analysis</b> Subgroup analysis which o	tudies in nission/El ris et al [ nmary es compared showed d	the meta-an D visit. A n enhanced] <sup>3</sup> timate with I studies tha	alysis dic neta-analy <sup>8</sup> or Haw similar ri th reporter erns of ef	In't affect finding ysis for composit es et al <sup>40</sup> were re sk ratio (RR 0.95 d all-cause readr ffect: the effect o	gs in all out e readmission emoved, the r; p=0.02 and nissions at f intervention	comes on/ED result d 0.03 earlier on was

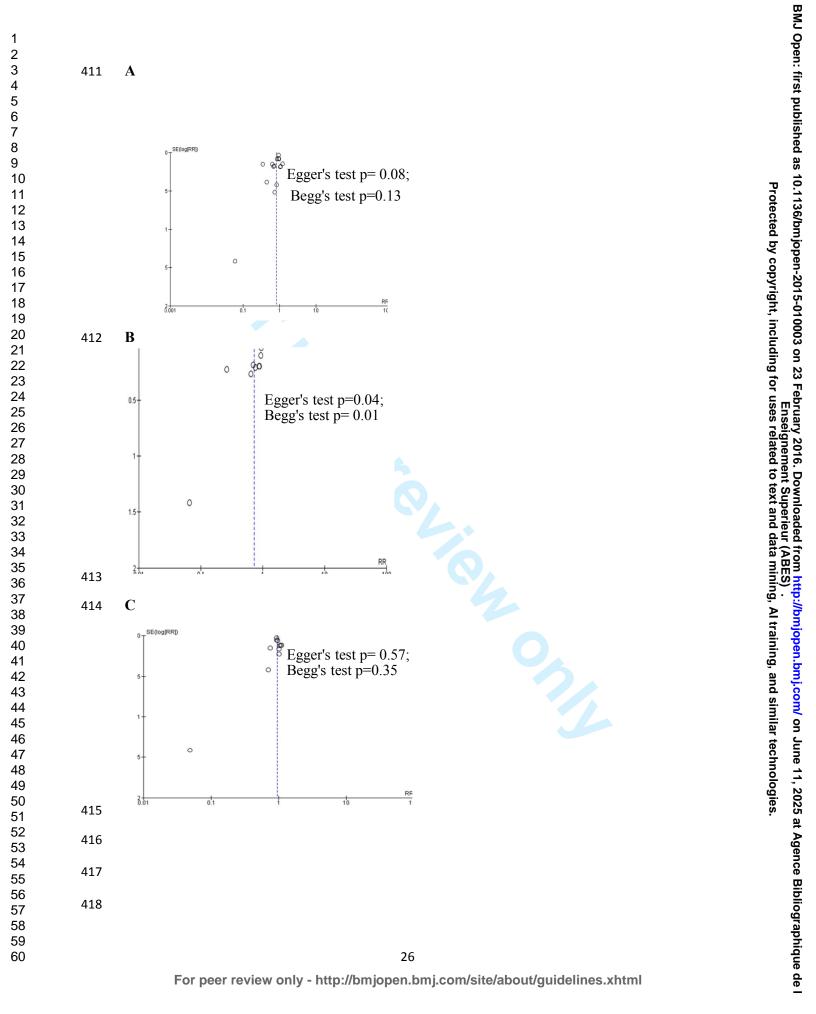
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0.60, 0.98, p=0.03). However, there was no significance difference between these two
subgroups. In addition, non-randomized studies showed a significant reduction in all-cause
readmission (RR 0.74, 95%CI 0.58, 0.94, p=0.01) and all-cause ED visit (RR 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 allcause 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).



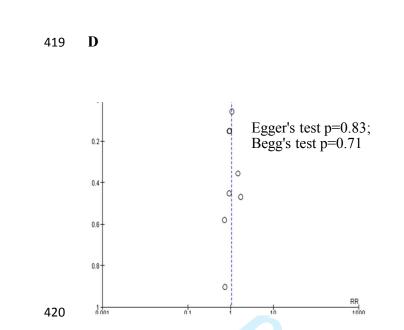


Figure 3 Funnel plots for the four outcomes for patients at hospital transitions. A) all-cause readmission B) all-cause ED visit C) composite readmission and/or ED visit D) all-cause mortality. The vertical line in the graphs corresponds to the pooled relative risk across studies.

#### 426 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). 

436 No previous reviews have been conclusively and consistently shown effectiveness of
437 medication reconciliation interventions; be it in the primary care,<sup>53</sup> long-term settings<sup>54</sup> or

hospital transitions.<sup>32,33</sup> 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. <sup>32, 33</sup> 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 <sup>55</sup> 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.<sup>43, 48</sup> Other studies also showed that medication discontinuity is the most common reason for discrepancy related ADE.<sup>56, 57</sup> Although Gillespie et al <sup>47</sup> 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; <sup>33</sup> 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

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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 <sup>58, 59</sup> 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<sup>58</sup> 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 <sup>59</sup> 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.

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A number of recent studies have investigated medication reconciliation interventions at the level of real practice models or as in integrated management of medicines.<sup>48-50</sup> 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-

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

#### 489 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<sup>60-63</sup> to 35-71% during discharge.<sup>5, 64,</sup> <sup>65</sup> Coleman et al <sup>66</sup> 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<sup>67</sup> 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.

#### 522 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.

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542 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.

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551 Competing interests

552 None declared.

553 Data sharing statement

554 No additional data are available.

**References** 

1. Kohn LT, Corrigan JM, Donaldson MS, editors. To Err is Human: Building a Safer

557 Health System: Committee on Quality of Health Care in America, Institute of Medicine.

558 Washington, DC: The National Academy Press; 2000.

2. Roughhead L, Semple S, Rosenfeld E. Literature review: Medication safety in
Australia. Australian Commission on Safety and Quality in Health Care, Sydney.2013.

#### **BMJ Open**

1		
2 3 4	561	Available at http://www.safetyandquality.gov.au/publications/literature-review-medication-
5 6	562	safety-in-australia/ (last accessed December 2014)
7 8	563	3. Rozich JD, Howard RJ, Justeson JM, et al. Standardization as a mechanism to
9 10	564	improve safety in health care. Jt Comm J Qual Saf 2004;30:5-14.
11 12 13	565	4. Cornish PL, Knowles SR, Marchesano R, et al. Unintended medication discrepancies
13 14 15	566	at the time of hospital admission. Arch Intern Med 2005;165:424-29.
16 17	567	5. Wong JD, Bajcar JM, Wong GG, et al. Medication reconciliation at hospital
18 19	568	discharge: evaluating discrepancies. Ann Pharmacother 2008;42:1373-79.
20 21	569	6. Pippins JR, Gandhi TK, Hamann C, et al. Classifying and predicting errors of
22 23 24	570	inpatient medication reconciliation. J Gen Intern Med 2008;23:1414-22.
24 25 26	571	7. Herrero-Herrero JI, Garcia-Aparicio J. Medication discrepancies at discharge from an
27 28	572	internal medicine service. Eur J Intern Med 2011; 22:43-48.
29 30	573	8. Geurts MM, Talsma J, Brouwers JR, <i>et al.</i> Medication review and reconciliation with
31 32	574	cooperation between pharmacist and general practitioner and the benefit for the patient: a
33 34 35	575	systematic review. Br J Clin Pharmacol 2012;74:16-33.
36 37	576	9. Allende Bandres MA, Arenere Mendoza M, Gutierrez Nicolas F, <i>et al.</i> Pharmacist-led
38 39	577	medication reconciliation to reduce discrepancies in transitions of care in Spain. Int J Clin
40 41	578	<i>Pharm</i> 2013; <b>35</b> :1083-90.
42 43	579	10. Howard RL, Avery AJ, Howard PD, et al. Investigation into the reasons for
44 45 46	580	preventable drug related admissions to a medical admissions unit: observational study. Qual
47 48	581	<i>Saf Health Care</i> 2003; <b>12</b> :280-85.
49 50	582	11. Witherington EM, Pirzada OM, Avery AJ. Communication gaps and readmissions to
51 52	583	hospital for patients aged 75 years and older: observational study. Qual Saf Health Care
53 54 55 56 57 58	584	2008; <b>17</b> :71-75.

585	12. Dedhia P, Kravet S, Bulger J, et al. A quality improvement intervention to facilitate
586	the transition of older adults from three hospitals back to their homes. J Am Geriatr Soc
587	2009; <b>57</b> :1540-46.
588	13. Schnipper JL, Hamann C, Ndumele CD, et al. Effect of an electronic medication
589	reconciliation application and process redesign on potential adverse drug events: a cluster-
590	randomized trial. Arch Intern Med 2009;169:771-80.
591	14. Jack BW, Chetty VK, Anthony D, <i>et al</i> . A reengineered hospital discharge program to
592	decrease rehospitalization: a randomized trial. Ann Intern Med 2009;150:178-87.
593	15. Institute for Healthcare Improvement. Medication reconciliation review: Available at
594	http://www.ihi.org/resources/Pages/Tools/MedicationReconciliationReview.aspx. (last
595	accessed 30 December 2014)
596	16. Joint Commission on Accreditation for Healthcare Organizations. National Patient
597	Safety Goals. 2006. Available at
598	http://www.jointcommission.org/Improving_Americas_Hospitals_The_Joint_Commissions_
599	Annual_Report_on_Quality_and_Safety2006/
600	17. National Institute for Health and Care Excellence. Technical patient safety solutions
601	for medicines reconciliation on admission of adults to hospital. London, 2007.
602	(NICE/NSPA/2007/PSG001). Available at: <u>www.nice.org.uk/PSG001</u> (last accessed 30
603	December 2014.
604	18. Canadian Council on Health Services Accreditation. Patient Safety Goals and
605	Required Organizational Practices. Ottawa, 2004. Available at: <u>www.accreditation.ca</u> (last
606	accessed 30 December 2014)
607	19. Australian Commission on Safety and Quality in Healthcare. Medication
608	reconciliation. Avialable at http://www.safetyandquality.gov.au/our-work/medication-
609	safety/medication-reconciliation/ (last accessed 30 December 2014)

#### **BMJ Open**

20. Duran-Garcia E, Fernandez-Llamazares CM, Calleja-Hernandez MA. Medication reconciliation: passing phase or real need? Inter J Clin Pharm 2012;34:797-802. Canadian Agency for Drugs and Techonlogies in Health. Medication reconciliation at 21. discharge: A review of the clinical evidence and guidelines. 2012. Available at http://www.cadth.ca/en/publication/3350 (last accessed 30 December 2014) 22. Gimenez Manzorro A, Zoni AC, Rodriguez Rieiro C, et al. Developing a programme for medication reconciliation at the time of admission into hospital. Int J Clin Pharm 2011;33:603-9. Schnipper JL, Liang CL, Hamann C, et al. Development of a tool within the 23. electronic medical record to facilitate medication reconciliation after hospital discharge. J Am Med Inform Assoc 2011;18:309-13. Moore P, Armitage G, Wright J, et al. Medicines reconciliation using a shared 24. electronic health care record. J Patient Saf 2011;7:148-54. 25. Bedard P, Tardif L, Ferland A, et al. A medication reconciliation form and its impact on the medical record in a paediatric hospital. J Eval Clin Pract 2011;17:222-7. 26. De Winter S, Vanbrabant P, Spriet I, et al. A simple tool to improve medication reconciliation at the emergency department. Eur J Intern Med 2011;22:382-5. De Winter S, Spriet I, Indevuyst C, et al. Pharmacist-versus physician-acquired 27. medication history: a prospective study at the emergency department. *Oual Saf Health Care* 2010;19:371-5. 28. Feldman LS, Costa LL, Feroli ER, et al. Nurse-pharmacist collaboration on medication reconciliation prevents potential harm. J Hosp Med 2012;7:396-401. 29. Greenwald JL, Halasyamani L, Greene J, et al. Making inpatient medication reconciliation patient centered, clinically relevant and implementable: a consensus statement on key principles and necessary first steps. J Hospital Med 2010;5:477-85.

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#### **BMJ Open**

635 30. Eggink RN, Lenderink AW, Widdershoven JW, *et al.* The effect of a clinical
636 pharmacist discharge service on medication discrepancies in patients with heart failure.
637 *Pharm World Sci* 2010;**32**:759-66.

Galvin M, Jago-Byrne MC, Fitzsimons M, *et al.* Clinical pharmacist's contribution to
medication reconciliation on admission to hospital in Ireland. *Int J Clin Pharm* 2013;**35**:1421.

641 32. Mueller SK, Sponsler KC, Kripalani S, *et al.* Hospital-based medication reconciliation
642 practices: a systematic review. *Arch Intern Med* 2012;**172**:1057-69.

643 33. Kwan JL, Lo L, Sampson M, et al. Medication reconciliation during transitions of
644 care as a patient safety strategy: a systematic review. *Ann Intern Med* 2013;158:397-403.

645 34. David Moher AL, Jennifer Tetzlaff, Douglas G. Altman, The PRISMA Group.
646 Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA
647 Statement. *PLoS Med* 2009;6:e1000097. doi:10.1371/journal.pmed.

648 35. Effective Practice and Organisation of Care (EPOC). [Data collection checklist and 649 risk of bias]. EPOC Resources for review authors. Oslo: Norwegian Knowledge Centre for 650 the Health Services; 2014. Available at: http://epoc.cochrane.org/epoc-specific-resources-651 review-authors (last accessed 30 Decmeber 2014).

652 36. Anderegg SV, Wilkinson ST, Couldry RJ, *et al.* Effects of a hospitalwide pharmacy
653 practice model change on readmission and return to emergency department rates. *Am J*654 *Health Syst Pharm* 2014;71:1469-79.

655 37. Eisenhower C. Impact of pharmacist-conducted medication reconciliation at discharge
656 on readmissions of elderly patients with COPD. *Ann Pharmacother* 2014;48:203-8.

657 38. Farris KB, Carter BL, Xu Y, *et al.* Effect of a care transition intervention by
658 pharmacists: an RCT. *BMC Health Serv Res* 2014;14:406.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

#### **BMJ Open**

39. Gardella JE, Cardwell TB, Nnadi M. Improving medication safety with accurate preadmission medication lists and postdischarge education. Jt Comm J Qual Patient Saf 2012;38:452-8. Hawes EM, Maxwell WD, White SF, et al. Impact of an outpatient pharmacist 40. intervention on medication discrepancies and health care resource utilization in posthospitalization care transitions. J Prim Care Community Health 2014;5:14-8. 41. Koehler BE, Richter KM, Youngblood L, et al. Reduction of 30-day postdischarge hospital readmission or emergency department (ED) visit rates in high-risk elderly medical patients through delivery of a targeted care bundle. J Hosp Med 2009;4:211-8. 42. Pal A, Babbott S, Wilkinson ST. Can the targeted use of a discharge pharmacist significantly decrease 30-day readmissions? Hosp Pharm 2013;48:380-8. 43. Schnipper JL, Kirwin JL, Cotugno MC, et al. Role of pharmacist counseling in preventing adverse drug events after hospitalization. Arch Intern Med 2006;166:565-71. 44. Walker PC, Bernstein SJ, Jones JN, et al. Impact of a pharmacist-facilitated hospital discharge program: A quasi-experimental study. Arch Intern Med 2009;169:2003-10. 45. Warden BA, Freels JP, Furuno JP, et al. Pharmacy-managed program for providing education and discharge instructions for patients with heart failure. Am J Health Syst Pharm 2014;71:134-9. Wilkinson ST, Pal A, Couldry RJ. Impacting readmission rates and patient 46. satisfaction: Results of a discharge pharmacist pilot program. Hosp Pharm 2011;46:876-83. 47. Gillespie U1, Alassaad A, Henrohn D, et al. A comprehensive pharmacist intervention to reduce morbidity in patients 80 years or older: a randomized controlled trial. Arch Intern Med 2009;169:894-900.

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#### Page 38 of 62

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Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies

#### **BMJ Open**

48. Hellstrom LM, Bondesson A, Hoglund P, *et al.* Impact of the Lund Integrated
Medicines Management (LIMM) model on medication appropriateness and drug-related
hospital revisits. *Eur J Clin Pharmacol* 2011;67:741-52.

49. Hellstrom LM, Hoglund P, Bondesson A, *et al.* Clinical implementation of systematic
medication reconciliation and review as part of the Lund Integrated Medicines Management
model--impact on all-cause emergency department revisits. *J Clin Pharm Ther* 2012;**37**:686-

688 92.

50. Scullin C, Scott MG, Hogg A, *et al.* An innovative approach to integrated medicines
management. *J Eval Clin Pract* 2007;**13**:781-8.

691 51. Bolas H, Brookes K, Scott M, *et al.* Evaluation of a hospital-based community liaison
692 pharmacy service in Northern Ireland. *Pharm World Sci* 2004;26:114-20.

52. Stowasser DA, Collins DM, Stowasser M. A randomised controlled trial of
medication liaison services - patient outcomes. *J Pharm Pract Res* 2002;**32**:133-40.

695 53. Bayoumi I, Howard M, Holbrook AM, *et al.* Interventions to improve medication
696 reconciliation in primary care. *Ann Pharmacother* 2009;43:1667-75.

697 54. Chhabra PT, Rattinger GB, Dutcher SK, *et al.* Medication reconciliation during the
698 transition to and from long-term care settings: a systematic review. *Res Social Adm Pharm*699 2012;8:60-75.

700 55. Rebecca Thomas ALH, Mala Mann, Dyfed Huws, *et al.* Pharmacist-led interventions
701 to reduce unplanned admissions for older people: a systematic review and meta-analysis of
702 randomised controlled trials. *Age Ageing* 2014; **43**:174–87.

703 56. Boockvar KS, Carlson LaCorte H, Giambanco V, et al. Medication reconciliation for

reducing drug-discrepancy adverse events. *Am J Geriatr Pharmacother* 2006;4:236-43.

#### **BMJ Open**

57. Mergenhagen KA, Blum SS, Kugler A, et al. Pharmacist versus physician-initiated admission medication reconciliation: impact on adverse drug events. Am J Geriatr Pharmacother 2012;10:242-50. Holland R, Desborough J, Goodyer L, et al. Does pharmacist-led medication review 58. help to reduce hospital admissions and deaths in older people? A systematic review and metaanalysis. Br J Clin Pharmacol 2008;65:303-16. 59. Christensen M, Lundh A. Medication review in hospitalised patients to reduce morbidity and mortality. Cochrane Database of Syst Rev 2013;2:CD008986. 60. Coffey M, Mack L, Streitenberger K, et al. Prevalence and clinical significance of medication discrepancies at pediatric hospital admission. Acad Pediatr 2009;9:360-5. 61. Gleason KM, Groszek JM, Sullivan C, et al. Reconciliation of discrepancies in medication histories and admission orders of newly hospitalized patients. Am J Health Syst Pharm 2004;61:1689-95. 62. Salanitro AH, Osborn CY, Schnipper JL, et al. Effect of patient- and medication-related factors on inpatient medication reconciliation errors. J Gen Intern Med 2012;27:924-32. 63. Villanyi D, Fok M, Wong RY. Medication reconciliation: identifying medication 

discrepancies in acutely ill hospitalized older adults. *Am J Geriatr Pharmacother* 2011;9:33944.

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64. Manias E, Gerdtz MF, Weiland TJ, *et al.* Medication use across transition points from
the emergency department: Identifying factors associated with medication discrepancies. *Ann Pharmacother* 2009;43:1755-64.

65. Grimes T, Delaney T, Duggan C, et al. Survey of medication documentation at
hospital discharge: Implications for patient safety and continuity of care. *Ir J Med Sci*2008;177:93-7.

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data mining, AI training, and similar technologies

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 prevalence and contributing factors. Arch Intern Med 2005;165:1842-7.

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

## PRISMA 2009 Checklist

Section/topic	ion/topic # Checklist item						
TITLE							
Title       1       Identify the report as a systematic review, meta-analysis, or both.							
ABSTRACT							
2 Structured summary 3 4	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.						
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.					
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.					
) 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 .səibo	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I <sup>2</sup> for each meta analysis ເວັ້ນງວ່າ ເຂົ້າເພື່ອກິນຮູ້ ອີນເປັນເຊິ່ງ ອີນເປັນເປັນເອົາອາຍຸລາວ ເວລາອີດອີນຮູ້ອີນເອົາຮູ້ອີນເອົາເອົາເຮັດໃຫ້ເຫັນເອົາ	7 and 8				
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## **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.					
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	I <u> </u>						
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				

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Appendix A

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**Electronic database Searches** 

Medline, IPA and PsychINFO

((medic\$ or drug\$) adj2 discrepanc\$).mp.

((medic\$ or drug\$) adj2 histor\$).mp.

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8 ((medic\$ or drug\$) adj2 management).mp.

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record\$)) adj2 review\$).mp.

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Searches

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**Results** 

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9 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8
10 patient admission.mp. or Patient Admission/
11 patient discharge.mp. or Patient Discharge
12 patient transfer.mp. or Patient Transfer/
13 Hospitalization/ or hospital transfer.mp.
14 "Continuity of Patient Care"/ or care transition.mp.
15 inpatients.mp. or Inpatients/
16 seamless care.mp.
17 continuum of care.mp.
18 "Delivery of Health Care, Integrated"/ or integrated health care.mp.
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# Searches	Results
S18 S14 AND S15 AND S16 Limiters-Peer Reviewed; English L Abstract Available	anguage; 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 Discharge+")	(MH "Patient 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	

#### Embase

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

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#### 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." <u>Pharmacotherapy:The Journal of Human Pharmacology & Drug Therapy</u> **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." <u>Annals of</u> Pharmacotherapy **46**(4): 484-494.

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

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

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

Midlov, P., et al. (2012). "The effect of medication reconciliation in elderly patients at hospital discharge." <u>International Journal of Clinical Pharmacy</u> **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." <u>American Journal of Health-System Pharmacy</u> **65**(9): 857-860.

#### **BMJ Open**

#### 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." <u>American Journal of Health-System Pharmacy</u> **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." <u>Archives of Internal Medicine</u> **169**(8): 771-780.

Showalter, J. W., et al. (2011). "Effect of standardized electronic discharge instructions on postdischarge 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." <u>European Journal of Internal Medicine</u> **23**(8): 696-700.

#### **Study Protocol**

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

#### <u>Not English</u>

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

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#### Medication reconciliation is not the primary intervention

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

Lisby M et al (2010). "The effect of systematic medication review in elderly patients admitted to an acute ward of Internal Medicine". <u>Basic & Clinical Pharmacology & Toxicology</u> 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." <u>Anaesthesia</u> <u>and Intensive Care</u> **39**(6): 1064-1070.

Nazareth, I., et al. (2001). "A pharmacy discharge plan for hospitalized elderly patients--a randomized controlled trial." <u>Age & Ageing 30(1)</u>: 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)." <u>American Journal of Medical Quality</u> **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." <u>J Am Geriatr Soc</u> **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." <u>Am J Med Qual</u> **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". <u>Arch Intern Med</u> 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." <u>Pharm Pract (Granada)</u> **12**(1): 360.

#### Ineligible study design/procedure

Carter, M. K., et al. (2006). "Pharmacist-acquired medication histories in a university hospital emergency department." <u>American Journal of Health-System Pharmacy</u> **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." <u>Annals of Pharmacotherapy</u> **43**(6): 1001-1010.

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Musgrave, C. R., et al. (2013). "Improving transplant patient safety through pharmacist discharge medication reconciliation." <u>American Journal of Transplantation</u> **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 techniciancentered 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." <u>American Journal of Geriatric Pharmacotherapy</u> **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." <u>American</u> 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." <u>Stroke</u> 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 <u>Pharmacy & Therapeutics</u> **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 <u>Care</u> **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". <u>Br J Clin Pharmacol</u> 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." <u>J Eval Clin</u> <u>Pract</u> **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." <u>Hospital Pharmacy</u> **47**(12): 927-932.

Bergkvist, A., et al. (2009). "Improved quality in the hospital discharge summary reduces medication errors--LIMM: Landskrona Integrated Medicines Management." <u>European Journal of Clinical Pharmacology</u> **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." <u>Emerg Med Australas</u> **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." <u>American Journal of Health-System</u> <u>Pharmacy</u>: 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.

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Grant, R. W., et al. (2003). "Improving Adherence and Reducing Medication Discrepancies in Patients with Diabetes." <u>Ann Pharmacother</u> **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." <u>BMJ Open 3(7)</u>.

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

Hick, H. L., et al. (2001). "The impact of the pharmacist on an elective general surgery preadmission clinic." <u>Pharmacy World & Science</u> **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." <u>International Journal of Pharmacy Practice</u> **13**(3): 179-185.

Tompson, A. J., et al. (2012). "Utilizing community pharmacy dispensing records to disclose errors in hospital admission drug charts." <u>International Journal of Clinical Pharmacology &</u> <u>Therapeutics</u> **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." <u>Healthcare Quarterly</u> 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, nursepharmacist intervention for improving the accuracy of the medication history." <u>J Patient Saf</u> **10**(2): 88-94.

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

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

		(2009). "Effectiveness ies for patients transition			
Journal	of	Health-System	Pharmacy	<b>66</b> (22):	2027-2031.

#### Appendix C

Summary of risk of bias assessment\*

Study reference	Randomiza tion	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;  -: unclea EPOC risk of bias asses	r; ?: not done sment; modified fo	or non- controlled s	studies							

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#### Appendix D

Subgroup analysis

#### 4.1 All-cause Readmission

#### 4.1.1 Subgroup analysis based on outcome timing

	-					-	
	Interve	ntion	Usual	care		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
2.2.1 Readmission, 30 d							
Anderegg 2014 [Overall]	258	1652	270	1664	7.8%	0.96 [0.82, 1.13]	+
Anderegg 2014 [High-risk]	44	358	58	325	6.0%	0.69 [0.48, 0.99]	
Eisenhower 2014	4	25	13	60	2.0%	0.74 [0.27, 2.05]	
Farris 2014 [Enhanced]	47	311	43	313	5.8%	1.10 [0.75, 1.61]	
Farris 2014 [Minimal]	40	312	43	313	5.6%	0.93 [0.62, 1.39]	
Gardella 2012	97	1624	961	7335	7.4%	0.46 [0.37, 0.56]	-
Hawes 2014	0	24	12	37	0.3%	0.06 [0.00, 0.98]	← ~
Pal 2013	90	537	50	192	6.5%	0.64 [0.47, 0.87]	
Stowasser 2002	9	113	12	127	2.7%	0.84 [0.37, 1.93]	
Walker 2009	79	358	66	366	6.6%	1.22 [0.91, 1.64]	+
Warden 2014	2	35	21	115	1.2%	0.31 [0.08, 1.27]	
Wilkinson 2011	36	229	95	440	6.1%	0.73 [0.51, 1.03]	
Subtotal (95% CI)		5578		11287		0.77 [0.60, 0.98]	◆
Total events	706		1644				
Heterogeneity: Tau <sup>2</sup> = 0.12; (		- df = 7		000011	I <sup>2</sup> = 80%		
Test for overall effect: Z = 2.1					1 - 00 %		
	- (, ,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	-,					
2.2.2 Readmission > 30 d							
Farris 2014 [Enhanced]	49	311	47	313	5.9%	1.05 [0.73, 1.52]	<u> </u>
Farris 2014 [Minimal]	51	312	47	313	5.9%	1.09 [0.76, 1.57]	_ <b>_</b>
Gardella 2012	44	1624	565	7335	6.5%	0.35 [0.26, 0.48]	
Gillespie 2009	106	182	110	186	7.7%	0.98 [0.83, 1.17]	
Hellstrom 2012	547	1216	1296	2758	8.2%	0.96 [0.89, 1.03]	-
Scullin 2007	141	371	172	391	7.7%	0.86 [0.73, 1.03]	-
Subtotal (95% CI)		4016		11296	42.0%	0.83 [0.66, 1.06]	•
Total events	938		2237				•
Heterogeneity: Tau <sup>2</sup> = 0.07; (		15 df = 1		10001\· P	<sup>2</sup> = 89%		
Test for overall effect: Z = 1.4			0.0	,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	- 00 %		
		·/					
Total (95% CI)		9594		22583	100.0%	0.80 [0.68, 0.94]	•
Total events	1644		3881				
Heterogeneity: Tau <sup>2</sup> = 0.08; (		.86. df=		0.00001	): I <sup>2</sup> = 85%	6	
Test for overall effect: Z = 2.7							0.01 0.1 1 10 1
Test for subgroup difference			= 1 (P = 0	1.63) I <sup>2</sup> =	0%		Favours intervention Favours usual care
i control constructor anteresso					• • •		

4.1.2 Subgroup	analysis ba	ased on s	study design
1.1.2 Subgroup	unurysis of	used on t	fudy design

Study or Subgroup	Interver Events		Usual		Weight	Risk Ratio M-H, Random, 95% Cl	Risk Ratio M-H, Random, 95% Cl
2.3.1 RCT	Erenta	10101	Lionta	Total	reight		
Farris 2014 [Enhanced]	49	311	47	313	6.9%	1.05 [0.73, 1.52]	<u> </u>
Farris 2014 [Minimal]	51	312	47	313	7.0%	1.09 [0.76, 1.57]	T
Gillespie 2009	106	182	110	186	10.1%	0.98 [0.83, 1.17]	T
Hawes 2014	0	24	12	37	0.3%	0.06 [0.00, 0.98]	• • • • • • • • • • • • • • • • • • •
Scullin 2007	141	371	172	391	10.1%	0.86 [0.73, 1.03]	*
Stowasser 2002	9	113	12	127	2.6%	0.84 [0.37, 1.93]	
Subtotal (95% CI)		1313		1367	37.1%	0.95 [0.83, 1.08]	•
Total events	356		400				
Heterogeneity: Tau² = 0.00; ( Test for overall effect: Z = 0.8			(P = 0.30	)); I² = 18	1%		
2.3.2 NRCT							
Anderegg 2014 [Overall]	258	1652	270	1664	10.3%	0.96 [0.82, 1.13]	4
	44	358	58	325	7.0%		
Anderegg 2014 [High-risk]						0.69 [0.48, 0.99]	
Eisenhower 2014	4	25	13	60	1.9%	0.74 [0.27, 2.05]	
Gardella 2012	44	1624	565	7335	8.0%	0.35 [0.26, 0.48]	
Hellstrom 2012	547	1216	1296	2758	11.3%	0.96 [0.89, 1.03]	1
Pal 2013	90	537	50	192	7.9%	0.64 [0.47, 0.87]	
Walker 2009	79	358	66	366	8.1%	1.22 [0.91, 1.64]	+
Warden 2014	2	35	21	115	1.1%	0.31 [0.08, 1.27]	
Wilkinson 2011	36	229	95	440	7.2%	0.73 [0.51, 1.03]	
Subtotal (95% CI)		6034		13255		0.74 [0.58, 0.94]	•
Total events	1104		2434				•
Heterogeneity: Tau <sup>2</sup> = 0.09; (		58 df = 9		100011-8	= 86%		
Test for overall effect: Z = 2.4			5 (r × 0.0	,0001),1	- 00%		
Total (95% CI)		7347		14622	100.0%	0.82 [0.70, 0.96]	•
Total events	1460		2834				
Heterogeneity: Tau <sup>2</sup> = 0.05; (	$Chi^{2} = 65.1$	13 df=1	14 (P < 0)	00001)	$ ^2 = 79\%$		0.01 0.1 1 10
.2 All-cause ED	visits						
.2.1 Subgroup an	alysis	base	ed on	outco	ome ti	iming	
	-					_	

	Interver	ntion	Usual	care		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% Cl
1.1.1 ED visit, 30 d							
Anderegg 2014 [High-risk]	22	358	31	325	7.8%	0.64 (0.38, 1.09)	
Anderegg 2014 (Overall)	155	1652	168	1664	10.0%	0.93 [0.76, 1.14]	+
Farris 2014 [Enhanced]	38	311	52	313	8.8%	0.74 [0.50, 1.08]	
Farris 2014 [Minimal]	49	312	52	313	9.1%	0.95 [0.66, 1.35]	-
Gardella 2012	37	1424	785	7199	9.3%	0.24 [0.17, 0.33]	
Hawes 2014	0	24	11	37	1.0%	0.07 [0.00, 1.07]	• · · · · · · · · · · · · · · · · · · ·
Walker 2009	34	358	45	366	8.6%	0.77 [0.51, 1.18]	
Subtotal (95% CI)		4439		10217	54.6%	0.61 [0.38, 0.99]	◆
Total events	335		1144				
Heterogeneity: Tau <sup>2</sup> = 0.33; (	Chi <sup>2</sup> = 60.9	98, df = 6	6 (P < 0.0	0001); P	²= 90%		
Test for overall effect: Z = 1.9	38 (P = 0.0	5)					
1.1.2 ED visit,> 30 d							
Farris 2014 [Enhanced]	41	311	46	313	8.8%	0.90 [0.61, 1.33]	
Farris 2014 [Minimal]	40	312	46	313	8.8%	0.87 [0.59, 1.29]	
	40 20	312 1424	46 381	313 7199	8.8% 8.4%	0.87 [0.59, 1.29] 0.27 [0.17, 0.41]	
Farris 2014 [Minimal]			10.00				
Farris 2014 (Minimal) Gardella 2012	20	1424 182 1216	381	7199 186 2758	8.4%	0.27 [0.17, 0.41]	
Farris 2014 [Minimal] Gardella 2012 Gillespie 2009	20 36	1424 182	381 52	7199 186	8.4% 9.0%	0.27 [0.17, 0.41] 0.71 [0.49, 1.03]	
Farris 2014 [Minimal] Gardella 2012 Gillespie 2009 Hellstrom 2012	20 36	1424 182 1216	381 52	7199 186 2758	8.4% 9.0% 10.5%	0.27 [0.17, 0.41] 0.71 [0.49, 1.03] 0.95 [0.89, 1.02]	
Farris 2014 [Minimal] Gardella 2012 Gillespie 2009 Hellstrom 2012 Subtotal (95% CI)	20 36 594 731	1424 182 1216 <b>3445</b>	381 52 1416 1941	7199 186 2758 <b>10769</b>	8.4% 9.0% 10.5% <mark>45.4</mark> %	0.27 [0.17, 0.41] 0.71 [0.49, 1.03] 0.95 [0.89, 1.02]	
Farris 2014 [Minimal] Gardella 2012 Gillespie 2009 Hellstrom 2012 Subtotal (95% CI) Total events	20 36 594 731 Chi <sup>2</sup> = 36.4	1424 182 1216 3445	381 52 1416 1941	7199 186 2758 <b>10769</b>	8.4% 9.0% 10.5% <mark>45.4</mark> %	0.27 [0.17, 0.41] 0.71 [0.49, 1.03] 0.95 [0.89, 1.02]	
Farris 2014 [Minimal] Gardella 2012 Gillespie 2009 Hellstrom 2012 Subtotal (95% CI) Total events Heterogeneity: Tau <sup>2</sup> = 0.18; (	20 36 594 731 Chi <sup>2</sup> = 36.4	1424 182 1216 3445	381 52 1416 1941	7199 186 2758 <b>10769</b> 0001); P	8.4% 9.0% 10.5% <mark>45.4</mark> %	0.27 [0.17, 0.41] 0.71 [0.49, 1.03] 0.95 [0.89, 1.02]	
Farris 2014 [Minimal] Gardella 2012 Gillespie 2009 Hellstrom 2012 Subtotal (95% CI) Total events Heterogeneity: Tau <sup>2</sup> = 0.18; Test for overall effect: Z = 1.6	20 36 594 731 Chi <sup>2</sup> = 36.4	1424 182 1216 3445 1, df = 4 7)	381 52 1416 1941	7199 186 2758 <b>10769</b> 0001); P	8.4% 9.0% 10.5% 45.4% *= 89%	0.27 (0.17, 0.41) 0.71 (0.49, 1.03) 0.95 (0.89, 1.02) 0.69 (0.46, 1.03)	
Farris 2014 [Minimal] Gardella 2012 Gillespie 2009 Hellstrom 2012 Subtotal (95% CI) Total events Heterogeneity: Tau <sup>2</sup> = 0.18; Test for overall effect: Z = 1.8 Total (95% CI) Total events	20 36 594 731 Chi <sup>2</sup> = 36.4 80 (P = 0.0 1066	1424 182 1216 3445 11, df = 4 7) 7884	381 52 1416 1941 4 (P < 0.0 3085	7199 186 2758 <b>10769</b> 0001); P <b>20986</b>	8.4% 9.0% 10.5% 45.4% <sup>2</sup> = 89% 100.0%	0.27 [0.17, 0.41] 0.71 [0.49, 1.03] 0.95 [0.89, 1.02] 0.69 [0.46, 1.03] 0.65 [0.49, 0.87]	
Farris 2014 [Minimal] Gardella 2012 Gillespie 2009 Hellstrom 2012 Subtotal (95% CI) Total events Heterogeneity: Tau <sup>2</sup> = 0.18; Test for overall effect: Z = 1.8 Total (95% CI)	20 36 594 731 Chi <sup>a</sup> = 36.4 80 (P = 0.0 1066 Chi <sup>a</sup> = 121	1424 182 1216 3445 41, df = 4 7) 7884 .03, df =	381 52 1416 1941 4 (P < 0.0 3085	7199 186 2758 <b>10769</b> 0001); P <b>20986</b>	8.4% 9.0% 10.5% 45.4% <sup>2</sup> = 89% 100.0%	0.27 [0.17, 0.41] 0.71 [0.49, 1.03] 0.95 [0.89, 1.02] 0.69 [0.46, 1.03] 0.65 [0.49, 0.87]	0.01 0.1 10 1 Favours intervention Favours usual care

#### 4.2.2 Subgroup analysis based on study design

	Interver	ntion	Usual	care		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
1.2.1 RCT							
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]	
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]	· · · · · · · · · · · · · · · · · · ·
Subtotal (95% CI)		829		849	36.4%	0.80 [0.61, 1.05]	•
Total events	117		155				
Heterogeneity: Tau <sup>2</sup> = 0.02; 0			(P = 0.25	); I² = 27	%		
Test for overall effect: Z = 1.6	i0 (P = 0.1	1)					
1.2.2 NRCT							
Anderegg 2014 [High-risk]	22	358	31	325	9.4%	0.64 [0.38, 1.09]	
Anderegg 2014 [Overall]	155	1652	168	1664	15.2%	0.93 [0.76, 1.14]	+
Gardella 2012	20	1424	381	7199	10.8%	0.27 [0.17, 0.41]	
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]	
Subtotal (95% CI)		5008		12312	63.6%	0.68 [0.48, 0.97]	$\bullet$
Total events	825		2041				
Heterogeneity: Tau <sup>2</sup> = 0.13; 0			4 (P < 0.0	0001); P	²= 89%		
Test for overall effect: Z = 2.1	5 (P = 0.0	3)					
Total (95% CI)		5837		13161	100.0%	0.72 [0.57, 0.92]	•
Total events	942		2196				
Heterogeneity: Tau <sup>2</sup> = 0.09; 0	Chi² = 42.2	26, df =	8 (P < 0.0	0001); P	²= 81%		0.01 0.1 1 10 100
Test for overall effect: Z = 2.6	3 (P = 0.0	09)					Favours intervention Favours usual care
Test for subgroup difference	s: Chi <sup>2</sup> = (	).49, df	= 1 (P = 0	.49), 12=	0%		avours intervention Tavours usual care

#### 4.3 All-cause mortality

#### 4.3.1 Subgroup analysis based on outcome timing

	Interver		Usual			Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% CI
1.4.1 Mortality, 30 d							
Stowasser 2002	2	113	3	127	0.3%	0.75 [0.13, 4.40]	
Subtotal (95% CI)		113		127	0.3%	0.75 [0.13, 4.40]	
Total events	2		3				
Heterogeneity: Not applic							
Test for overall effect: Z =	0.32 (P = 1)	J.75)					
1.4.2 Mortality, >30 d							
Bolas 2004	17	119	12	124	1.9%	1.48 [0.74, 2.96]	
Farris 2014 [Enhanced]	12	311	7	313	1.1%	1.73 [0.69, 4.32]	+
Farris 2014 [Minimal]	5	312	7	313	0.7%	0.72 [0.23, 2.23]	
Gillespie 2009	70	199	75	201	13.6%	0.94 [0.73, 1.22]	+
Hellstrom 2011	9	109	9	101	1.2%	0.93 [0.38, 2.24]	
Hellstrom 2012	330	1325	685	2965	70.7%	1.08 [0.96, 1.21]	
Scullin 2007	67	371	76	391	10.5%	0.93 [0.69, 1.25]	+
Subtotal (95% CI)		2746		4408	99.7%	1.05 [0.95, 1.15]	•
Total events	510		871				
Heterogeneity: Tau <sup>2</sup> = 0.0			= 6 (P = 0	.67); l² =	= 0%		
Test for overall effect: Z =	0.97 (P = I	).33)					
Total (95% CI)		2859		4535	100.0%	1.05 [0.95, 1.15]	•
Total events	512		874				
Heterogeneity: Tau <sup>2</sup> = 0.0			= 7 (P = 0	.75); l² =	= 0%		0.001 0.1 1 10
Test for overall effect: Z =							Favours intervention Favours usual care
Test for subgroup differer	nces: Chi²	= 0.14,	df = 1 (P	= 0.71),	l² = 0%		

#### 4.3.1 Subgroup analysis based on study design

	Interver	ntion	Usual	care		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% CI
1.5.1 RCT							
Bolas 2004	17	119	12	124	1.9%	1.48 [0.74, 2.96]	+
Farris 2014 [Enhanced]	12	311	7	313	1.1%	1.73 [0.69, 4.32]	+
Farris 2014 [Minimal]	5	312	7	313	0.7%	0.72 [0.23, 2.23]	
Gillespie 2009	70	199	75	201	13.6%	0.94 [0.73, 1.22]	+
Scullin 2007	67	371	76	391	10.5%	0.93 [0.69, 1.25]	+
Stowasser 2002	2	113	3	127	0.3%	0.75 [0.13, 4.40]	
Subtotal (95% CI)		1425		1469	28.2%	0.98 [0.82, 1.17]	•
Total events	173		180				
Heterogeneity: Tau <sup>2</sup> = 0.0	0; Chi² = 3	.39, df=	= 5 (P = 0	.64); l² =	= 0%		
Test for overall effect: Z =	0.22 (P = 1	D.83)					
1.5.2 NRCT							
Hellstrom 2011	9	109	9	101	1.2%	0.93 [0.38, 2.24]	
Hellstrom 2012	330	1325	685	2965	70.7%	1.08 [0.96, 1.21]	<b>.</b>
Subtotal (95% CI)		1434		3066	71.8%	1.08 [0.96, 1.20]	•
Total events	339		694				
Heterogeneity: Tau <sup>2</sup> = 0.0	0; Chi <sup>2</sup> = 0	.11, df=	= 1 (P = 0	.74); l <sup>2</sup> =	= 0%		
Test for overall effect: Z =	1.26 (P = 1	0.21)					
Total (95% CI)		2859		4535	100.0%	1.05 [0.95, 1.15]	•
Total events	512		874				
Heterogeneity: Tau <sup>2</sup> = 0.0	0; Chi <sup>2</sup> = 4	.22, df=	7 (P = 0	.75); I <sup>2</sup> =	= 0%		0.002 0.1 1 10 500
Test for overall effect: Z =	0.95 (P = 1	0.34)					Favours intervention Favours usual care
Test for subgroup differer	ices: Chi²	= 0.72,	df = 1 (P :	= 0.40).	l² = 0%		Favours intervention Favours usual care

#### 4.4 Composite readmission and/or ED admission

4.4.1 Subgroup analysis based on outcome timing

Study or Subgroup 2.5.1 Composite readmission Anderegg 2014 [Overall] Anderegg 2014 [High-risk] Farris 2014 [Enhanced] Farris 2014 [Minimal] Hawes 2014 Koehler 2009				1664	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl
Anderegg 2014 (Overall) Anderegg 2014 (High-risk) Farris 2014 (Enhanced) Farris 2014 (Minimal) Hawes 2014	373 62 81	1652 358	389		14 7%		
Anderegg 2014 (High-risk) Farris 2014 (Enhanced) Farris 2014 (Minimal) Hawes 2014	62 81	358			14 7%		
Farris 2014 [Enhanced] Farris 2014 [Minimal] Hawes 2014	81		75		1 1.1 70	0.97 [0.85, 1.09]	+
Farris 2014 (Minimal) Hawes 2014		311		325	2.9%	0.75 [0.56, 1.01]	
Hawes 2014	88		87	313	3.9%	0.94 [0.72, 1.21]	-
		312	87	313	4.1%	1.01 [0.79, 1.30]	
Koehler 2009	0	24	15	37	0.0%	0.05 [0.00, 0.78]	·
	2	20	8	21	0.1%	0.26 [0.06, 1.09]	
Schnipper 2006	28	92	25	84	1.3%	1.02 [0.65, 1.61]	
Walker 2009	98	358	94	366	4.4%	1.07 [0.84, 1.36]	+
Subtotal (95% CI)		3127		3123	31.4%	0.94 [0.82, 1.08]	•
Total events	732		780				
2.5.2 Composite readmission	n and/or	ED visit,	> 30 d				
Farris 2014 [Enhanced]	97	312	88	313	4.4%	1.11 [0.87, 1.41]	
Farris 2014 [Minimal]	90	311	88	313	4.2%	1.03 [0.80, 1.32]	+
Gillespie 2009	134	182	147	186	17.0%	0.93 [0.83, 1.04]	•
Hellstrom 2011	45	109	41	101	2.5%	1.02 [0.73, 1.41]	+
Hellstrom 2012	645	1216	1555	2758	40.2%	0.94 [0.88, 1.00]	•
Koehler 2009	6	20	9	21	0.4%	0.70 [0.30, 1.61]	
Subtotal (95% CI)		2150		3692	68.6%	0.95 [0.90, 1.00]	•
Total events	1017		1928				
Heterogeneity: Tau² = 0.00; C	hi² = 2.89	, df = 5 (	(P = 0.72	); I <sup>2</sup> = 0	%		
Test for overall effect: Z = 1.95	5 (P = 0.0	5)					
Total (95% CI)		5277		6815	100.0%	0.95 [0.91, 1.00]	•
Total events	1749		2708				
Heterogeneity: Tau <sup>2</sup> = 0.00; Cl	hi <sup>2</sup> = 14.0	0, df = 1	3 (P = 0.	37); l² =	: 7%		0.01 0.1 1 10
Test for overall effect: Z = 1.77	7 (P = 0.0	8)	2223				Favours intervention Favours usual care

#### 4.4.2 Subgroup analysis based on study design

	Interven	ntion	Usual o	are		<b>Risk Ratio</b>	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
2.6.1 RCT							
Farris 2014 [Enhanced]	90	312	88	313	4.2%	1.03 [0.80, 1.32]	+
Farris 2014 (Minimal)	97	311	88	313	4.5%	1.11 [0.87, 1.41]	+
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]	·
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]	
Subtotal (95% CI)		941		954	28.5%	0.98 [0.85, 1.13]	•
Total events	355		372				
Heterogeneity: Tau <sup>2</sup> = 0.01; 0	Chi² = 6.95	i, df = 5	(P = 0.22	); I <sup>2</sup> = 2	8%		
Test for overall effect: Z = 0.2	6 (P = 0.7	9)					
2.6.2 NRCT							
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]	
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]	•
Walker 2009	98	358	94	366	4.5%	1.07 [0.84, 1.36]	+
Subtotal (95% CI)		3693		5214	71.5%	0.95 [0.90, 1.00]	•
Total events	1223		2154				
Heterogeneity: Tau <sup>2</sup> = 0.00; 0	Chi <sup>2</sup> = 3.53	, df = 4	(P = 0.47)	); $I^2 = 0$	%		
Test for overall effect: Z = 2.0	6 (P = 0.0	4)					
Total (95% CI)		4634		6168	100.0%	0.95 [0.90, 1.00]	
Total events	1578		2526				
Heterogeneity: Tau <sup>2</sup> = 0.00; C	Chi <sup>2</sup> = 10.6	2, df = 1	10 (P = 0.	39); l² =	: 6%		
Test for overall effect: Z = 1.8	0 (P = 0.0	7)					0.01 0.1 1 10 100 Favours intervention Favours usual care
Test for subaroup difference			= 1 (P = 0	.64), I <sup>2</sup>	= 0%		Favours intervention Favours usual Care

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

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1	Effectiveness of pharmacist-led medication reconciliation programmes on clinical
2	outcomes at hospital transitions: A systematic review and meta-analysis
3	
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#### 26 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. 

#### 75 INTRODUCTION

Medication reconciliation has been recognised as a major intervention tackling the burden of medication discrepancies and subsequent patient harm at care transitions.<sup>1</sup> 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,<sup>2</sup> and up to one-third could have the potential to cause harm.<sup>3</sup> Unintentional medication changes are common at care transitions,<sup>3-8</sup> and are one of the reasons for a huge utilization of healthcare resources.<sup>9-13</sup> 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, <sup>14</sup> and later the WHO and collaborators, <sup>15-17</sup> 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,<sup>18</sup> and there is no previous clinical evidence as to which member of the healthcare professional (s) or strategies effectively perform medication reconciliation.<sup>19</sup> A number of medication reconciliation strategies were utilized for safe patient transitions: electronic reconciliation tools,<sup>20-22</sup> use of standardised forms,<sup>23, 24</sup> collaborative models,<sup>25, 26</sup> patient engagement <sup>27</sup> and pharmacist-led. <sup>28, 29</sup>

The impact of medication reconciliation on clinical outcomes at hospital transitions were reported so far, however, two recently published systematic reviews <sup>30, 31</sup> 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, <sup>30</sup> Kwan et al <sup>31</sup> 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 Page 5 of 66

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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.

103 METHODS

#### 104 Data sources and searches

The study was conducted utilising PRISMA group (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines, <sup>32</sup> 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. 

118 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* 

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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*". <sup>1</sup> 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-andafter 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** 

146 One review author (ABM) was responsible for data extraction from full-texts using a 147 modified adopted Cochrane EPOC data collection checklist, <sup>33</sup> including quality assessment 148 of studies. The following information was extracted from each included study: name of first 149 author, year of publication, country and setting where the study conducted, study design,

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150 sample size, target of intervention, patient characteristics, components of intervention and 151 relevant outcomes and results. If insufficient details were reported, study authors were 152 contacted for further information.

153 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.<sup>34</sup> 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

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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<sup>2</sup>, Chi-square (O),  $I^2$  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.<sup>33</sup> 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** 

#### 192 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 Page 9 of 66

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reconciliation was not the primary intervention (n=11) (Appendix B). After applying all the
inclusion criteria, we finally included 17 articles (Figure 1).

# 202 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), <sup>35-45</sup> and the remainder were in Sweden (three studies), <sup>46-48</sup> Ireland (two studies) <sup>49</sup>, <sup>50</sup> and Australia (one study).<sup>51</sup> 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.<sup>38, 49, 51</sup> Most studies reported outcomes up to 30 days of follow-up after selection of eligible patients; only six studies<sup>37, 46-50</sup> reported longer follow-up of 3 month or more. Interventions were initiated at different care transitions; most were conducted at multiple transitions, <sup>35, 37-40, 42, 44, 46-51</sup> and all studies targeting a single transition intervention were carried out at hospital discharge.<sup>36, 41, 43, 45</sup> 

Most studies recruited high-risk patients (including elderly patients, patients with multiple medications and patients at risk of medication-related events). Five studies<sup>36, 37, 39, 44, 48</sup> focused on a specific patient population, mainly patients with heart failure and chronic obstructive pulmonary disease (COPD). Methodologically, one study <sup>35</sup> stratified patients in two groups: general population and high-risk patients, and another study <sup>37</sup> 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,<sup>44, 48, 51</sup> patient
 counselling <sup>35, 38, 41, 45</sup> or both telephone/home visit and patient counselling.<sup>37, 40, 42, 43, 46, 49, 50</sup>
 After medication reconciliation, few studies <sup>42, 46-49</sup> additionally included a formal medication

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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.

	227	pharmacist-led intervention.
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 2 2	229	
5 1 5	230	
5 5 7	231	
3 9	232	
)	233	
2 3	234	
+ 5 6	235	
7 3	236	
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 2	238	
3 4 5	239	
5 5 7	240	
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1 5		
5 7		
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1		

# 23 Table 1 Characteristics of included studies

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10

1

5												
A <b>G</b> hor, Year	Country, Setting	Study design	Intervention	Comparator	Target of	Inclusion	Exclusion	Components of	Comparator	Follow-	Relevant	Main results
7					intervention			intervention		up	outcomes	
8 9												
9 10										Period		
11												
And regg et al.	USA, single centre	Before-after	1664	1652	Admission,	Age 18 years or	Mental illness /alcohol	Admission MedRec,	Control group	30 days	Readmission,	30 day readmission and/or ED
13 2014 15 16					discharge	older, discharge	or drug use; discharge	Discharge MedRec,	(admission		Readmission	visit (general population): NS
15						from internal	to a rehabilitation unit/	patient education,	MedRec as		and/or ED visit	30 day readmission (high-risk)
16 17						medicine,	long-term care	medication calendar	needed)			: 12.3% (I) vs 17.8% (U);
18						family	facility, readmission					p=0.042
19 20						medicine,	for chemotherapy/					
21						cardiology, or	radiation therapy/					
22						orthopaedic	rehabilitation therapy					
23						Î						
24 25						surgery						
26						medical						
27								1.				
Bolag et al.	Ireland, single	RCT	81	81	In-patient	Age 55 years or	Transfer to another	Medication liaison	Standard	3	Readmission,	Readmission rate: p>0.05;
21 22 23 24 25 26 27 B28 <i>et al.</i> 200950 30 21	centre				stay,	older, at least 3	hospital or nursing	service	clinical	month	hospital stay	Length of stay: p>0.05
30 31					discharge,	regular	home, unable to	(comprehensive	pharmacy		(following	
32					post-discharge	medications	communicate, mental	medication history,	service (not		readmission)	
32 33 34 35							illness or alcohol	discharge letter faxed	include			
34							related admission,	to GP and	discharge			
36							, ,		-			
36 37							follow up was	community	counselling			
38												
39												
40 41												
41 42												
43							11					
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4 5							declined	pharmacist,	and liaison			
6								medicines record	service)			
7 8								sheet, discharge				
9								counselling, home				
10 11								visit/telephone call)				
12								visit telephone can)				
12 Eiseshower 14 2015 <sup>36</sup> 16 17	US, single centre	Before -after	25	60	Discharge	Age 65 years or	Left the hospital	MedRec at	Usual care	30 days	Readmission	Readmission rate, 16% (I) Vs
<sup>20</sup> /5 <sup>36</sup>						older, with	without medical	discharge,	(pharmacist			22.2% (U)
16						history of	advice, death within	Medication	was not			
17 18						COPD	30 d of discharge	reconciliation form,	present			
19								discharge summary	during			
20									baseline data			
21									collection)			
23									)			
21 22 23 24 Farris <i>et al.</i> 25	USA, Single centre	RCT	Minimal=312	313	Admission,	18 years or	Admission to	Admission MedRec,	Usual care (	90 days	ADEs,	16% experienced an AE,
2026			<b></b>		in-patient	older, English	psychiatry, surgery or	patient education	admission		readmission,	
27 28			Enhanced=		stay,	or Spanish	haematology/oncology	during inpatient stay,	MedRec,		ED visit,	Health care utilization at 30
29			311		discharge	speaker,	service, could	discharge	nurse-led		readmission	days and 90 days: NS
30						diagnosis of		counselling,	discharge		and/or ED visit	
31 32						HPN,	not use a telephone,	discharge medication	counselling			
33						hyperlipidemia,	had life expectancy <6	list, telephone call,	and			
34 35						HF, CAD, MI,	months, had dementia	care plan faxed to	medication			
32 33 34 35 36 37						stroke, TIA,	or cognitive	primary care	list)			
						asthma, COPD	impairment	physician/community				
38 39								physician community				
40						or receiving						
41 42												
42							12					
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4 5						oral		pharmacist				
6						anticoagulation		pharmacist				
7 8						anticoaguiation						
G <b>g</b> della et al.	US, multicentre	Before-after	1624	7335	Pre-admission	NA	NA	Preadmission	Historical	60 days	ADE, ED	30 day readmission: 6% (I)
2019 <sup>38</sup> 11					to post			medication list,	control group		visits and	vs 13.1% (U) [OR 2.34, 95%
12					discharge			patient education	(preadmission		readmission	CI;1.87-2.94, p<0.001];
13 14									medication			60 day readmission: 2.7% (I)
15									list gathered			
16 17									by nurse)			vs 7.7% (U) [OR 3.02, 95%
10												CI; 2.18-4.19, p<0.001]
Gillespie <i>et al.</i> 2029 <sup>46</sup> 222 23 24 25 26 27 29	Sweden, single	RCT	182	186	Admission,	Age 80 or older	Previous admission	Admission MedRec,	Usual care (	12	Readmissions,	Readmissions: 58.2% (I) vs
2029 <sup>46</sup>	centre				in-patient stay		during the study	discharge	without	month	ED visits,	59.1% (U) [OR 0.96, 95% CI;
22					and discharge		period	counselling,	pharmacist		mortality	0.64 - 1.4]);
23								medication review,	involvement)			ED visits per patient: 0.35 (I)
25 26								faxing discharge				vs 0.66 (U) [OR 0.53, 95%
27								summary to primary				CI; 0.37 - 0.75]
27 28 29 30 31 32 33 Hawes et al. 34 2085 <sup>39</sup> 36 37 38								care physicians,				01, 0.57 - 0.75]
30								telephone follow up				
31 32								at 2 months				
33 Hawes <i>et al.</i>	US, single centre	RCT	24	37	Discharge and	High risk	Age < 18 yrs, inability	Post-discharge	Usual care	30 days	Readmission,	ED visit: 0 (I) vs 29.7% (U),
34 20 <b>35</b> <sup>39</sup>	,				post discharge	patients [ HF,	to communicate in	medication	(with no		ED visit,	p=0.004;
36					1	COPD,	English, unable to	reconciliation	pharmacist		readmission	I
37 38						hyperglycaemic	follow up ( no		intervention)		and /or ED visit	Readmission: 0 (I) vs 32.4%
39						crisis, stroke	transportation and		,			(U), p=0.002;
40 41												
42							13					
43 44												
45												
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2 3												
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5						,NSTEM, more	telephone					Composite of hospitalization
6 7						than 3	access), transfer to					or ED visit: 0 (I) vs 40.5% (C),
8						hospitalizations	other facilities other					p< 0.001
9 10						in the past 5	than primary care,					
11						yrs., 8 or more	decisional impairment,					
12						medications on	incarceration					
13 14						discharge]						
15												
Helletrom <i>et</i> 17 <i>al</i> 12911 47	Sweden, single	Before-after	109	101	Admission,	Age 65 or	Staying during the	LIMM model,	Standard care	3	Readmission	ED visit and readmission:
<i>al</i> <b>128</b> <sup>11 47</sup>	centre				in-patient	older, at least	implementation period	admission and	(no formal	month	and ED visit,	45/108 (I) vs 41/100 (U)
19					stay,	one regular		discharge MedRec,	MedRec by			
20 21					discharge	medication		medication review	clinical		ADE related	Mortality, 3 month: 9/108 (I)
22								and monitoring,	pharmacists)		hospital visit	vs 9/100 (U)
23								quality control of				ADE related revisit: 6/108 (I)
24								discharge MedRec				vs 12/100 (U)
26												
21 22 23 24 25 26 27 Helstrom <i>et</i> 28 212 <sup>48</sup>	Sweden, single	Before- after	1216	2758	Admission,	High risk	NA	Admission MedRec,	Usual care	6	ED visits,	ED visit: 48.8% (I) vs 51.3%
al <b>29</b> 12 48	centre				inpatient stay	patients[ age		structured	(no clinical	month	hospital	(U) [HR 0.95, 95%CI:0.86-
30 31						$\geq$ 65 with any of		medication reviews,	pharmacists		admissions and	1.04];
32						HF, RF]		follow up at least two	working in		mortality	
32 33 34 35 36								times a week	the wards)			All ED visits, hospitalization
34 35												or death: 58.9% (I) vs 61.2%
36												(U) [HR 0.96, 95% CI: 0.88-
37 38 39												1.04]
39												
40												Mortality: 18.2% (I) vs 17.3%
41 42												
43							14					
44												
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4 5 6												(U); p=0.55
Koehler <i>et al.</i> 8 2009 <sup>9 40</sup>	US, single centre	RCT	20	21	Admission,	age 70 years or	Primarily surgical	Targeted care	Usual care	60 days	Readmission	30 d readmission/ED visits:
20 <b>9</b> 9 40					discharge and	older, $\geq 5$	procedure, life	bundle, medication	(nurse and		and/or ED	2/20 (I) vs 8/21 (U) ( p= 0.03);
10 11					post discharge	medications, $\geq 3$	expectancy≤6	reconciliation and	care		visits	60 d readmission/ED visits:
12						chronic	months, residence in	education, follow up	coordination			6/20 (I) vs 9/21 (U); p= 0.52
13 14						comorbid	long term care facility,	call, enhanced	staff			
15 16						conditions,	refusal to participate,	discharge form	providing			
16 17						assisted living,	not enrolled within 72		care)			
18						English	hrs.					
19 20						language,						
20 21						phone contact						
<b>22</b> Pa <b>2</b> al. 2013	US, single centre	NRCT	537	192	Discharge	Age 18 years or	NA	Patient counselling,	Usual care	30 days	Readmission	30 d readmission: 16.8% (I) vs
<sub>41</sub> 24	-				-	older, at least		pharmacist	(without			26.0% (U), p=0.006
25 26						10 regular		medication	discharge			
27						medications		reconciliation,	review by			ADE prevented: 52.8%
28 29								medication calendar	pharmacist)			
30												
31												
31 32 33 Schipper <i>et</i> 34 <i>al</i> 35906 <sup>42</sup> 36 37	US, single centre	RCT	92	84	In-patient	Discharge to	NA	Discharge	Usual care (		ADEs related	Preventable ADE: 1% (I) vs
al <b>35</b> 06 <sup>42</sup>					stay,	home,		medication	medication		hospital visit,	11% (U), p=0.01;
36 37					discharge,	contacted 30		reconciliation,	review by a		readmission	
38					post discharge	days after		telephone follow up,	pharmacist		and/or ED visit	ED visit/readmission: 30% (I)
39 40						discharge,		medication review,	and discharge			vs 30% (U) ;p>0.99
41												
42 43							15					
44												
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5 6						spoke English,		standard email	counselling			preventable medication related
7						cared for		template, patient	by a nurse)			healthcare utilization: 1% (I)
8						primary care		counselling				vs 8% (U), p= 0.03
9 10						physician/						
11						internal						
12						medicine						
13						resident						
14						resident						
13 14 15 Schein <i>et al.</i>	Ireland, multicentre	RCT	371	391	Admission,	Age 65 or	Scheduled admissions	Integrated medicines	Usual care	12	Length of	LoS reduced by 2 days for
17 <sup>20</sup> 08 <sup>49</sup> 19					in-patient	older, at least 4	and admissions from	management service	(did not	month	hospital stay,	intervention vs usual care,
19					stay,	regular	private nursing homes	-admission and	receive		readmission	p=0.003
20 21							private nursing nomes				readmission	p=0.005
21					discharge	medications,		discharge MedRec,	integrated			Readmissions per patient:0.8
22 23						taking		inpatient medication	medicines			(I) vs 1 (U)
24						antidepressants,		review and	management			() ()
25						previous		counselling,	service)			
26 27						admission in		telephone follow-up				
28						the last 6						
29 30 31 32						months, taking						
30 31						IV antibiotics						
32						IV antibiotics						
Stowasser et al.	Australia,	RCT	113	127	Admission,	Return to the	Outpatients, discharge	Medication liaison	Usual care	30 days	Mortality,	Mortality, 30 d: 2/113 (I) vs
32 Stowasser <i>et al.</i> 34 2095 <sup>51</sup> 36 37	multicentre					community	to hostel or nursing	service - medication	(no		readmission,	3/127 (U): NS
36					discharge	following	home, previous	history confirmation	medication		ED visit	
37						-	· •				ED VISI	Readmissions: 12/113 (I) vs
38 39						discharge	enrolment, unable to	with community	liaison			17/127 (U)
40							provide consent and	health care				
41												
42							16					
43 44												
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46			rechnologies.	elimisebne.eo	iiniewufa.ep	itinu/kepipoe	enxandi pane(aitsda	aniphopiane	by င <b>ှည့်ပု</b> ဖွှ	rotected	d	
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W <b>5</b> rden <i>et al.</i>	US, single centre	Before-after	35	115	Admission,	Age 18-85	Diastolic dysfunction,	Medication	Historical	30 days	Readmission	Al- cause readmission, 30 day
2014 44					in-patient	years, systolic	valve replacement/left	reconciliation	control group			:17% (I) vs 38% (U) [RR 0.45,
8					stay,	dysfunction	ventricular assist	(admission and	(physicians -			95% CI:0.21-0.96, p=0.02],
9					discharge	(EF ≤40)	device	discharge), discharge	admission			
10 11								instructions,	MedRec;			30 d HF related readmission:
12								telephone follow-up	nurses-			6%(I) vs 18% (U) [RR 0.31,
13 14									discharge			95% CI: 0.08-1.27, p=0.11]
15									-			
16 17									counselling)			
<b>17</b> Wilkinson <i>et</i>	US, single centre	NRCT	229	440	Discharge	Age 18 years or	Refusal of pharmacist	Medication history at	Control group	30 days	Readmission	Readmission rate: 15.7% (I)
<i>al</i> . <sup>129</sup> 11 <sup>45</sup>						older, English	education, transfer to a	admission, during	(pharmacists			vs 21.6% (U) [RR 0.728, 95%
<i>al</i> .12911 <sup>45</sup> 20 21						speaking,	skilled nursing	hospitalization and	not provide			CI: 0.514-1.032, p =0.04]
21 22						patients with		discharge, patient	medication			ei. 0.511 1.052, p 0.01]
23							facility, or discharge	0.71				
24						depression,	when the pharmacist	education upon	counselling at			
22 23 24 25 26						receiving	was not available	discharge	discharge)			
27						high-risk						
28 29						medications						
30						and						
31												
32 33						polypharmacy,						
34						poor health						
35 36						literacy,						
36 37						having an						
38						-						
39						absence of						
40 41												
42							18					
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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. 

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### 243 Risk of bias assessment

Patients included in the study were similar in the baseline characteristics except five studies <sup>36, 38, 39, 45, 48</sup> which were not clear or different in patient characteristics. However, in only three studies<sup>43, 48, 51</sup> that baseline clinical outcomes were reported or some form of adjustment analysis was performed. Eight out of 17 studies <sup>37, 39, 40, 42, 46, 49-51</sup> provided enough details on randomization procedure to be judged as adequate. Among these studies, allocation concealment was fully described in all reports except one.<sup>51</sup> All but three studies, <sup>43, 45, 50</sup> either care providers and outcome assessors were blinded or objective health outcomes were reported. Five studies <sup>37, 41, 47, 48, 51</sup> 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.<sup>35, 37, 41, 47</sup> At least one of our outcomes of interest was selectively reported in four studies<sup>36, 49-51</sup> 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).

### **257 Effect of interventions**

Of the 14 studies that reported data on all-cause readmissions, thirteen were eligible for meta-analysis. One study<sup>35</sup> measured this outcome for a high-risk population separately; and another study<sup>37</sup> reported it for two different interventions. Thus, fifteen interventions were meta-analysed. Eight studies reported this outcome at 30 days<sup>35, 36, 39, 41, 43-45, 51</sup> while three <sup>46,</sup> <sup>48, 49</sup> reported long-term data and two studies<sup>37, 38</sup> reported both. Seven studies<sup>35, 38, 39, 41, 44, 45,</sup> <sup>49</sup> showed a significant reduction (p < 0.05) in rehospitalizations although two <sup>39, 44</sup> 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<sup>35, 37-39, 43, 46, 48</sup> which measured ED visit as an outcome were pooled. 

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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 <sup>38</sup> 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 <sup>35, 37, 39, 40, 42, 43, 46-48</sup> 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 <sup>37, 46-51</sup> 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<sup>50</sup> and Farris et al <sup>37</sup> 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 allcause mortality (RR 1.05; 95% CI: 0.95 - 1.16) (Figure 2E). 

### 284 Other outcomes

Studies reporting other clinically important outcomes are summarized in table 2. Some studies <sup>46-49</sup> furnished information on the proportion of patients who did not revisit the hospital. The intervention group in the 3 studies <sup>46, 48, 49</sup> 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.

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293	Table 2 Other clinically relevant outcomes
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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.

295 it showed success)

†p<0.01

297 ‡p>0.05

ADE, adverse drug event; ED, emergency department; RR, risk ratio; CI, confidence interval;

299 WMD, weighted mean difference.

300 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]<sup>37</sup> or Hawes et al <sup>39</sup> 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,<sup>52</sup> long-term settings<sup>53</sup> or hospital transitions.<sup>30,31</sup> 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.<sup>30, 31</sup> 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 <sup>54</sup> 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.<sup>43, 47</sup> Other studies also showed that medication discontinuity is the most common reason for discrepancy related ADE.<sup>55, 56</sup> Although Gillespie et al <sup>46</sup> 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; <sup>31</sup> 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 

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of the intervention, and this was supported by non-significance differences between the subgroups. Moreover, non-randomized studies showed a slight significant reduction in allcause 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 <sup>57, 58</sup> 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 <sup>57</sup> 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 <sup>58</sup> 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.

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

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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.

391 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 <sup>59-62</sup> to 35-71% during discharge.<sup>4</sup>, <sup>63, 64</sup> Coleman et al <sup>65</sup> 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 <sup>38</sup> in the ADE-related hospital visit and Hellstrom et al <sup>48</sup> in the mortality forest plots were accounted for a large proportion of the studied subjects, yet these studies possessed low quality score. 

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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 metaanalyses 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 <sup>66</sup> 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. BMJ Open: first published as 10.1136/bmjopen-2015-010003 on 23 February 2016. Downloaded from http://bmjopen.bmj.com/ on June 11, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES)

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### 427 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

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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.

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### **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.

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- 455 None declared.
- **Data sharing statement**
- 457 No additional data are available.

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465	REFERENCES
466	1. Institute for Healthcare Improvement. Medication reconciliation review: Available a
467	http://www.ihi.org/resources/Pages/Tools/MedicationReconciliationReview.aspx. (las
468	accessed 30 December 2014).
469	2. Rozich JD, Howard RJ, Justeson JM, et al. Standardization as a mechanism to
470	improve safety in health care. Jt Comm J Qual Saf 2004;30:5-14.
471	3. Cornish PL, Knowles SR, Marchesano R, et al. Unintended medication discrepancie
472	at the time of hospital admission. Arch Intern Med 2005;165:424-29.
473	4. Wong JD, Bajcar JM, Wong GG, et al. Medication reconciliation at hospita
474	discharge: evaluating discrepancies. Ann Pharmacother 2008;42:1373-79.
475	5. Pippins JR, Gandhi TK, Hamann C, et al. Classifying and predicting errors o
476	inpatient medication reconciliation. J Gen Intern Med 2008;23:1414-22.
477	6. Herrero-Herrero JI, Garcia-Aparicio J. Medication discrepancies at discharge from an
478	internal medicine service. <i>Eur J Intern Med</i> 2011; <b>22</b> :43-48.
479	7. Geurts MM, Talsma J, Brouwers JR, et al. Medication review and reconciliation with
480	cooperation between pharmacist and general practitioner and the benefit for the patient:
481	systematic review. Br J Clin Pharmacol 2012;74:16-33.
482	8. Allende Bandres MA, Arenere Mendoza M, Gutierrez Nicolas F, et al. Pharmacist-lee
483	medication reconciliation to reduce discrepancies in transitions of care in Spain. Int J Clin
484	<i>Pharm</i> 2013; <b>35</b> :1083-90.

485	9. Howard RL, Avery AJ, Howard PD, et al. Investigation into the reasons for
486	preventable drug related admissions to a medical admissions unit: observational study. Qual
487	Saf Health Care 2003;12:280-85.
488	10. Witherington EM, Pirzada OM, Avery AJ. Communication gaps and readmissions to
489	hospital for patients aged 75 years and older: observational study. Qual Saf Health Care
490	2008; <b>17</b> :71-75.
491	11. Dedhia P, Kravet S, Bulger J, et al. A quality improvement intervention to facilitate
492	the transition of older adults from three hospitals back to their homes. J Am Geriatr Soc
493	2009; <b>57</b> :1540-46.
494	12. Schnipper JL, Hamann C, Ndumele CD, et al. Effect of an electronic medication
495	reconciliation application and process redesign on potential adverse drug events: a cluster-
496	randomized trial. Arch Intern Med 2009;169:771-80.
497	13. Jack BW, Chetty VK, Anthony D, <i>et al.</i> A reengineered hospital discharge program to
498	decrease rehospitalization: a randomized trial. Ann Intern Med 2009;150:178-87.
499	14. Joint Commission on Accreditation for Healthcare Organizations. National Patient
500	Safety Goals. 2006. Available at:
501	http://www.jointcommission.org/Improving_Americas_Hospitals_The_Joint_Commissions_
502	Annual_Report_on_Quality_and_Safety2006/
503	15. National Institute for Health and Care Excellence. Technical patient safety solutions
504	for medicines reconciliation on admission of adults to hospital. London, 2007.
505	(NICE/NSPA/2007/PSG001). Available at: www.nice.org.uk/PSG001 (last accessed 30
506	December 2014).
507	16. Canadian Council on Health Services Accreditation. Patient Safety Goals and
508	Required Organizational Practices. Ottawa, 2004. Available at: www.accreditation.ca (last
509	accessed 30 December 2014).

### **BMJ Open**

510	17. Australian Commission on Safety and Quality in Healthcare. Medication
511	reconciliation. Avialable at http://www.safetyandquality.gov.au/our-work/medication-
512	safety/medication-reconciliation/ (last accessed 30 December 2014).
513	18. Duran-Garcia E, Fernandez-Llamazares CM, Calleja-Hernandez MA. Medication
514	reconciliation: passing phase or real need? Inter J Clin Pharm 2012;34:797-802.
515	19. Canadian Agency for Drugs and Techonlogies in Health. Medication reconciliation at
516	discharge: A review of the clinical evidence and guidelines. 2012. Available at:
517	https://www.cadth.ca/medication-reconciliation-discharge-review-clinical-evidence-and-
518	guidelines ( last accessed 24 November 2015).
519	20. Gimenez Manzorro A, Zoni AC, Rodriguez Rieiro C, et al. Developing a programme
520	for medication reconciliation at the time of admission into hospital. Int J Clin Pharm
521	2011; <b>33</b> :603-9.
522	21. Schnipper JL, Liang CL, Hamann C, et al. Development of a tool within the
523	electronic medical record to facilitate medication reconciliation after hospital discharge. J Am
524	Med Inform Assoc 2011;18:309-13.
525	22. Moore P, Armitage G, Wright J, et al. Medicines reconciliation using a shared
526	electronic health care record. J Patient Saf 2011;7:148-54.
527	23. Bedard P, Tardif L, Ferland A, et al. A medication reconciliation form and its impact
528	on the medical record in a paediatric hospital. J Eval Clin Pract 2011;17:222-7.
529	24. De Winter S, Vanbrabant P, Spriet I, et al. A simple tool to improve medication
530	reconciliation at the emergency department. Eur J Intern Med 2011;22:382-5.
531	25. De Winter S, Spriet I, Indevuyst C, et al. Pharmacist- versus physician-acquired
532	medication history: a prospective study at the emergency department. Qual Saf Health Care
533	2010; <b>19</b> :371-5.

BMJ Open: first published as 10.1136/bmjopen-2015-010003 on 23 February 2016. Downloaded from http://bmjopen.bmj.com/ on June 11, 2025 at Agence Bibliographique de I Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.

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Feldman LS, Costa LL, Feroli ER, et al. Nurse-pharmacist collaboration on 26. medication reconciliation prevents potential harm. J Hosp Med 2012;7:396-401. Greenwald JL, Halasyamani L, Greene J, et al. Making inpatient medication 27. reconciliation patient centered, clinically relevant and implementable: a consensus statement on key principles and necessary first steps. J Hospital Med 2010;5:477-85. 28. Eggink RN, Lenderink AW, Widdershoven JW, et al. The effect of a clinical pharmacist discharge service on medication discrepancies in patients with heart failure. Pharm World Sci 2010;32:759-66. 29. Galvin M, Jago-Byrne MC, Fitzsimons M, et al. Clinical pharmacist's contribution to medication reconciliation on admission to hospital in Ireland. Int J Clin Pharm 2013;35:14-21. Mueller SK, Sponsler KC, Kripalani S, et al. Hospital-based medication reconciliation 30. practices: a systematic review. Arch Intern Med 2012;172:1057-69. 31. Kwan JL, Lo L, Sampson M, et al. Medication reconciliation during transitions of care as a patient safety strategy: a systematic review. Ann Intern Med 2013;158:397-403. 32. David Moher AL, Jennifer Tetzlaff, Douglas G. Altman, The PRISMA Group. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. *PLoS Med* 2009;6:e1000097. doi:10.1371/journal.pmed. 33. Effective Practice and Organisation of Care (EPOC). [Data collection checklist and risk of bias]. EPOC Resources for review authors. Oslo: Norwegian Knowledge Centre for the Health Services; 2014. Available at: http://epoc.cochrane.org/epoc-specific-resources-review-authors (last accessed 30 Decmeber 2014). 34. Higgins JPT, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions. Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011. Available at: www.cochrane-handbook.org.

Page 33 of 66

### **BMJ Open**

35. Anderegg SV, Wilkinson ST, Couldry RJ, et al. Effects of a hospitalwide pharmacy practice model change on readmission and return to emergency department rates. Am J Health Syst Pharm 2014;71:1469-79. 36. Eisenhower C. Impact of pharmacist-conducted medication reconciliation at discharge on readmissions of elderly patients with COPD. Ann Pharmacother 2014;48:203-8. 37. Farris KB, Carter BL, Xu Y, et al. Effect of a care transition intervention by pharmacists: an RCT. BMC Health Serv Res 2014;14:406. 38. Gardella JE, Cardwell TB, Nnadi M. Improving medication safety with accurate preadmission medication lists and postdischarge education. Jt Comm J Qual Patient Saf 2012;38:452-8. 39. Hawes EM, Maxwell WD, White SF, et al. Impact of an outpatient pharmacist intervention on medication discrepancies and health care resource utilization in posthospitalization care transitions. J Prim Care Community Health 2014;5:14-8. 40. Koehler BE, Richter KM, Youngblood L, et al. Reduction of 30-day postdischarge hospital readmission or emergency department (ED) visit rates in high-risk elderly medical patients through delivery of a targeted care bundle. J Hosp Med 2009;4:211-8. Pal A, Babbott S, Wilkinson ST. Can the targeted use of a discharge pharmacist 41. significantly decrease 30-day readmissions? Hosp Pharm 2013;48:380-8. 42. Schnipper JL, Kirwin JL, Cotugno MC, et al. Role of pharmacist counseling in preventing adverse drug events after hospitalization. Arch Intern Med 2006;166:565-71. 43. Walker PC, Bernstein SJ, Jones JN, et al. Impact of a pharmacist-facilitated hospital discharge program: A quasi-experimental study. Arch Intern Med 2009;169:2003-10. 44. Warden BA, Freels JP, Furuno JP, et al. Pharmacy-managed program for providing education and discharge instructions for patients with heart failure. Am J Health Syst Pharm 2014;71:134-9.

BMJ Open: first published as 10.1136/bmjopen-2015-010003 on 23 February 2016. Downloaded from http://bmjopen.bmj.com/ on June 11, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.

45. Wilkinson ST, Pal A, Couldry RJ. Impacting readmission rates and patient satisfaction: Results of a discharge pharmacist pilot program. Hosp Pharm 2011;46:876-83. Gillespie U1, Alassaad A, Henrohn D, et al. A comprehensive pharmacist 46. intervention to reduce morbidity in patients 80 years or older: a randomized controlled trial. Arch Intern Med 2009;169:894-900. 47. Hellstrom LM, Bondesson A, Hoglund P, et al. Impact of the Lund Integrated Medicines Management (LIMM) model on medication appropriateness and drug-related hospital revisits. Eur J Clin Pharmacol 2011;67:741-52. 48. Hellstrom LM, Hoglund P, Bondesson A, et al. Clinical implementation of systematic medication reconciliation and review as part of the Lund Integrated Medicines Management model--impact on all-cause emergency department revisits. J Clin Pharm Ther 2012;37:686-92. 49.. Scullin C, Scott MG, Hogg A, et al. An innovative approach to integrated medicines management. J Eval Clin Pract 2007;13:781-8. 50. Bolas H, Brookes K, Scott M, et al. Evaluation of a hospital-based community liaison pharmacy service in Northern Ireland. *Pharm World Sci* 2004;26:114-20. 51. Stowasser DA, Collins DM, Stowasser M. A randomised controlled trial of medication liaison services - patient outcomes. J Pharm Pract Res 2002;32:133-40. 52. Bayoumi I, Howard M, Holbrook AM, et al. Interventions to improve medication reconciliation in primary care. Ann Pharmacother 2009;43:1667-75. 53. Chhabra PT, Rattinger GB, Dutcher SK, et al. Medication reconciliation during the transition to and from long-term care settings: a systematic review. Res Social Adm Pharm 2012;8:60-75.

### **BMJ Open**

54. Rebecca Thomas ALH, Mala Mann, Dyfed Huws, et al. Pharmacist-led interventions to reduce unplanned admissions for older people: a systematic review and meta-analysis of randomised controlled trials. Age Ageing 2014; 43:174-87. 55. Boockvar KS, Carlson LaCorte H, Giambanco V, et al. Medication reconciliation for reducing drug-discrepancy adverse events. Am J Geriatr Pharmacother 2006;4:236-43. 56. Mergenhagen KA, Blum SS, Kugler A, et al. Pharmacist versus physician-initiated admission medication reconciliation: impact on adverse drug events. Am J Geriatr Pharmacother 2012;10:242-50. 57. Holland R, Desborough J, Goodyer L, et al. Does pharmacist-led medication review help to reduce hospital admissions and deaths in older people? A systematic review and meta-analysis. Br J Clin Pharmacol 2008;65:303-16. 58. Christensen M, Lundh A. Medication review in hospitalised patients to reduce morbidity and mortality. Cochrane Database of Syst Rev 2013;2:CD008986. 59. Coffey M, Mack L, Streitenberger K, et al. Prevalence and clinical significance of medication discrepancies at pediatric hospital admission. Acad Pediatr 2009;9:360-5. 60. Gleason KM, Groszek JM, Sullivan C, et al. Reconciliation of discrepancies in medication histories and admission orders of newly hospitalized patients. Am J Health Syst *Pharm* 2004;**61**:1689-95. Salanitro AH, Osborn CY, Schnipper JL, et al. Effect of patient- and medication-61. related factors on inpatient medication reconciliation errors. J Gen Intern Med 2012;27:924-32. 62. Villanyi D, Fok M, Wong RY. Medication reconciliation: identifying medication discrepancies in acutely ill hospitalized older adults. Am J Geriatr Pharmacother 2011;9:339BMJ Open: first published as 10.1136/bmjopen-2015-010003 on 23 February 2016. Downloaded from http://bmjopen.bmj.com/ on June 11, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.

44.

631	63. Manias E, Gerdtz MF, Weiland TJ, <i>et al.</i> Medication use across transition points from
632	the emergency department: Identifying factors associated with medication discrepancies. Ann
633	<i>Pharmacother</i> 2009; <b>43</b> :1755-64.
634	64. Grimes T, Delaney T, Duggan C, et al. Survey of medication documentation at
635	hospital discharge: Implications for patient safety and continuity of care. Ir J Med Sci
636	2008;177:93-7.
637	65. Coleman EA, Smith JD, Raha D, et al. Posthospital medication discrepancies:
638	prevalence and contributing factors. Arch Intern Med 2005;165:1842-7.
639	66. Sanchez Ulayar A, Gallardo Lopez S, Pons Llobet N, et al. Pharmaceutical
640	intervention upon hospital discharge to strengthen understanding and adherence to
641	pharmacological treatment. Farm Hosp 2012;36:118-23.
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Figure 1 PRISMA flow diagram of the selection of eligible studies.	yrigh
Figure 2 Forest plots of intervention effects on the proportion of patients with all-cause	t, incl
readmission (A), emergency department (ED) visits (B), composite rate of readmissions	Protected by copyright, including for uses related
and/or ED visits (C), Adverse drug event-related hospital revisits (D) and mortality (E).	for us
Pooled estimates (diamond) calculated by the Mantel-Haenszel random effects model.	inseig es reli
Horizontal bars and diamond widths represent 95% CIs. Anderegg et al <sup>35</sup> stratified patients	ated to
in two groups: general population and high-risk patients. Farris et al <sup>37</sup> randomised the	Enseignement Superieur (Al Protected by copyright, including for uses related to text and data
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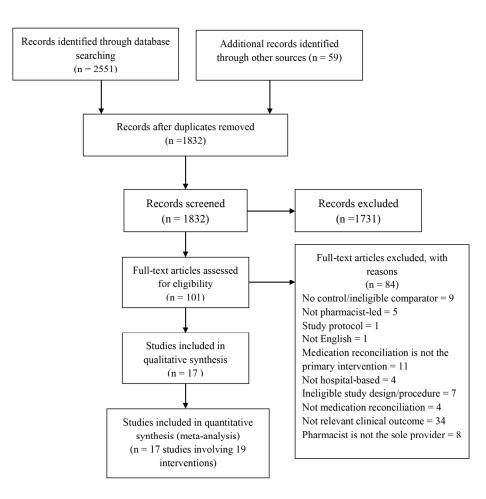


Figure 1 PRISMA flow diagram of the selection of eligible studies. 200x231mm (300 x 300 DPI)

### A. All-cause readmission

	Interver	ntion	Usual	care		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
Anderegg 2014 [Overall]	258	1652	270	1664	10.1%	0.96 [0.82, 1.13]	+
Anderegg 2014 [High-risk]	44	358	58	325	6.9%	0.69 [0.48, 0.99]	
Eisenhower 2014	4	25	13	60	1.9%	0.74 [0.27, 2.05]	
Farris 2014 [Enhanced]	49	311	47	313	6.8%	1.05 [0.73, 1.52]	+
Farris 2014 [Minimal]	51	312	47	313	6.9%	1.09 [0.76, 1.57]	+
Gardella 2012	44	1624	565	7335	7.8%	0.35 [0.26, 0.48]	+
Gillespie 2009	106	182	110	186	9.9%	0.98 [0.83, 1.17]	+
Hawes 2014	0	24	12	37	0.3%	0.06 [0.00, 0.98]	
Hellstrom 2012	547	1216	1296	2758	11.0%	0.96 [0.89, 1.03]	
Pal 2013	90	537	50	192	7.8%	0.64 [0.47, 0.87]	
Scullin 2007	141	371	172	391	9.9%	0.86 [0.73, 1.03]	+
Stowasser 2002	9	113	12	127	2.6%	0.84 [0.37, 1.93]	
Walker 2009	79	358	66	366	8.0%	1.22 [0.91, 1.64]	-
Warden 2014	6	35	44	115	2.9%	0.45 [0.21, 0.96]	
Wilkinson 2011	36	229	95	440	7.1%	0.73 [0.51, 1.03]	-
Total (95% CI)		7347		14622	100.0%	0.81 [0.70, 0.95]	•
Total events	1464		2857				
Heterogeneity: Tau <sup>2</sup> = 0.05; (	Chi <sup>2</sup> = 66.2	20, df = 1	14 (P < 0.)	00001);	I <sup>2</sup> = 79%		
Test for overall effect: Z = 2.65 (P = 0.008)							0.001 0.1 1 10 1000 Favours intervention Favours usual care

### B. All-cause emergency department (ED) visits

	Interver	tion	Usual	care		<b>Risk Ratio</b>	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% Cl
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]	1 m m
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: Tau <sup>2</sup> = 0.09; 0	Chi <sup>2</sup> = 42.2	6, df = 1	8 (P < 0.0	10001); P	²= 81%		
Test for overall effect: Z = 2.6	i3 (P = 0.0	09)					0.01 0.1 1 10 100 Favours intervention Favours usual care

### C. Composite rate of readmissions and/or ED visits

	Interver	ntion	Usual o	care		<b>Risk Ratio</b>	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	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: Tau <sup>2</sup> = 0.00; •	Chi <sup>2</sup> = 10.8	62, df = 1	10 (P = 0)	39); I <sup>z</sup> =	6%		tor de la con
Test for overall effect: Z = 1.8	80 (P = 0.0	7)	2				0.01 0.1 1 10 100 Favours intervention Favours usual care

227x297mm (300 x 300 DPI)

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### D. Adverse drug event-related hospital revisits

2

Heterogeneity: Tau<sup>2</sup> = 0.00; Chi<sup>2</sup> = 3.94, df = 7 (P = 0.79); l<sup>2</sup> = 0%

Test for overall effect: Z = 1.03 (P = 0.30)

10.8%

73.0%

10.9%

0.3%

Farris 2014 [Minimal]

Gillespie 2009

Hellstrom 2011

Hellstrom 2012

Stowasser 2002

Total (95% CI)

Total events

Scullin 2007

	Interver	ntion	Usual	care		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total			Weigh	t M-H, Random, 95% C	
Gardella 2012	10	1624	183	7335	57.69	6 0.25 [0.13, 0.47]	
Hellstrom 2011	6	108	12	100	26.19	6 0.46 [0.18, 1.19]	i —•
Schnipper 2006	4	92	7	84	16.39	6 0.52 [0.16, 1.72]	i —•+
Total (95% CI)		1824		7519	100.09	6 0.33 [0.20, 0.53]	▲
Total events	20		202				
Heterogeneity: Tau² = Test for overall effect:	CE.500004 (2010)			P = 0.3	7); I² = 09	16	0.01 0.1 1 10 10
			,				Favours intervention Favours usual care
2. All-cause mor	tality	ntion	Usual c	аге		Risk Ratio	Risk Ratio
Study or Subgroup	Events				Veight N	I-H, Random, 95% CI	M-H, Random, 95% Cl
Bolas 2004	17	119	12	124	2.0%	1.48 [0.74, 2.96]	+
Farris 2014 [Enhanced]	12	311	7	313	1.1%	1.73 [0.69, 4.32]	

0.72 [0.23, 2.23]

0.95 [0.71, 1.29]

0.93 [0.38, 2.24]

1.08 [0.96, 1.21]

0.93 [0.69, 1.25]

0.75 [0.13, 4.40]

1.05 [0.95, 1.16]

0.001

0.1

Favours intervention Favours usual care

0.7%

1.2%

4520 100.0%

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 <sup>35</sup> stratified patients in two groups: general population and high-risk patients. Farris et al <sup>37</sup> 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	7 and 8



# PRISMA 2009 Checklist

Dago	1	of	2
Page		0I	2

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

48

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# **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.

, (2009). Preferred Rep.

# 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

'inpatients'/exp OR 'inpatients'

'patient transfer'/exp OR 'patient transfer'

'patient discharge'/exp OR 'patient discharge'

'patient admission'/exp OR 'patient admission'

# Searches	Results
S14 AND S15 AND S16 Limiters-Peer Reviewed; English Language;	267
Abstract Available	
S17S14 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	335
AND [abstracts]/lim	
23 #1.15 OR #1.16 OR #1.17 OR #1.18 OR #1.19 #1.5 OR #1.6 OR #1.7 OR #1.8 OR #1.9 OR #1.10 OR #1.11 OR #1.12 OR	375,805
22 #1.3 OR #1.0 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' 18 'inpatients' OR 'inpatients'	74,696

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108,750

40,927

96,003

137,129

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ining,

, Al training, and similar technologies.

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 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.

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.

Reeder, T. A. and A. Mutnick (2008). "Pharmacist- versus physician-obtained medication histories." <u>American Journal of Health-System Pharmacy</u> **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." <u>American Journal of Health-System Pharmacy</u> **65**(15): 1451-1457.

Midlov, P., et al. (2008). "Medication report reduces number of medication errors when elderly patients are discharged from hospital." <u>Pharmacy World & Science</u> **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." <u>Archives of Internal Medicine</u> **169**(8): 771-780.

Showalter, J. W., et al. (2011). "Effect of standardized electronic discharge instructions on postdischarge 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." <u>European Journal of Internal Medicine</u> **23**(8): 696-700.

## **Study Protocol**

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

#### <u>Not English</u>

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

#### **BMJ Open**

## Medication reconciliation is not the primary intervention

Nester TM et al (2002)." Effectiveness of a pharmacist acquired medication history in promoting patient safety". <u>Am J Health-Syst Pharm</u> 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". <u>Basic & Clinical Pharmacology & Toxicology</u> 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." <u>Anaesthesia</u> <u>and Intensive Care</u> **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." <u>J Am Geriatr Soc</u> **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." <u>Am J Med Qual</u> **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". <u>Arch Intern Med</u> 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." <u>Pharm Pract (Granada)</u> **12**(1): 360.

## Ineligible study design/procedure

Carter, M. K., et al. (2006). "Pharmacist-acquired medication histories in a university hospital emergency department." <u>American Journal of Health-System Pharmacy</u> **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." <u>Annals of Pharmacotherapy</u> **43**(6): 1001-1010.

Musgrave, C. R., et al. (2013). "Improving transplant patient safety through pharmacist discharge medication reconciliation." <u>American Journal of Transplantation</u> **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 techniciancentered 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." <u>American Journal of Geriatric Pharmacotherapy</u> **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." <u>American</u> 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." <u>J Crit Care</u> **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." <u>Stroke</u> 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 <u>Pharmacy & Therapeutics</u> **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". <u>Br J Clin Pharmacol</u> 1997; 44: 163–165.

Michels R et al (2003). "Programme using pharmacy technicians to obtain medication histories." <u>American Journal of Health-System Pharmacy</u> 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." <u>J Eval Clin</u> <u>Pract</u> **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." <u>Hospital Pharmacy</u> **47**(12): 927-932.

Bergkvist, A., et al. (2009). "Improved quality in the hospital discharge summary reduces medication errors--LIMM: Landskrona Integrated Medicines Management." <u>European Journal of</u> 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." <u>Emerg Med Australas</u> **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." <u>American Journal of Health-System</u> <u>Pharmacy</u>: 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." <u>BMJ Open 3(7)</u>.

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

Hick, H. L., et al. (2001). "The impact of the pharmacist on an elective general surgery preadmission clinic." <u>Pharmacy World & Science</u> **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.

#### **BMJ Open**

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." <u>International Journal of Clinical Pharmacology & Therapeutics</u> **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." <u>Healthcare Quarterly</u> 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, nursepharmacist intervention for improving the accuracy of the medication history." <u>J Patient Saf</u> **10**(2): 88-94.

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

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

Journal	of	Health-System	Pharmacy	<b>66</b> (22):	2027-203
Journal	01	<u>Incartiti-System</u>	<u>I narmac y</u>	00(22).	2027-20.

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# **Appendix C**

## Summary of risk of bias assessment\*

Study reference	Randomiza tion	Allocation concealment	Similarity of baseline	Similarity of baseline	Incomplete outcome data	Assessors blind to	Absence of contamination	Selective	Free of other biases	Total†
			characteristics	outcomes		outcome		reporting		
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.

<sup>†</sup>Studies with *clear* data' each of the domains given of 1. а on were a score

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## Appendix D

Subgroup analysis

## 4.1 All-cause Readmission

## 4.1.1 Subgroup analysis based on outcome timing

11 J	Interve		Usual			Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% CI
2.2.1 Readmission, 30 d							
Anderegg 2014 [Overall]	258	1652	270	1664	7.8%	0.96 [0.82, 1.13]	+
Anderegg 2014 [High-risk]	44	358	58	325	6.0%	0.69 [0.48, 0.99]	
Eisenhower 2014	4	25	13	60	2.0%	0.74 [0.27, 2.05]	
Farris 2014 [Enhanced]	47	311	43	313	5.8%	1.10 [0.75, 1.61]	
Farris 2014 [Minimal]	40	312	43	313	5.6%	0.93 [0.62, 1.39]	
Gardella 2012	97	1624	961	7335	7.4%	0.46 [0.37, 0.56]	+
Hawes 2014	0	24	12	37	0.3%	0.06 (0.00, 0.98) 🔸	
Pal 2013	90	537	50	192	6.5%	0.64 [0.47, 0.87]	
Stowasser 2002	9	113	12	127	2.7%	0.84 [0.37, 1.93]	
Walker 2009	79	358	66	366	6.6%	1.22 [0.91, 1.64]	
Warden 2014	2	35	21	115	1.2%	0.31 [0.08, 1.27]	
Wilkinson 2011	36	229	95	440	6.1%	0.73 [0.51, 1.03]	
Subtotal (95% CI)		5578		11287	58.0%	0.77 [0.60, 0.98]	◆
Total events	706		1644				
Test for overall effect: Z = 2. 2.2.2 Readmission > 30 d	12 (P = 0.0	13)					
Farris 2014 [Enhanced]	49	311	47	313	5.9%	1.05 [0.73, 1.52]	<u> </u>
Farris 2014 [Minimal]	51	312	47	313	5.9%	1.09 [0.76, 1.57]	<b></b>
Gardella 2012	44	1624	565	7335	6.5%	0.35 [0.26, 0.48]	-
Gillespie 2009	106	182	110	186	7.7%	0.98 [0.83, 1.17]	+
Hellstrom 2012	547	1216	1296	2758	8.2%	0.96 [0.89, 1.03]	+
Scullin 2007	141	371	172	391	7.7%	0.86 [0.73, 1.03]	-
Subtotal (95% CI)		4016		11296	42.0%	0.83 [0.66, 1.06]	•
Total events	938		2237				
Heterogeneity: Tau <sup>2</sup> = 0.07;	Chi <sup>2</sup> = 46.	15, df = 1	5 (P < 0.0	0001); P	<sup>2</sup> = 89%		
Test for overall effect: Z = 1.	48 (P = 0.1	4)					
Total (95% CI)		9594		22583	100.0%	0.80 [0.68, 0.94]	•
Total events	1644		3881				
Heterogeneity: Tau <sup>2</sup> = 0.08;	Chi <sup>2</sup> = 113	.86, df=	17 (P <	0.00001	); I <sup>2</sup> = 859	5 E	01 0.1 1 10
Test for overall effect: Z = 2.						υ.	01 0.1 1 10 Favours intervention Favours usual care
			= 1 (P = 0	.63), I <sup>z</sup> =	0%		Favours intervention Favours usual care
Test for subgroup differenc							
Test for subgroup differenc							

# 4.1.2 Subgroup analysis based on study design

	Interver		Usual			Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
2.3.1 RCT							
Farris 2014 [Enhanced]	49	311	47	313	6.9%	1.05 [0.73, 1.52]	-
Farris 2014 [Minimal]	51	312	47	313	7.0%	1.09 [0.76, 1.57]	+-
Gillespie 2009	106	182	110	186	10.1%	0.98 [0.83, 1.17]	
Hawes 2014	0	24	12	37	0.3%	0.06 (0.00, 0.98)	•
Bcullin 2007	141	371	172	391	10.1%	0.86 [0.73, 1.03]	*
Stowasser 2002	9	113	12	127	2.6%	0.84 [0.37, 1.93]	
Subtotal (95% CI)		1313		1367	37.1%	0.95 [0.83, 1.08]	•
Fotal events	356		400				
Heterogeneity: Tau² = 0.00; 0			(P = 0.30	); I <sup>z</sup> = 18	%		
Fest for overall effect: Z = 0.8	0 (P = 0.4	2)					
2.3.2 NRCT							
Anderegg 2014 [Overall]	258	1652	270	1664	10.3%	0.96 [0.82, 1.13]	+
Anderegg 2014 [High-risk]	44	358	58	325	7.0%	0.69 [0.48, 0.99]	
Eisenhower 2014	4	25	13	60	1.9%	0.74 [0.27, 2.05]	
Gardella 2012	44	1624	565	7335	8.0%	0.35 [0.26, 0.48]	-
Hellstrom 2012	547	1216	1296	2758	11.3%	0.96 [0.89, 1.03]	+
Pal 2013	90	537	50	192	7.9%	0.64 [0.47, 0.87]	
Valker 2009	79	358	66	366	8.1%	1.22 [0.91, 1.64]	+
Warden 2014	2	35	21	115	1.1%	0.31 [0.08, 1.27]	
Vilkinson 2011	36	229	95	440	7.2%	0.73 [0.51, 1.03]	
Subtotal (95% CI)		6034		13255	62.9%	0.74 [0.58, 0.94]	•
Fotal events	1104		2434				
Heterogeneity: Tau <sup>2</sup> = 0.09; C	;hi² = 58.5	58, df = 8	3 (P < 0.0	0001); P	²= 86%		
Fest for overall effect: Z = 2.4	7 (P = 0.0	1)					
Fotal (95% CI)		7347		14622	100.0%	0.82 [0.70, 0.96]	•
Fotal events	1460		2834				
Heterogeneity: Tau <sup>2</sup> = 0.05; C	hi <sup>2</sup> = 65.1	3, df = 1	14(P < 0.)	00001);	I <sup>2</sup> = 79%		0.01 0.1 1 10 1
Fest for overall effect: Z = 2.5	4 (P = 0.0	1)					U.U1 U.1 1 1U 1 Favours intervention Favours usual care
Fest for subgroup difference	s: Chi² = 3	8.10, df=	= 1 (P = 0	.08), I <sup>2</sup> =	67.7%		ravours intervention ravours usual care
.2 All-cause ED	visits						
.2 All-Cause ED	v 15113						
.2.1 Subgroup an	alveio	hase	nd on	outor	nma ti	iming	
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# 4.2 All-cause ED visits

# 4.2.1 Subgroup analysis based on outcome timing

	Interver	tion	Usual	care		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
1.1.1 ED visit, 30 d							
Anderegg 2014 [High-risk]	22	358	31	325	7.8%	0.64 [0.38, 1.09]	
Anderegg 2014 [Overall]	155	1652	168	1664	10.0%	0.93 [0.76, 1.14]	+
Farris 2014 [Enhanced]	38	311	52	313	8.8%	0.74 [0.50, 1.08]	
Farris 2014 (Minimal)	49	312	52	313	9.1%	0.95 [0.66, 1.35]	-+-
Gardella 2012	37	1424	785	7199	9.3%	0.24 [0.17, 0.33]	
Hawes 2014	0	24	11	37	1.0%	0.07 [0.00, 1.07]	· · · · · · · · · · · · · · · · · · ·
Walker 2009	34	358	45	366	8.6%	0.77 [0.51, 1.18]	
Subtotal (95% CI)		4439		10217	54.6%	0.61 [0.38, 0.99]	◆
Total events	335		1144				
Heterogeneity: Tau <sup>2</sup> = 0.33; C	chi² = 60.9	18, df = 1	6 (P < 0.0	0001); P	²= 90%		
Test for overall effect: Z = 1.9	8 (P = 0.0	5)					
1.1.2 ED visit,> 30 d							
Farris 2014 [Enhanced]	41	311	46	313	8.8%	0.90 [0.61, 1.33]	
Farris 2014 (Minimal)	40	312	46	313	8.8%	0.87 [0.59, 1.29]	
Gardella 2012	20	1424	381	7199	8.4%	0.27 [0.17, 0.41]	
Gillespie 2009	36	182	52	186	9.0%	0.71 [0.49, 1.03]	
Hellstrom 2012	594	1216	1416	2758	10.5%	0.95 [0.89, 1.02]	. 1
Subtotal (95% CI)		3445		10769	45.4%	0.69 [0.46, 1.03]	•
Total events	731		1941				
Heterogeneity: Tau <sup>2</sup> = 0.18; C	chi² = 36.4	1, df = -	4 (P < 0.0	0001); P	²= 89%		
Test for overall effect: Z = 1.8	0 (P = 0.0	7)					
Total (95% CI)		7884		20096	100.0%	0.65 [0.49, 0.87]	
Total events	1066	1004	3085	20500	100.0%	0.05 [0.45, 0.07]	•
		02 46-		000041	V IZ - 010		
Heterogeneity: Tau <sup>2</sup> = 0.21; C			: I I (P < I	0.00001	, = 91%	0	0.01 0.1 1 10 100
Test for overall effect: Z = 2.8	•		- 1 /D - 0	701 17	.00		Favours intervention Favours usual care
Test for subgroup difference:	s: Uni*= U	. 13, at:	= 1 (P = 0	.72), [*=	0%		

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# 4.2.2 Subgroup analysis based on study design

	Interver	tion	Usual	are		Risk Ratio	Risk Ratio
Study or Subgroup	Events		Events		Weight	M-H, Random, 95% CI	M-H, Random, 95% Cl
1.2.1 RCT							
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]	
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]	• • • • • • • • • • • • • • • • • • •
Subtotal (95% CI)		829		849	36.4%	0.80 [0.61, 1.05]	•
Total events	117		155				
Heterogeneity: Tau <sup>2</sup> = 0.02; C	hi <sup>2</sup> = 4.11	, df = 3	(P = 0.25)	); I <sup>2</sup> = 27	%		
Test for overall effect: Z = 1.6	0 (P = 0.1	1)					
1.2.2 NRCT							
Anderegg 2014 (High-risk)	22	358	31	325	9.4%	0.64 [0.38, 1.09]	
Anderegg 2014 [Overall]	155	1652	168	1664	15.2%	0.93 [0.76, 1.14]	+
Gardella 2012	20	1424	381	7199	10.8%	0.27 [0.17, 0.41]	
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]	
Subtotal (95% CI)		5008		12312	63.6%	0.68 [0.48, 0.97]	$\bullet$
Total events	825		2041				
Heterogeneity: Tau <sup>2</sup> = 0.13; C			4 (P < 0.0	0001); P	²= 89%		
Test for overall effect: Z = 2.1	5 (P = 0.0	3)					
Total (95% CI)		5837		13161	100.0%	0.72 [0.57, 0.92]	•
Total events	942		2196				
Heterogeneity: Tau <sup>2</sup> = 0.09; C	hi² = 42.2	6, df = 1	8 (P < 0.0	0001); P	²= 81%		
Test for overall effect: Z = 2.63	3 (P = 0.0	09)					Favours intervention Favours usual care
Test for subgroup differences	s: Chi <sup>2</sup> = 0	.49, df=	= 1 (P = 0	.49), I <sup>2</sup> =	0%		avours intervention Tavours usual care

## 4.3 All-cause mortality

# 4.3.1 Subgroup analysis based on outcome timing

	Interver	ntion	Usual	care		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
1.4.1 Mortality, 30 d							
Stowasser 2002	2	113	3	127	0.3%	0.75 [0.13, 4.40]	
Subtotal (95% CI)		113		127	0.3%	0.75 [0.13, 4.40]	
Total events	2		3				
Heterogeneity: Not applic	able						
Test for overall effect: Z =	0.32 (P = 0	0.75)					
1.4.2 Mortality, >30 d							
Bolas 2004	17	119	12	124	1.9%	1.48 [0.74, 2.96]	
Farris 2014 [Enhanced]	12	311	7	313	1.1%	1.73 [0.69, 4.32]	<u>+</u>
Farris 2014 (Minimal)	5	312	7	313	0.7%	0.72 [0.23, 2.23]	
Gillespie 2009	70	199	75	201	13.6%	0.94 [0.73, 1.22]	+
Hellstrom 2011	9	109	9	101	1.2%	0.93 [0.38, 2.24]	
Hellstrom 2012	330	1325	685	2965	70.7%	1.08 [0.96, 1.21]	· · · · · · · · · · · · · · · · · · ·
Scullin 2007	67	371	76	391	10.5%	0.93 [0.69, 1.25]	+
Subtotal (95% CI)		2746		4408	99.7%	1.05 [0.95, 1.15]	•
Total events	510		871				
Heterogeneity: Tau <sup>2</sup> = 0.0	0; Chi <sup>2</sup> = 4	.08, df=	= 6 (P = 0	.67); l² =	= 0%		
Test for overall effect: Z =	0.97 (P = 0	D.33)					
Total (95% CI)		2859		4535	100.0%	1.05 [0.95, 1.15]	•
Total events	512		874				
Heterogeneity: Tau <sup>2</sup> = 0.0	0; Chi <sup>2</sup> = 4	.22, df=	= 7 (P = 0	.75); l² =	= 0%		0.001 0.1 1 10 100
Test for overall effect: Z =	0.95 (P = 0	0.34)					Favours intervention Favours usual care
Test for subgroup differer	nces: Chi²	= 0.14,	df = 1 (P	= 0.71),	I <sup>2</sup> = 0%		Favours intervention Favours usual care

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## 

# 4.3.1 Subgroup analysis based on study design

	Interver	ntion	Usual	care		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
1.5.1 RCT							
Bolas 2004	17	119	12	124	1.9%	1.48 [0.74, 2.96]	
Farris 2014 [Enhanced]	12	311	7	313	1.1%	1.73 [0.69, 4.32]	+
Farris 2014 [Minimal]	5	312	7	313	0.7%	0.72 [0.23, 2.23]	
Gillespie 2009	70	199	75	201	13.6%	0.94 [0.73, 1.22]	+
Scullin 2007	67	371	76	391	10.5%	0.93 [0.69, 1.25]	+
Stowasser 2002 Subtotal (95% CI)	2	113 1425	3	127 1469	0.3%	0.75 [0.13, 4.40] 0.98 [0.82, 1.17]	•
Total events	173		180				
Heterogeneity: Tau <sup>2</sup> = 0.0	0: Chi <sup>2</sup> = 3	.39. df=	= 5 (P = 0	.64); I <sup>2</sup> =	= 0%		
Test for overall effect: Z =		-					
1.5.2 NRCT							
Hellstrom 2011	9	109	9	101	1.2%	0.93 [0.38, 2.24]	
Hellstrom 2012	330	1325	685	2965	70.7%	1.08 [0.96, 1.21]	<b>—</b>
Subtotal (95% CI)		1434		3066	71.8%	1.08 [0.96, 1.20]	•
Total events	339		694				
Heterogeneity: Tau <sup>2</sup> = 0.0	0; Chi <sup>2</sup> = 0	.11, df=	= 1 (P = 0	.74); l² =	= 0%		
Test for overall effect: Z =	1.26 (P = 1	0.21)					
Total (95% CI)		2859		4535	100.0%	1.05 [0.95, 1.15]	•
Total events	512		874				
Heterogeneity: Tau <sup>2</sup> = 0.0	0; Chi <sup>2</sup> = 4	.22, df=	7 (P = 0	.75); l² =	= 0%		0.002 0.1 1 10 500
Test for overall effect: Z =	0.95 (P = 1	0.34)					Favours intervention Favours usual care
Test for subgroup differen	nces: Chi <sup>2</sup>	= 0.72	df = 1 (P)	= 0.40	$l^2 = 0\%$		Favours intervention Favours usual care

# 4.4 Composite readmission and/or ED visit

## 4.4.1 Subgroup analysis based on outcome timing

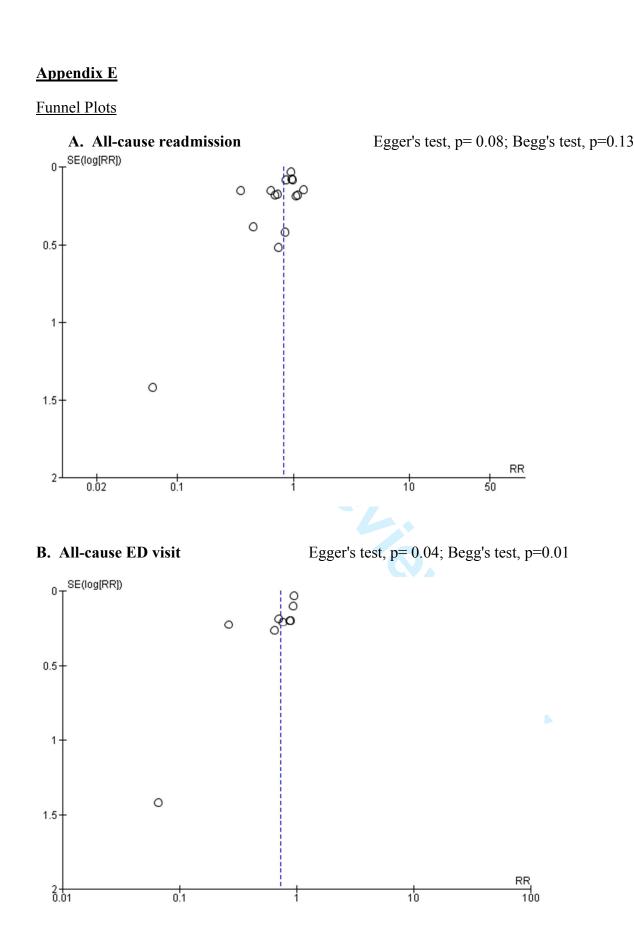
$\begin{array}{ c c c c c c c c c c c c c c c c c c c$								
2.5.1 Composite readmission and/or ED visit, 30 d         Anderegg 2014 [Overall]       373       1652       399       1664       14.7%       0.97       0.05, 1.09]         Anderegg 2014 [Enhanced]       81       311       87       313       3.9%       0.94 [0.72, 1.21]         Farris 2014 [Minimal]       88       312       87       313       4.1%       1.01 [0.72, 1.21]         Farris 2014 [Minimal]       88       312       87       313       4.1%       1.01 [0.00, 0.78]         Koehler 2009       2       20       8       21       0.9%       0.05 [0.00, 0.78]         Schipper 2006       28       92       25       84       1.3%       1.02 [0.65, 1.61]         Walker 2009       98       358       94       366       4.4%       1.07 [0.84, 1.36]         Subtotal (95% CI)       3127       3123       31.4%       0.94 [0.82, 1.08]       1.04         Total events       732       780       1.03 [0.80, 1.32]       1.04       1.11 [0.87, 1.41]         Farris 2014 [Minimal]       90       311       88       313       4.2%       1.03 [0.80, 1.32]       1.03 [0.80, 1.32]         Gillespie 2009       134       182       147       186		Interver	ntion	Usual	care		Risk Ratio	Risk Ratio
Anderegg 2014 [Overall] 373 1652 309 1664 14.7% 0.97 [0.65, 1.09] Anderegg 2014 [High-risk] 62 358 75 325 2.9% 0.75 [0.56, 1.01] Farris 2014 [Enhanced] 81 311 87 313 3.9% 0.94 [0.72, 1.21] Farris 2014 [Minimal] 88 312 87 313 4.1% 1.01 [0.79, 1.30] Hawes 2014 0 24 15 37 0.0% 0.05 [0.00, 0.78] Koehler 2009 2 2 20 8 21 0.1% 0.26 [0.66, 1.09] Schnipper 2006 28 92 25 84 1.3% 1.02 [0.65, 1.61] Walker 2009 9 8 358 94 366 4.4% 1.07 [0.84, 1.36] Subtotal (95% CI) 3127 3123 31.4% 0.94 [0.82, 1.08] Total events 732 780 Heterogeneity: Tau <sup>2</sup> = 0.01; Chi <sup>2</sup> = 11.33, df = 7 (P = 0.13); P = 38% Test for overall effect Z = 0.90 (P = 0.37) 2.5.2 Composite readmission and/or ED visit, > 30 d Farris 2014 [Minimal] 90 311 88 313 4.2% 1.03 [0.80, 1.32] Gillespie 2008 134 182 147 186 17.0% 0.93 [0.83, 1.04] Hellstrom 2011 45 109 41 101 2.5% 1.02 [0.73, 1.41] Hellstrom 2012 645 1216 1555 2758 40.2% 0.94 [0.88, 1.00] Koehler 2009 6 20 9 21 0.4% 0.70 [0.30, 1.61] Subtotal (95% CI) 2150 3692 68.6% 0.95 [0.91, 1.00] Total events 1749 2708 Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 2.89, df = 5 (P = 0.72); I <sup>2</sup> = 0% Test for overall effect Z = 1.77 (P = 0.08) Total (95% CI) 5277 6815 100.0% 0.95 [0.91, 1.00] Total events 1749 2708 Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 1.400, df = 13 (P = 0.37); I <sup>2</sup> = 7% Total (95% CI) 5277 6815 100.0% 0.95 [0.91, 1.00] Total events 1749 2708 Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 1.400, df = 13 (P = 0.37); I <sup>2</sup> = 7% Test for overall effect Z = 1.77 (P = 0.08)	Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
Anderegg 2014 [High-risk] 62 358 75 325 2.9% 0.75 [0.56, 1.01] Farris 2014 [Enhanced] 81 311 87 313 3.9% 0.94 [0.72, 1.21] Farris 2014 [Minimal] 88 312 87 313 4.1% 1.01 [0.79, 1.30] Hawes 2014 0 24 15 37 0.0% 0.05 [0.00, 0.78] Schnipper 2006 28 92 25 84 1.3% 1.02 [0.65, 1.61] Walker 2009 98 358 94 366 4.4% 1.07 [0.84, 1.36] Subtotal (95% Cl) 3127 3123 31.4% 0.94 [0.82, 1.08] Total events 732 780 Helstrom 2011 4 (Minimal] 90 311 88 313 4.4% 1.11 [0.87, 1.41] Farris 2014 [Enhanced] 97 312 88 313 4.4% 1.11 [0.87, 1.41] Farris 2014 [Enhanced] 97 312 88 313 4.4% 1.02 [0.63, 1.03] Cillespie 2009 134 182 147 186 17.0% 0.93 [0.80, 1.32] Gillespie 2009 134 182 147 186 17.0% 0.93 [0.80, 1.32] Gillespie 2009 6 20 9 21 0.4% 0.70 [0.30, 1.81] Subtotal (95% Cl) 2150 3692 68.6% 0.95 [0.90, 1.00] Total events 1017 1928 Heterogeneity: Tau <sup>2</sup> = 0.00; Ch <sup>2</sup> = 2.89, df = 5 (P = 0.72); P = 0% Test for overall effect: Z = 1.95 (P = 0.05) Total events 1749 2708 Heterogeneity: Tau <sup>2</sup> = 0.00; Ch <sup>2</sup> = 2.89, df = 5 (P = 0.37); P = 7% Test for overall effect: Z = 1.77 (P = 0.08)	2.5.1 Composite readmissi	on and/or	ED visit	, 30 d				
Farris 2014 [Enhanced] 81 311 87 313 3.9% 0.94 [0.72, 1.21] Farris 2014 [Minimal] 88 312 87 313 4.1% 1.01 [0.79, 1.30] Hawes 2014 0 24 15 37 0.0% 0.05 [0.00, 0.78] Hawes 2014 0 24 15 37 0.0% 0.05 [0.00, 0.78] Koehler 2009 2 20 8 21 0.1% 0.26 [0.66, 1.09] Schnipper 2006 28 92 25 84 1.3% 1.02 [0.65, 1.61] Walker 2009 98 358 94 366 4.4% 1.07 [0.84, 1.36] Subtotal (95% CI) 3127 3123 31.4% 0.94 [0.82, 1.08] Total events 732 780 Heterogeneity: Tau <sup>2</sup> = 0.01; Chi <sup>2</sup> = 11.33, df = 7 ( $P = 0.13$ ); $P = 38\%$ Test for overall effect: $Z = 0.90$ ( $P = 0.37$ ) 2.5.2 Composite readmission and/or ED visit, > 30 d Farris 2014 [Enhanced] 97 312 88 313 4.4% 1.11 [0.87, 1.41] Farris 2014 [Minimal] 90 311 88 313 4.2% 1.03 [0.80, 1.32] Gillespie 2009 134 182 147 186 17.0% 0.93 [0.83, 1.04] Hellstrom 2011 45 109 41 101 2.5% 1.02 [0.73, 1.41] Hellstrom 2012 645 1216 1555 2758 40.2% 0.94 [0.88, 1.00] Koehler 2009 6 20 9 21 0.4% 0.70 [0.30, 1.61] Subtotal (95% CI) 2150 3692 68.6% 0.95 [0.90, 1.00] Total events 1017 1928 Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 2.89, df = 5 ( $P = 0.72$ ); $P = 0\%$ Test for overall effect: $Z = 1.95$ ( $P = 0.05$ ) Total events 1749 2708 Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 14.00, df = 13 ( $P = 0.37$ ); $P = 7\%$ Total (95% CI) 5277 6815 100.0% 0.95 [0.91, 1.00] Total events 1749 2708 Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 14.00, df = 13 ( $P = 0.37$ ); $P = 7\%$	Anderegg 2014 [Overall]	373	1652	389	1664	14.7%	0.97 [0.85, 1.09]	+
Farris 2014 [Minimal] 88 312 87 313 4.1% $1.01 [0.79, 1.30]$ Hawes 2014 0 24 15 37 0.0% $0.05 [0.00, 0.78]$ Koehler 2009 2 20 8 21 0.1% $0.26 [0.06, 1.09]$ Schnipper 2006 28 92 25 84 1.3% $1.02 [0.65, 1.61]$ Walker 2009 98 358 94 366 4.4% $1.07 [0.84, 1.36]$ Subtotal (95% CI) 3127 3123 31.4% $0.94 [0.82, 1.08]$ Total events 732 780 Heterogeneity: Tau <sup>2</sup> = 0.01; Chi <sup>2</sup> = 11.33, df = 7 (P = 0.13); l <sup>2</sup> = 38% Test for overall effect: Z = 0.90 (P = 0.37) 2.5.2 Composite readmission and/or ED visit, > 30 d Farris 2014 [Enhanced] 97 312 88 313 4.4% $1.11 [0.87, 1.41]$ Farris 2014 [Enhanced] 97 312 88 313 4.2% $1.03 [0.80, 1.32]$ Gillespie 2009 134 182 147 186 17.0% $0.33 [0.83, 1.04]$ Helistrom 2011 45 109 41 101 2.5% $1.02 [0.73, 1.41]$ Helistrom 2011 45 109 41 101 2.5% $0.94 [0.88, 1.00]$ Koehler 2009 6 20 9 21 0.4% $0.70 [0.30, 1.61]$ Subtotal (95% CI) 2150 3692 68.6% $0.95 [0.91, 1.00]$ Total events 1017 1928 Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 2.89, df = 5 (P = 0.72); l <sup>2</sup> = 7% Test for overall effect: Z = 1.95 (P = 0.05) Total events 1017 1928 Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 14.00, df = 13 (P = 0.37); l <sup>2</sup> = 7% Test for overall effect: Z = 1.77 (P = 0.08)	Anderegg 2014 [High-risk]	62	358	75	325	2.9%	0.75 [0.56, 1.01]	
Hawes 2014 0 24 15 37 0.0% 0.05 [0.00, 0.78] Koehler 2009 2 20 8 21 0.1% 0.26 [0.06, 1.09] Schnipper 2006 28 92 25 84 1.3% 1.02 [0.65, 1.61] Walker 2009 98 358 94 366 4.4% 1.07 [0.84, 1.36] Subtotal (95% CI) 3127 3123 31.4% 0.94 [0.82, 1.08] Total events 732 780 Heterogeneity: Tau <sup>2</sup> = 0.01; Chi <sup>2</sup> = 11.33, df = 7 (P = 0.13); P = 38% Test for overall effect: Z = 0.90 (P = 0.37) 2.5.2 Composite readmission and/or ED visit, > 30 d Farris 2014 [Enhanced] 97 312 88 313 4.4% 1.11 [0.87, 1.41] Farris 2014 [Minimal] 90 311 88 313 4.2% 1.03 [0.80, 1.32] Gillespie 2009 134 182 147 186 17.0% 0.93 [0.83, 1.04] Hellstrom 2011 45 109 41 101 2.5% 1.02 [0.73, 1.41] Hellstrom 2012 645 1216 1555 2758 40.2% 0.94 [0.88, 1.00] Koehler 2009 6 20 9 21 0.4% 0.70 [0.30, 1.61] Subtotal (95% CI) 2150 3692 68.6% 0.95 [0.90, 1.00] Total events 1017 1928 Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 2.89, df = 5 (P = 0.72); I <sup>2</sup> = 0% Test for overall effect: Z = 1.95 (P = 0.05) Total events 1017 1927 Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 14.00, df = 13 (P = 0.37); I <sup>2</sup> = 7% Test for overall effect: Z = 1.77 (P = 0.08) $D_{10} = 10000$ Chi <sup>2</sup> = 14.00, df = 13 (P = 0.37); I <sup>2</sup> = 7% Test for overall effect: Z = 1.77 (P = 0.08)	Farris 2014 [Enhanced]	81	311	87	313	3.9%	0.94 [0.72, 1.21]	-
Koehler 2009       2       20       8       21       0.1%       0.26       [0.06, 1.09]         Schnipper 2006       28       92       25       84       1.3%       1.02       [0.06, 1.61]         Walker 2009       98       358       94       366       4.4%       1.07       [0.84, 1.36]         Subtotal (95% CI)       3127       3123       31.4%       0.94       [0.82, 1.08]         Total events       732       780         Heterogeneity: Tau <sup>2</sup> = 0.01; Ch <sup>2</sup> = 11.33, df = 7 (P = 0.13); P = 38%         Test for overall effect: Z = 0.90 (P = 0.37)         2.5.2 Composite readmission and/or ED visit, > 30 d         Farris 2014 [Enhanced]       97       312       88       313       4.4%       1.11 [0.87, 1.41]         Farris 2014 [Minimal]       90       311       88       313       4.2%       1.03 [0.80, 1.32]         Gillespie 2009       134       182       147       186       17.0%       0.93 [0.83, 1.04]         Helstrom 2011       45       109       41       101       2.5%       1.02 [0.73, 1.41]         Subtotal (95% CI)       2150       3692       68.6%       0.95 [0.90, 1.00]       100         Total events       1017       1	Farris 2014 (Minimal)	88	312	87	313	4.1%	1.01 [0.79, 1.30]	+
Schnipper 2006 28 92 25 84 1.3% 1.02 [0.65, 1.61] Walker 2009 98 358 94 366 4.4% 1.07 [0.84, 1.36] Subtotal (95% CI) 3127 3123 31.4% 0.94 [0.82, 1.08] Total events 732 780 Heterogeneity: Tau <sup>2</sup> = 0.01; Chi <sup>2</sup> = 11.33, df = 7 (P = 0.13); I <sup>2</sup> = 38% Test for overall effect: $Z = 0.90$ (P = 0.37) 2.5.2 Composite readmission and/or ED visit, > 30 d Farris 2014 [Enhanced] 97 312 88 313 4.4% 1.11 [0.87, 1.41] Farris 2014 [Enhanced] 97 312 88 313 4.2% 1.03 [0.80, 1.32] Gillespie 2009 134 182 147 186 17.0% 0.93 [0.83, 1.04] Hellstrom 2011 45 109 41 101 2.5% 1.02 [0.73, 1.41] Hellstrom 2012 645 1216 1555 2758 40.2% 0.94 [0.88, 1.00] Koehler 2009 6 20 9 21 0.4% 0.70 [0.30, 1.61] Subtotal (95% CI) 2150 3692 68.6% 0.95 [0.90, 1.00] Total events 1017 1928 Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 2.89, df = 5 (P = 0.72); I <sup>2</sup> = 0% Test for overall effect: $Z = 1.95$ (P = 0.05) Total events 1749 2708 Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 14.00, df = 13 (P = 0.37); I <sup>2</sup> = 7% Test for overall effect: $Z = 1.77$ (P = 0.08)	Hawes 2014	0	24	15	37	0.0%	0.05 [0.00, 0.78]	• • • • • • • • • • • • • • • • • • • •
Walker 2009       98       358       94       366       4.4%       1.07       [0.84, 1.36]         Subtotal (95% Cl)       3127       3123       31.4%       0.94       [0.82, 1.08]         Total events       732       780         Heterogeneity: Tau <sup>2</sup> = 0.01; Chi <sup>2</sup> = 11.33, df = 7 (P = 0.13); P = 38%         Test for overall effect: Z = 0.90 (P = 0.37)         2.5.2 Composite readmission and/or ED visit, > 30 d         Farris 2014 [Enhanced]       97       312       88       313       4.4%       1.11 [0.87, 1.41]         Farris 2014 [Minimal]       90       311       88       313       4.2%       1.03 [0.80, 1.32]         Gillespie 2009       134       182       147       186       17.0%       0.93 [0.83, 1.04]         Hellstrom 2011       45       109       41       101       2.5%       1.02 [0.73, 1.41]         Hellstrom 2012       645       1216       1555       2758       40.2%       0.94 [0.88, 1.00]       •         Koehler 2009       6       20       9       21       0.4%       0.70 [0.30, 1.61]       •         Subtotal (95% Cl)       2150       3692       68.6%       0.95 [0.90, 1.00]       •       •         Total events	Koehler 2009	2	20	8	21	0.1%	0.26 [0.06, 1.09]	
Subtotal (95% CI) $3127$ $3123$ $314\%$ $0.94$ ( $0.82$ , $1.08$ ]         Total events $732$ $780$ Heterogeneity: Tau <sup>2</sup> = 0.01; Chi <sup>2</sup> = 11.33, df = 7 (P = 0.13); P = 38%         Test for overall effect: $Z = 0.90$ (P = 0.37)         2.5.2 Composite readmission and/or ED visit, > 30 d         Farris 2014 [Enhanced]       97 $312$ $88$ $313$ $4.4\%$ $1.11$ [ $0.87$ , $1.41$ ]         Farris 2014 [Enhanced]       97 $312$ $88$ $313$ $4.2\%$ $1.03$ [ $0.80$ , $1.32$ ]         Gillespie 2009       134       182       147       186 $1.03$ [ $0.83$ , $1.04$ ]         Hellstrom 2011       45       109       41 $101$ $2.5\%$ $0.94$ [ $0.88$ , $1.00$ ]         Koehler 2009       6       20       9 $21$ $0.4\%$ $0.70$ [ $0.30$ , $1.61$ ]         Subtotal (95% CI)       2150 $3692$ $68.6\%$ $0.95$ [ $0.90$ , $1.00$ ] $0.95$ [ $0.91$ , $1.00$ ]         Total events $1017$ $1928$ $0.95$ [ $0.91$ , $1.00$ ] $0.95$ [ $0.91$ , $1.00$ ] $0.95$ [ $0.91$ , $1.00$ ]         Total events $1749$ $2708$ $0.95$ [ $0.91$ , $1.00$ ] $0.1$ $10$ $1$	Schnipper 2006	28	92	25	84	1.3%	1.02 [0.65, 1.61]	
Heterogeneity: Tau <sup>2</sup> = 0.01; Chi <sup>2</sup> = 11.33, df = 7 (P = 0.13); l <sup>2</sup> = 38% Test for overall effect: $Z = 0.90$ (P = 0.37) 2.5.2 Composite readmission and/or ED visit, > 30 d Farris 2014 [Enhanced] 97 312 88 313 4.4% 1.11 [0.87, 1.41] Farris 2014 [Minimal] 90 311 88 313 4.2% 1.03 [0.80, 1.32] Gillespie 2009 134 182 147 186 17.0% 0.93 [0.83, 1.04] Hellstrom 2011 45 109 41 101 2.5% 1.02 [0.73, 1.41] Hellstrom 2012 645 1216 1555 2758 40.2% 0.94 [0.88, 1.00] Koehler 2009 6 20 9 21 0.4% 0.70 [0.30, 1.61] Subtotal (95% CI) 2150 3692 68.6% 0.95 [0.90, 1.00] Total events 1017 1928 Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 2.89, df = 5 (P = 0.72); l <sup>2</sup> = 0% Test for overall effect: $Z = 1.95$ (P = 0.05) Total (95% CI) 5277 6815 100.0% 0.95 [0.91, 1.00] Total events 1749 2708 Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 14.00, df = 13 (P = 0.37); l <sup>2</sup> = 7% Test for overall effect: $Z = 1.77$ (P = 0.08)		98		94				<b>↓</b>
Test for overall effect: $Z = 0.90 (P = 0.37)$ 2.5.2 Composite readmission and/or ED visit, > 30 d Farris 2014 [Enhanced] 97 312 88 313 4.4% 1.11 [0.87, 1.41] Farris 2014 [Minimal] 90 311 88 313 4.2% 1.03 [0.80, 1.32] Gillespie 2009 134 182 147 186 17.0% 0.93 [0.83, 1.04] Hellstrom 2011 45 109 41 101 2.5% 1.02 [0.73, 1.41] Hellstrom 2012 645 1216 1555 2758 40.2% 0.94 [0.88, 1.00] Koehler 2009 6 20 9 21 0.4% 0.70 [0.30, 1.61] Subtotal (95% CI) 2150 3692 68.6% 0.95 [0.90, 1.00] Total events 1017 1928 Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 2.89, df = 5 (P = 0.72); I <sup>2</sup> = 0% Test for overall effect: Z = 1.95 (P = 0.05) Total events 1749 2708 Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 14.00, df = 13 (P = 0.37); I <sup>2</sup> = 7% Test for overall effect: Z = 1.77 (P = 0.08)	Total events	732		780				
Farris 2014 [Minimal]       90       311       88       313       4.2%       1.03 [0.80, 1.32]         Gillespie 2009       134       182       147       186       17.0%       0.93 [0.83, 1.04]         Hellstrom 2011       45       109       41       101       2.5%       1.02 [0.73, 1.41]         Hellstrom 2012       645       1216       1555       2758       40.2%       0.94 [0.88, 1.00]         Koehler 2009       6       20       9       21       0.4%       0.70 [0.30, 1.61]         Subtotal (95% CI)       2150       3692       68.6%       0.95 [0.90, 1.00]         Total events       1017       1928         Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 2.89, df = 5 (P = 0.72); P = 0%       0.95 [0.91, 1.00]         Total (95% CI)       5277       6815       100.0%       0.95 [0.91, 1.00]         Total (95% CI)       5277       6815       100.0%       0.95 [0.91, 1.00]         Total events       1749       2708       0.95 [0.91, 1.00]       10         Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 14.00, df = 13 (P = 0.37); P = 7%       0.01       0.1       10       1         Test for overall effect: Z = 1.77 (P = 0.08)       Fayours intervention       Fayours usual care       10 <t< td=""><td>Test for overall effect: Z = 0.9</td><td>90 (P = 0.3</td><td>7)</td><td></td><td>3); I<sup>z</sup> = 1</td><td>38%</td><td></td><td></td></t<>	Test for overall effect: Z = 0.9	90 (P = 0.3	7)		3); I <sup>z</sup> = 1	38%		
Farris 2014 [Minimal]       90       311       88       313       4.2%       1.03 [0.80, 1.32]         Gillespie 2009       134       182       147       186       17.0%       0.93 [0.83, 1.04]         Hellstrom 2011       45       109       41       101       2.5%       1.02 [0.73, 1.41]         Hellstrom 2012       645       1216       1555       2758       40.2%       0.94 [0.88, 1.00]         Koehler 2009       6       20       9       21       0.4%       0.70 [0.30, 1.61]         Subtotal (95% CI)       2150       3692       68.6%       0.95 [0.90, 1.00]         Total events       1017       1928         Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 2.89, df = 5 (P = 0.72); I <sup>2</sup> = 0%       0.95 [0.91, 1.00]         Total (95% CI)       5277       6815       100.0%       0.95 [0.91, 1.00]         Total events       1749       2708       0.95 [0.91, 1.00]       10         Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 14.00, df = 13 (P = 0.37); I <sup>2</sup> = 7%       0.01       0.1       10       1         Favours intervention       Favours usual care       10       1       10       1       10       1					313	4 4 %	1 11 (0 87 1 41)	-
Gillespie 2009       134       182       147       186       17.0%       0.93 [0.83, 1.04]         Hellstrom 2011       45       109       41       101       2.5%       1.02 [0.73, 1.41]         Hellstrom 2012       645       1216       1555       2758       40.2%       0.94 [0.88, 1.00]         Koehler 2009       6       20       9       21       0.4%       0.70 [0.30, 1.61]         Subtotal (95% CI)       2150       3692       68.6%       0.95 [0.90, 1.00]       10         Total events       1017       1928         Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 2.89, df = 5 (P = 0.72); I <sup>2</sup> = 0%       0.95 [0.91, 1.00]       10         Total events       1749       2708       0.95 [0.91, 1.00]       10         Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 14.00, df = 13 (P = 0.37); I <sup>2</sup> = 7%       0.01       0.1       10       1         Test for overall effect: Z = 1.77 (P = 0.08)       Favours usual care       10       1       10       1							ALLOW A MODELING & COMPLEX IN	+
Hellstrom 2011       45       109       41       101       2.5%       1.02 [0.73, 1.41]         Hellstrom 2012       645       1216       1555       2758       40.2%       0.94 [0.88, 1.00]         Koehler 2009       6       20       9       21       0.4%       0.70 [0.30, 1.61]         Subtotal (95% CI)       2150       3692       68.6%       0.95 [0.90, 1.00]         Total events       1017       1928         Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 2.89, df = 5 (P = 0.72); I <sup>2</sup> = 0%         Test for overall effect: Z = 1.95 (P = 0.05)         Total events       1749       2708         Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 14.00, df = 13 (P = 0.37); I <sup>2</sup> = 7%       0.01       0.1       1         Test for overall effect: Z = 1.77 (P = 0.08)       100       10       1       10       1	Gillespie 2009	134	182	147	186	17.0%	0.93 [0.83, 1.04]	•
Hellstrom 2012       645       1216       1555       2758       40.2%       0.94 [0.88, 1.00]         Koehler 2009       6       20       9       21       0.4%       0.70 [0.30, 1.61]         Subtotal (95% Cl)       2150       3692       68.6%       0.95 [0.90, 1.00]       1         Total events       1017       1928       1928       1928       1928         Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 2.89, df = 5 (P = 0.72); I <sup>2</sup> = 0%       0.95 [0.91, 1.00]       1       1         Total (95% Cl)       5277       6815       100.0%       0.95 [0.91, 1.00]       1         Total events       1749       2708       1       1       1       1         Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 14.00, df = 13 (P = 0.37); I <sup>2</sup> = 7%       0.01       0.1       1       10       1         Test for overall effect: Z = 1.77 (P = 0.08)       1       10       1       10       1 </td <td></td> <td>45</td> <td>109</td> <td>41</td> <td>101</td> <td>2.5%</td> <td></td> <td>+</td>		45	109	41	101	2.5%		+
Subtotal (95% CI)         2150         3692         68.6%         0.95 [0.90, 1.00]           Total events         1017         1928           Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 2.89, df = 5 (P = 0.72); I <sup>2</sup> = 0%         0.95 [0.90, 1.00]           Total (95% CI)         5277         6815         100.0%         0.95 [0.91, 1.00]           Total events         1749         2708         1749         2708           Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 14.00, df = 13 (P = 0.37); I <sup>2</sup> = 7%         0.01         0.1         10         1           Test for overall effect: Z = 1.77 (P = 0.08)         Favours intervention         Favours usual care         Favours usual care	Hellstrom 2012	645	1216	1555	2758	40.2%		•
Total events       1017       1928         Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 2.89, df = 5 (P = 0.72); I <sup>2</sup> = 0%         Test for overall effect: Z = 1.95 (P = 0.05)         Total (95% CI)       5277       6815       100.0%       0.95 [0.91, 1.00]         Total events       1749       2708         Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 14.00, df = 13 (P = 0.37); I <sup>2</sup> = 7%       0.01       0.1       1       10       1         Test for overall effect: Z = 1.77 (P = 0.08)       Favours intervention       Favours usual care       5000000000000000000000000000000000000	Koehler 2009	6	20	9	21	0.4%	0.70 [0.30, 1.61]	
Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 2.89, df = 5 (P = 0.72); i <sup>2</sup> = 0% Test for overall effect: Z = 1.95 (P = 0.05) Total (95% CI) 5277 6815 100.0% 0.95 [0.91, 1.00] Total events 1749 2708 Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 14.00, df = 13 (P = 0.37); i <sup>2</sup> = 7% Test for overall effect: Z = 1.77 (P = 0.08)	Subtotal (95% CI)		2150		3692	68.6%	0.95 [0.90, 1.00]	•
Test for overall effect: Z = 1.95 (P = 0.05)         Total (95% CI)       5277       6815       100.0%       0.95 [0.91, 1.00]         Total events       1749       2708         Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 14.00, df = 13 (P = 0.37); l <sup>2</sup> = 7%       0.01       0.1       1       10       1         Test for overall effect: Z = 1.77 (P = 0.08)       Eavours intervention       Favours usual care	Total events	1017		1928				
Total events         1749         2708           Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 14.00, df = 13 (P = 0.37); l <sup>2</sup> = 7%         0.01         0.1         10         1           Test for overall effect: Z = 1.77 (P = 0.08)         Eavours intervention         Favours usual care         Favours intervention         Favours usual care				(P = 0.72	?); I² = 0	%		
Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 14.00, df = 13 (P = 0.37); l <sup>2</sup> = 7% Test for overall effect: Z = 1.77 (P = 0.08) Favours intervention Favours usual care	Total (95% CI)		5277		6815	100.0%	0.95 [0.91, 1.00]	•
Test for overall effect: Z = 1.77 (P = 0.08)	Total events	1749		2708				
Test for overall effect: Z = 1.77 (P = 0.08) Favours intervention Favours usual care				13 (P = 0	.37); l² =	: 7%		
Test for subgroup differences: Chi <sup>2</sup> = 0.02 df = 1 (P = 0.88) l <sup>2</sup> = 0%		•	· ·					
$(a_1, a_2, a_3, a_4, a_4, a_4, a_4, a_4, a_4, a_4, a_4$	Test for subgroup difference	es: Chi <sup>z</sup> = 0	1.02, df=	= 1 (P = 0	).88), <mark>I</mark> ²:	= 0%		

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# 4.4.2 Subgroup analysis based on study design

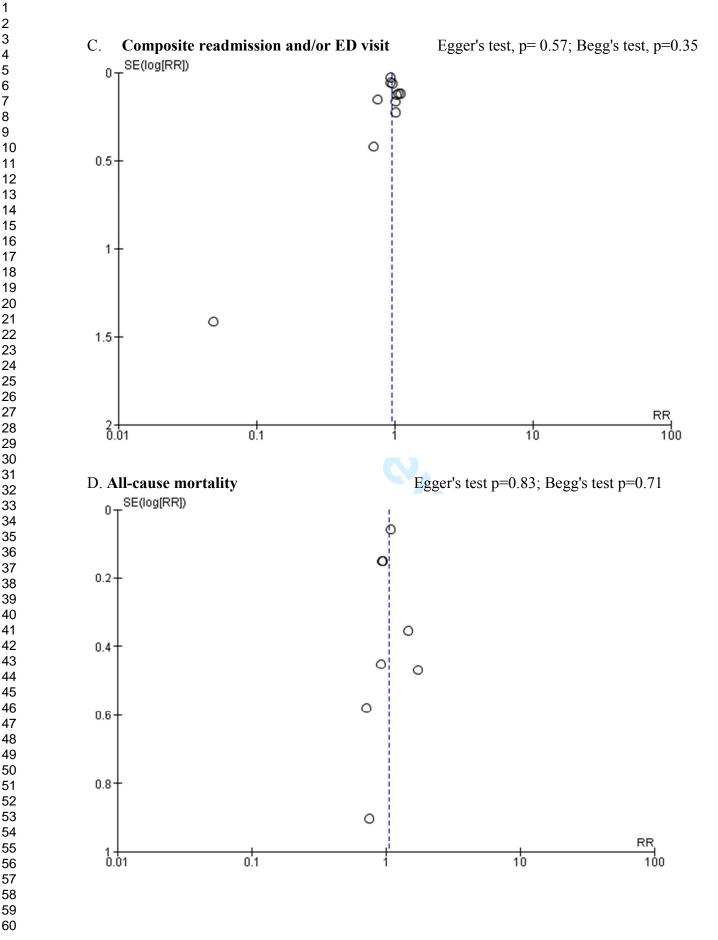
	Interver		Usual			Risk Ratio	Risk Ratio
Study or Subgroup	Events	lotal	Events	lotal	Weight	M-H, Random, 95% CI	M-H, Random, 95% Cl
2.6.1 RCT							
Farris 2014 [Enhanced]	90	312	88	313	4.2%	1.03 [0.80, 1.32]	+
Farris 2014 [Minimal]	97	311	88	313	4.5%	1.11 [0.87, 1.41]	
Gillespie 2009	134	182	147	186	18.0%	0.93 [0.83, 1.04]	
Hawes 2014	0	24	15	37	0.0%	0.05 [0.00, 0.78]	·
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]	- <u>+</u> -
Subtotal (95% CI)		941		954	28.5%	0.98 [0.85, 1.13]	•
Total events	355		372				
Heterogeneity: Tau <sup>2</sup> = 0.01; (	Chi <sup>2</sup> = 6.95	i, df = 5	(P = 0.22)	); $ ^2 = 2$	8%		
Test for overall effect: Z = 0.2	26 (P = 0.7	9)					
2.6.2 NRCT							
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]	
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]	
Walker 2009	98	358	94	366	4.5%	1.07 [0.84, 1.36]	+-
Subtotal (95% CI)		3693		5214	71.5%	0.95 [0.90, 1.00]	•
Total events	1223		2154				
Heterogeneity: Tau <sup>2</sup> = 0.00;	Chi <sup>2</sup> = 3.53	, df = 4	(P = 0.47)	); $I^2 = 0^4$	%		
Test for overall effect: Z = 2.0	)6 (P = 0.0	4)	2				
Total (95% CI)		4634		6168	100.0%	0.95 [0.90, 1.00]	
Total events	1578		2526				
Heterogeneity: Tau <sup>2</sup> = 0.00; (	Chi <sup>2</sup> = 10.8	i2, df = 1	10 (P = 0.	39); l² =	6%		0.01 0.1 1 10
Test for overall effect: Z = 1.8	30 (P = 0.0	7)					Favours intervention Favours usual care
Test for subgroup difference	c: Chiz - C	122 df-	- 1 /P - 0	641 12.	- 0%		Favours intervention Favours usual care





4

5



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.

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data mining, AI training, and similar technologies

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