



# Pharmacy-supported interventions at transitions of care: an umbrella review

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## Abstract

**Background** Medication discrepancies arising at care transitions are prevalent and are linked with adverse drug events and increased healthcare utilization. Evidence is lacking about which pharmacy-supported interventions at care transitions are most effective for both the patient and the healthcare system. **Aim of the review** To investigate the content and effect of pharmacy-supported interventions at transitions of care. **Method** The PubMed, Ovid/Medline and Cochrane Database of Systematic Reviews databases were used. The search was limited to systematic reviews and meta-analyses published in English up to May 2018. Included reviews investigated any intervention related to medication therapy performed by pharmacists or multiple healthcare professionals, including a pharmacist, at transition points in any healthcare setting. Reviews were excluded if interventions were not clearly defined or were not performed at care transitions or were not related to medications. A quality assessment was performed using the PRISMA guidelines. The data extracted included general characteristics, methodology, point of transition, pharmacy-supported interventions and outcomes. For systematic reviews, narrative conclusions were extracted. For meta analyses, reported relative risks or odds ratios were extracted along with the 95% confidence intervals. **Results** Nine systematic reviews and 5 meta-analyses reporting 162 studies were included. The interventions analysed included medication reconciliation (7 reviews) and composite interventions (7 reviews). Six studies reviewed interventions performed by pharmacists alone, while 8 studies explored interventions by different healthcare professionals, including a pharmacist. A positive effect on either medication discrepancies or (potential) ADEs was observed in all reviews. Mixed effects were observed for hospitalizations rates (9 reviews) and costs (4 reviews), regardless of the intervention applied. Mixed effects were also observed for both medication reconciliation and composite interventions on the number of emergency department visit. Interventions showed no significant effect on mortality (4 reviews). The quality of the reviews showed significant variability. **Conclusion** Pharmacy-supported interventions at transitions of care are heterogeneous and potentially improve medication safety, but show no significant effect on mortality. The effect on healthcare utilization and costs is inconclusive.

**Keywords** Care transitions · Medication reconciliation · Pharmacists · Umbrella review

## Impact on practice

- As pharmacy-supported interventions seem to have a positive effect on medication discrepancies and ADEs, the implementation of such interventions, especially at the hospital level, can be beneficial.
- Although it is not yet clear which interventions benefit the most, numerous reviews concluded that pharmacy-supported interventions are effective when nurses and physicians are in close collaboration with pharmacists and when medication interventions are bundled with other patient-tailored interventions.
- Focusing the pharmacy supported interventions on high-risk patients could improve clinical outcomes.

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## Introduction

Transitions of care represent a period of high vulnerability for the patient, also in terms of medication management [1]. Evidence shows that errors in medication history are present in more than half of the patients admitted to the hospital and up to two thirds of patients experience adverse drug events (ADEs) or report medications omissions after discharge [2–4]. The possibility of medication errors, omissions and involuntary non-adherence is increased and further enhanced by poor communication and loss of important information at transition points [3, 5]. These errors can have clinically important consequences. It has been estimated that 25% of all ADEs are the results of medication errors. Medication errors also cause prolonged hospital stay, early hospital readmissions, decrease patients' quality of life and increase healthcare costs [6–8]. The medication-related problems arising at transitions of care are also one of the main focus areas of the WHO's Third Global Patient Safety Challenge—Medications Without Harm [9]. Most importantly, medication errors, omissions and non-adherence at transitions of care are potentially preventable.

Pharmacists can have a crucial role in providing medication management interventions at transitions of care and thus preventing medication errors and ADEs [10–12]. Medication reconciliation, patient education and counselling, patient follow-up are some of the possible interventions performed at various points of transition [13]. Despite a large number of interventions being performed, the question remains of what outcomes do these interventions actually address. Furthermore, these interventions represent a burden in the work organization and healthcare utilization and are also time-consuming for both the patient and the provider [14, 15]. It is therefore crucial to better understand what the effect of these interventions is and which intervention assures the greatest effect for both the patient and the healthcare system.

## Aim of the review

Pharmacy-supported interventions at transitions of care have been addressed by several systematic reviews and also meta-analyses. However, these reviews addressed different interventions (e.g. medication reconciliation, medication review) at different time points (admission, discharge) and assessed diverse outcomes (from medication discrepancies to hospital admissions). The aim of our umbrella review is thus to review the published systematic reviews and meta-analyses investigating the content and effect of pharmacy-supported interventions at transitions of care.

## Method

The Cochrane guideline for the overview of reviews was used as a guide in the preparation of this umbrella review. The protocol for this umbrella review was accepted to the PROSPERO—International prospective registry of systematic reviews (no. CRD42018091612).

## Data sources

The PubMed, Ovid/Medline and Cochrane Database of Systematic Reviews bibliographic databases were used. The search was limited to systematic reviews and meta-analyses published in English language from inception up to May 2018.

A set of terms was selected prior to beginning the search. With the terms selection we aimed to cover three main areas: transitions of care (and related terms such as integrated care) with a relation to medicines (e.g. medication use, drug related problem) at all possible transition points (e.g. admission, discharge). A full search strategy is provided in the Appendix 1.

The bibliography of the selected studies was hand searched by two researchers for additional relevant studies. Titles, abstracts, and full-text articles were screened against eligibility criteria independently by 2 reviewers. Any issues regarding the inclusion were discussed and resolved between researchers. Inter-rater agreement for full-text assessment was calculated using the proportion of agreed inclusions/exclusions (number of agreed inclusions plus number of agreed exclusion per number of all full-texts assessed) and Kappa statistics ( $\kappa$ ). In case of doubt or disagreement, a third member of the research team was consulted and consensus was obtained.

## Selection of reviews and meta-analyses

We included reviews that investigated any intervention related to medication therapy performed by pharmacists or multiple healthcare professionals, including a pharmacist, at points of transition of care. We included reviews that investigated transitions between any type of healthcare setting (primary, secondary or tertiary care). Comparison groups could include usual care, any other intervention or no intervention. Reviews in which it has not been clearly defined what type of interventions were performed by pharmacists were excluded from the selection. Excluded were reviews analysing the effect of pharmacists' interventions in non-transition of care settings and reviews analysing interventions not related to medications.

## Data extraction

One reviewer extracted the relevant data, which were later verified by two other reviewers. The data extracted included general characteristics of the review (healthcare setting, population included), methodology (aim, number and type of studies included, review type, inclusion and exclusion criteria), point of transition, pharmacy-supported interventions and outcomes. The outcomes reported were categorized into adverse drug events (ADEs) and medication discrepancies, hospital readmissions and emergency department visits, mortality and costs. For systematic reviews, the narrative conclusions of authors were extracted. For meta-analyses, the pooled relative risks (RR), odds ratios (OR) or mean differences were extracted along with the 95% confidence intervals (CI).

## Data synthesis and analysis

Given variable study designs, interventions and outcomes presented across all reviews, statistical pooling in meta-analyses was not appropriate. Findings are presented in a narrative form.

## Quality of studies

The quality of the studies was assessed using the PRISMA 2009 Checklist quality assessment tool [16]. Two reviewers rated each study. In case of doubt or disagreement, a third member of the research team was consulted and consensus was obtained. Studies were assessed for each checklist item and the score proportion (the number of items fulfilled divided by all items) was calculated. The checklist item number 2—Structured summary—was assessed and reported separately. The quality of the studies was not a criterion for exclusion.

## Results

Figure 1 summarizes the selection process. From a total of 175 identified studies, 35 were retrieved in full text. The observed similarity between the 2 reviewers for full-text screening was 89% (inter-rater agreement  $\kappa = 0.77$ ). Ten studies were excluded because the interventions performed by pharmacists were not clear, 7 were not related to transitions of care, 3 reviews did not include a pharmacist and 2 were narrative or umbrella reviews on a different, but related topic. One additional review was identified through review of the references of the included studies. In total, 14 reviews were selected for final inclusion, of which 5 were meta-analyses [17–21] and 9 were systematic reviews [22–30].

## General characteristics of included reviews and meta-analyses

A total of 243 studies were included in these reviews and after removal of duplicates, all reviews included 162 original studies. All reviews were published between 2011 and 2018. Most reviews reported usual clinical care as comparator, while five reviews did not specifically define the comparator group [22, 24, 25, 28, 29]. The inclusion and exclusion criteria of the included reviews are presented in Appendix 2.

Six studies reviewed interventions performed by pharmacists alone [18–21, 25, 28], while 8 studies explored interventions by different healthcare professionals in collaboration with pharmacists [17, 22–24, 26, 27, 29, 30]. All reviews included general patient populations at points of transition; one review, summarizing studies in long-term care facilities, focused on elderly patients [24] and one review included both adults and children [28].

## Setting

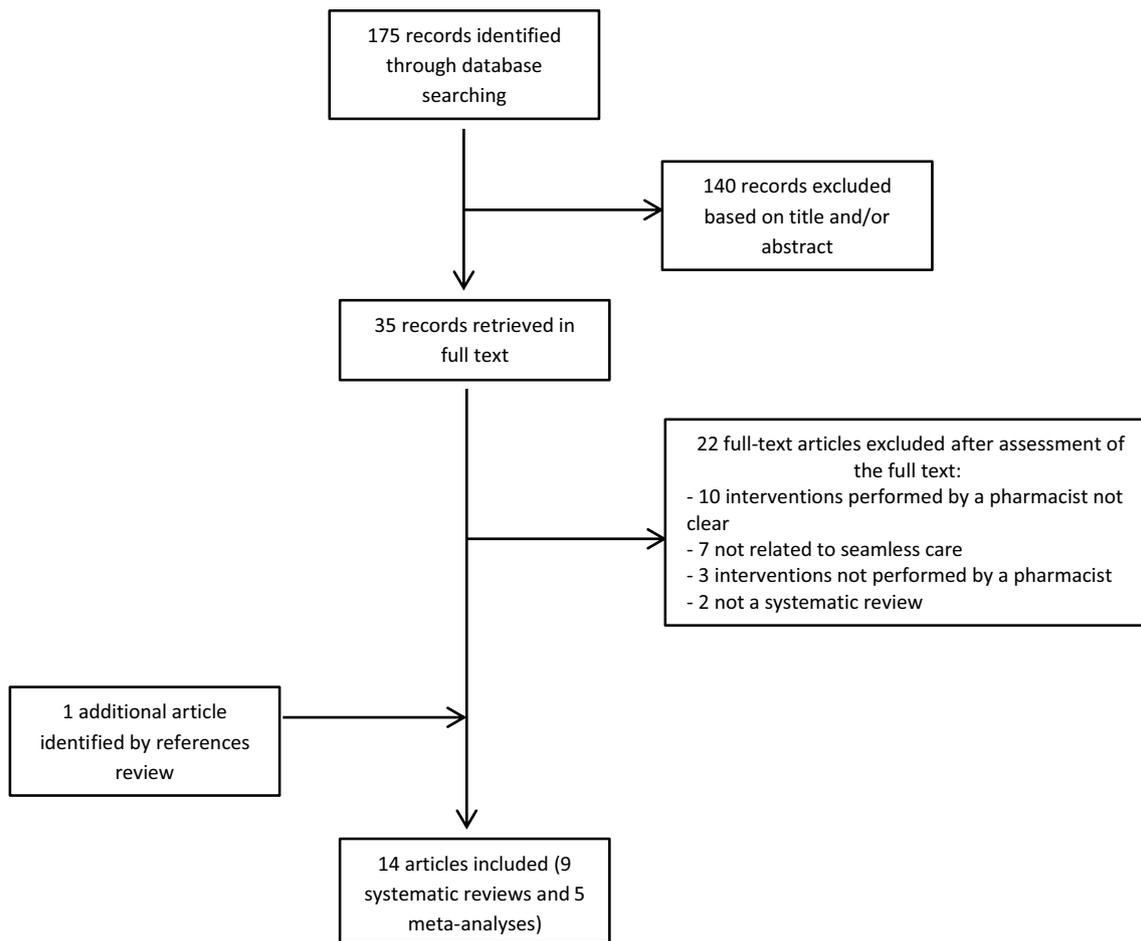
The majority of studies reviewed activities performed at admission or discharge from the hospital [17–23, 25, 27, 28, 30]. One review included studies at transitions to or from hospital, community setting and residential aged care facilities [29], one reviewed the transition between ambulatory and hospital care [26] and one to or from long-term care facilities [24].

## Interventions

Studies reported various interventions performed at transitions of care. Eight studies reported medication reconciliation as the main intervention at transitions of care [17–19, 21, 22, 24, 28, 29]. However, the description of medication reconciliation showed some variance among the studies. Some described it as a single intervention [17, 21, 22, 24, 29], while others bundled it with e.g. medication review and patient counselling [18, 19, 28]. Different names were used for such intervention, e.g. supplemented medication reconciliation [28] and comprehensive medication reconciliation [18, 19]. Six reviews included studies assessing a composite of different interventions at transitions of care [20, 23, 25–27, 30]. The interventions are described in detail in Table 1.

## Outcomes

The reported outcomes were in the majority of cases related to the safety of medication use (ADEs, number of medication discrepancies). Nine reviews aimed to relate the interventions to harder outcomes, such as mortality and hospital



**Fig. 1** Flowchart of study inclusion

readmissions [18, 20–22, 25, 27–30]. The outcomes are summarized in Table 2.

**ADEs and medication discrepancies** Outcomes related to safety of medication use were most frequently analysed. Medication reconciliation studies reported mixed results. Mekonnen et al. [19] in their review focusing on pharmacists alone reported no significant difference in mean number of discrepancies per patient, however they observed a two-thirds reduction in the proportion of patients with discrepancies after interventions at single transitions. The effect was not observed at multiple transitions. In a review by the same group on electronic medication reconciliation, which included studies related to pharmacists and other healthcare professionals, no significant difference in ADRs or medication discrepancies was observed [17]. Kwan et al. [22] also investigated interventions performed by pharmacists and other professionals and found a decrease in number of preventable ADEs in the intervention group of 2 studies, but no significant difference in total ADEs. Mueller et al. [30] reported a reduction in medication discrepancies in all 10 studies analysed and a reduction in

potential ADEs, whereas the effect on preventable ADEs was mixed. McNab et al. [20] found an increased identification and resolution of medication discrepancies as well as a reduction in clinically relevant discrepancies in 2 out of 4 studies.

The effect of composite interventions on drug-related safety was analysed in two reviews. De Oliveira et al. [21] reported a favourable effect of pharmacists' involvement on the incidence of medication errors during transitions of care. Nazar et al. [25] concluded that identification and rectification of medication errors was significantly improved when community pharmacists were involved.

**Hospital readmissions and ED visits** Medication reconciliation showed no reduction in hospital readmissions in three reviews, one review concluded mixed effects. The meta-analysis by Mekonnen et al. [18] reported a one-third reduction in ED visits (95% CI 0.57 to 0.92) and a 19% reduction in hospital readmissions 30 days after discharge (95% CI 0.70 to 0.95). Similar results were reported by Lehnbohm et al. [29] in the setting of residential aged care facilities. Mueller et al. [30] reported mixed effects.

**Table 1** Methodology of included systematic reviews and meta-analysis

Author	Type of review	Number of studies	Study objective	Population	Description of the intervention	Intervention performed by	Comparator	Setting	Point of transition
Chhabra et al. [22]	SR	7 experimental or quasi-experimental studies	To systematically review the literature and evaluate studies performing medication reconciliation interventions in patients transferred to and from long-term care settings	Older adults	Medication reconciliation	Pharmacists & other HCPs	NR	Long-term care settings	Transitions from long-term care settings
De Oliveira et al. [19]	MA	13 RCTs	to quantitatively estimate the effect of pharmacist-based intervention on the reduction of medication errors during transitions of care	Standard patient population	Pharmacist interventions (i.e. medication reconciliation and/or patient education)	Pharmacists	usual care	Hospital	From hospital to the community

Table 1 (continued)

Author	Type of review	Number and type of studies	Study objective	Population	Description of the intervention	Intervention performed by	Comparator	Setting	Point of transition
Ensing et al. [21]	SR	30 RCTs	To identify the components of pharmacist intervention that improve clinical outcomes during care transitions	Standard patient population	Admission reconciliation, patient counselling at admission, medication review, discharge reconciliation, patient counseling at discharge, patient discharge letter, transmission to next HCP, patient-centered follow-up, health care provider-centered follow-up, extra post-discharge follow-up, tailored intervention, provision of adherence aides, dispensing/logistic aides	Pharmacists & other HCPs	usual care	Hospital	Admission and discharge

**Table 1** (continued)

Author	Type of review	Number and type of studies	Study objective	Population	Description of the intervention	Intervention performed by	Comparator	Setting	Point of transition
Hammad et al. [26]	SR	13 studies (3 RCTs and 10 non-RCTs)	To review the evidence for the effects and costs/cost-effectiveness of complete pharmacy-led medication reconciliation in hospital settings	Adults and children	Primarily medication reconciliation and supplementation medication reconciliation (bundled with pharmacotherapy consultation and medication review, discharge counseling, patient and carer education, written medication information handed to patient, ward round and bedside care, medication supply)	Pharmacists	NR	Hospital	Hospital transitions
Kwan et al. [20]	SR & MA	18 studies (RCTs; before-and-after evaluations; and post-intervention studies)	To summarize evidence about the effectiveness of hospital-based medication reconciliation interventions	Standard patient population	Medication reconciliation	Pharmacists & other HCPs	NR	Hospital	Hospital transitions
Lehnbom et al.* [27]	SR	40 RCTs and non-RCTs	To examine the evidence regarding the effectiveness of medication reconciliation and review and to improve clinical outcomes in hospitals, the community, and aged care facilities	Standard patient population	Medication reconciliation	Pharmacists & other HCPs	NR	Hospital, community residential aged care facilities	Admission and discharge (from hospital or residential care aged facilities)

Table 1 (continued)

Author	Type of review	Number and type of studies	Study objective	Population	Description of the intervention	Intervention performed by	Comparator	Setting	Point of transition
McNab et al. [18]	MA	14 studies (5 RCTs, 6 cohort studies, 3 pre-post intervention studies)	To determine the effectiveness of medication reconciliation performed by community and primary care pharmacists after hospital discharge on overall discrepancy identification and resolution, the clinical relevance of resolved discrepancies and healthcare utilization in terms of readmission rates, emergency department attendance and primary care workload	Patients discharged from hospital to their permanent residence	Medication reconciliation completed by a pharmacist based in the community	Community pharmacists	usual care	Hospital/community	From hospital to permanent residence
Mekonnen et al. [16]	MA	17 studies (8 RCTs; 6 before-after study; and 3 non-RCTs)	To investigate the effect of pharmacist-led medication reconciliation programs on clinical outcomes at hospital transitions	Standard adult patient population	Medication reconciliation and comprehensive medication reconciliation (bundled with medication review, telephone follow-up/home visit, patient counselling)	Pharmacists	usual care	Hospital	Hospital transitions

Table 1 (continued)

Author	Type of review	Number and type of studies	Study objective	Population	Description of the intervention	Intervention performed by	Comparator	Setting	Point of transition
Mekonnen et al. [17]	MA	19 studies (11 RCTs; 5 before-after study; 1 prospective study; and 2 non-RCTs)	To evaluate the impact of pharmacy-led medication reconciliation interventions on medication discrepancies at hospital transitions and to categorize these interventions as single transition interventions or multiple transitions interventions	Standard adult patient population	Medication reconciliation and comprehensive medication reconciliation (bundled with medication review, telephone follow-up/home visit, patient counselling)	Pharmacists	usual care	Hospital	Hospital transitions
Mekonnen et al. [15]	MA	10 studies (1 RCT; 8 pre-post implementation; and 1 non-RCT)	To evaluate the impact of electronic medication reconciliation interventions on the occurrence of medication discrepancies at hospital transitions	Standard patient population	Electronic medication reconciliation	Pharmacists & other HCPs	usual care	Hospital	Hospital transitions

Table 1 (continued)

Author	Type of review	Number and type of studies	Study objective	Population	Description of the intervention	Intervention performed by	Comparator	Setting	Point of transition
Mueller et al. [28]	SR	26 controlled studies	To summarize available evidence on medication reconciliation interventions in the hospital setting and identify the most effective practices	Standard patient population	Medication reconciliation practices (medication history taking, medication reconciliation, patient counseling, communication with outpatient providers, review appropriateness of medications, post-discharge communication with patient)	Pharmacists & other HCPs	usual care	Hospital	Hospital transitions (admission and discharge)

**Table 1** (continued)

Author	Type of review	Number and type of studies	Study objective	Population	Description of the intervention	Intervention performed by	Comparator	Setting	Point of transition
Nazar et al. [23]	SR	14 studies (9 RCTs and 5 non-RCTs)	To determine the potential contribution of community pharmacists to improve the transfer of care of patients from secondary to primary care settings	Post-discharge patients	Interventions focused on continuity of care, transfer of care or follow-up care, occurred post-discharge (categorized into information, coordination and communication).	Community pharmacists	NR	Hospital	Discharge
					Information-quality of information exchanged between care settings in terms of completeness, accuracy and clarity.				
					Coordination of care: quality of assessment, planning and organization of follow-up services. Communication: quality of exchanging information in terms of personal and direct contact, accessibility, timelines				

Table 1 (continued)

Author	Type of review	Number and type of studies	Study objective	Population	Description of the intervention	Intervention performed by	Comparator	Setting	Point of transition
Simoens et al. [29]	SR	8 cost-effectiveness analysis	To assess the evidence and its methodological quality relating to the cost-effectiveness of interventions to improve seamless care focusing on medication	Standard patient population related to transitions	Counselling by pharmacist at discharge, phone call by pharmacist after discharge, counselling heart failure patients at discharge and telephone follow-up, patient education at discharge with subsequent reinforcement by pharmacist, counselling visit at discharge, tailored counselling for depressive patients at discharge, intervention to prevent medication errors at admission	Pharmacists & other HCPs	usual care	Community and hospital	Transition between ambulatory (including nursing homes) and hospital care
Spinewine et al. [25]	SR	14 RCTs and CTs	To synthesize the impact of approaches to optimize the continuity of care in medication management upon hospital admission and/or discharge	Standard patient population	Medication histories conducted by pharmacists, communication of discharge information to primary care providers, patient education and counseling before and after discharge	Pharmacists & other HCPs	usual care	Hospital	Admission and discharge

\*The review by Leimbom included 2 types of interventions: medication reconciliation and medication review. As the results were presented separately, the number of studies and outcomes are presented for medication reconciliation only

CTs clinical trials, HCPs healthcare professionals, MA meta-analysis, NR not reported, RCTs randomized clinical trials, SR systematic review

**Table 2** Outcomes of included systematic reviews and meta-analyses

Outcome	References	Findings
ADEs and medication discrepancies	De Oliveira et al. [19]	Pharmacists effect on incidence of medication errors during transitions favored over control (OR 0.44; 95% CI 0.31 to 0.63; 10 studies)
	Kwan et al. [20]	Evaluated the effect of medication reconciliation on medication discrepancy and reported less preventable ADEs in the intervention group, but no difference in number of total ADEs (2 studies)
	Lehnbom et al. [27]	Medication reconciliation identified unintentional medication discrepancies in 3.4 to 98.2% of patients. Most discrepancies had little potential or actual impact on clinical outcomes.
	McNab et al. [18]	Medication reconciliation in the community setting increased identification and resolution of medication discrepancies (4 of 4 studies) and reduced clinically relevant discrepancies (2 of 4 studies)
	Mekonnen et al. [17]	No difference in mean number of discrepancies per patient (mean 2.03; 95% CI 2.69 to 1.38); 66% reduction in proportion of patients with discrepancies at single transition points (RR 0.34; 95% CI 0.23 to 0.50; 12 studies); 31% reduction if only RCTs included (RR 0.69; 95% CI 0.51 to 0.92; 5 studies) No difference at multiple transition points (RR 0.88; 95% CI 0.77 to 1.02; 5 studies).
	Mekonnen et al. [15]	<i>Electronic medication reconciliation</i> Significant reduction in the incidence of medications with unintentional discrepancies over total number of medications reconciled at hospital transitions (RR 0.55, CI 0.51 to 0.58; 4 studies) 80% reduction in proportion of omission errors over total number of medications reconciled (RR 0.20; 95% CI 0.06 to 0.66; 3 studies) No difference in mean number of discrepancies (mean difference -0.18; 95% CI 0.45 to 0.09; 3 studies) No difference in proportion of patients with discrepancies (RR 0.37; 95% CI 0.08 to 1.70; 4 studies)
	Mueller et al. [28]	Reduction of medication discrepancies (17 of 17 studies/10 of 10 included studies related to pharmacists) Reduction in potential ADEs, mixed effects on preventable ADEs (improvement in 1 of 2 studies)
	Nazar et al. [23]	Identification and rectification of medication errors were significantly improved with community pharmacists involvement (4 studies)
	Spinewine et al. [25]	Patient education and counselling provided upon discharge and reinforced after discharge—sometimes together with improved communication with HCPs—was shown to reduce the risk of ADEs in some, but not all studies. (2 studies) Composite interventions: no difference in ADEs, lower rates of medication discrepancies (1 study). Communication with healthcare professionals: no conclusion given; no difference in the rate of medication discrepancies (1 study).

**Table 2** (continued)

Outcome	References	Findings	
Hospital readmissions and ED visits	De Oliveira et al. [19]	No significant effect of pharmacists interventions compared with control (OR 0.73; 95% CI 0.47 to 1.13; 8 studies); Pharmacists effect on the incidence of emergency room visits favored over control in 4 studies (OR 0.42; 95% CI 0.22–0.78, NNT 6.2 (3.4–31.4).	
	Hammad et al. [26]	Supplemented medication reconciliation has positive impact on readmission rate after 30 days (6 of 6 studies, pooled reduction 4%) and length of stay (2 of 5 studies).	
	Kwan et al. [20]	<i>Meta-analysis</i> Readmissions and emergency department visits were reduced by 23% (95% CI 0.05 to 0.37) (3 studies) <i>Systematic review</i> No reduction in ED visits within 30 days of discharge No reduction in readmissions within 30 days of discharge	
	Lehnbom et al. [27]	Medication reconciliation found no significant difference in the rate readmissions in the hospital setting (5 of 5 studies); significantly fewer ED visits and readmissions and shorter hospital stays in the residential aged care facilities (2 of 3 studies).	
	McNab et al. [18]	Meta-analysis did not demonstrate a significant reduction in readmission rate (RR 0.91; 95% CI 0.66 to 1.25; 7 studies) No consistent evidence of reduction in emergency department attendance. (3 studies)	
	Mekonnen et al. [16]	<i>Medication reconciliation</i> 28% reduction in all-cause ED visits (RR 0.72; 95% CI 0.57 to 0.92; 7 studies) 19% reduction in all-cause hospital readmissions (RR 0.81; 95% CI 0.70 to 0.95; 13 studies) No difference in composite rate of readmissions and/or ED visits (RR 0.95; 95% CI 0.90 to 1.00; 9 studies) 67% reduction in adverse drug event-related hospital revisits (RR 0.33; 95% CI 0.20 to 0.53; 3 studies)	
	Mueller et al. [28]	Mixed effects on healthcare utilization in studies examining pharmacist-related interventions (improvement in 2 of 8 studies)	
	Nazar et al. [23]	No significant difference/little agreement between trials.	
	Spinewine et al. [25]	Education before and after discharge resulted in fewer hospital readmissions at 6 and 12 months post-discharge (1 out of 2 studies); significant reduction in rate of preventable medication-related visits to the ED or hospital readmissions (1 out of 2 studies) Composite interventions had a mixed effect on both outcomes (2 studies lower rates, 2 studies no difference)	
	Mortality	Hammad et al. [26]	No conclusion possible (3 studies)
		Mekonnen et al. [16]	Medication reconciliation showed no difference in all-cause mortality (RR 1.05; 95% CI 0.95 to 1.16; 7 studies)
Nazar et al. [23]		Interventions showed no significant difference/little agreement between trials (5 studies)	
Costs	Spinewine et al. [25]	Interventions showed no difference in mortality (4 studies)	
	Hammad et al. [26]	No conclusion possible due to lack of evidence. Providing a comprehensive pharmacy-led medication reconciliation may be desirable	
	Kwan et al. [20]	Probably cost-effective for reducing (potential) ADEs (1 study)	
	Simoens et al. [29]	Methodological limitations, not possible to recommend a specific intervention to improve seamless care	
Mortality, readmissions, ED visits, ADEs	Spinewine et al. [25]	Conclusion not possible	
	Ensing et al. [21]	Studies presented as “effective” or “ineffective”. Effective studies indicated strong evidence for pharmacist involvement during admission by performing a level 3 medication review, implemented individual patient tailoring, partly a multidisciplinary team (especially nurse + pharmacist) and medication reconciliation on admission plus post-discharge intervention in collaboration with physicians.	

**Table 2** (continued)

Outcome	References	Findings
Other	Chhabra et al. [22]	The authors did not provide any conclusion on the studied outcomes
	Nazar et al. [23]	Adherence and clinical control not unanimously positively or negatively influenced
	Spinewine et al. [25]	Some studies reported increased patient knowledge, while others mixed effects (4 studies)

ADEs adverse drug events, CI confidence interval, ED emergency department, NNT number needed to treat, OR odds ratio, RCT randomized control trial, RR risk ratio

For composite interventions, 3 reviews reported contrasting results. Hammad et al. [28] concluded that supplemented medication reconciliation has a positive impact on readmission rate (pooled reduction 4% after 30 days) as well as length of stay. De Oliveira et al. [21] favoured pharmacists interventions over usual care in terms of ED visits (OR 0.42; 95% CI 0.22 to 0.78), but not hospital readmissions (OR 0.73; 95% CI 0.47 to 1.13). The positive effects were not supported by the review by Nazar et al. [25] who reported no significant difference or little agreement between trials of interventions performed by community pharmacists. Mixed outcomes were reported also by Spinewine et al. [27].

**Mortality** One meta-analysis and 3 systematic reviews reported this outcome. None of them reported a significant difference in all-cause mortality or were able to provide a conclusion based on the results available [18, 25, 27, 28].

**Costs** Four reviews assessed the effect of interventions on costs and none reported a unanimous conclusion [22, 26–28]. The review by Simoens et al. focused specifically on cost-effectiveness of interventions related to medications. Eight studies were included in the review, all focusing on discharge interventions and mostly performed by clinical pharmacists. The authors reported that interventions to improve seamless care focusing on medications were associated with cost savings, although the evaluation suffered numerous methodological limitations. Hence the authors concluded it is not possible to recommend a specific intervention to improve seamless care focusing on medications based on cost-effectiveness [26]. In the review by Hammad et al. [28] no conclusion regarding cost-effectiveness could be made due to limited and heterogeneous data. Kwan et al. reported that medication reconciliation is probably cost-effective in reducing potential ADEs. However, cost-effectiveness was not the primary outcome of this review and the conclusion was based on 1 study [22].

**Mixed outcomes** The review by Ensing et al. [23] united various outcomes and assessed which interventions were most effective in achieving them. Effective studies indicated strong evidence for pharmacist involvement during admission by performing level 3 medication review, implemented individual patient tailoring and partly a multidisciplinary team, especially a nurse and pharmacists. Medication

reconciliation on admission and post-discharge was also one of the core interventions in the “effective” studies, especially when performed in close collaboration with physicians. Nazar et al. [25] aimed to assess the impact of community pharmacists’ interventions on adherence and clinical control, but could not report a unanimous effect. One review also addressed the effect of different pharmacists’ interventions on patient knowledge and reported mixed effects [27].

### Quality of the included reviews

The quality of the included reviews showed a significant variability. The average score proportion was 0.79 and ranged from 0.58 to 0.96. The criteria for which most studies failed were protocol registration, additional results analysis and risk of bias presentation. A detailed summary of the quality assessment is provided in Tables 3 and 4.

### Discussion

Our umbrella review attempted to summarize systematic reviews and meta-analyses investigating the effects of medications-related interventions at transitions of care. To our knowledge, this is the first umbrella review on the topic. Half of the included reviews focused on medication reconciliation as the main intervention and half reported composite interventions. Most reviews reported positive effects in terms of medication safety—decrease in medication discrepancies and (potential) ADEs. No effect was observed on mortality. The effect on healthcare utilization and costs was inconclusive, mostly due to heterogeneity of the included reviews and/or lack of data.

From all the included reviews, most assessed medication reconciliation as the core intervention at transitions of care. However, the intervention was diversely defined in different reviews. In a limited number of reviews, medication reconciliation followed the definition of the National institute of Clinical Excellence (NICE): *Medicines reconciliation is the process of identifying an accurate list of a person’s current medicines and comparing it with the current list in use. [...] The result is a complete list of*

**Table 3** Quality assessment—PRISMA 2009 Checklist

Study	PRISMA 2009 checklist item																											Score
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	
Chhabra et al. [22]					x						x	x	x	x	x	x			x		x	x	x				x	0.58
De Oliveira et al. [19]					x			x										x										0.88
Ensing et al. [21]					x																							0.96
Hammad et al. [26]															x								x					0.92
Kwan et al. [20]				x								x	x	x	x	x			x			x	x					0.62
Lehboom et al. [27]			x								x				x				x			x	x					0.69
McNab et al. [18]					x										x				x			x	x					0.81
Mekonnen et al. [16]					x										x							x	x					0.96
Mekonnen et al. [17]					x																							0.96
Mekonnen et al. [15]					x										x							x						0.88
Mueller et al. [28]					x										x					x		x	x					0.77
Nazar et al. [23]					x										x					x		x	x					0.73
Simoens et al. [29]			x												x							x	x	x		x		0.58
Spinewine et al. [25]					x									x	x	x						x	x	x				0.69
Score proportion	0.86	1.00	0.93	0.07	1.00	0.93	1.00	0.93	0.64	1.00	0.93	0.79	0.79	0.86	0.57	0.36	1.00	0.93	0.57	1.00	0.79	0.36	0.36	1.00	0.93	1.00	0.93	

x = checklist item not fulfilled. Checklist items: 1—Title; 2—Structured Summary (presented in Table 4); 3—Introduction, rationale; 4—Introduction, objectives; 5—Methods, protocol and registration; 6—Methods, eligibility criteria; 7—Methods, information sources; 8—Methods, search; 9—Methods, study selection; 10—Methods, data collection process; 11—Methods, data items; 12—Methods, risk of bias in individual studies; 13—Methods, summary measures; 14—Methods, synthesis of results; 15—Methods, risk of bias across studies; 16—Methods, additional analysis; 17—Results, study selection; 18—Results, study characteristics; 19—Results, risk of bias within studies; 20—Results, results of individual studies; 21—Results, synthesis of results; 22—Results, risk of bias across studies; 23—Results, additional analysis; 24—Discussion, summary of evidence; 25—Discussion, limitations; 26—Discussion, conclusions; 27—Funding

**Table 4** Quality assessment—PRISMA 2009 Checklist item 2: Structured summary

Study	Background	Objectives	Data sources	Study eligibility criteria, participants and interventions	Study appraisal and synthesis methods	Results	Limitations	Conclusion and implications of key findings	Systematic review registration number	Score proportion
Chhabra et al. [22]					x		x		x	0.67
De Oliveira et al. [19]							x		x	0.78
Ensing et al. [21]							x		x	0.78
Hammad et al. [26]							x		x	0.78
Kwan et al. [20]							x		x	0.78
Lehnbom et al. [27]	x				x		x		x	0.56
McNab et al. [18]							x		x	0.78
Mekonnen et al. [16]							x		x	0.78
Mekonnen et al. [17]					x		x		x	0.67
Mekonnen et al. [15]						x	x		x	0.78
Mueller et al. [28]							x		x	0.78
Nazar et al. [23]							x		x	0.78
Simoens et al. [29]	x				x		x		x	0.44
Spinewine et al. [25]	x						x		x	0.67
Score proportion	0.79	1.00	0.93	1.00	0.71	0.93	0.07	1.00	0.00	

x = checklist item not fulfilled

medicines, accurately communicated to all health and social care professionals involved in the person's care, in which any issues with the medicines, such as wrong dosage or omission, have been addressed [31]. Others however, addressed medication reconciliation as a multiple stage intervention, including medication review, patient consultation and follow-up, etc. In line with this, many reviews analysed interventions beyond simple medication reconciliation. The discrepancy in the definition and understanding of medication reconciliation has also been addressed by the Pharmaceutical Care Network Europe recently [32]. Such diversities limit the ability to draw conclusions on the most effective pharmacy-supported intervention at transition of care. Since medication reconciliation is treated as a multidisciplinary and multidimensional health process, the relevance of assessing its effects in isolation of other activities might be questionable [28, 32]. Despite limited data available, multiple reviews concluded that medication reconciliation bundled with other interventions might be most effective [22, 23, 28].

Studies assessed various outcomes from softer, e.g. ADEs, to harder, e.g. hospital readmissions and mortality. The effects on ADEs and medication discrepancies were the most pronounced and most often assessed as positive. As our interventions of interest were directed at medications, this could be expected. Pharmacy-supported interventions have been attributed to increased medication-related safety [33], an effect which seems to be observed also at transitions of care. The clinical impact of these reduced discrepancies and potential ADEs was however less homogeneous, but might also be more pronounced in the long-run and hence difficult to observe in studies of shorter duration.

Multiple reviews aimed to assess the effect of interventions at transitions of care on healthcare use, with conclusions reaching little agreement. Two meta-analyses at hospital level reported a significant reduction in readmissions and ED visits [18, 22], while a meta-analysis and a systematic review focusing on community pharmacists showed no reduction in readmission rates [20, 25]. Similarly as the clinical effects of medication discrepancies and ADEs, the hard outcomes might also be better detected in the long run; only a limited number of studies followed patients for more than 30 days.

Economic evaluations were very limited in the presented reviews. In those that addressed this question, studies revealed heterogeneity in terms of outcomes measured (costs, cost-effectiveness, etc.) and methodologic limitations. It is therefore not possible to draw robust conclusions on the effect of transition of care interventions on health-care-related costs.

Most reviews did not include specific patient populations. However, the reviews included in our umbrella review often

included so called “high-risk patients”. These were either patients with a specific condition (e.g. heart failure, acute admission, etc.), on polypharmacy or elderly, multimorbid patients. Numerous reviews also emphasized that the effectiveness of the interventions is increased when applied to such high-risk populations [20, 23, 30].

The current umbrella review should only be interpreted within the context of its limitations. First of all, the diversity of the terminology in the field of seamless care/transitions of care/integrated care etc. represented a challenge and has made an effective retrieval of all published reviews uncertain. Nevertheless, our search was extensive and our search profile broad, hence assuring the majority of applicable reviews were identified and included. Secondly, we did not manage to correlate specific interventions with positive and negative outcomes. This was due to the diversity of interventions analysed in the reviews, despite the common nomenclature. Third, the systematic reviews and meta-analyses showed considerable heterogeneity, which made comparison and drawing of strong conclusion challenging. Many studies did not have adequate power to detect significant differences.

Nevertheless, our review has also several strengths. It is the first umbrella review to investigate pharmacy-supported interventions at transitions of care. A comprehensive search strategy was utilized including three bibliographic databases with no limitation placed on date of publication and an in-depth quality assessment of the included studies. It therefore provides a comprehensive and methodologically-robust overview of the currently published reviews on the topic.

Future research should focus on the composite of the optimum medication reconciliation as it is not standardized. Our umbrella review calls for further discussion and high-quality studies with well-defined interventions and outcomes. Focus on assessing actual harm and patient-oriented outcomes is also needed.

## Conclusion

Pharmacy-supported interventions at transitions of care seem to have a positive effect on ADEs and medication discrepancies and show no effect on mortality. The effect on health resources use is inconsistent, while evidence on the cost-effectiveness of such interventions is lacking. Overall, the evidence on the most effective interventions at transitions of care remains limited and heterogeneous. Future high quality studies with well-defined interventions and outcomes are needed.

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**Conflicts of interest** The authors declare that they have no conflict of interest.

## Appendix 1:

Search profile:

Search: (“transition of care”[Title/Abstract] OR “transitions of care”[Title/Abstract] OR “seamless care”[Title/Abstract] OR “integrated care”[Title/Abstract] OR “continuity of care”[Title/Abstract] OR “continuity of patient care”[Title/Abstract] OR “delivery of health care, integrated”[Title/Abstract] OR “transmural care”[Title/Abstract] OR “coordinated care”[Title/Abstract] OR “continuum of care”[Title/Abstract] OR “transitional care”[Title/Abstract] OR “medication reconciliation”[Title/Abstract] or “comprehensive care”[Title/Abstract]) AND (“drug” OR “medicament” OR “medicine” OR “drug prescriptions” OR “electronic prescribing” OR “medication” OR “medical product” OR “drug related problems” OR “medication related problems” OR “medication use” OR “medication errors” OR “medication review” OR “pharmacy”) AND (“patient admission” OR “hospital admission” OR “patient discharge” OR “hospital discharge” OR “patient readmission” OR “patient transfer” OR “transition” OR “transitional”)

Filters: Meta-Analysis, Systematic Reviews

## Appendix 2:

Inclusion and exclusion criteria of included systematic reviews and meta-analyses

Author	Inclusion criteria	Exclusion criteria
Chhabra et al. [22]	Studies that evaluated an intervention involving medication reconciliation in patients transferred to and/or from long-term care settings, such as nursing homes, skilled nursing facility, residential care facilities, assisted living facilities, homes for the aged, and hospice care	Studies involving transitions to or from home health care agencies were excluded because they typically serve patients for a short duration and are in contact with a patient’s health care provider, family members, and/or caregivers. Studies published before 2000, not written in English, that were not empirical, that did not involve medication reconciliation as an intervention, or that were not experimental or quasi-experimental also were excluded

Author	Inclusion criteria	Exclusion criteria
De Oliveira et al. [19]	RCTs that compared a pharmacist intervention (i.e., reconciliation and/or patient education) with an inactive (“usual care”) control group in patients undergoing transitions of care from a hospital setting back to the community. Studies had to report at least on medication errors or healthcare utilization (hospital readmissions and/or emergency room visits) as outcomes. No minimum sample size was required for inclusion in the metaanalysis	Excluded were trials reporting on the effect of pharmacist interventions in non-transition of care settings or involving pediatric patients. Trials that evaluated the effect of the pharmacist intervention compared with an active comparator (e.g., nurse intervention, community health worker) were excluded to optimize clinical homogeneity. Studies containing a concurrent use of an alternative intervention (e.g., bundle interventions) were excluded if a direct comparison of pharmacist and control could not be established
Ensing et al. [21]	<i>Study design</i> (quasi) (cluster) randomized controlled trial published in English <i>Population</i> Adult participants admitted to a hospital and discharged home <i>Setting</i> Intervention conducted in hospital and/or community pharmacy and/or patients’ home <i>Intervention</i> The intervention involved a pharmacist, pre-graduate pharmacist, or pharmacy technician. The pharmacist had a proactive role, meaning for all interventions, patients received an active pharmacist intervention (e.g., excluding reactively responding to physician questions during ward rounds). Interventions were performed before, during, or up to 30 days after hospitalization. The post-discharge time limit was chosen to ensure connection to transitional care. The intervention was designed to improve transitional care and aimed at medication-related issues <i>Comparison</i> The intervention was compared with a control group that received usual care <i>Clinical outcomes</i> At least 1 of the following outcomes was measured: mortality, readmissions, emergency department visits, and adverse drug events	<i>Participant</i> Intervention conducted solely on pediatric patients or psychiatric patients due to their specific population characteristics <i>Setting</i> Interventions in a palliative care setting or in an intensive care ward due to their specific setting characteristics <i>Intervention</i> Interventions solely targeted at specific drugs (e.g., improving adherence of statins) Interventions not aimed at transitional care (e.g., interventions in outpatient clinics without transmission of relevant information from earlier health care provider encounters in the hospital or interventions on heart failure guideline adherence)

Author	Inclusion criteria	Exclusion criteria	Author	Inclusion criteria	Exclusion criteria
Hammad et al. [26]	Adults and children receiving pharmacy-led medication reconciliation within hospital inpatient settings	Studies evaluating non-pharmacy-led medication reconciliation at only one end of patient care or transfer were not included. Studies evaluating pharmacy-led medication reconciliation 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 medication reconciliation and suspected to influence readmissions and health care utilization	McNab et al. [18]	<i>Population</i> Patients discharged from hospital to their permanent residence (home, residential unit or nursing home) <i>Intervention of interest</i> Medicines reconciliation completed by a pharmacist based in the community <i>Comparator</i> Usual care processes for medication reconciliation <i>Outcome measure</i> Discrepancy identification, Discrepancy categorisation, Healthcare usage (readmission, emergency department attendance, GP attendance), Workload/efficiency measures—time to complete medicines reconciliation, effect on number of primary and secondary care appointments needed, and economic outcomes <i>Study design</i> RCTs, cluster RCTs, quasi-RCTs, cluster quasi-RCTs, controlled pre–post intervention studies, interrupted-time-series, cohort studies (prospective or retrospective), case–control studies, uncontrolled pre–post intervention studies <i>Language</i> No limitation <i>Publication date</i> No limitation	Studies focused on medication review (e.g., recommendations to optimise medication regimens) were excluded
Kwan et al. [20]	Studies evaluating medication reconciliation with an eligible outcome reported	Studies in which the person conducting medication reconciliation provided the sole assessment of clinical significance for identified discrepancies were excluded. The authors also required that studies explicitly distinguish unintentional discrepancies from other (intentional) medication changes through direct communication with the medical team	Mekonnen et al. [16]	Studies reporting medication reconciliation intervention primarily and that provide data on any of these clinical end points (all-cause readmission, emergency department visits, mortality, adverse drug events)	The following types of studies were excluded: 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
Lehnbom et al. [27]	Studies evaluating medication reconciliation or medication review that also reported the impact of identifying and rectifying discrepancies and medication-related problems	Articles that only reported the number of identified discrepancies or medication-related problems but failed to identify the potential or actual impact of these discrepancies on patient outcomes were excluded. Articles were also excluded if the sample size was fewer than 50 patients because the impact on clinical outcomes could not be reliably evaluated with such a small sample size			

Author	Inclusion criteria	Exclusion criteria
Mekonnen et al. [17]	Studies comparing pharmacy-led medication reconciliation interventions with usual care and measured medication discrepancies as an outcome of interest	Interventions with medication reconciliation where physicians or nurses assessed medication discrepancies were excluded. Studies assessed discrepancies in medical histories, for example – documentation of allergy, were excluded
Mekonnen et al. [15]	Studies which reported data related to the effectiveness of electronic medication reconciliation intervention, and provided data on medication discrepancies or errors	Studies with a focus on other types of medication errors (e.g. prescribing errors) that were identified through the non-reconciliation process were excluded
Mueller et al. [28]	Medication reconciliation was the primary focus of the intervention. English language, hospital setting, intervention during hospitalization and/or transition, quantitative results	Not reported
Nazar et al. [23]	Patients who were identified as post-discharged from hospital, intervention performed by a community pharmacist, intervention focused on continuity of care, CT or RCT. Outcomes reported	Not reported
Simoens et al. [29]	Studies had to compare an intervention to improve seamless care focusing on medication with usual care	Not reported
Spinewine et al. [25]	Inclusion of patients admitted to and/or discharged from hospital	The following exclusion criteria were applied: (i) studies where the focus of the intervention was broader than medications and without specific measure to evaluate the effect of the intervention on the medication component; (ii) studies where the intervention focused on medications but with a scope that was broader than continuity of care (e.g. clinical pharmacists doing admission histories and discharge counselling along with interventions to improve prescribing during hospital stay) and without specific measure to evaluate the effect of the intervention on the continuity of care component; (iii) studies with no control group or 'before-after studies' with no control group (i.e. in which the control group is an historical group) and (iv) studies with <30 patients per group. Systematic reviews and meta-analyses on related topics were not included as such, but the list of articles included in the corresponding reviews was checked for eligibility

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