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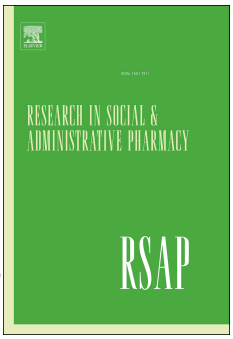

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Pharmacy led medicine reconciliation at hospital: a systematic review of effects and costs

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Abstract

Background: Transition of patients care between settings presents an increased opportunity for errors and preventable morbidity. A number of studies outlined that pharmacy-led medication reconciliation (MR) might facilitate safer information transfer and medication use. MR practice is not well standardised and often delivered in combination with other healthcare activities. The question regarding the effects and costs of pharmacy-led MR and the optimum MR practice is warranted of value. **Objectives:** To review the evidence for the effects and costs/ cost-effectiveness of complete pharmacy-led MR in hospital settings. **Methods:** A systematic review searching the following database was conducted up to the 13th December 2015; EMBASE & MEDLINE Ovid, CINAHL and the Cochrane library. Studies evaluating pharmacy-led MR performed fully from admission till discharges were included. Studies evaluated non-pharmacy-led MR at only one end of patient care or transfer were not included. Articles were screened and extracted independently by two investigators. Studies were divided into those in which: MR was the primary element of the intervention and labelled as "primarily MR" studies, or MR combined with non-MR care activities and labelled as "supplemented MR" studies. Quality assessment of studies was performed by independent reviewers using a pre-defined and validated tool. **Results:** The literature search identified 4,065 citations, of which 13 implemented complete MR. The lack of evidence precluded addressing the effects and costs of MR. **Conclusions:** The composite of optimum MR practice is not widely standardised and requires discussion among health professions and key organisations. Research focused on evaluating cost-effectiveness of pharmacy-led MR is lacking.

Keywords: Medicine/ medication reconciliation, care transition errors, costs, hospital pharmacy, pharmacy-led medicine reconciliation

Abbreviation:

MR: medicine reconciliation

Introduction

Transition of patient care between settings presents an increased opportunity for error. Poor communication of clinical information at healthcare transitions is responsible for over 50% of all medication errors and up to 20% of adverse events.[1-4] At least half of discrepancies at discharge originate from discrepancies in medication histories, and 72% of all potentially harmful discrepancies in admission or discharge orders were due to errors related to compiling pre-admission medicines list.[5, 6].It is also estimated that 12% of adverse drug events upon hospital admission were related to medicine use and that each adverse event increase hospital stay by 8.5 days on average..[3,7]

Medicine reconciliation (MR) is proposed as a solution for communication deficits between healthcare settings.[2, 8, 9,10] In the US, the Joint Commission for health care organizations accreditation defines MR as the process of "obtaining and maintaining an accurate, detailed list of all medicines taken by a patient and using this list to provide correct medicines anywhere within the health care system".[10] In the UK, MR is described similarly and recommended to be performed every time a transfer of care takes place.[11]

Studies have outlined that MR facilitates safer medication use after patient transfer of care.[12-18] Of note, two systematic reviews of hospital-based MR, Kwan et al.,[17]and Mueller et al.,[18] supported MR interventions that relied on pharmacists to improve the transfer of medication information. It was highlighted also that MR when bundled with other healthcare activities such as medication review and discharge planning might improve clinical and healthcare utilisation post discharge. [17] However, the cost/cost-effectiveness of MR was not fully addressed, and MR was not always fully

implemented. Thus little was concluded whether the observed beneficial effects may justify costs and what would be the composites of optimised MR practice.

The Institute of Healthcare Improvement stated that occasionally MR is not fully implemented. For some organisations, MR is widely accepted as a medication history-taking task, and in others it includes only discharge reconciliation. [19] MR continues to be a challenge for many hospitals and care settings. This is due to the lack of clear ownership of MR and the need for developing a standardised approach to implement MR. [19] Thus, exploring the existing evidence to identify the features of MR practice and the resources necessary to deliver is warranted.

This systematic review aimed to synthesise evidence to determine the effects and costs associated with complete MR; in which MR is implemented at admission and continued through the hospital stay until discharge and where patient information is fully and accurately communicated to the next health provider. This would enable service purchasers and health policymakers to make more informed decisions regarding MR optimum practice and cost implications.

Methods

Identification of studies

PRISMA guidelines were used to inform this systematic review. A literature search was carried out from the start date of the database (noted in parentheses) to the 13th December 2015. The following databases were reviewed; EMBASE (1946) & MEDLINE Ovid (1950), CINAHL (1961) and the Cochrane library including Cochrane Database of Systematic Review (1988), Database of Abstracts of Reviews of Effects and the NHS Economic Evaluation Database (1991), the Centre of Reviews and

Dissemination and PHARMLINE provided by the National electronic Library for Medicines (1970).

Search terms were set by the authors prior to the beginning of the electronic search. Scoping searches reviewing published MR articles and citation searches using the SCOPUS database were conducted to identify all relevant search terms. Search terms were discussed with peer researchers with mixed professional and research backgrounds in an open forum. Search terms were revised accordingly. Bibliographies and reference lists of the identified studies and systematic reviews were revised to identify additional relevant articles. Authors and key institutions including the UK National Patient Safety Agency and National Prescribing Centre, Institute of healthcare improvement, the Agency of Healthcare research and Quality and Joint Commission in the US were contacted by email to obtain any relevant work. Search terms included: medicine/medication reconciliation, medical record review or assessment, drug history-taking, seamless care plus information communication and care transfer. Truncations (*), wild cards ($), hyphens and other relevant Boolean operators were used where permitted. The search strategy (Appendix 1) is available upon request. No restriction on language or publication date was applied. Non-English studies were translated to English language by an independent researcher who speaks fluently in several languages.

Inclusion and exclusions criteria

Eligible studies were those evaluating adults and children receiving pharmacy-led MR within hospital inpatient settings. All types of admissions and ward specialities were considered. Only studies describing clearly that MR was implemented fully upon admission through the hospital stay until discharge and with patient information

being communicated accurately to the next health provider were included. The term 'complete MR' was used for this review. Studies evaluating non- pharmacy-led MR at only one end of patient care or transfer were not included. Studies evaluating pharmacy-led MR using a qualitative approach and studies evaluating enhanced interventions, including telephone helpline and post discharge follow-up calls, were excluded. Telephone helpline and follow-up calls were not considered part of MR and suspected to influence readmissions and healthcare utilisation.[20, 21] Thus; these were excluded to avoid bias in favour of the intervention.

Study selection and Data extraction

Screening of titles and abstracts for relevance and data extraction was performed independently by two authors; EH and AB. Discrepancies were discussed to obtain consensus, disagreement was resolved by a third author (DB).

Abstracted data were related to study design, authors, country of correspondence, year of publication and setting, study population, number of participants, demographics and baseline comparability if applicable. Details of the study intervention, including who and when implemented MR and what comprised the MR service, and the standard care in the study site, were extracted. Studies evaluating complete MR performed by pharmacy staff in a hospital setting were relevant to the review. Non-pharmacy-led MR was considered out of the scope of this review. Studies were divided into two subsets: those in which MR was the primary element of the intervention and labelled as "primarily MR" studies, and studies in which the MR intervention was performed in bundle with other non-MR healthcare activities. The latter were labelled as "supplemented MR" studies. This classification was to

enable better understanding of the dynamic of MR practice and the true impact of MR on patient outcomes and health costs.

Outcomes and cost estimation

Details related to the effect of MR were recorded as process-oriented outcomes such as medication discrepancy rate, clinical significance of medication discrepancy and resources necessary to implement MR including time and training. Patient-oriented outcomes included health resource use in hospital and community, health related quality of life and mortality rate.

Costs related to the extra time commitment needed to implement MR and savings due to reductions in medicines taken during the hospital stay were extracted. Cost savings related to hospital and emergency department revisits, health resource use in community and the time of doctors and nurses freed from obtaining accurate medication histories and transcribing medications changes were extracted.

High heterogeneity due to disparate study designs and measured of outcomes deemed meta-analytic data reporting inappropriate. However, where a common unit of outcome measure we reported the effect and/or costs was pooled. The central tendency and range/SD were estimated using Microsoft Excel (Microsoft, Seattle, Washington). This approach has been used in similar systematic reviews.[17, 22]

Cost estimation

Pooled outcomes were valued in monetrary units using the unit costs reported by personal social services research units and Department of Health reference costs in UK for the financial year 2012/2013, avalible at: www.pssru.ac.uk/. The average cost per patient was

146 calculated for each pooled outcome by multiplying the pooled health resouce
147 consumed/saved by the relevant average unit cost.

148 *Assessing risk of bias*

149 Two of the investigators independently assessed risk of bias using a tool based on
150 the Cochrane Collaboration risk of bias tool for randomised controlled studies. [23] In
151 addition to the Cochrane risk domains for randomised controlled studies, the
152 following risk domains were assessed: design, baseline comparability, standardised
153 intervention delivery and outcome measurement and sample size calculation. These
154 domains were to enable more comprehensive evaluation for the quality of non-
155 randomised and uncontrolled studies. The tool was piloted and validated to fit the
156 purpose of this review (Appendix 2); it was presented to researchers with systemic
157 review experience from different disciplines. They were invited independently to
158 assess the quality of two articles using the tool and provide interactive feedback via
159 group and one to one discussions. Disagreements were referred and resolved by a
160 third reviewer (DB).

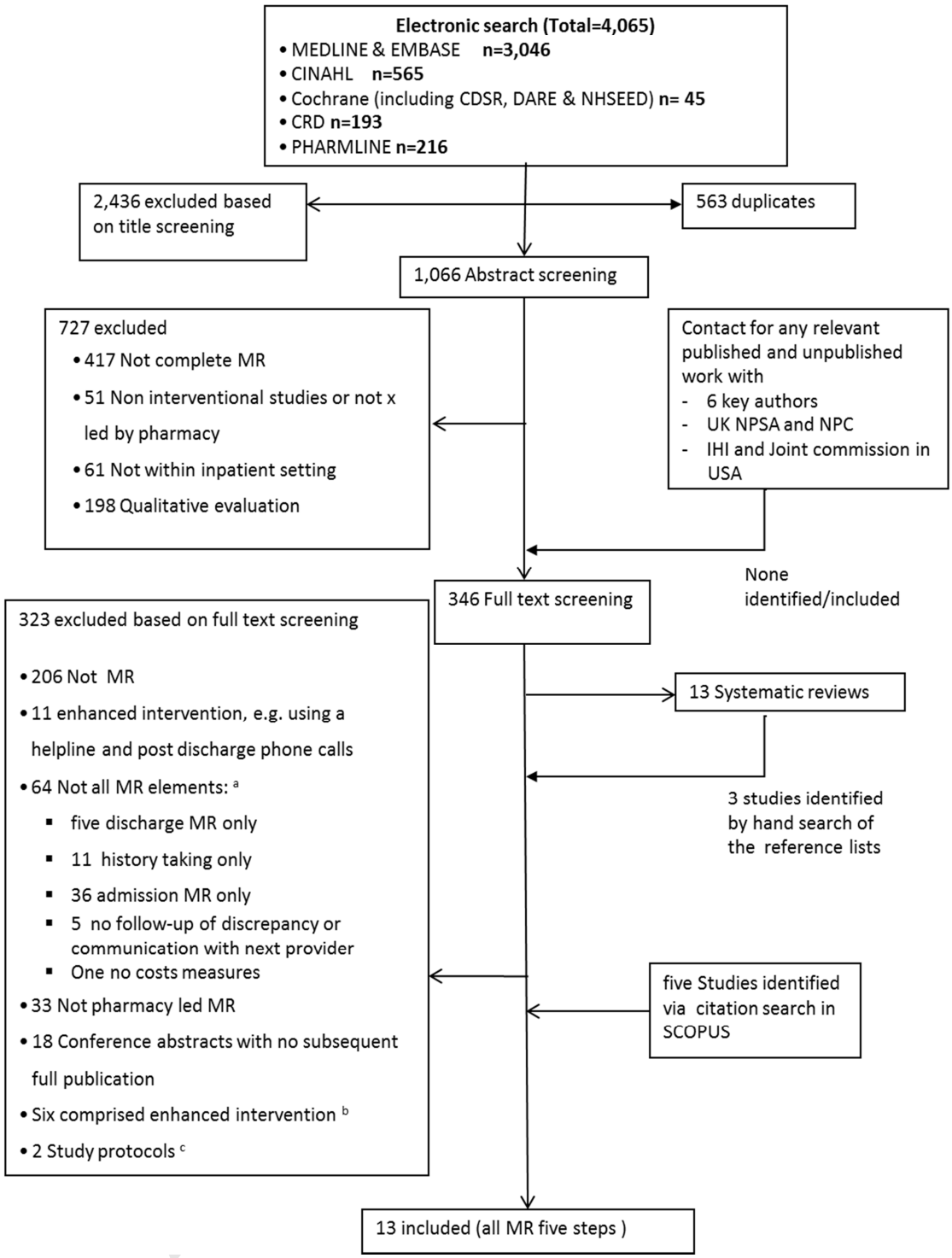
161 This review registration number at the international prospective register of systematic
162 reviews (PROSPERO) is CRD42012002386.

163

Results

The literature search identified 4,065 citations, of which 13 met the inclusion criteria. The study selection process and number of papers excluded at each stage of the review are summarised in Figure 1. Studies were most frequently excluded because they were not pharmacy-led and were not evaluating complete MR. Box 1 highlights the composite of MR practices across a selection of excluded articles.

The majority of studies were conducted in Europe of which three were in Northern Ireland.[24-26] Five studies were based in the USA and Canada [27-31] and one study in Australia.[32] One study was reported in French [33] and the remainder were in English. Table 1 summarises the characteristics of included studies with respect to study design. There were seven controlled studies [24, 26-29, 32,34] of which three were randomised, [26, 27, 30, 32] one non-randomised prospective observational [24] and three before and after study designs.[28, 31, 34] The remaining were prospective uncontrolled studies.[25, 29, 33, 35, 36] A detailed description of comparators and the study inclusion criteria are also presented in Table 1. It can be seen that what constituted a standard care varied across the reviewed studies.



[a] Full text was revised to enable decisions for exclusion, incase of uncertainty authors were contacted. [b] e.g. follow up phone call and medicine help line. [b] Authors were contacted; no published or unpublished relevant data were available.

Figure 1. Study selection and reasons for exclusion

Table 1. Summary of included studies

Authors, Year	Study design (sample size)	Control	Inclusion criteria
Andregg, 2014 [31]	Before and after Pre-implementation (n=1664) Post-implementation (n=1652)	Standard care included MR upon admission only to all patient	*Age:*≥18years Condition: discharged from internal medicine, family medicine, cardiology, or orthopaedic surgery medical services
Brookes, 2000 [25]	Prospective uncontrolled (n=109)	-	*Age:*≥60 years *Number of medications:*≥4 medicines *Others:* Admitted via the medical admission unit
Hellstrom, 2011 [34]	Before and after Pre-implementation (n=101) Post-implementation (n=109)	Standard care included only MR upon discharge	*Age:*≥ 65 years *Number of medications:*≥one medicines for regular use
Hick, 2001 [24]	Prospective controlled (n=50) in each group	Standard post-admission pharmacist ward visit involving checking and resolving medication chart errors and omissions	*Age:*≥ 29 years

187

Continued

Table 1 Summary of included studies

Authors, Year	Study design (sample size)	Control	Inclusion criteria
Israel, 2013 [30]	Randomised controlled study Standard care (n=246) Minimal intervention (n=245) Enhanced intervention (n=241)	Usual care included no medication education but did receive a discharge medication list and oral information from a hospital unit nurse.	*Age:*≥18 years *Condition:* admitted with a diagnosis of hypertension, hyperlipidemia, heart failure, coronary artery disease, myocardial infarction, stroke, transient ischemic attack, asthma, chronic obstructive pulmonary disease, or diabetes or were receiving oral anticoagulation. Others: admitted to the internal medicine, family medicine, cardiology, or orthopaedics service and receive their usual medical care in the community and their prescriptions from a community pharmacy.
Kramer, 2007 [28]	Before and after study Pre-implementation (n=147) Post-implementation (n=136)	Pre-implementation phase included admission medication histories and discharge medication counselling followed standard care process which included a nurse-led MR	*Age:*≥18years
Makowsky, 2009 [27]	Multi-centre, quasi controlled clinical trial Intervention (n=220) Control (n=231)	Usual care included traditional reactive clinical pharmacy by either ward-based or dispensary-based staff pharmacists	*Age:*>18 years *Condition:* Primary diagnosis of coronary artery disease, community acquired pneumonia, chronic obstructive pulmonary disease, heart failure, or type 2 diabetes mellitus and not due palliative cancer
Perennes, 2012 [33]	Prospective uncontrolled (n=61)	-	*Age:* ≥65 years old or more.

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Continued

Table 1. Summary of included studies

Authors, Year	Study design (sample size)	Control	Inclusion criteria
Rabi and Dahdal, 2007 [36]	Prospective uncontrolled (n=150)	-	All patients offered intervention
Scullin, 2007 [26]	Randomised controlled study Intervention (n=371) Control (n=391)	Usual care	*Age:*≥65 years *Number of medications*: ≥four regular medications, taking a high risk medicine(s) or anti-depressant *Others*: A previous hospital admission within the last six months, prescribed intravenous antibiotics on the day of admission
Stowasser, 2002 [32]	Randomised controlled study Intervention (n=104) Control (n=105)	Usual care by a clinical pharmacist included review of medication history and current medication, medication supply, counselling on medications and preparing discharge medicines	Patients returning to community following discharge
Vira, 2006 [29]	Prospective uncontrolled =60)	Usual care included Pharmacist or nurse verification of the patients' medication history only if requested by the physician or evidence of incomplete or unusual drug orders. At discharge, pharmacists provided medication education if requested by a physician and for additional patients as time permitted	All new admission in the previous 24 hours

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Table 2 summarises the composite of the reviewed interventions. Four studies were primarily MR. [28, 29, 33, 36] The remainder were supplemented MR. MR was often bundled with pharmacotherapy consultation or medication review, patient consultation and discharge planning. Patients were very similar in terms of demographic characteristics. Average age ranged between 55 and 93 years and equal male to female ratio. Patients were prescribed a mean (SD) of 7 (4.3) medicines. Characteristics of included patients are summarised in Box 2.

Quality of the evidence

Outcomes of bias assessment by study and type of bias are presented in Figures 2 and 3, respectively. Studies were considered at high risk for design bias particularly randomisation and allocation concealment. Risk of bias in terms of selection was often low, specifically in relation to baseline comparability and patient selection (10 out of 13). Performance bias with respect to delivery of the intervention and outcome measurements was generally low (9 out of 13). Detection bias was low for five studies, [25-27, 32, 34] and most studies were considered not susceptible to selective reporting (11 out of 13). Only five studies introduced no concerns regarding the adequacy of the study power and the statistical analysis.[26, 27, 30, 34, 35]

208 **Table 2 Components of pharmacy-led MR by study**

Study	All MR elements	Pharmacotherapy consultation & medication review	Discharge counselling/planning	Patient and carer education	Written medication information handed to patient	Ward round and bedside care	Medication supply/patient own drugs management
Andregg, 2014**[31]	✓	×	✓	✓	✓	×	×
Brookes 2000**[25]	✓	✓	✓	×	✓	×	✓
Hellstrom 2011**[34]	✓	✓	×	×	×	×	×
Hick 2001**[24]	✓	✓	×	✓	×	×	×
Israel, 2013**[30]	✓	✓	✓	✓	✓	×	×
Karapinar-Carkit 2012**[35]	✓	✓	✓	×	×	×	×
Kramer 2007*[28]	✓	×	✓	×	×	×	×
Makowsky 2009**[27]	✓	✓	✓	×	×	✓	×
Perennes 2012*[33]	✓	×	✓	×	✓	×	×
Rabi and Dahdal. 2007*[36]	✓	×	✓	×	×	✓	×
Scullin 2007**[26]	✓	✓	×	✓	×	×	×
Stowasser 2002**[32]	✓	✓	×	✓	×	×	✓
Vira 2006*[29]	✓	×	×	×	×	×	×
Frequency	**13**	**8**	**8**	**5**	**4**	**2**	**2**

209 *Primarily MR studies; i.e. MR the primary element of the intervention. ** Supplemented MR studies; i.e. MR supplemented often with pharmacotherapy consultation or medication review,
210 patient consultation and discharge planning

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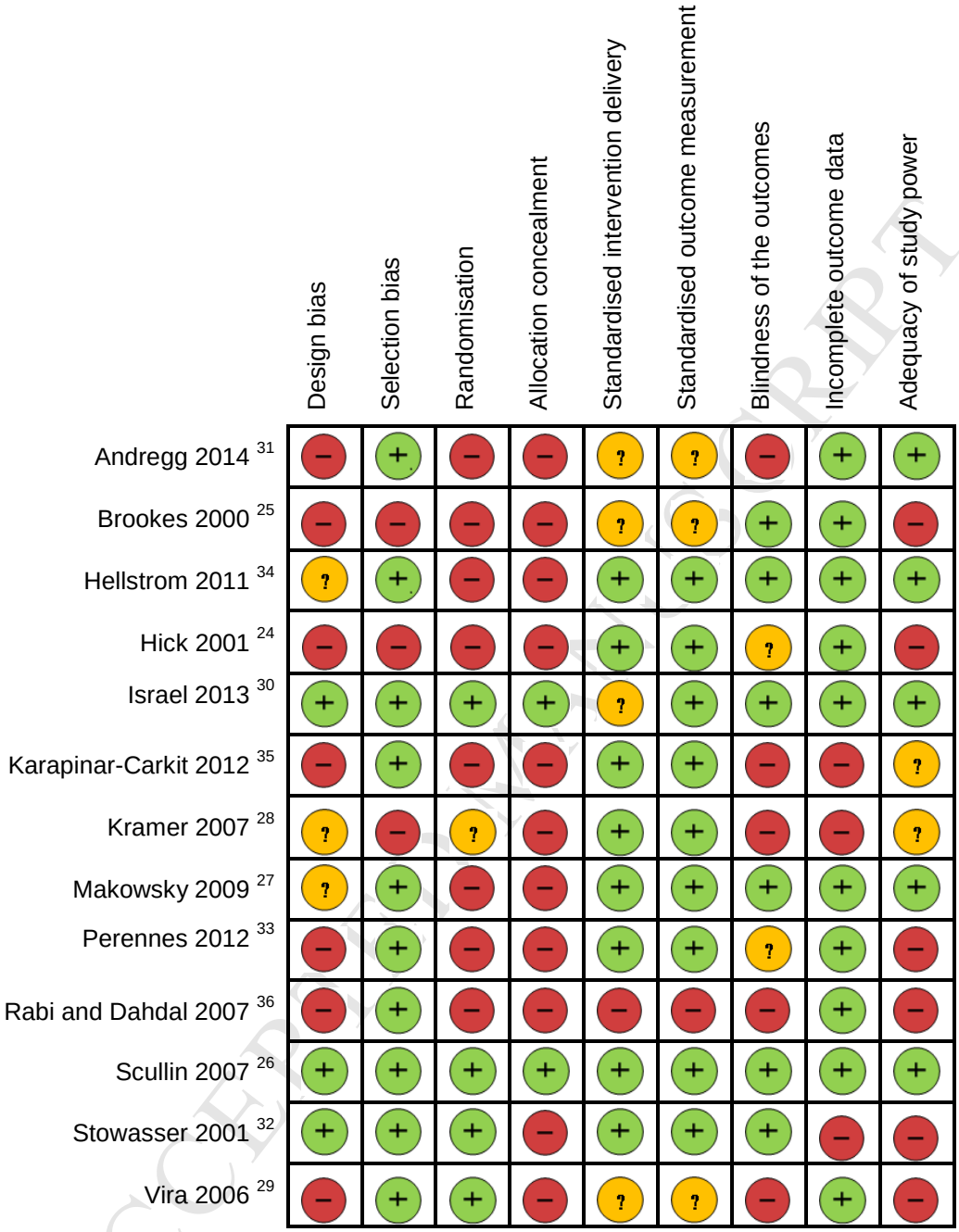

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213 **Figure 2 Risk of bias assessment by study** Low risk of bias High risk of bias Risk of bias
214 unclear

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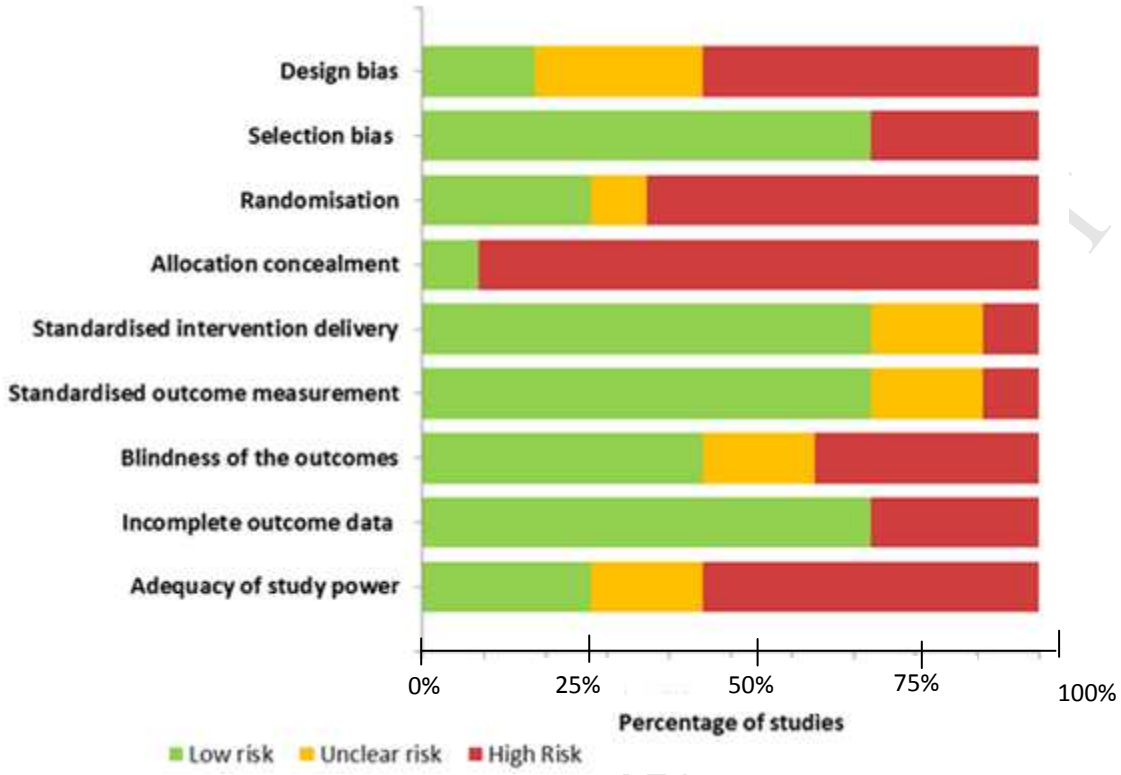
216 **Figure 3 Outcomes of bias assessment by type of bias**



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Effects of pharmacy-led MR

Table 3 summarises the effect of MR on process and patient-oriented outcomes. The mean number of discrepancies reported per patient varied considerably between studies ranging from 0.35 to 4.85. [28, 36,33,29, 24, 35,26,32, 27] Supplemented MR studies appeared to report more often a positive impact, particularly on readmission rate and length of hospital stay, compared to primarily MR studies. At 30 days, the pooled median (range) reduction in readmission and emergency department visits was 4% (1%, 5.9%).[28, 32, 31, 35] Anderegg et al.[31] reported a significant reduction in 30-day readmission rate for patients with high risk; 5.5% (p=0.042). Those were patients hospitalized with acute myocardial infarction, congestive heart failure or pneumonia and chronic obstructive pulmonary disease and on oral anticoagulation. At three months, the reduction in readmission and emergency department visits ranged from 6.4% to 9.3%.[27, 34] This effect was statistically significant (p= 0.045 and 0.047, respectively). However, the effect was not significant at six months post discharge.[27] At twelve months post discharge, Scullin et al. found a significant reduction readmissions rate in the intervention group compared to the control group. Patients also took longer time to be readmitted; 262 days and 242 days, respectively.[21]

There was a mixed effect of MR on hospital stay with a pooled median (IQ) increase in hospital stay of 8.4 (0, 16) hours [26-29, 31-35] for the intervention. Makowsky et al.[27] reported that patients in the intervention group stayed longer in the hospital. The adjusted median ratio of hospital stay [95% CI] was 1.16 [1.01, 1.34] (p=0.031).[27] In contrast, Scullin et al. reported two days reduction in hospital stay with patients in the intervention group (p=0.003).[26]

Health resource use in community and heath related quality of life were evaluated by only one Australian study using a postal survey 30 days post discharge.[32] The total number of health visits and resource use post discharge was significantly lower in the intervention group. Mortality at 12 months was assessed by three studies, none identified a significant impact.[26, 32,34]

Table3 Summary of MR effects on process and patient oriented outcomes

Intervention type	Study	Process oriented outcomes		Patient oriented outcomes				
		Overall discrepancies (per patient)	Clinically significant unintentional discrepancies (per patient)	Readmission and emergency visit rate	Average hospital stay	Health resource use	Quality of life	Mortality
Primarily MR	Kramer, 2007 [28]	0.35	-	⊕	No change	-	-	-
	Rabi and Dahdal,2007 [36]	1	-	-	-	-	-	-
	Perennes, 2012 [33]	0.62	0.033	-	⊖	-	-	-
	Vira, 2006 [29]	2.3	0.33	-	⊕	-	-	-
Supplemented MR	Anderegg, 2014 [31]	-	-		⊖	??	-	-
	Brookes, 2002 [25]	-	-	⊕	-	-	-	-
	Hellstrom, 2011 [34]	-	-	⊕	⊖	-	-	⊖
	Hick,2001 [24]	2.48	-	⊕	-	-	-	-
	Isreal, 2013 [30]	-	-	-	-	-	-	-
	Karapinar-Carkit, 2012 [35]	2.98	-	-	⊖	-	-	-
	Makwosky, 2009 [27]	4.85	-	⊕	⊖	-	-	-
	Scullin, 2007 [26]	5.5	-	⊕	⊕	-	-	⊕
	Stowasser , 2002 [32]	0.77	-	⊕	⊕	⊕	⊕	⊕

249 ⊕: not statistically significant ⊕: statistically significant. ??: the author reported no direction of change but stated this to be overall statistically
250 nonsignificant.

Costs and savings associated with Pharmacy-led MR

Time spent by pharmacists to implement complete MR was estimated in six studies; the pooled median (IQ) time was 50 (14, 50) minutes.[24, 28, 29, 33, 35,36] Details of the time spent in each study are shown in Box 3.

None of the included studies incorporated a full economic evaluation of the cost and/or cost-effectiveness of MR. Karapinar-Carkit et al.[35] performed a cost analysis from a health insurer's perspective. MR was performed by a team of pharmaceutical consultants who were pharmacy technicians completed an additional three-year degree and obtained further pharmacotherapy and patient communication training. Savings in medicine costs were €21.77/patient (USD $24.79) at one month and €96.65/patient (USD $110.07) at six months. The savings did not outweigh the pharmacy consultant's labour cost after one month, but did outweigh the labour costs at six months post discharge with a net saving of €55.62 /patient (USD $63.34) (sensitivity analysis €37.25-€71.10; USD $42.42- 80.97). Saving was estimated if MR was provided by a clinical pharmacist or a pharmacy technician. Net savings were €47.41/patient (USD $53.99) (€25.37-€65.98; US$ 28.89-75.14) with the clinical pharmacist, and €63.82/patient (USD $72.68) (€49.13-€76.21; USD $55.95-86.79) with the pharmacy technician.

Cost savings related to reconciliation of the patient's own drugs upon admission were evaluated by Brookes et al.[25] The extra prescription costs that would have been saved if home medications of 13 patients were reconciled and taken during hospital stay was on average £25.22 (USD $35.93). Annually, this would translate to £15,000 (USD $21,367).

Cost savings related to prevention of readmissions and hospital stay was outlined in three studies. Brookes et al.[25] estimated that eighteen readmissions were prevented

and extrapolated this to 72 readmissions with average stay of 7.7 days. Consequently, total cost savings was estimated as £80,000 (USD $113,958) annually. Andereeg et al.[31] estimated that the pharmacy team interventions could prevent approximately 75 readmissions of high-risk patients per year. At an average direct cost of USD $10,446 per readmission including the cost for medications, laboratory testing, imaging, and other resource charges, the potential annual cost savings would be USD $783,450. With overhead expenses, the annual estimated saving were estimated as USD $1,121,850. Scullin et al. estimated over £3 million (USD $4,273,41) annual savings due to reductions in hospital stay. [26]

Two studies estimated savings related to the time of other members of the healthcare team.[24, 28] The time spared for doctors and nurses was 14 minutes per patient [24] and one hour, respectively.[28] However, this was not valuated in monetary units.

Cost estimation

The valuation of doctor and nurse time using the reference unit cost reported by the Personal and Social Services Research Unit in the UK for the year 2012/2013, estimates savings of £85 (USD $121.08) per patient in nurse time and £8.75 (USD $12.46) per patient for doctor time. The average cost of pharmacist time to implement MR would be £14.7(USD $20.93) (£13.8-£49.2; USD $19.65- USD $70.08) per patient. The average costs of excess hospital stay can be estimated as £92.4 (USD $131.62) (£0-£176; USD $0-$250.70). Savings in terms of preventing readmissions at 30 days post discharge can be estimated at £5,744 (USD $8,182) (£2,872-£8,472; USD $4,091-$12,068). At three months, savings can be estimated as £1,344 (US$ 1,914) (£9,190-£13,354; US$ 13,090- US$19,022).

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Discussion

MR is a well-defined process and recommended to take place each time the patient is transferred between health settings or different levels of care within the same setting.[1,2,4, 10, 11,19] However, MR is prioritised and delivered differently across countries and health organizations.[10,11,19] Thus, the composite of the optimum practice of MR is not widely standardised and requires further discussion among health professions and organizations. The current review identified only a limited number of studies; 13 implemented MR fully from admission until discharge and communicated updated information to the next health provider. In some institutions and healthcare systems, MR is delivered at admission namely through medication history-taking, or simply at discharge alone or bundled with more specialised service such as medication review.[37,38] MR provided at one end of patient care or transfer was considered incomplete in this review.

Additionally, MR is often bundled with pharmacotherapy consultation and reviews ,[25-27,30,35,36] and discharge counselling.[25,27,28,30,31,35,33,36] MR appears to be a multidisciplinary and multidimensional health process; i.e. it requires collaboration of various health providers at various care levels. Thus, MR can be integrated with a multicomponent care bundle designed to improve patient outcomes. Hence, the relevance of assessing MR effects in isolation of other care activities might be questionable in some contexts, and implementation of MR fully faces number of challenges. This has been highlighted in a number of professional and health management meetings.[39,19] Therefore, developing a well-defined MR process and highlighting the role of pharmacists in optimising the delivery and application of MR are needed. Further research and discussion among healthcare systems and world organisations to encourage

organisations to define their own MR process and adopt MR within their routine workflows is warranted.

This review highlighted that continuity of care was improved by MR pharmacist intercepting and clarifying medication discrepancies.[28,29,33,36] However, these discrepancies were not always considered clinically significant, and thus little can be said as to whether intercepting MR discrepancies precludes actual patient harm. This corroborates previous MR reviews requesting future studies to focus on evaluating actual harm and patient-oriented outcomes.[17, 18, 40]

Kwan et al.,[17] suggested that MR alone probably does not reduce post discharge hospital utilisation but may do so when bundled with interventions aimed at improving care transitions. This review found the evidence is lacking and was of poor quality, precluding confirmative conclusions for the effects of MR alone or when bundled with other care activities. Without detailed investigation of the nature of each unit of resource used, it is not possible to draw definitive conclusions. Thus, the effects on readmissions, length of hospital stay, post discharge health resource use, mortality and quality of life will remain uncertain unless these details were collected compressively.

Strengths and limitations

There is no other comprehensive review that scoped effects and costs of implementing full MR and highlighted the features of MR practice in the context of non-MR healthcare activities. The empirical valuation for the costs of MR was useful to highlight the potential cost drivers and data needed to conduct useful cost/ cost-effectiveness evaluation in future. This review implemented a comprehensive search strategy by independent reviewers. All key terms systematically were searched through all relevant databases, key authors and institutions with no limitations to study language, year of publication or design. No other MR review implemented a comprehensive

quality assessment that enable the reader to understand the quality of each study and weighted them differently based on the robustness of their findings.

However, this systematic review is subject to a number of limitations. The reviewed studies were limited and of inadequate quality. They were mainly non-randomised and/or uncontrolled designs. Additionally, the composite of the reviewed interventions varied widely and represented very heterogynous MR practice. Thus, the generalizability of this review must be considered in light of the differences existing between worldwide health care systems, processes for sharing information, and funding of patient care.[41].

Conclusion

This review provided an empirical valuation of MR costs and highlighted that the extra time commitment to implement MR and details of post discharge resource use are potentially the main cost drivers to inform policy makers as to the cost implications of MR. Research focused on evaluating cost-effectiveness of pharmacy-led MR should be a priority because evidence is scant. Providing a comprehensive pharmacy-led MR service to patients may be desirable; however, it is essential to identify the situations most likely to benefit from pharmacy-led MR and to target areas where MR impact is maximised.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article. There is no financial and personal relationships with other people or organizations that could inappropriately influence (bias) their work.

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Appendix 1. Example of search strategy applied in EMBASE and MEDLINE Ovid database in 23.11.2012

	Search terms
1.	medicine$.ti,ab.
2.	Medication$.ti,ab.
3.	drug$.ti,ab.
4.	medicament$.ti,ab
5.	prescription$.ti,ab.
6.	(medic$ adj2 chart$).ti,ab.
7.	(medic$ adj2 record$).ti,ab.
8.	1 or 2 or 3 or 4 or 5 or 6 or 7
9.	((medicine$ or medication$ or drug$ or medicament$ or prescription$ or (medic$ adj2 chart$) or (medic$ adj2 record$)) adj2 reconciliation).ti,ab.
10.	((medicine$ or medication$ or drug$ or medicament$ or prescription$ or (medic$ adj2 chart$) or (medic$ adj2 record$)) adj2 management).ti,ab.
11.	((medicine$ or medication$ or drug$ or medicament$ or prescription$ or (medic$ adj2 chart$) or (medic$ adj2 record$)) adj2 assessment).ti,ab.
12.	((medicine$ or medication$ or drug$ or medicament$ or prescription$ or (medic$ adj2 chart$) or (medic$ adj2 record$)) adj2 review$).ti,ab.
13.	((medicine$ or medication$ or drug$ or medicament$ or prescription$ or (medic$ adj2 chart$) or (medic$ adj2 record$)) adj2 histor$).ti,ab.
14.	information.ti,ab.
15.	(information adj2 transfer$).ti,ab.
16.	information adj2 continu$).ti,ab.
17.	((medicine$ or medication$ or drug$ or medicament$ or prescription$ or (medic$ adj2 chart$) or (medic$ adj2 record$)) adj2 system$).ti,ab.
18	((medicine$ or medication$ or drug$ or medicament$ or prescription$ or (medic$ adj2 chart$) or (medic$ adj2 record$)) adj2 congruence$).ti,ab.
19	((medicine$ or medication$ or drug$ or medicament$ or prescription$ or (medic$ adj2 chart$) or (medic$ adj2 record$)) adj2 communication).ti,ab.
20	(information adj2 communication).ti,ab.
21	((medicine$ or medication$ or drug$ or medicament$ or prescription$ or (medic$ adj2 chart$) or (medic$ adj2 record$)) adj2 liaison).ti,ab.

22	care.ti,ab.
23	(seamless adj2 care).ti,ab.
24	discrepanc$.ti,ab.
25	Error$.ti,ab.
26	transition$.ti,ab.
27	9 or 10 or 11 or 12 or 13 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 23 or 25 or 26
28	Secondary adj1 care).ti,ab.
29	hospital$.ti,ab.
30	inpatient$.ti,ab.
31	interface$.ti,ab.
32	dicharge$.ti,ab.
33	admission$.ti,ab.
34	28 or 29 or 30 or 31 or 32 or 33
35	pharmacist$.ti,ab.
36	pharmacy.ti,ab.
37	pharmacies.ti,ab.
38	35 or 36 or 37
39	27 and 34 and 38
40	Remove duplicate from 39
41	Export to Endnote and further remove of duplicate

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Appendix 2. Risk of bias assessment tool

Domain	Low risk	High risk	Unclear

1. Design bias (focus study question & design)	• The study clearly described all of the following:
	  ◦ Targeted population
	  ◦ The intervention
	  ◦ The comparator
	  ◦ Outcomes measured
	• The study design is the best to answer the question, e.g. RCT for intervention
	• The study addressed the intended research question
		The study is not fulfilling any of these criteria	Insufficient information to permit judgment of 'Low risk' or 'High risk'

2. Selection bias (external and internal variations)	• The study sample is representative of the intended population • There is nothing special about the sample with any potential to effect intervention or outcomes • All patients were included/ excluded as per the stated inclusion and exclusion criteria • The study groups are comparable at baseline	The study is not fulfilling any of these criteria	Insufficient information to permit judgment of 'Low risk' or 'High risk'[1]
3. Selection bias (randomisation)	The investigators describe a random component in the sequence generation process [2]	The description of the sequence generation involve some systematic but non- random approach [3]	Insufficient information permit judgment of 'Low risk' or 'High risk'
4. Selection bias (allocation concealment)	Participants and investigators enrolling participants could not foresee the study group assignment [4]	Participants and investigators enrolling participants could possibly foresee the study group assignments [5]	Insufficient information permit judgment of 'Low risk' or 'High risk'

Domain	Low risk	High risk	Unclear
5. Performance bias (Standardised intervention delivery)	The investigators used a standardised process which followed by all the service providers delivering the intervention [6]	The process of intervention delivery was not standardised	Insufficient information to permit judgment of 'Low risk' or 'High risk'
6. Performance bias (Standardised outcome measurement)	The investigators used a standardised process which followed by all investigators recording and measuring t outcomes[7]	The process for recording /measuring outcomes was not standardised	Insufficient information to permit judgment of "'Low risk' or 'High risk'
7. Detection bias (Blindness of the outcomes)	• Blinding of outcome assessment ensured, and unlikely it was broken. • No blinding of the outcome assessment, but this unlikely to influence outcome assessment	Outcomes measurement was not blind [8]	Insufficient information to permit judgement of 'Low risk' or 'High risk'
8. Incomplete outcome data	• No missing outcome data and all study participants accounting for at conclusion [9] • All pre-specified (primary and secondary) outcomes have been reported • The reported outcomes are appropriate to answer the study question	The study is not fulfilling any of these criteria	Insufficient information to permit judgement of 'Low risk' or 'High risk'
9. Adequacy of study power (appropriate Statistical analysis)	• The study used appropriate/justifiable statistical testing • Power calculation or sample size calculation was performed • Results do not match up or add up but with no major concern	The study is not fulfilling any of these these criteria	Insufficient information to permit judgement of 'Low risk' or 'High risk'

Explanatory notes:

1. For example, groups were reported comparable but with no evidence to support this or groups reported different but no way of knowing if this is significant
2. For example referring to a random number table, using a computer random number generator, coin tossing, shuffling cards or envelopes, throwing dice or drawing of lots
3. For example generating sequence by odd or even date of birth, sequence generated by some rule based on date (or day) of admission, sequence generated by some rule based on hospital or clinic record number or other non- random approaches such as allocation by judgment of the clinician, the preference of the participant, on the results of a laboratory test or a series of tests or the availability of the intervention.
4. For example the study allocation was concealed by central allocation (including telephone, web-based and pharmacy – controlled randomisation), sequentially numbered drug containers of identical appearance or sequentially numbered, opaque, sealed envelopes
5. For example the study allocation based on using open random allocation schedule (e.g a list of random numbers), assignment envelopes were used without appropriate safeguards (e.g. if envelopes were unsealed or nonopaque or not sequentially numbered, alternation or rotation, date of birth, case recorded number or any other explicitly unconcealed procedure.
6. For example the investigator used a standardised form or checklist or undertook a training
7. I.e. the investigators used a structured review of medical chart, independent and double identification of medication discrepancies and demonstrate satisfactory agreement between the intervention assessors
8. Detection bias criteria related to blinding of outcomes is considered of importance in assessing the measurement of medication discrepancies and their clinical significance. However, blinding of outcome assessors not particularly relevant to the end-points of hospital revisits or deaths and therefore it was assessed whether studies confirmed outcome data by using a subjective standardised reporting system such as hospital data or self-report data.
9. I.e. attrition rate is similar between study groups, the study follow up is complete, patients were analysed as allocated at the study commencement, reasons for missing outcome data unlikely to be related to true outcome , missing outcome data balanced in numbers across intervention groups, with similar reasons for missing data across groups. In case of dichotomous outcome data, the proportion of missing outcomes compared with observed event risk not enough to have a clinically relevant impact on the intervention effect estimate. For continuous outcome data, plausible effect size (difference in means or standardized difference in means) among missing outcomes not enough to have a clinically relevant impact on observed effect size and missing data have been imputed using appropriate methods.

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Box 1. Composites of MR practice across a selection of excluded articles.

Author, year	country	Admission MR		Discharge MR			
		Collection of medicine history	Clarification drug allergy	Comparing collected information with inpatient chart	Comparing inpatient with discharge charts	Pharmacist intervene to resolve discrepancy	Documenting changes and communicate to next provider
George et al., 2011[1]	Australia	●	–	●	●	–	–
Schnipper et al., 2009 [2]	USA	●	–	●	–	●	–
Cohen et al., 2008 [3]	USA	●	–	●	–	–	–
Abuyassin et al., 2011[4]	Saudi Arabia	●	–	●	–	●	–
Winter et al., 2010 [5]	Belgium	●	–	●	–	●	–
Marino et al., 2010 [6]	US	●	●	–	–	–	–
Steurbaut et al., 2010 [7]	Belgium	●	●	●	–		
Lisby et al., 2010 [8]	Denmark	–	–	●	–	●	–
Green et al., 2010 [9]	UK	●	–	●	–	–	–
Coffey et al., 2010 [10]	Canada	●	–	●	–	●	–
Brownlie et al., 2014[11]	UK	●	–	●	–	●	–
Conklin et al., 2014[12]*	USA	●	–	●	●	●	●

*involved follow calls within 72 hours of discharge

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Box 2. Characteristics of patients in the studies reviewed.

Authors, Year	Demographics	Measurement	Intervention	Control
Andregg, 2014[31]	Age	Mean (SD)	54.2 (16.4)	54.2 (17.1)
	Gender (male)	N (%)	832 (50.4%)	878 (52.8%)
	No. of medication	Mean (SD)		
	Admission		11.8 (8.0)	11.2 (7.8)
	Discharge		12.4 (7.0)	12.2 (7.2)
	New at discharge		3.8 (3.1)	3.4 (2.8)
	Type of admission (planned)	N (%)	No details	No details
Brookes, 2000[25]				
	Age	Mean (Range)	75 (60-92)	-
	Gender (male)	N (%)	No details	No details
	No. of medication	Mean (Range)	8.0 (4-14)	-
	Type of admission (planned)	N (%)	No details	No details
Hellstrom,2011 [34]	Age	Mean (SD)	83.0 (7.0)	81.8 (7.4)
	Gender (male)	N (%)	49 (45%)	50 (49.4%)
	No. of medications*	Mean (IQ)	8 (5-11)	7 (5-11)
	Type of admission (planned)	N (%)	No details	No details
Hick, 2001 [24]	Age	Mean (SD)	67.4 (15.5)	63.0 (16.1)
	Gender (male)	N (%)	21(42.0%)	26 (52.0%)
	No. of medications	Mean (SD)		
	Admission *		2.78 (2.31)	2.52 (2.58)
	Discharge		4.36 (2.51)	3.60 (3.0)
	Type of admission (planned)	N (%)	100%	100%
Israel, 2013 [30]	Age	Mean (SD)	No details	No details
	Gender (male)	N (%)	112 (45.7)	133 (54.3)
	No. of medication	Mean (SD)	No details	No details
	Type of admission (planned)	N (%)	No details	No details

Continued

Box 2. Characteristics of patients in the studies reviewed.

Authors, Year	Demographics	Measurement	Intervention	Control
Karapinar-Carkit, 2012 [35]	Age	Mean (SD)	65 (17)	-
	Gender (male)	N (%)	131 (50%)	-
	No. of medications	Mean (SD)		
	Admission		6.6 (3.8)	-
	Discharge		9.1 (4.7)	-
	Type of admission (planned)	N (%)	35 (13%)	-
Kramer 2007 [28]	Gender (male)	N (%)	74(51.0%)	69 (52.0%)
	No. of medications	Mean (SD)	8.3 (5.2)	6.0 (4.0)
	Type of admission (planned)	N (%)	No details	No details
Makowsky, 2009 [27]	Age	Mean (SD)	74.9 (13.9)	73.2 (14.7)
	Gender (male)	N (%)	104 (47.1%)	102 (44.2%)
	No. of medications	Mean (SD)	No details	No details
	Type of admission (planned)	N (%)	No details	No details
Perennes, 2012 [33]	Age	Mean (SD)	78 (7.4)	-
	Gender (male)	N (%)	20 (31.2%)	-
	No. of medications	Mean (SD)	7 (2.9)*	-
	Type of admission (planned)	N (%)	46 (75%)	-
Rabi and Dahdal, 2007 [36]	Age	Mean (SD)	No details	No details
	Gender (male)	N (%)	No details	No details
	No. of medications**	Mean (SD)	No details	No details
	Type of admission (planned)	N (%)	No details	No details

Continued

Box 2. Characteristics of patients in the studies reviewed.

Authors, Year	Demographics	Measurement	Intervention	Control
Scullin, 2007 [26]	Age	Mean (SD)	70.3 (13.8)	69.9 (4.8)
	Gender (male)	N (%)	167 (45.0%)	192(49.0%
	No. of medications	Mean (SD)	No details	No details
	Type of admission (planned)	N (%)	0%	0%
Stowasser, 2002 [32]	Age	Mean (SD)	67.4 (13.0)	65.6 (14.0)
	Gender (male)	N (%)	63(56.0%)	69 (54.0%)
	No. of medications	Mean (SD)		
	Admission		7 (3.7)	7.2 (3.6)
	Discharge		7.6 (3.5)	7.6 (3.8)
Vira, 2006 [29]	Age	Mean (SD)	56.0 (24.0)	-
	Gender (male)	N (%)	30 (50%)	-
	No. of medications	Mean (SD)		
	Admission		3.6 (3.5)	-
	Type of admission (planned)	N (%)	13 (22%)	-

** Regular medicines only

Box 3. Time to implement medication reconciliation, by study reviewed.

Author, Year	Measure	Time per patients
Hick, 2001 [24]	Mean	▪ Medication history extra 5 minutes. Range (4 to 6) minutes, this equates to approximately 22.5 hours/month for an average caseload of 270 patients. ▪ The mean additional time commitment per patient was 11.5 minutes, which for an average caseload of 270 patients per month is equivalent to approximately 52 hours of the pharmacist's time.
Karapinar-Carkit,. 2012 [35]	Mean (SD)	Total 62.7 (14.6) minuets ▪ Admission and discharge medication reconciliation 32.9 (6.6) minutes ▪ Patient counselling 26.6 (9.8) minutes ▪ Transfer of medication information (including adjustments in final discharge prescriptions 3.3 (2.8) minutes
Kramer, 2007 [28]	Mean (S.D)	▪ Time required for nurses to enter allergies in the computer - Nurse time; Before vs. after MR intervention: 69.1 ± 98 vs.141.1 ± 238.8, p = 0.0315 - Pharmacist time; Before vs. after MR intervention : 112.9 ± 70 minutes vs.64.1 ±38.7 minutes, p < 0.000 ▪ Time required to initiate the admission medication history after receiving trigger notification: 18.8 ± 20.2 minutes (range, 1–140 minutes) ▪ Time required to completed the admission medication history 12.9 ± 9.34 minutes ▪ Time required to clarify medications 1.18 ± 5.84 minutes ▪ Time required to perform interventions 1.4 ± 2.25 minutes.

Continued

Table 3. Time to implement medication reconciliation, by study reviewed.

Author, Year	Measure	Time per patients
Perennes, 2012 [33]	Mean (range)	Total time 46 minutes ▪ Patient interview or family member 16 (5-40) minutes ▪ Obtain medication information from patient notes and GP letter 12 (5-15) minutes ▪ Obtain faxed copy of the medication dispensed by the community pharmacies 21 (10-45) minutes
Rabi and Dahda, 2007 [36]	Mean	▪ 15 minutes for admission interview ▪ 10 minutes for discharge counselling including list of discharge medications prepared by study pharmacist and given to patient
Vira T et al. 2006 [29]	Median (IQR)	▪ Admission reconciliation 15 minutes (IQR 10–21). ▪ Time required for discharge reconciliation was not record

Highlights

- **T**ransition of patients care between settings presents an increased opportunity for errors and preventable morbidity.
- Medicine reconciliation is proposed as a solution for deficits at the health interface
- Exploring the existing evidence to identify the features of MR practice and the resources necessary to deliver MR is warranted.
- The lack of evidence precluded addressing the effects and costs of MR.
- The composite of optimum MR practice is not widely standardised and requires discussion among health professions and key organizations.