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REVIEW

Effects of hospital pharmacist interventions on health outcomes in older polymedicated inpatients: a scoping review

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Key summary points

Aim Do patients receiving polypharmacy benefit from interventions by hospital pharmacists, individually or as part of a multidisciplinary team?

Findings Some beneficial effects were found of pharmacist interventions in 15 of 26 studies, specifically on hospital readmission, visits to the emergency department and healthcare costs.

Message Evidence in favour of hospital pharmacist interventions in polymedicated older patients is scarce. Well-designed studies, with clearly defined interventions, outcomes and follow-up times should be conducted in the future to define the role of pharmacists in the geriatric team.

Abstract

Purpose To identify the evidence that supports the effect of interventions made by hospital pharmacists, individually or in collaboration with a multidisciplinary team, in terms of healthcare outcomes, a more effective utilization of resources and lower costs in older polymedicated inpatients.

Methods We searched the following databases: MEDLINE, EMBASE and the Cochrane Library. We also conducted a hand search by checking the references cited in the primary studies and studies included in reviews identified during the process of research. Four review authors working by pairs searched for studies, extracted data, and drew up the results tables.

Results Twenty-six studies were included in the review. In 13 of them pharmacists carried out their intervention exclusively while the patients were in hospital, whereas in 13 interventions were delivered during admission and after hospital discharge. Outcomes identified were mortality, length of stay, visits to the emergency department, readmissions and reported quality of life, among others. Pharmacist interventions were found to be beneficial in fifteen studies, specifically on hospital readmissions, visits to the emergency department and healthcare costs.

Conclusion There is no hard evidence demonstrating the effectiveness of hospital pharmacist interventions in older polymedicated patients. Mortality does not show as a relevant outcome. Other health care outcomes, such as hospital readmissions, visits to the emergency department and healthcare costs, seem to be more relevant and amenable to change. Interventions that include pharmacists in multidisciplinary geriatric teams seem to be more promising that isolated pharmacist interventions. Interventions prolonged after hospital discharge seem to be more appropriate that interventions delivered only during

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hospital admission. Better-designed studies should be conducted in the future to provide further insight into the effect of hospital pharmacist interventions.

Keywords Polypharmacy · Aged · Hospital pharmacists · Health care outcome · Review literature

Background

It was not until 1989 that Hepler and Strand introduced the term pharmaceutical care [1]. The new term brought about a major transformation in clinical pharmacy practice. From that moment onwards, the work of pharmacists is gradually transforming into a more cooperative and patient-centred effort aimed at obtaining specific and positive results to enhance patients' quality of life (QoL). In this sense, close cooperation between clinical pharmacists and other healthcare specialists, especially physicians and nurses, and with patients and their relatives, are mandatory to succeed in many pharmaceutical interventions, beyond the usual role of pharmacist to ensure that patients properly take their medications as prescribed and avoid any harmful effects.

At first, the value of pharmacists was only measured through simple and intermediate outcomes such as reduction of medication errors [2], avoidance of drug misuse [3], prevention of adverse drug reactions [4], and minimization of the potential for unnecessary anticholinergic burden [5]. Furthermore, the benefits of pharmacist interventions were also measured in terms of cost savings and the generation of economic value [6–8]. This value was not related to pharmacists' daily everyday activities, such as medication reconciliation, counselling, or drug review. Indeed, as pharmacists walked out their pharmacy departments and started to collaborate with other healthcare providers and to join multidisciplinary teams, their value started to become noteworthy. Pharmacist-led interventions in multidisciplinary teams in hospital settings seem to improve clinical outcomes [9]. For example, their work has a positive impact on clinical outcomes and healthcare-resource utilization, reducing the number of hospitals visits [10] and mortality [11], and improving QoL or other patient-reported outcomes [12]. Their value has also been recognised in the care of non-hospitalised patients [13], in long-term care settings [14], and even in the delivery of home visits [15, 16].

In the case of older patients, the contribution made by pharmacists could be significant. Ageing places individuals at risk of multi-morbidity due to associated physiological and pathological changes and increases their chances of being prescribed multiple medications [17]. This increases their risk of developing adverse reactions, drug-drug interactions or adherence problems, all of them issues that pharmacists feel comfortable dealing with. Ageing is also associated with pharmacokinetic and pharmacodynamic changes [18]. Drugs and their formulations usually differ in liberation, absorption, distribution, metabolism, and clearance patterns and pharmacists are the experts to consult. Moreover, tools have been developed to review treatments administered to older patients to make prescriptions safer and more effective [19, 20]. In this regard, pharmacists have demonstrated their skill in applying these tools [21, 22]. For all the reasons above, pharmacists are in a unique position to improve heath and QoL in this particular population. Although the literature is scarce in this regard, some systematic reviews have been conducted to look into the impact that pharmacists exert on the lives of older patients [8, 23, 24]. In general, studies in this area are of low-to-medium quality, and underpowered to estimate the contribution of pharmacists to older patients' hard health outcomes such as mortality or hospital readmission, as many pharmacists fulfil their role as members of multidisciplinary teams. This issue remains clearly unexplored. Moreover, the exact interventions conducted by pharmacists in different studies are heterogeneous, which makes it difficult to determine which interventions produce the best results in complex older patients [25].

This scoping review seeks to identify and discuss the evidence that supports the effect of the interventions made by hospital pharmacists, either individually or as part of a multidisciplinary team, in terms of better healthcare outcomes, a more effective utilization of resources and lower costs in older polymedicated inpatients.

Methods

A scoping review was conducted according to the guidelines set out in the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) extension for Scoping Reviews (PRISMA-ScR) [26].

First, the research question was formulated following the PICO(d) format, as shown in Table 1.

Literature search strategy

A search was launched in MEDLINE (through OvidSP, all PubMed), EMBASE (Elsevier), and the Cochrane Library (Wiley). All databases were searched from inception to the 3rd March 2020. The search strategy is described in Appendix 1. The search was not filtered by language.

We did not register a review protocol for the search.

Table 1 Research question based on the PICO (d) format

Population	Hospitalised patients older than 65 years taking four or more regular medications on a regular basis (polymedicated)
Intervention	Interventions carried out by a hospital pharmacist individually or in collaboration with an interdisciplinary team
Comparator	Any comparator; usual care
Outcomes	Clinical outcomes: Mortality; quality of life (QoL) Use of healthcare resources: Hospital usage (length of hospitalization, readmission rates, visits to an emergency department or visits to a general practitioner) Health-related costs and cost savings
Design	Randomised controlled trials (RCTs), non-randomized or quasi-randomised controlled trials (Quasi RCT), before-after studies without historical controls

Selection of studies and data extraction

Studies were selected based on the criteria established in the PICO question (Table 1).

Duplicate references across the different literature databases were deleted. Title and abstract screening were undertaken in pairs by four independent reviewers to detect studies matching the inclusion criteria. In a second round, full-text articles were reviewed by four reviewers working in pairs to obtain the final set of studies to be included. In addition, a manual search was performed by reviewing the references in the narrative or systematic reviews found in the literature search. Discrepancies were discussed and resolved by a third reviewer.

A data extraction sheet was designed to collect the information of interest from the included studies. A pilot extraction process was performed to test this extraction sheet. This was done by the reviewers that would subsequently perform the final extraction process. Once the data extraction sheet was ready, three of the review authors collected the data from the selected studies and filled out the extraction sheet. Two review authors summarised the collected information by grouping the results of the included studies by setting, intervention performed, and outcome assessed. No formal quality assessment of the included studies was carried out as this is not mandatory when conducting a scoping review.

Results

Results of the literature search

The systematic search resulted in the identification of 3982 references, 166 of which were selected following title and abstract screening. After the full-text review process, 21 references were included, corresponding to 20 studies. Seven further references were included from hand searching [27–33]. Again, two of these references came from the same study but reported different outcomes [30, 34]. Finally, 26 studies were included in the review (see Fig. 1).

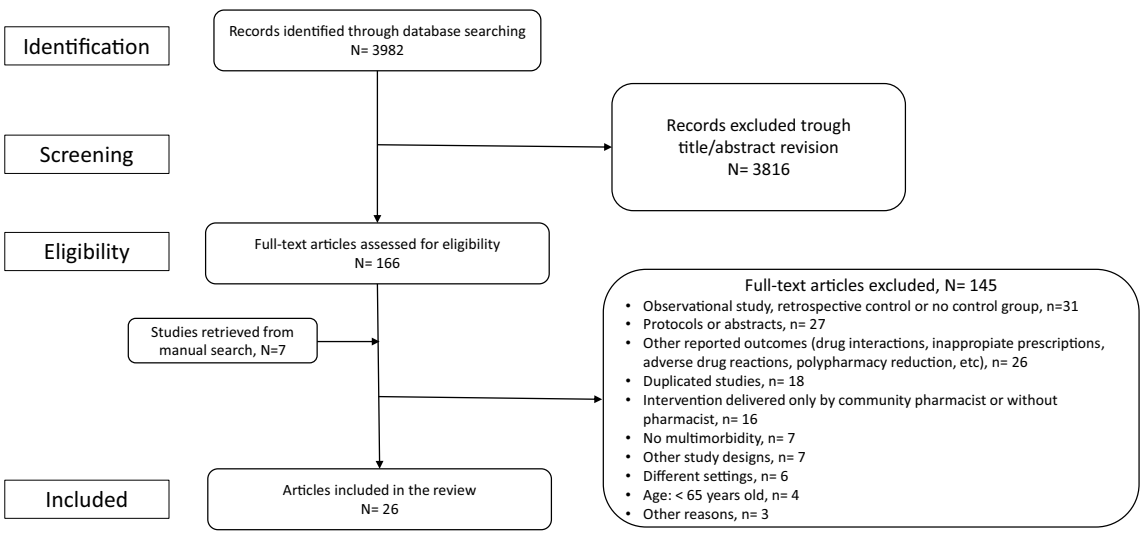

Fig. 1 Flow chart of the study revision process

Included studies

The characteristics of the included studies are detailed in Tables 2 and 3.

Setting

After data extraction, the included studies were classified into two main groups according to the setting where the intervention was performed. Studies classified under the acute care group included interventions delivered during hospitalization. In studies classified under the transitional care group, interventions were delivered during hospitalization and after hospital discharge.

Interventions delivered by setting

Acute setting In 13 studies, hospital pharmacists delivered the interventions only while patients were in hospital. The most frequent interventions were medication reconciliation at admission (11 out of 13 studies) [30, 32–41], comprehensive medication review during hospitalization (10 out of 13 studies) [30, 32–38, 40–42], and counselling at hospital discharge, delivering a discharge summary to the patient [33, 40, 41, 43], to the patients' general practitioner (GP) [35, 37, 44, 45] and to the GP and/or to the community pharmacist (CP) [32, 36, 38] (10 out of 13 studies) [30, 32–38, 40, 41, 43–45].

Pharmacists delivered their interventions individually, i.e. without being part of a team, in nine studies [30, 33–35, 40, 42–45], in which the hospital pharmacist made drug recommendations to the attending physician. In another three studies, the pharmacist was part of a multidisciplinary team [37, 38, 41]. In a single study, pharmacy technicians were also part of the multidisciplinary team together with hospital pharmacists [32]; in one, the hospital pharmacist worked along with a clinical pharmacologist [39] and in one, the hospital pharmacist worked in collaboration with the GP and the CP [36].

Transition from the acute care setting to the community Thirteen studies assessed interventions conducted by the hospital pharmacist during transition of care from the hospital to the community [10, 27–29, 31, 46–53]. During hospitalization, pharmacists performed some interventions as drug reconciliation at admission [10, 28, 48, 52] or after admission [31, 46], and medication management, including medication review and giving advice on potential drug-related adverse events and drug–drug interactions [10, 27, 28, 31, 46, 48, 52]. Other interventions conducted at discharge included medication reconciliation [10, 28, 31, 49], a patient interview giving counsel on discharge medication and on how to prevent or manage drug problems [10, 28, 29, 31, 47, 49, 53], and sending a discharge summary to the GP or CP [48, 50–53].

After discharge, interventions consisted of: follow-up phone calls by the hospital pharmacist [10, 28, 29, 31, 48, 51, 52] or by other member of the team [46] in eight studies, and personal follow-up by pharmacist [47, 49, 53] or by a nurse [52] in four studies. During follow-up, pharmacists made drug-related recommendations, provided counselling, and reinforced adherence [31, 47, 48, 50, 53]. Contact with the GP in case any problems were detected or if changes to the medication were required was done by the pharmacist in six studies [10, 31, 47, 50, 51, 53] and by some other member of the team in an additional study [27]. In two studies, the pharmacist met with the patient's responsible team if there were any problems related with the patients' drug treatment [46, 50].

The drug treatment was followed by a hospital pharmacist in seven studies [10, 28, 29, 31, 48, 49, 52], a community pharmacist in two [47, 50] and by other members of the team in four studies [27, 46, 51, 52].

The hospital pharmacist was part of a multidisciplinary team in seven studies [28, 29, 31, 46, 47, 51, 52]. The composition of the team varied among the different studies: in some it comprised the hospital physician [31, 52], or the patient's GP [29] or patient's GP and patient's community nurse [46, 51], a community pharmacist [47] or a study care coordinator (SCC) [28]; in other, the hospital pharmacist was considered an external expert who provided advice and formulated recommendations when asked to do so, or was called on to address a specific issue [27], in five studies [10, 48–50, 53] pharmacists worked on their own.

Outcomes

The included studies reported on a wide variety of health-related and economic outcomes. Detailed information for every considered outcome is showed in Tables 2 and 3 (only numerical information of the statistically significant outcomes is reported).

A. Outcomes resulting from interventions in the acute care setting.

I. Effects of clinical pharmacist interventions during the index hospitalization. 1. Length of hospital stay (LOS):

Ten out of 13 studies measured the length of the index hospitalization. Only one study found a LOS reduction in the intervention group compared to the control group [32]. Eight studies showed no differences in LOS between the study groups [30, 34, 36, 39–42, 44, 45]. In one study, LOS was longer in the intervention group than in the control group [38].

Table 2 Description of the studies which intervention was delivered during the acute care

Study characteristics			Baseline population characteristics			
Author, year	Country	Desing	*N*, (% female)	Age (years), mean (SD)	Patient's conditions	Number of drugs, mean (SD)
Bladh 2011 [44], Wallerstedt 2012 [45]	Sweden	RCT	Intervention group: 164 (60) Control group: 181 (61) Patients with EQ-5 utility scores: - Intervention group: 116 (61) - Control group 124 (63)	All participants: 82 (35–99)	No data	Number of drugs, median (IQR): Intervention group: 7 (4–9) Control group: 7 (4–10)
Cossette 2017 [42]	Canada	RCT	Intervention group: 126 (61.9) Control group: 128 (58.6)	Intervention group: 81.5 (7.7) Control group: 80.5 (7.0)	CCI, mean (SD): Intervention group: 1.9 (2.1) Control group: 2.7 (2.8)	No data
Dedhia 2009 [41]	EEUU	Pre-post design	Preintervention group: 237 (60.3) Intervention group: 185 (61.8)	Preintervention group: 77.3 (7.0) Intervention group: 76.7 (7.7)	Most common diagnoses: hypertension, congestive heart failure; coronary heart disease; COPD; diabetes mellitus	Preintervention group: prescribed medication 6.8 (4.3); OTC 1.7 (1.5) Intervention group: prescribed medication 7.3 (3.8); OTC 1.8 (1.6)
Graabaek 2019 [40]	Denmark	RCT	Basic intervention group (ED): 200 (48) Extended intervention group (STAY): 200 (50) Control group: 200 (49)	Age, median (IQR): Basic intervention group (ED): 75 (70–82) Extended intervention group (STAY): 74 (69–80) Control group: 75 (70–82)	No data	Number of drugs, median (IQR): Basic intervention group (ED): 6 (3–10) Extended intervention group (STAY): 6 (3–10) Control group: 6 (3–10)
Lenssen 2018 [33]	Germany	RCT	Intervention group: 31 (61.3) Control group: 29 (58.6)	Intervention group: 75.9 (6.87) Control group: 79.5 (8.62)	No data	Intervention group: 16.3 (6.3) Control group: 17.3 (7.3)
Lisby 2010 [39]	Denmark	RCT	Intervention group: 50 (60) Control group: 49 (61)	Age, mean (95% CI): Intervention group: 80.2 (95% CI 78.3–82.1) Control group: 78.2 (95% CI 76.2–80.2)	Most common diagnoses: pneumonia, COPD and suspected myocardial infarction	Number of drugs, mean (95% CI): Intervention group: 10.2 (95% CI 8.9–11.5) Control group: 10.1 (95% CI 8.8–11.5)
Makowsky 2009 [38]	Canada	Quasy RCT	Intervention: 221 (52.9) Control: 231 (55.8)	Intervention group: 74.9 (13.9) Control group: 73.2 (14.7)	Most common diagnoses: coronary artery disease, community adquired pneumonia, COPD, heart failure and type 2 diabetes mellitus	No data
O´Sullivan 2016 [30]; Gallagher 2016 [34]	Ireland	RCT	Intervention 361 (50,1) Control 376 (49,5)	Age, median (IQR) Intervention group: 77 (71–83) Control group: 78 (72–84)	CIRS, median (IQR): Intervention group: 5 (3–6) Control group: 4 (3–6)	Number of drugs, median (IQR) Intervention group: 9 (6–12) Control group: 8 (6–11)
Sánchez-Ulayar 2012 [43]	Spain	RCT	Intervention: 50 (42) Control: 50 (42)	Intervention group: 75 (11) Control group: 77 (10)	No data	Intervention group: 9.7 (2.9) Control group: 10 (3.5)
Scullin 2007 [32]	UK	RCT	Intervention: 371 (55) Control: 391 (51)	Intervention group: 70.3 (13.8) Control group: 69.9 (14.8)	No data	No data (patients were included if they were taking at least four medications regularly)

Table 2 (continued)

Study characteristics			Baseline population characteristics			
Author, year	Country	Desing	*N*, (% female)	Age (years), mean (SD)	Patient's conditions	Number of drugs, mean (SD)
Spinewine 2007 [37]	Belgium	RCT	Intervention: 96 (71.9) Control: 90 (66.7)	Intervention group: 82.4 (6.9) Control group: 81.9 (6.2)	CCI, mean (SD): Intervention group: 2.0 (1.6) Control group: 2.0 (1.5)	Intervention group: 7.9 (3.5) Control group: 7.3 (3.3)
Stowasser 2002 [36]	Australia	RCT	Intervention: 113 (44); Control: 127 (14)	Intervention group: 67.4 (13); Control group: 65.6 (14)	Number of ICD codes for comorbidity, mean (SD): Intervention group: 6.2 (3.3) Control group: 5.8 (2.4)	Intervention group: 7.0 (3.7) Control group: 7.2 (3.6)
Van del Linden 2017 [35]	Belgium	Quasi-RCT	Intervention 91 (48) Control 81 (56)	All participants: 84.5 (4.8)	CCI, median (IQR): Intervention group 7 (5–8) Control group: 6 (5–8)	Number of drugs, median (IQR): Intervention group: 9 (7–12) Control group: 10 (7–13)
Study characteristics			Description of the intervention			
Author, year	Country	Desing	At admission	During hospitalization	At discharge	In the community setting
Bladh 2011 [44], Wallerstedt 2012 [45]	Sweden	RCT	–	The composite intervention consisted of (1) medication reviews by the pharmacist including oral feedback on prescribing to physicians	(2) Drug treatment discussion with the patient at discharge and (3) a medication report including a summary of the drug treatment changes during the hospital stay and a medication list, given to the patient and sent to the patient's general practitioner (GP) at discharge	–
Cossette 2017 [42]	Canada	RCT	–	The pharmacist analyzed the computerized alerts system on a daily basis and determined their clinical relevance based on their clinical experience. For clinically relevant alerts, the pharmacist then developed a geriatric pharmaco-therapeutic plan to be discussed with the treating physician to reduce potentially inapropriate medication use	–	–

Table 2 (continued)

Study characteristics			Description of the intervention			
Author, year	Country	Desing	At admission	During hospitalization	At discharge	In the community setting
Dedhia 2009 [41]	EEUU	Pre-post design	Physician–Pharmacist Collaborative Medication Reconciliation: Hospital providers carefully documented the preadmission medication regimen using a medication intake form that prompted them to consider whether to continue, change, or hold these medications considering the patient's age, comorbidities, and presenting illness	Inpatient pharmacist reviewed the history and physical medication intake, and inpatient medication orders. Specific feedback about each patient´s regimen was informed to the responsible faculty member	Scheduled Discharge Meeting: This meeting of the discharge planning nurse, discharging hospitalist provider, and the patient (with or without caregiver) was arranged to review the hospital course and follow-up recommendations before discharge. Written discharge information and instructions were discussed. Medication discharge instructions were presented on a grid with straightforward instructions about how, when, and why to take each medication. Contact information for their hospitalist providers were shared in case patients had additional questions after returning home	–
Graabaek 2019 [40]	Denmark	RCT	Both, the ED group and the STAY group received a pharmacist-led medication review (including a patient interview and medication reconciliation process) at admission	Patients in the STAY group transferred to a specialized ward received a medication review during inpatient stay. Recommendations about changing regimens for economic reason were only conducted if it would affect the patient. The recommendations for medical changes were reported to the physician electronically in the patient record and supplemented with dialogue with the physician whenever possible	Patients in the STAY group received counselling and a medication report at discharge (a note in the electronical medical record where the pharmacist listed all changes to the patient´s medication use during inpatient stay)	–

Table 2 (continued)

Study characteristics			Description of the intervention			
Author, year	Country	Desing	At admission	During hospitalization	At discharge	In the community setting
Lenssen 2018 [33]	Germany	RCT	The comprehensive pharmaceutical care service (made by clinical pharmacist) included face-to-face counselling with the patients and a previous study (a medication review, medication reconciliation and a medication safety check) after inclusion	The comprehensive pharmaceutical care service (made by clinical pharmacist) included face-to-face counselling with the patients and a previous study (a medication review, medication reconciliation and a medication safety check) during the entire stay on the wards	Medication reconciliation at discharge and providing recomendations for the discharge letter (performed by clinical pharmacist)	After discharge, the comprehensive pharmaceutical care service ended, and all study patient received their "standard care"
Lisby 2010 [39]	Denmark	RCT	Intervention delivered within 24 h of admission or in the first-coming day of the week. Medication review and drug counselling by a clinical pharmacist and a clinical pharmacologist after the usual routine medication review in the ward by the ward physician. First, a clinical pharmacist collected information about the patients' medication and second, the collected medical histories were discussed with a clinical pharmacologist. Discrepancies, inappropriate drugs, doses, routes, dosing schedules or inappropriate interactions between drugs would be described in an advisory note with recommendations about the patients' medication	–	–	–
Makowsky 2009 [38]	Canada	Quasy RCT	At admission, the pharmacist performed a comprehensive medication history and performed medication reconciliation	Pharmacists provided proactive clinical services at the bedside as part of the medical team: clarified and documented pharmacotherapy history, participated in bedside patient care rounds, identified and resolved actual and potential drug related problems, communicated patient-specific therapeutic recommendations to the team	Medication reconciliation prior to patient discharge. The pharmacist reviewed changes of the medication regimen with the patient, and if necessary provided to the patient a written summary and contacted to the patient's CP or GP	–

Table 2 (continued)

Study characteristics			Description of the intervention			
Author, year	Country	Desing	At admission	During hospitalization	At discharge	In the community setting
O´Sullivan 2016 [30]; Gallagher 2016 [34]	Ireland	RCT	The structured pharmacist review of medication/clinical decision support software intervention consisted of four elements: the first of which was direct contact with the patient's community pharmacy and or general practitioner in order to reconcile the patient's medication history	The second element was deplopment of the clinical decision support software to review the patient's list of medications in order to identify any drug related problems and drug appropriateness. Third, the intervention pharmacist then reviewed clinical decision support software output and interpreted which potential interventions were clinically relevant and the likely risk: benefit ratio of each recommendation. A economic evaluation consisted of a trial-based analysis conducted alongside the RCT	At 7–10 days post-admission or at discharge (whichever came first), the primary researcher conducted a follow-up review of each randomised patient's medical notes, nursing notes and medication Kardex	–
Sánchez-Ulayar 2012 [43]	Spain	RCT	–	–	At discharge, clinical pharmacists provided a personalised medication planning to the patients and medication counselling	–
Scullin 2007 [32]	UK	RCT	The clinical pharmacist performed an accurate medication history. Any discrepancies with the hospital prescription list were dealt with	Drug treatment was reviewed daily, taking into account therapeutic goals, relevant clinical chemistry and haematology results, and, where appropriate, therapeutic drug monitoring. Counselling to each patient, was provided focusing on drugs which had been started or discontinued, high-risk drugs, use of devices. In addition, the technician highlighted medication list queries to the pharmacist	At discharge, the pharmacist provided counselling to the patient and generated a medicines record sheet with dosage instructions and other relevant information as steroid cards or anticoagulation booklets. It also included information of changes to the patient's medications and laboratory findings. It was faxed to the GP and CP	–

Table 2 (continued)

Study characteristics			Description of the intervention			
Author, year	Country	Desing	At admission	During hospitalization	At discharge	In the community setting
Spinewine 2007 [37]	Belgium	RCT	A comprehensive pharmaceutical care in addition to GEM care. On admission: review of medication history and appropriateness of treatment. A pharmaceutical care plan was prepared	The pharmacist participated in medical and multidisciplinary rounds and discussed any opportunity for treatment optimization with the prescriber, who could accept or reject the pharmacist intervention	At discharge, the pharmacist provided written and oral information on treatment changes to the patient or caregiver, as well as written information to the general practitioner	During the follow-up, two pharmacists performed phone calls only asking for some outcome-related data
Stowasser 2002 [36]	Australia	RCT	MLS. On admission: review of the medication history and current medication. In addition, the medication history was confirmed by the CP and GPs	During admission, supply of and counselling on medication were undertaken by the ward pharmacist	On discharge: preparation of the MLS discharge summary (including list of medications, reason for medication changes, medication-related problems, and actions required by the GP within 2 weeks postdischarge) posted and faxed to the CP and GP within 24 h postdischarge	–
Van del Linden 2017 [35]	Belgium	Quasi-RCT	A trained clinical pharmacist performed medication reconciliation with a subsequent two-stage medication review. In a first step of medication review, a pharmacist aplied the Rationalization of home medication by an Adjusted STOPP in older Patients list to the drugs reconciled on admission	A second step comprised an additional comprehensive medication review by the clinical pharmacist, focusing on polypharmacy, quality of prescribing, and clinical outcomes in geriatric inpatients	In the intervention group, accepted recommendations by the doctor were included in the discharge letter to the general practitioner	–

Table 2 (continued)

Study characteristics			Description of the comparison	Length of follow up (after discharge)	Outcomes assessed		Summary of the results
Author, year	Country	Desing			During hospitalization	During follow up	
Bladh 2011 [44], Wallerstedt 2012 [45]	Sweden	RCT	Patients in the control group received normal care (the regular discharge summary was sent to the patient's GP)	6 months	1. LOS (days)	2. HRQL and EQ-5D score 3. Costs during 6 months after discharge from the hospital in all patients (all direct costs, reimbursed drugs and cost for the intervention) 4. The incremental cost-effectiveness ratio per quality-adjusted life year (QALY) in patients with EQ-5 utility scores	1. There was no difference in LOS 2. Per-protocol analysis revealed significantly better HRQL in the intervention group at six-month follow-up as measured by global health (mean: 3.14 (SD: 0.87) vs. 2.77 (SD 0.94), $p = 0.020$), but not as measured by summarised EQ-5D score 3. No significant difference in costs between the randomisation groups was found; the mean total costs per individual, intervention costs included, were €10.748 (SD 13.799) (intervention patients) and €10.344 (SD 14.728) (control patients) ($p = 0.79$) 4. For patients in the cost-effectiveness analysis, the corresponding costs were €10.912 (SD 13.999) and €9.290 (SD 12.885). Intervention patients gained an additional 0.0051 QALYs (unadjusted) and 0.0035 QALYs (adjusted for baseline EQ-5D utility score)

Table 2 (continued)

Study characteristics			Description of the comparison	Length of follow up (after discharge)	Outcomes assessed		Summary of the results
Author, year	Country	Desing			During hospitalization	During follow up	
Cossette 2017 [42]	Canada	RCT	No computerized alert system was reviewed by the pharmacist during the patients' hospital stay. The clinical relevance of the computerized alerts system in the control group was only determined by the pharmacists after the control patient was discharged from the hospital	1 month	1. LOS (days). 2. Mortality	3. Number of ED visits. 4. Number of hospital readmissions	The differences in LOS, in-hospital death, emergency room visits and readmissions were not statistically different
Dedhia 2009 [41]	EEUU	Pre-post design	Preintervention: None of the components at admission, during stay or at discharge had been implemented in any systematic way before the intervention	1 month	1. LOS (days)	2. ED visits 3. Hospital readmissions	1. There was no difference in LOS between groups 2. Return to the emergency department within 3 days of discharge was lower in the intervention period (10% vs. 3%, OR = 0.25, 95% CI = 0.10–0.62). At 30 days, there was a lower rate of readmission (22% vs. 14%, OR = 0.55, 95% CI = 0.32–0.94) in the intervention group 3. At 30 days, fewer visits to the emergency department in the intervention group (21% vs. 14%, OR = 0.58, 95% CI = 0.34–0.99)

Table 2 (continued)

Study characteristics			Description of the comparison	Length of follow up (after discharge)	Outcomes assessed		Summary of the results
Author, year	Country	Desing			During hospitalization	During follow up	
Graabaek 2019 [40]	Denmark	RCT	All patients received usual care including medication history, medication reconciliation, and medication review by a physician without any structured instrument as part of the normal procedure. The Control group was not offered any pharmacist-led intervention	3 months	1. LOS (days) 2. Mortality	3. Number of patients with a medication-related readmission within 30 days from discharge 4. Mortality within 30 days after discharge or 180 days after discharge 5. Patients with readmissions within 30 days after discharge 6. Number of vitis to the ED, the hospital or a GP within 180 dias after discharge	No differences were observed between study arms in any of the considered outcomes
Lenssen 2018 [33]	Germany	RCT	Usual care	1 year	-	1. Drug related readmissions (DRR) over 1 year (rehospitalization of a discharged patient due to an adverse drug reaction in any hospital) 2. Preventable DRR	1. Drug-related readmissions (DRR): regarding the 1 year follow, the median time until onset od DRR was longer compared to the control group, but not significant ($p=0.068$). The risk for DRR was higher under standard care compared to comprehensive pharmaceutical care (HR: 3.276, $p=0.0864$) 2. Preventable DRR: four preventable DRR ocurred in the control group and one in the intervention group
Lisby 2010 [39]	Denmark	RCT	Usual routine for medication prescription by a junior physician on admission and within 24 h an assessment by a senior physician, specialized in internal medicine	3 months	1. LOS (hours)	2. Time to first admission 3. Number of readmissions 4. Number of emergency department visits 5. Visits to outpatient care 6. Visits to general practitioners 7. Deaths 8. Quality-of-life (EQ-5D)	No differences were observed between study arms in any of the considered outcomes

Table 2 (continued)

Study characteristics			Description of the comparison	Length of follow up (after discharge)	Outcomes assessed		Summary of the results
Author, year	Country	Desing			During hospitalization	During follow up	
Makowsky 2009 [38]	Canada	Quasy RCT	Usual care: clinical pharmacy services provided by either ward-based or dispensary-based staff pharmacists, identifying drug-related problems in the dispensary; not performing medication reconciliation neither attending patient care rounds. Only occasionally, pharmacist participated in patient education activities (usually at the request of a physician)	6 months	1. LOS (days)	2. Number of all-cause hospital readmission (hospital admission or ED visit) at 90 and 180 days postdischarge	1. The median LOS was increased in the team care group as compared with the usual care group in the adjusted analysis (OR: 1.16; 95% CI 1.01–1.34) 2. Patients assigned to team care experienced a lower rate of 3-month hospital readmission in the adjusted analysis (OR 0.63; 95% CI 0.42–0.94). No differences were observed between groups in 6-month readmissions
O´Sullivan 2016 [30]; Gallagher 2016 [34]	Ireland	RCT	Usual pharmaceutical care, which consisted of ad hoc pharmaceutical review from a hospital pharmacist employed at the study site. This involved hospital pharmacists performing an unstructured pharmaceutical review with communication of any suggested interventions to the attending medical team via handwritten notes attached to the patient's hospital Kardex. In some cases, medicines reconciliation was also performed. The hospital pharmacists performed pharmaceutical reviews within 24–72 h of admission	No follow up after discharge	1.LOS (days) 2. Hospital mortality rate 3. Healthcare cost. Both outcomes assesed from randomizarion to discharge or 10-day follow-up, whichever came first	–	1, 2. LOS and hospital mortality were not significantly different between groups 3. The intervention was associated with a decrease of 807 € (95% CI 3.443–1.829 $p=0.548$) in mean healthcare cost, the intervention group is likely to be considered cost effective

Table 2 (continued)

Study characteristics			Description of the comparison	Length of follow up (after discharge)	Outcomes assessed		Summary of the results
Author, year	Country	Desing			During hospitalization	During follow up	
Sánchez-Ulayar 2012 [43]	Spain	RCT	Usual care: discharge without medication planning neither medication counselling	2 months	–	1. Number of patients with any hospital readmission at 1 and 2 months postdischarge	1. Patients from the intervention group had less readmissions than patients in the control group at 1 and 2 months after discharge: 3 vs. 10 ($p<0.05$) and 3 vs. 13 ($p<0.01$), respectively
Scullin 2007 [32]	UK	RCT	Normal care group: Traditional clinical pharmacy services	12 months	1. LOS (days) and cost savings per patient	2. Number of unplanned readmission 3. Time to be readmitted (days) 4. LOS during hospital readmissions (days) 5. Mortality	1. LOS was reduced 2 days ($p=0.003$; t-test loge). This is a potential cost saving of £424 per patient (considering the cost of a medical bed is £212 per day) 2. The 40.8% and 49.3% of patients from the intervention group and normal care group were readmitted, respectively ($p=0.027$) 3. Patients from the intervention group took significantly longer time (262 days) to be readmitted to hospital than the normal care patients (242 days; $p=0.0356$) 4–5. There were no difference in reduction of LOS due to readmissions neither in mortality after 12 monts of follow up
Spinewine 2007 [37]	Belgium	RCT	Usual care: GEM care by a multidisciplinary team (geriatricians, nurses, physiotherapists, social workers, psychologists, and occupational therapists) providing medical care, rehabilitation, and discharge planning	12 months	–	1. Readmission rates 2. Rate of deaths 3. Rate of emergency visits	No differences were observed between study arms in any of the considered outcomes

Table 2 (continued)

Study characteristics			Description of the comparison	Length of follow up (after discharge)	Outcomes assessed		Summary of the results
Author, year	Country	Desing			During hospitalization	During follow up	
Stowasser 2002 [36]	Australia	RCT	Routine clinical pharmacist service. On admission: review of the medication history and current medication. During admission, supply of and counselling on medication were undertaken by the ward pharmacist (blinded to the patient's randomisation status). On discharge: preparation of the standard discharge summary (including list of discharge medication) and posted to the GP within 2–7 days postdischarge	1 month	1. LOS (days)	2. Number of readmissions 3. Number of unplanned readmissions 4. Number of total contacts per patient (planned and unplanned) with healthcare professionals (medical specialist, GP, community and hospital pharmacist, domiciliary nurse, outpatient clinics) 5. Changes in SF-36 score 6. Mortality	1–3, 6. There was no significant effect on length of stay, number of readmissions, or mortality 4. MSL group had significantly fewer total healthcare professional visits than control group: 7.54 (SD 7.4) vs. 9.94 (SD 10) ($p<0.05$) 5. MLS subjects improved significantly (SF-36 Score) only for Body Pain and Physical Functioning
Van del Linden 2017 [35]	Belgium	Quasi-RCT	Usual care: medication reconciliation at admission	3 months	1. Mortality	2. Mortality 3. Patients with one or more readmissions 4. Electively readmitted patients 5. Patients with one or more ED visits 6. Patients with one or more ED visits without readmission 7. QOL improvement (EQ-5D-3L)	1–5. There were no significant differences between groups 6. Only there was a reducciont in ED visits without hospitalization in the intervention group 1/87 (1.1) vs. control group 7/79 (8.9) ($p=0.021$) 7. Participant in the intervention group increased QOL with an average of 0.358 (SE 0.016), vs. 0.294 (SE 0.018) in the control group. This is a difference of 0.064 points (SE 0.024; $p=0.008$) in favor of the intervention group

CCI Charlson Comorbidity Index, *CI* Confidence Interval, *CIRS* Cumulaive illness rating scale, *CP* community pharmacist, *COPD* Chronic Obstructive Pulmonary Disease, *EQ-5D* EuroQol survey, *GEM* Geriatric Evaluation and Management, *GP* General Practitioner, *ICD* International Classification of Diseases, *IQR* interquartile range, *LOS* Length of hospital stay, *MLS* Medication Liason Service, *OTC* over the counter, *QOL* Quality of Life, *RCT* Randomized Controlled Trial, *SD* Standard deviation, *SF-36* 36-item Short Form Health Survey

Table 3 Description of the studies which intervention was delivered during the transtition of care

Study characteristics			Baseline population characteristics			
Author, year	Country	Desing	*N*, (% female)	Age (years), mean (SD)	Patient's conditions	Number of drugs, mean (SD)
Al-Rashed 2002 [53]	UK	RCT	Intervention group: 43 (37.2) Control group: 40 (50)	Intervention group: 80.2 (5.7) Control group: 81.1 (5.8)	No data	Intervention group: 7.1 (1.8) Control group: 7.1 (2.3)
Basger 2015 [49]	Australia	RCT	Intervention group: 114 (83) Control group: 102 (72)	Intervention group: 82.7 (7.3) Control group: 80.3 (6.7)	Number of documented conditions, mean (SD): Intervention group 8.8 (3.4) Control group (8.1 (3.0)	Intervention group: 11.7 (3.4) Control group: 12.4 (3.3)
Cohen 2002 [27]	EEUU	RCT (two-by-two factorial design)	All participants: 1388 (2). Four study groups: GEMU–UCOP 348 (–) UCIP–GEMC 346 (–) UCIP–UCOP 348 (–) GEMU–GEMC 346 (–)	All participants: 74,2 (–)	CCI, mean (SD): All participants: 2.6 (1.9)	No data
Crotty 2004 [50]	Australia	RCT	Intervention group: 56 (58.9) Control group: 54 (63)	Age, mean (95% CI): Intervention group: 82 (80.2–83.7) Control group: 83.4 (81.7–85.1)	CCI, mean (95% CI): Intervention group 3.9 (3.2–4.7) Control group 4.9 (4.1–5.8)	Number of drugs, mean (95% CI): Intervention group: 6.6 (5.6–7.6) Control group: 7.7 (6.5–8.8)
Fretwell 1990 [51]	EEUU	RCT	Intervention group: 221 (71.5) Control group: 215 (71.6)	Intervention group: 83.5 (5.3) Control group: 83.0 (5.7)	No data	No data
Gillespie 2009 [48]	Sweeden	RCT	Intervention group: 105 (57.7) Control group: 186 (59.7)	Intervention group: 86.4 (4.2) Control group: 87.1 (4.1)	Most common patient's conditions: hypertension, heart failure, coronary artery disease, arrhythmia, diabetes mellitus, pulmonary disease, past cerebral vascular lesion, malignant disease, and dementia	Intervention group: 8.7 (4.5); Control group: 7.3 (4.4)
Koeheler 2009 [28]	USA	RCT	Intervention group: 20 (85) Control group: 21 (62)	Intervention group: 77.2 (5.3) Control group: 79.8 (5.6)	CCI, mean (SD): Intervention group 3.7 (1.1) Control group 3.2 (1.3) Most common diagnoses: congestive heart failure, syncope, COPD, cellulitis and gastrointestinal disorder	Intervention group: 12 (5) Control group: 11 (3)
Lipton 1994 [29]	USA	RCT	Intervention group: 350 (–) Control group: 356 (–)	Intervention group: 74.6 (–) Control group: 74.4 (–)	Number of diagnoses at hospital admission, mean (SD) Intervention group: 4.75 (–) Control group: 4.72 (–)	No data. Inclusion criteria: at least 3 or more drugs taken for chronic conditions

Table 3 (continued)

Study characteristics			Baseline population characteristics			
Author, year	Country	Desing	*N*, (% female)	Age (years), mean (SD)	Patient's conditions	Number of drugs, mean (SD)
Low 2017 [46]	Singapore	RCT	Intervention group: 420 (50) Control group: 420 (53)	Intervention group: 70.3 (13.7) Control group: 70.5 (13.5)	CCI, mean (SD): Intervention group 3.3 (1.7) Control group 3.3 (1.8) Most common diagnoses: heart failure, diabetes mellitus, stroke, and chronic obstructive pulmonary disease	No data
Nazareth 2001 [47]	UK	RCT	Intervention group: 181 (62) Control group: 181 (66)	Intervention group: 84 (5.2) Control group: 84 (5.4)	Number of chronic conditions, mean (SD): 3 (−)	All participants: 6 (2)
Ravn-Nielsen 2018 [10]	Denmark	RCT	Basic intervention group: 493 (50.2) Extended intervention group: 476 (55.0) Control group: 498 (55.8)	Age, median (IQR): Basic intervention group: 72 (63–80) Extended intervention group: 71 (63–79) Control group: median 73 (65–80)	CCI, median (IQR): Basic intervention group: 2 (1–4); Extended intervention group: 2 (1–4); Control group: 2 (1–4)	Number of drugs, median (IQR): Basic intervention group: 10 (7–13) Extended intervention group: 10 (7–12) Control group: 9 (7–12)
Rottman-Sagebiel 2018 [31]	USA	Quasi-RCT	Intervention group: 388 (14) Control group: 1.189 (26)	Intervention group: 74.9 (7.6) Control group: 75.2 (8.4)	CCI, mean (SD): Intervention group 4.4 (2.8) Control group 4.3 (2.9)	No data. Inclusion criteria: prescribed ≥ 12 outpatient medications
Torisson 2013 [52]	Sweden	Quasi-RCT	Intervention group: 99 (64) Control group: 101 (66)	Intervention group: 84.6 (7.3) Control group: 82.3 (8.7)	CCI, mean (SD): Intervention group 2.4 (1.4) Control group 2.1 (1.6)	The average number of prescribed daily medications were between 7 and 8 drugs

Table 3 (continued)

Study characteristics			Description of the intervention			
Author, year	Country	Desing	At admission	During hospitalization	At discharge	In the community setting
Al-Rashed 2002 [53]	UK	RCT	–	–	Pre-discharge counselling by the clinical pharmacist. During this counselling session patients received information about their medicines and they were given a medicine reminder card. The number of doses together with the times of day (tick in box for breakfast, lunchtime, teatime and bedtime as appropriate) were also included. All patients were given 14 days of medication on discharge and informed to show their GP and community pharmacist the MIDS and medicine card during their first visit post discharge	Each patient's GP was sent a copy on discharge. Predischarge a pharmacist counselled study patients about their medicines and compliance. A research pharmacist visited patients in their home approximately 2–3 weeks and at 3 months post-discharge to determine their drug knowledge, compliance, home medicine stocks and any healthcare related events

Table 3 (continued)

Study characteristics			Description of the intervention			
Author, year	Country	Desing	At admission	During hospitalization	At discharge	In the community setting
Basger 2015 [49]	Australia	RCT	–	–	The SF-36 health survey was administered to each patient the day before discharge. Intervention patients then received medication counselling and an in-depth interview from the clinical pharmacist to facilitate completion of a medication review, sent to their GP within 3 days of discharge. Medication review consisted of medication reconciliation, identification of (potential) causes of DRPs and recommendations for their resolution and prevention. Opportunities for self-management were discussed with the patient. Intervention patients received a copy of the review	Three months after discharge, both patient groups were contacted for follow-up in their home. This time periodwas chosen to enable implementation of changes made by their GP as a result of pharmacist recommendations. All current medications were recorded and the criteria-set applied to each patient for a second time. The SF-36 health survey was re-administered. The clinical pharmacist assessed the following: changes in medication between discharge and follow-up of control and intervention patients; implementation of medication review recommendations made to GPs by comparison between follow-up and discharge medication history; and contribution of the criteria-set to the total number of (potential) causes of DRPs, identified during medication review
Cohen 2002 [27]	EEUU	RCT (two-by-two factorial design)	–	Inpatient care in a geriatric evaluation and management unit. A plan of care was developed, and the team (a geriatrician, a social worker, and a nurse) met at least twice a week to discuss the plan. Preventive and management services (dietetics, physical and occupational therapy, and clinical pharmacy) were coordinated to address the problems identified, with a general emphasis on maintaining the patient's functional status	–	Outpatient care in a geriatric evaluation and management clinic. After the initial site visits, the process of care was evaluated with the use of annual questionnaires, as well as a specific checklist for each part of the intervention, in order to ensure compliance with the study protocol

Table 3 (continued)

Study characteristics			Description of the intervention			
Author, year	Country	Desing	At admission	During hospitalization	At discharge	In the community setting
Crotty 2004 [50]	Australia	RCT	–	–	On the patient's discharge from the hospital to the long term care facility, both the CPC and the CP were faxed a medication transfer summary compiled by the transition pharmacist and signed by the hospital medical officer. This communication suplemented the usual hospital discharge summary and included specific information on changes to medications that had been made in the hospital and aspects of medication management that required monitoring	After transfering the patient to the long term care facility, the transition pharmacist coordinated an evidence based medication review that was to be performed by the CP contracted to the facility within 10 to 14 days of the transfer. The transition pharmacist also coordinated a case conference involving him or her self, the CPC, the CP, and a registered muse at the facility within 14 to 28 days of the transfer. At this case conference, the transition pharmacist provided infomation concerning medication use and appropriateness. Eight weeks after discharge, independent pharmacists who were blinded to study group allocation assessed patients' medication charts and case notes
Fretwell 1990 [51]	EEUU	RCT	–	–	Before patient discharge, an updated care plan documenting the problems that remained unresolved at discharge was prepared by the hospital pharmacist	Follow-up telephone calls were made weekly for 1 month, and once 2 months after hospital discharge. After each contact, a written summary of the patient's follow-up status was sent to the attending physician, other team members, and staff nurses. Urgent problems were communicated directly to the patient 's physician by telephone

Table 3 (continued)

Study characteristics			Description of the intervention			
Author, year	Country	Desing	At admission	During hospitalization	At discharge	In the community setting
Gillespie 2009 [48]	Sweeden	RCT	A comprehensive list of current medications was compiled from several information sources, including an interview with the patient on admission to complement that obtained in the ED, ensuring that the medication list received by the ward was correct	A comprehensive review of patient's drug therapy addressing issues of indication, effectiveness, safety, and adherence. Relevant drug related problems were discussed to the health care team during ward rounds and reccomendations were made. Pharmacist provided counseling to individual patients regarding newly commenced or discontinued drugs when appropriate	Information about discharge medications (eg, rationale for changes, therapeutic goals, and monitoring needs for newly commenced drugs) was communicated to the PCP by the pharmacist	The pharmacist contacted by telephone 2 months after discharge to ensure adequate home management of medications, counselling about drug adherence and answering drug-related questions
Koeheler 2009 [28]	USA	RCT	Medication reconciliation by a clinical pharmacist	Daily medication review and education regarding any new agents started during the hospitalization and gave medication change recommendations if they were indicated by a clinical pharmacist. In addition, the SCC instructed patients daily on specific health conditions	Medication reconciliation and counselling on discharge medication regimen by a clinical pharmacist. The SCC provide an extra discharge teaching focusing on optimizing home self-care and contingency plans if problems arose	Follow-up call at 5–7 days postdischarge: the clinical pharmacist asked to the patient about any symptoms or medication side effects. At the follow-up call, the SCC reinforces patient education on managing their conditions
Lipton 1994 [29]	USA	RCT	–	–	At discharge, clinical pharmacists provided booklets to patients in which to record medication information. After reviewing the records, the pharmacists conducted a face-to-face consultation with the patient before hospital discharge to discuss the purpose and use of their medications and potential drug-related problems	Postdischarge consultations by telephone, in the pharmacists' hospital office or in the patient's home. When significant prescribing problems were detected, consultations were provided with the patient's physician

Table 3 (continued)

Study characteristics			Description of the intervention			
Author, year	Country	Desing	At admission	During hospitalization	At discharge	In the community setting
Low 2017 [46]	Singapore	RCT	–	Inpatient care team (an attending family physician, medical officer, a nurse case manager, and a part-time pharmacist): provided general medical care, identified and addressed patient risk factors for readmission and focused on intensive discharge planning. The pharmacists assist in medication reconciliation and advise on potentially harmful drug adverse events and interactions. The nurse case managers provided patient education for chronic diseases	An individualized care plan complete with written discharge instructions, patients' appointments, medication changes and the contact information of the outpatient nurse case manager is provided by the impatien team care	Outpatient virtual ward team (an attending family physician and two nurse case managers). The outpatient nurse case manager follows up with a telephone call within 72 h of discharge to assess the patient's condition and ensure adherence to the prescribed care plans and successful activation of community services. A home assessment is performed by the outpatient nurse case manager within one week of discharge. During the home assessment, the nurse case manager assessed the patient's medical condition and health literacy, competency of the care-giver, availability of nursing and home care equipment, adequacy of social support, safety of the home environment and adherence to medication. A multidisciplinary team meeting was conducted in the morning of every working day. Patients with urgent problems are referred to the early review clinic. Patients who are doing well are reviewed less frequently at the team meetings. Patients were discharged at the end of the intervention period of three months to a primary care provider in the community

Table 3 (continued)

Study characteristics			Description of the intervention			
Author, year	Country	Desing	At admission	During hospitalization	At discharge	In the community setting
Nazareth 2001 [47]	UK	RCT	–	–	The hospital pharmacist intervention included: at discharge, an assessment of the patients' medication, assessment of patients' ability to manage their medication, information on discharge medication given to the patient, the patient's community pharmacist and general practitioner and any other professionals or cares involved	Between 7–14 days postdischarge, the CP intervention included: check for discrepancies between the drugs that the patient was taking and those prescribed at discharge, assessment of the patient's understanding of and adherence to the medication prescribed, counselling patients or cares and liasing with general practitioners. Further visits were arranged if needed. A revised care plan was issued if a patient was re-admitted to hospital during the 6-month study period
Ravn-Nielsen 2018 [10]	Denmark	RCT	In both basic and extended intervention groups, a structured, patient centered medication review was conducted by a clinical pharmacist. Medication were assessed by the indication for treatment, drug dose, adverse drug events, therapeutic duplication, dosage time and interval, drug formulation and strength, interactions, contraindications, precautions, and specific patient characteristics. If needed, the treatment was proposed to be discontinued to the patient's responsible phsycian	–	In the extended intervention group, the clinical pharmacist performed a medication reconciliation and counselling through a patient interview with a motivational approach, given information of medication changes, drug administration, adverse drug events, and adherence to prevent drug related problems	In the extended intervention group, the clinical pharmacist mailed or faxed any drug related problem not resolved during hospitalization to the PCP, in addition to a summary note containing changes in drug therapy. The PCP, caregiver, and primary care pharmacist were contacted by telephone 3 workdays after discharge when any change in medication was made during the index hospitalization. The primary pharmacy was called to delete old prescriptions or address problems concerning dose-dispensed medication. Two follow-up telephone calls at 1 week and 6 months after discharge were performed. The interviews were based on principles of motivational interview. If required, additional follow ups were arranged

Table 3 (continued)

Study characteristics			Description of the intervention			
Author, year	Country	Desing	At admission	During hospitalization	At discharge	In the community setting
Rottman-Sagebiel 2018 [31]	USA	Quasi-RCT	–	Meeting between a clinical pharmacist and the patient; reconciliation; medication education. The clinical pharmacist worked with a internist/geriatrician	The clinical pharmacist performed medication reconciliation and provided medication education regarding administration and usage of the patient's medications. The clinical pharmacist communicated recommendations regarding appropriateness of therapy (including any potential barriers to medication adherence) to the medical team	Telephone visit 2–3 days to discharge performed by the same clinical pharmacist: reconciliation; identify and rectify errors; drug education and assist in facilitating appropriate follow-up by the patient's primary care provider, if required. Follow-up questions were asked as needed to clarify and identify potential medication problems
Torisson 2013 [52]	Sweden	Quasi-RCT	A clinical pharmacist performed a medication review, using a method called the Lund Integrated Medicines Management Model: 1. Reconciliation (the patient's most accurate list of medications was established from structured interviews, records from primary care, community care, and the National Pharmacy Register)	2. Medication review during hospitalization 3. Developing drug-related recommendations to be considered by the ward physician	4. Drug information to discharge. The ordinary discharge summary sent to GP was accompanied by a separate document containing cognitive test results and a recommendation on how to proceed with investigations. The GPs had the opportunity to discuss the results and recommendations with the study physician	Telephone follow-up at home within a week after discharge (by a nurse). If a problem had occurred, the communication nurse could provide counseling, book an appointment at the community health center, or initiate a home visit from social services, usually on the same day

Table 3 (continued)

Study characteristics			Description of the comparison	Length of intervention and follow-up	Outcomes assessed	Summary of the results
Author, year	Country	Desing			During intervention period and follow up	
Al-Rashed 2002 [53]	UK	RCT	Normal discharge was provided to control patients	Intervention and follow up: 2–3 weeks and 3 months postdischarge	1. Unplanned visits to GP and hospital readmissions at 2–3 weeks and at 3 months	1. Unplanned visits to the GP and readmissions to hospital between the intervention group were 19 and 5, respectively, which were both significantly less ($p < 0.05$) than 27 and 13 in the control group at 2–3 weeks. For the study group the 24 unplanned GP visits and three re-admissions were significantly ($p < 0.05$) less than the respective 32 and 15 in the control group at 3 months postdischarge
Basger 2015 [49]	Australia	RCT	Patients receiving usual care	Intervention: 1 day before hospital discharge to 3 months postdischarge Follow-up: 3 months postdischarge	1. Changes in SF-36 health-related quality of life health (HRQoL) at discharge and at 3 months	1. There was no significant difference in SF-36 domain scores at discharge between patient groups prior to the intervention. However, while the difference between groups was positive at follow-up (except for mental health), the only domain that reached statistical significance between control and intervention patients was that for vitality ($p = 0.04$)

Table 3 (continued)

Study characteristics			Description of the comparison	Length of intervention and follow-up	Outcomes assessed	Summary of the results
Author, year	Country	Desing			During intervention period and follow up	
Cohen 2002 [27]	EEUU	RCT (two-by-two factorial design)	Inpatient usual care: appropriate hospital services except for those provided by the team on the geriatric evaluation and management unit Outpatient usual care: at least one follow-up appointment in an appropriate clinic	Intervention: From admission to 12 months after randomization	1. In-hospital LOS (days) 2. Health-relate quality of life (SF-36) at discharge and at 12 months 3. Costs of health care services 4. Utilization of health services in hospital 5. Clinic visits after discharge 6. Mortality	1. The LOS was greater for the group of patients assigned to the geriatric evaluation and management unit than for those assigned to usual inpatient care (35.3 vs. 28.3; $p < 0.001$) 2. At discharge patients assigned to the inpatient geriatrics units had significantly improvement in the scores for four of the eight SF-36 items. At 1 year had better scores on SF-36 mental health 3. The total costs at 1 year were similar 4. The mean numbers of medical and surgical consultations were higher for patients assigned to the geriatric evaluation and management unit than for those assigned to usual inpatient care (medical consultations, 2.8 vs. 1.3; surgical consultations, 2.1 vs. 1.2; $p < 0.001$) 5. There were no significant differences in the number of clinics visits between the groups 6. Neither the inpatient nor the outpatient intervention had a significant effect on mortality
Crotty 2004 [50]	Australia	RCT	The usual hospital discharge process received by the control group included a standard hospital discharge summary	Intervention: from hospital discharge to 2 months after discharge	1. LOS (at discharge) 2. Unplanned visits to the emergency department 3. Hospital readmissions at 2 months	1–3. There were no significant differences between the groups

Table 3 (continued)

Study characteristics			Description of the comparison	Length of intervention and follow-up	Outcomes assessed	Summary of the results
Author, year	Country	Desing			During intervention period and follow up	
Fretwell 1990 [51]	EEUU	RCT	Usual care	Intervention: From discharge to 2 months after discharge Follow-up: 6 months postdischarge	1. LOS and mortality (at discharge) 2. Hospital charges 3. Mortality 4. Any change in physical or mental function All measured at 6 weeks, 3 months and 6 months	1–4. There were no significant differences between the groups
Gillespie 2009 [48]	Sweeden	RCT	Standard (non pharmacist) care	Intervention: from admission to discharge and a phone call 2 months after discharge. Follow-up: 1 year after discharge	1. Number of drug-related readmissions 2. Number of visits to the emergency department 3. Number of hospital readmissions 4. Number of patients readmitted 5. Mortality 6. Cost of hospital care All measured at 12 months postdischarge	1. Drug-related readmissions were reduced by 80%: OR 0.20 (95% CI 0.10–0.41) 2. There was a reduction of 47% in visits to the ED: OR 0.53 (95% CI 0.37–0.75) 3–5. No differences were found for the other outcomes 6. The direct costs savings per patient of ED visits and readmissions were $100 and $300, respectively. After inclusion of the intervention costs ($170 per patient), the total cost per patient in the intervention group was $230 lower than in the control group
Koeheler 2009 [28]	USA	RCT	Usual care bundle: Medication reconciliation and medication education is generally performed by floor nursing staff. Pharmacist staff perform medication review for new orders as needed and provide medication change recommendations. Hospital care coordinator and social worker perform a need assessment on admission and a discharge planning	Intervention: From randomization to the phone call at 5–7 days after discharge Follow-up: 2 months postdischarge	1. LOS (days) during hospital stay 2. Number of unplanned readmission and ED visits at 1 month postdischarge 3. Number of unplanned readmission and ED visits at 2 months postdischarge	1. There was not possible to compare the effects of the intervention on LOS between groups. 2. Intervention group readmission and ED visits rates were reduced at 1 month compared to the control group. 3. There were no differences on readmissions and ED visits at 2 months

Table 3 (continued)

Study characteristics			Description of the comparison	Length of intervention and follow-up	Outcomes assessed	Summary of the results
Author, year	Country	Desing			During intervention period and follow up	
Lipton 1994 [29]	USA	RCT	Clinical pharmacists provided patients with booklets in which to record medication information at discharge. Postdischarge consultations	Intervention: at discharge and at 1 week, 2–4 weeks, 2 months, and 3 months postdischarge Follow-up: 6 months after discharge (including intervention at 3 months postdischarge)	1. Readmission rates and LOS (days) at 3 months 2. Inpatient readmission charges (costs) at 3 months 3. Readmission rates and LOS (days) at 6 months 4. Inpatient readmission charges (costs) at 6 months	1 and 3–4. No differences were observed between the study arms in any of the considered outcomes. 2. Only there were statistically significant reductions in the readmitted experimental vs. control patients in hospital charges for the first readmission, for all readmissions during the first month and the first three months after study enrollment
Low 2017 [46]	Singapore	RCT	Standard hospital care. On discharge, patients may be referred to primary care provider, specialists in the outpatient clinic and ambulatory community services as necessary. Patients receive an standardized patient copy of the hospital discharge summary listing their medical diagnoses and medications	Intervention: From randomization to 6 months postdischarge	1. Number of hospital unplanned readmissions 2. Number of ED visits 3. LOS (days) 4. Outpatient specialist clinic visits (excluding the early review clinic). All measured at 1, 3 and 6 months postdischarge 5. The probability without readmission or death up to 6 months 6. Index admission and postdischarge mortality rate at 3 months 7. Costs	1–2. Patients in the intervention group had a significant reduction in the number of 30-day readmissions: IRR 0.67 (95% CI 0.52–0.86, $p=0.001$), and in the number of 30-day emergency department attendances: IRR 0.60 (95% CI, 0.46 to 0.79, $p<0.001$) compared to those receiving standard hospital care. The effectiveness was sustained at 90 and 180 days 3. The intervention group utilized 1,164 fewer hospital bed days at 90-day post discharge (reduction in costs). LOS: reduction statiscally significant at 30, 90 and 180 days 4. Outpatient specialist clinic visits: no difference was found 5. Probability without readmission or death up to 180 days: HR 0.72; 95% CI, 0.61 to 0.86; ($p<0.001$) 6. Index mortality and at 90 days postdischarge: No difference was found 7. Total costs (including Readmission bed days, Emergency Department visits, and Outpatient specialist clinic visits and Incremental cost of intervention over standard care) of intervention and hospital services utilization in the intervention group (S$ 6,546,008) was lower than the costs of hospital services utilization in the control group (S$ 6,944,651). The difference between study groups in total cost savings (from reduced hospital utilization and additional costs of outpatient specialist clinic visits) was S$1,240,524 (SD S$2,954) saved per patient who received the intervention

Table 3 (continued)

Study characteristics			Description of the comparison	Length of intervention and follow-up	Outcomes assessed	Summary of the results
Author, year	Country	Desing			During intervention period and follow up	
Nazareth 2001 [47]	UK	RCT	Usual care: discharge letter to the GP including the diagnoses, investigations and current medications. Hospital pharmacist did not review the patient's medication at discharge neither the CP did the follow-up	Intervention: at discharge and between 7–14 days postdischarge Follow-up: 6 months	1. Hospital readmissions 2. Mortality 3. Visits at outpatient clinic or general practice at 3 and 6 months 4. Days in hospital as percentage of follow-up days 5. General well being questionnaire score (the British adaptation)	1–5. No differences were found between groups for these outcomes
Ravn-Nielsen 2018 [10]	Denmark	RCT	Standard care	Intervention: at admission, at discharge, and at 1 week and six months after inlcusion Follow-up: 6 months post-discharge	1. Number of readmissions at 1 and 3 months 2. Composite end point: number of readmissions and ED visits at 6 months 3. Number of drug-related readmissions at 1 and 6 months 4. Mortality	2. The extended intervention had a significant effect on the numbers of patients who were readmitted and ED visits within 1 or 6 months. 3–4. There was a non-significant reduction in drug-related readmissions within 1 and 6 months neither in number of deaths
Rottman-Sagebiel 2018 [31]	USA	Quasi-RCT	Usual care	Intervention: from admission to a 2–3 days after discharge Follow up: 1 month postdischarge	1. 30-day readmission	1. The 30-day readmission was 15.6% for the Intev group and 21.9% for the control group. After adjustment, the OR for readmission was 0.54 (95% CI, 0.32–0.90, $p=0.02$)
Torisson 2013 [52]	Sweden	Quasi-RCT	In the control group, all baseline measurements were performed but none of the interventions. Regular staff were informed of cognitive test results verbally and through the electronic medical record. Apart from this, the control group received standard care	Intervention: from admission to one week after discharge Follow up: 12 months after hospitalization	1. In-hospital LOS 2. Readmissions and ED visits at 12 months after discharge 3. LOS during follow up	1. No significant differences were found 2. The control group had more readmissions and ED visits compared with the intervention group ($p=0.02$) 3. The number of hospital nights (1,228) was higher in the control than in the intervention group (492) ($p=0.009$)

CCI Charlson Comorbidity Index, *CI* Confidence Interval, *CP* community pharmacist, *DRP* Drug-related problem, *ED* emergency department, *EQ-5D* EuroQol survey, *GEMC* geriatric evaluation and management clinic, *GEMU* geriatric evaluation and management unit, *GP* General practitioner, *IRR* incidence rate ratios, *LOS* Length of hospital stay, *PCP* Primary care physician, *OR* Odds Ratio, *RCT* Randomized Controlled Trial, *SCC* Study Care Coordinator, *SD* Standard deviation, *SF-36* 36-item Short Form Health Survey, *UCIP* inpatient usual care, *UCOP* outpatient usual care

2. In-hospital mortality:

Five studies assessed in-hospital mortality finding no differences during the index hospitalization [30, 34, 35, 40, 42].

II. Residual effects of clinical pharmacist interventions after discharge (without any intervention by the clinical pharmacist after discharge) 1. Hospital readmission:

Ten out of 13 studies assessed hospital readmission rates during the follow-up period (after discharge). Three studies found a significant reduction in the number of hospital readmissions in the intervention group: two at one month [41, 43], one at 2 months [43] and one at 12 months follow-up [32]. Five studies did not find any difference in the number of readmissions: three at one month [36, 40, 42], three at 3 months [35, 39, 40], and one at 12 months' follow-up [37]. Finally, two studies counted the number of patients with a medication-related readmission, after 30 days from discharge, no differences were found regarding the hospital readmission rate between groups [40], and after 1 year from discharge, the median time until a first readmission was no longer in the intervention group, but the risk for drug-related readmission was higher under standard care [33].

2. Visits to the emergency department (ED):

Six out of 13 studies calculated the number of ED visits after discharge. One study found a reduction in the number of ED visits in the intervention group [41] at one-month post-discharge, whereas two studies did not find any significant differences [39, 42]. Three studies did not observe a reduction in the number of ED visits in the intervention group at 3 months post-discharge [35, 39, 40]. Only one study considered the number of patients visiting the ED but who did not require further hospitalization and found a significant reduction [35]. One study did not find a reduction of ED visits in the intervention group at 12 months of post-discharge [37].

3. All cause hospital readmissions:

Only one study considered all cause hospital readmissions including both hospital readmissions and ED visits during the post-discharge period [38]. The authors observed a statistically significant reduction in number of readmissions at 3 months for the intervention group. However, there were no differences between groups at 6 months of post-discharge.

4. Visits to a healthcare provider:

Three studies assessed changes in the number of visits to a healthcare provider after hospital discharge. Only one study found a significant reduction in the number of visits to the GP and to outpatient clinics in the intervention group at one-month post-discharge [36]. The other two studies did not find any differences in the number of visits to the GP at one-month post-discharge [40], or at 3 months of post-discharge [39, 40].

5. Quality of life:

Four studies assessed post-discharge QoL. One study found a significant QoL improvement (measured with the EQ-5D questionnaire) [54] at three months post-discharge [35] but another study did not [39]. One study found a significantly better health-related QoL in the intervention group at 6 months' follow-up measured by self-rated global health (answering the question, "In your opinion, how is your state of health?"), but not when measured by the EQ-5D [44, 45]. One study found a significant improvement in SF-36 score [55] in the intervention group as compared to the control group at one-month post-discharge, but only with regard to body pain and physical function [36].

6. Mortality:

Six out of 13 studies assessed mortality after discharge. No study found a significant reduction in mortality after the index intervention at any of the time points assessed: 1 month [36, 40], 3 months [35, 39, 40] and 12 months [32, 37].

B. Outcomes resulting from the interventions delivered during transition of care

1. Length of hospital stay: Eight out of 13 studies assessed LOS [27–29, 46, 47, 50–52]. In four, the authors did not find statistically significant differences in LOS during the index hospitalization [28, 50–52]. Regarding the LOS of the readmissions after discharge, two studies found a statistically significant reduction in LOS at 30, 90 and 180 days [46] and at 12 months [52]. However, two studies did not find a reduction in LOS of readmissions after discharge at 3 months [29] and 6 months [29, 47] for the patients received pharmacist care.

In a third study, the number of days in hospital was higher for the group of patients assigned to the geriatric assessment team (including a geriatrician, a social worker, a nurse) than for those assigned to usual inpatient care during their hospital stay [27].

2. Hospital readmission: Ten studies assessed all-cause hospital readmissions [10, 28, 29, 31, 46–49, 52, 53] and two studies assessed drug-related readmissions (DRR) [10, 48]. Interventions delivered in the community setting lasted from one day to 6 months after discharge and the follow-up times lasted up to 12 months after discharge. Three studies showed a statistically significant reduction in hospital readmission rates during the intervention period of 2–3 weeks [53], 1 month [10, 46], 3 months [10, 46] and 6 months [46] after discharge. Two studies did not find a reduction in hospital readmission rates during the intervention period of 2 months [50] and 3 months [29] after discharge. Four studies showed that the reduction in hospital readmissions persisted at one month [28, 31, 46, 52], at 3 months [53],

and at 12 months [52] from discharge, spite of the end of the intervention in the community setting. By other hand, four studies did not find a persistent reduction on hospital readmissions at 2 months [28], 6 months [29, 47] and 12 months [48] after discharge.

Similarly, one study found a reduction in DRR at 12 months from the beginning of the intervention [48], while other study did not find DRR neither at one nor 6 months after discharge [10].

3. Visits to the emergency department: Five studies measured the impact of pharmacist interventions on the number of visits to the ED. In two of them authors found a statistically significant reduction in the number of visits to the ED for the duration of intervention [10, 46], and at 6 months [10]. When the impact of the intervention was measured during the follow-up period the results were variable [28, 46, 48, 50, 52]. Only two studies found the effect of the intervention to persist in the longer term: one of them at 6 months [46] and the other at 12 months [48].

4. Visits to the GP or to a specialist outpatient clinic: Of the four studies that looked into this outcome, [27, 46, 47, 53] only one showed a statistically significant reduction in unplanned visits to the GP for the intervention group [53].

5. Mortality: There were no studies showing significant differences in the number of deaths during follow-up. This outcome was included in six studies [10, 27, 46–48, 51].

6. Quality of life: QoL was measured in three studies [27, 47, 49]. One study used the British adaptation of the general well-being questionnaire designed to assess the impact of pharmaceutical treatment on QoL in older patients, but no differences were found between the groups at 3 and 6 months [47]. Two studies used the SF-36 questionnaire to measure health-related QoL [27, 49]. In one, there was no significant difference between patient groups in the SF-36 subscales at discharge, except for the vitality subscale [49]. In the other study, patients assigned to inpatient geriatric units showed significantly greater improvement in the scores for four of the eight SF-36 subscales at discharge. The scores on the SF-36′s mental health subscale also improved after 1 year [27].

C. Economic outcomes

Eight of the 26 studies reported economic outcomes. Healthcare costs were measured in different ways across the studies, including the cost of health services, hospitalization days or visits to outpatient clinics [27, 29, 32, 34, 45, 46, 48, 51]. In three studies, the cost of pharmacist interventions was also calculated to obtain the final balance in cost savings [45, 46, 48]. Only one study performed a cost-effectiveness analysis in a subgroup of patients where the EQ-5D utility scores had been calculated. The authors calculated a cost of €10,912 for the intervention group and of €9,290 for the control group. Intervention patients gained 0.0035 QALYs, which amounts to an incremental cost-effectiveness ratio per QALY of more than €460,000 in that group [45]. Five studies found a reduction in healthcare cost measured as cost-effectiveness of pharmacist intervention [34], cost savings per patient [32], inpatient readmission charges [29], total costs of intervention and hospital services utilization [46] and cost of hospital care [48]. In three studies, the authors did not find differences between study groups on hospital charges [51], costs of health care services [27], direct costs, reimbursed drugs and cost for the intervention [45].

Discussion

This scoping review intends to show the state of the art of hospital pharmacist interventions during and after hospitalization in different health outcomes in polymedicated older patients. There is enough evidence of the beneficial role that hospital pharmacists can play in reducing medication-related problems [37, 48], improving drug adherence [38, 53, 56] and the patients' understanding of their medication as well as other aspects related to pharmacotherapy and drug safety. However, evidence is not so strong when it comes to other health outcomes or the use of healthcare resources. Intermediate results (improved drug regimens) are only relevant if they have an impact on more relevant health outcomes, such as mortality, QoL, or healthcare utilization.

Our findings were heterogeneous both in the characteristics of the intervention and on the impact on outcomes. Some studies explored the impact of simple interventions with few professionals involved [25, 45, 57, 58], while other planned complex interventions where the pharmacist was part of a geriatric interdisciplinary team [25, 28]. In other studies, pharmacists only acted on demand [56, 59]. Globally, interventions developed by a pharmacist within a multidisciplinary team seem to provide greater benefits in terms of clinical outcomes and economic results than those carried out by individual pharmacists. In these multidisciplinary teams, with the collaboration of the hospital pharmacist, significant reductions were achieved in visits to the ED, visits to the primary care physician, hospital readmission rates [28, 32, 38, 41, 53] and length of hospital stay [32, 46]. Making pharmacists part of the geriatric team seems to be the most productive way to impact on outcomes, although studies comparing teams with a and without a pharmacist in intermediate and final outcomes are lacking.

Given the heterogeneity of the findings, it is not easy to establish whether there is any single type of pharmacist

intervention that is associated with a higher rate of success in terms of specific health outcomes. Medication reconciliation is the most frequent intervention at admission and at discharge; review of drugs is most common during admission; and advice and education is typical in the discharge phase. In addition, in transition of care studies, telephone reinforcement is usually carried out after discharge and the CP or GP are usually contacted to report changes in treatment. In our review, data did not allow to compare different interventions or the intensity of combined interventions. Other reviews that focussed on single component interventions, treatment review [60], medication counselling prior to discharge [61] or deprescription [62] did not find positive results. It has to be remembered that the success of pharmacist-led interventions depends on cooperation with prescribing physicians. In general, evidence shows that highly-complex multifaceted pharmacist-led interventions delivered from admission through to discharge obtain the best results in reducing hospital visits [28, 48, 53], LOS [44, 49] and DDR [48]. Very few studies have measured the degree of acceptance of such interventions; this may be an interesting aspect to be looked into in future analysis [63]. Further research is also required to provide an answer to whether multifaceted interventions are more effective than single-faceted interventions. This would contribute to a clearer definition of pharmacist interventions.

We found no evidence that any pharmacist intervention reduces mortality at any time point. These results were also found in other studies [8, 9, 25, 60]. This may be related to the high complexity of the patients studied, often with limited life expectancies, where the aim of care is usually to preserve or improve QoL or maintain function. In such patients, mortality may not be an outcome to use to test the effect of interventions, as agreed by others [64].

QoL is considered a relevant patient-reported outcome for many health care interventions. It may also be an indirect measure of unreported side effects of drug therapy, so it is worth exploring in interventions assessing drug use. We found some evidence that pharmacist interventions could improve QoL after hospital discharge. However, the number of studies is small and only two QoL instruments (EQ-5D and SF-36) were used. Specific instruments for drug-related QoL that include a range of medicine-related issues with potential impact on patients' day-to-day lives [65] may need to be developed in order to better understand impact of pharmacy (and other) interventions on QoL.

Health care use is a relevant outcome both for patients and care systems. In practise, it is usually measured with hospital length of stay, readmissions, visits to the emergency department or visits to other health care providers. We found variable results of pharmacist interventions on such outcomes. The outcome with more positive studies were readmission rates, especially in studies where pharmaceutical care was continued after hospital discharge in cooperation with other professionals (GP, nurse, community pharmacist). This suggests that, to obtain satisfactory results, interventions must be maintained over time and should not be limited to the hospitalization period. Several previous reviews showed that the long-term effects of interventions are limited, and very few studies have found that pharmacist interventions are able to reduce the number of ED visits [23, 60, 66]. When considering the effect of interventions on hospital length of stay, only three studies out of 18 included in this review showed a significant shortening. These unsatisfactory results could be due to the fact that such outcome is not ideal to determine the effectiveness of pharmaceutical interventions. Using medication-related hospital readmissions may be more relevant [8, 60], but such readmissions are ill-defined and studies using this outcome are mostly negative. The field is probably ready for an international multicentre trial to define if a standardised pharmaceutical intervention continued after discharge does reduce hospital use.

Another interesting aspect is to determine if the results obtained by interventions are maintained over the time. In the different studies found the effect of the intervention lasts between 1 and 12 months. If the intervention is carried out continuously, it does seem reasonable to measure its effect in terms of health outcomes over time. However, for interventions carried out only in the hospital setting it seem logical to expect that their effects will disappear soon. In addition, it must be remembered that health and function of older patients with complex conditions may change rapidly during follow-up.

Finally, economic outcomes were evaluated in eight studies, five of them showing a reduction in healthcare costs. Cost analysis tends to be complex and, although the results are generally in favour of pharmacist interventions, the relevance of such cost reductions is unclear. The reasons for this are twofold. First, the evaluated outcomes in different studies were heterogeneous and cannot be pooled. Second, none of the included studies had an economic variable as their main outcome, which means that they were not specifically designed to evaluate such outcomes. Post-discharge readmissions of older adults due to drug effects is estimated to cost the UK National Health Service £396 million annually, of which £243 million are potentially preventable [67]. Some authors suggest that, although pharmacist interventions can be cost-effective, the matter requires further evaluation as an inappropriate estimation of input costs usually leads to an overestimation of cost savings, rendering it impossible to make an informed decision regarding the true value of pharmacist interventions in this regard [6, 9, 68, 69].

Our scoping review has some strengths: it was conducted following a systematic search process, which can be replicated; used several key databases supplemented by hand search of the literature; only included RCTs and controlled

prospective studies; used pairs along all the review process; and piloted data extraction. It has also some limitations. The risk of bias of the included studies was not assessed, as a critical appraisal of the risk of bias is not considered mandatory in scoping reviews [26, 70]. Also, it includes a wide range of interventions, which are hard to aggregate.

It can be concluded that there is no hard evidence demonstrating the effectiveness of hospital pharmacist interventions in older polymedicated patients. Some ways forward to improve research in this area seem to arise from the review. First, mortality does not show as a relevant outcome of pharmacist interventions in older complex patients. Other health care outcomes, such as hospital readmissions, seem to be more relevant and amenable to change. Frailty, functional and mental outcomes, relevant in most areas of geriatric research, merit exploration as outcome measures for intervention studies on drugs. Moreover, patient-reported outcome, including QoL, need to be considered using well-validated methods. Interventions that include pharmacists in multidisciplinary geriatric teams seem to be more promising that isolated pharmacist interventions. Also, interventions prolonged after hospital discharge seem to be more appropriate that interventions delivered only during hospital admission. Standardization of interventions in future research would allow for comparison between studies performed in different countries and settings. Better-designed studies, with clearly-defined interventions, outcomes and follow-up times should be conducted in the future to provide further insight into the effect of pharmacist interventions.

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Declarations

Conflict of interest We declare that we have no competing interest.

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