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The effect of early in-hospital medication review on health outcomes: a systematic review

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AIMS

Adverse drug events are an important cause of emergency department visits, unplanned admissions and prolonged hospital stays. Our objective was to synthesize the evidence on the effect of early in-hospital pharmacist-led medication review on patient-oriented outcomes based on observed data.

METHODS

We systematically searched eight bibliographic reference databases, electronic grey literature, medical journals, conference proceedings, trial registries and bibliographies of relevant papers. We included studies that employed random or quasi-random methods to allocate subjects to pharmacist-led medication review or control. Medication review had to include, at a minimum, obtaining a best possible medication history and reviewing medications for appropriateness and adverse drug events. The intervention had to be initiated within 24 h of emergency department presentation or 72 h of admission. We extracted data in duplicate and pooled outcomes from clinically homogeneous studies of the same design using random effects meta-analysis.

RESULTS

We retrieved 4549 titles of which seven were included, reporting the outcomes of 3292 patients. We pooled data from studies of the same design, and found no significant differences in length of hospital admission (weighted mean difference [WMD] −0.04 days, 95% confidence interval [CI] −1.63, 1.55), mortality (odds ratio [OR] 1.09, 95% CI 0.69, 1.72), readmissions (OR 1.15, 95% CI 0.81, 1.63) or emergency department revisits at 3 months (OR 0.60, 95% CI 0.27, 1.32). Two large studies reporting reductions in readmissions could not be included in our pooled estimates due to differences in study design.

CONCLUSIONS

Wide confidence intervals suggest that additional research is likely to influence the effect size estimates and clarify the effect of medication review on patient-oriented outcomes. This systematic review failed to identify an effect of pharmacist-led medication review on health outcomes.

Introduction

Prescription and over the counter medications account for 19% of healthcare spending in countries belonging to the Organization for Economic Co-operation and Development (OECD), with the United States reporting the highest per capita spending at US$ 1010 per year [1]. In addition to the direct costs of medications, indirect costs occur when patients suffer from adverse drug events, their unintended and harmful effects. Adverse drug events are a leading cause of unplanned admissions and prolonged hospital stays, and increase healthcare costs [2–7]. Identifying effective drug use interventions to optimize the treatment benefit of medications while minimizing their potential for harm is a public health priority [8, 9].

Medication review, a structured and critical examination of an individual patient's medications by a qualified healthcare provider aims to accomplish exactly these goals [10]. Medication review is performed by a qualified healthcare provider, usually a pharmacist, and includes establishing an individualized treatment plan, obtaining an accurate medication history, identifying and discontinuing any inappropriate or harmful drugs, and ensuring that indicated medications are taken correctly to optimize their effectiveness [10]. An evolving body of evidence has linked a variety of medication review interventions to improved process outcomes, including reductions in the number of medications and reduced medication errors [10–12]. The value of medication reviews is generally accepted among clinicians, despite lack of robust research evidence demonstrating clinical or cost effectiveness compared with usual care which remains a barrier to more widespread implementation of this costly intervention. The only quantitative systematic review on the effect of in-hospital medication review on patient-oriented outcomes excluded non-randomized studies, did not evaluate its effect on the length of admission and extrapolated 12 month outcomes for all but one of the included studies [13]. Our objective was therefore to summarize the available evidence on the effect of pharmacist-led medication review initiated early within a patient's hospital course on the length of hospital stay, and on 3 month mortality, hospital readmissions and emergency department revisits based on observed data.

Methods

Study design

This was a systematic review to determine the effect of early in-hospital pharmacist-led medication review on health outcomes. Ethics approval was not required because the study did not involve the use of human subjects. We registered the study protocol with PROSPERO [14].

Data searches and sources

We developed a systematic search strategy with a professional medical librarian (MMDW). The search concepts included ((pharmacists AND medication review) OR pharmaceutical services) AND (emergency department OR acute care OR intensive care). We developed the search in MEDLINE (OvidSP) and included Medical Subject Headings terms for each concept (Appendix 1). We reviewed scope notes for each term for alternate and previous indexing terms and added keywords to increase the sensitivity of our search. We did not use any language or age restrictions. We adapted and applied our MEDLINE search to: Embase, the Cochrane Central Register of Controlled Trials, the Cochrane Database of Systematic Reviews, the Database of Abstracts of Reviews of Effects, International Pharmaceutical Abstracts, the Cumulative Index to Nursing and Allied Health Literature and Web of Science. All searches were from 1990 to March 2013, as medication review is a relatively recent intervention developed as a result of changes in pharmacists' scope of practice [15].

We searched 20 medical journals from 2000 to 2013, and the proceedings of 10 pharmacy conferences between 2008 and 2013 (Appendix 2). We used abstracts to identify manuscripts that were subsequently published, and contacted authors for the protocols and results of unpublished studies. We searched the following trial registries: Biomed, metaRegister of Current Controlled Trials, the NHA National Research Register, Clinical Practice Research Datalink and ClinicalTrials.gov. We completed grey literature searches using Google and relevant keywords from our bibliographic reference database searches. We hand searched the bibliographies of all relevant retrieved articles and contacted content experts for additional studies. During the course of the review, we completed periodic environmental scans of the literature to find newly published studies by searching Google using the key word 'medication review'.

Study selection

We included randomized controlled trials and controlled clinical trials that used quasi-randomized, interrupted time series, and stepped wedge designs to study the effect of medication review in adults (>18 years) who presented to an acute care hospital for an unexpected illness. We excluded studies without comparator groups. We defined medication review as an intervention including (i) a best-possible medication history, and (ii) a review of a patient's medications to optimize medication use and identify and resolve medication-related problems including adverse drug events. The intervention had to target a broad group of patients (targeting patients with more than one diagnosis of interest), and not health professionals (i.e. not academic detailing). While other healthcare providers could obtain the medication

history, pharmacists had to complete the medication review. Medication review had to be initiated within 24 h of emergency department presentation or within 72 h of an unplanned hospital admission. Medication reconciliation interventions were eligible if both of the required components of medication review had been completed. We excluded interventions conducted only over the phone or focusing on information technology. Studies had to report at least one outcome of interest and follow patients for at least 30 days.

Data extraction and quality assessment

Two authors independently reviewed all titles (CMH and SG) using standardized forms. Titles that either or both of the reviewers felt were potentially relevant underwent abstract review. Two authors independently reviewed all abstracts (CMH and EL) using standardized review forms. Abstracts that either or both reviewers felt were potentially relevant underwent full text review. Two pairs of authors independently reviewed all full texts (CMH and MLAS, CMH and JJP) for inclusion/exclusion criteria, and resolved disagreements by reaching consensus through discussion. The reviewers were not blinded to study title, authorship or journal of publication. Two reviewers (RH and MW) independently extracted data from included studies and extracted details on the design, setting, participants, intervention and outcomes of each study. We extracted outcome data according to intention-to-treat analysis. Disagreements were resolved by achieving consensus through discussion. We contacted study authors to clarify study methodology and results, and for patient-level data. Two reviewers (CMH and PB) independently assessed the quality of studies using the Risk of Bias quality assessment tool recommended by Cochrane and resolved disagreements though discussion [16].

Data synthesis and analysis

We decided *a priori* to pool data from studies of the same design, conducted in comparable patient populations, and that reported the same outcomes observed over the same period of follow-up. We analyzed data in an intention-to-treat analysis. Patients who died inhospital were retained for the analysis of mortality even if those patients had been excluded from the analysis of the trial. For continuous outcomes, we pooled results using a random effects model, and reported the weighted mean difference (WMD) with 95% confidence intervals (CIs). For dichotomous outcomes, we pooled results using random effects meta-analysis, and reported odds ratios (OR) with 95% CIs [17]. We used Forest plots, the I^2 statistic and Cochran's Q test to assess studies for heterogeneity [18, 19]. We used StatsDirect 2.8 for all analyses.

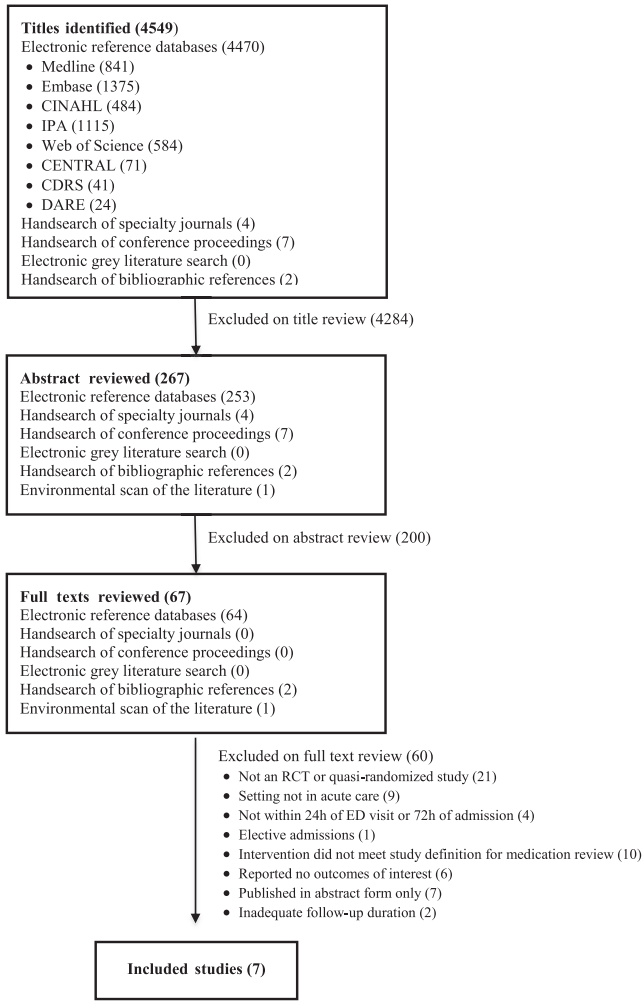

Figure 1
Flow diagram of included studies

Results

Main results

Our search revealed 4549 titles of which 67 proceeded to full text review (Figure 1). Seven studies met inclusion criteria and reported data on 3292 patients [20–26]. Six studies were conducted in Europe [20–23, 25, 26] and one in Canada [24]. Five studies were randomized controlled trials [20, 22, 23, 25, 26]. We re-classified one study as quasi-randomized because the order of patient allocation was predictable [21]. One study was unpublished. However, we obtained the protocol and patient-level data from the study authors [22].

All studies were conducted on hospital wards and none in the emergency department setting. The mean age of participants ranged from 70.1 to 86.6 years and the length of follow-up from 3 to 12 months. The number of pharmacists delivering the medication review interventions ranged from 1 to 10 per study, and most had postgraduate or residency training in pharmacy

Table 1

Risk of bias in included studies for outcomes of the systematic review

Study	Random sequence generation	Allocation concealment	Blinding: Participants	Blinding: Personnel	Blinding: Outcomes	Incomplete outcome assessment	Selective reporting	Other
Randomized controlled trials								
Bladh *et al.* [26]	Unclear	Low	High	High	**Mortality**: Unclear **LOA**: Unclear	**Mortality**: High **LOA**: Low	High	
Gillespie *et al.* [25]	High	Unclear	Unclear	Unclear	**Mortality**: Unclear **Re-admissions**: Low **ED revisits**: Low	**Mortality**: Low **Re-admissions**: Low **ED revisits**: Low	Low	Low
Lisby *et al.* [23]	Unclear	Unclear	Unclear	High	**Mortality**: Unclear **LOA**: Unclear **Re-admissions**: Unclear **ED revisits**: Unclear	**Mortality**: Low **LOA**: Low **Re-admissions**: Low **ED revisits**: Low	Low	
Lisby *et al.* [22]	Unclear	Unclear	Low	High	**Mortality**: Unclear **LOA**: High **Re-admissions**: Unclear **ED revisits**: Unclear	**Mortality**: Low **LOA**: Low **Re-admissions**: Low **ED revisits**: Low	Low	High
Scullin *et al.* [20]	High	Unclear	High	High	**Mortality**: NA **LOA**: High **Re-admissions**: High	**Mortality**: Low **LOA**: Unclear **Re-admissions**: Unclear	Low	NA
Controlled clinical trials								
Makowsky *et al.* [24]	High	Unclear	Low	High	**LOA**: High **Re-admissions**: Unclear **ED revisits**: Unclear	**LOA**: Low **Re-admissions**: Low **ED revisits**: Low	Low	High
Spinewine *et al.* [21]	High	Unclear	Low	High	**Mortality**: Low **Re-admissions**: High **ED re-visits**: High	**Mortality**: High **Re-admissions**: High **ED re-visits**: High	Unclear	NA

CCT, controlled clinical trial; HRQL, health-related quality of life; LOA, length of admission; NA, not applicable; RCT, randomized controlled trial.

or pharmacology. Pharmacists were fully integrated into healthcare teams in five studies [20, 21, 24–26], yet were only able to enact their own recommendations independently in one study [20]. Details of the characteristics of individual studies and the medication review interventions are described in Appendices 3 and 4.

Quality of included studies

Table 1 summarizes the Risk of Bias assessments. All studies were felt to be of unclear or high risk of selection bias, as the methods of random sequence generation were inadequately described [20, 23, 26] or deemed high risk [20, 25]. Allocation concealment for randomized studies was unclear in all but one study, which was considered low risk [26]. Blinding of participants and personnel was not feasible given the nature of the intervention. Thus, blinding of the outcomes assessment was judged highly relevant in this context, yet generally inadequately described, even for outcomes least susceptible to bias (i.e. mortality). In three studies, a high risk of bias was deemed to be present due to the risk of contamination between the intervention and control groups because the patients' physicians were the same in both groups [22, 23, 26]. One study reported on differences in non-primary outcomes without adjusting for multiple comparisons [26] and one study was at high risk of multiple testing bias [22]. Detection bias for the length of admission was at unclear or high risk due to unclear definitions of how the data were measured. Mortality, re-admission and emergency department revisit data were deemed at unclear or low risk of detection bias. All studies were at low risk of attrition bias.

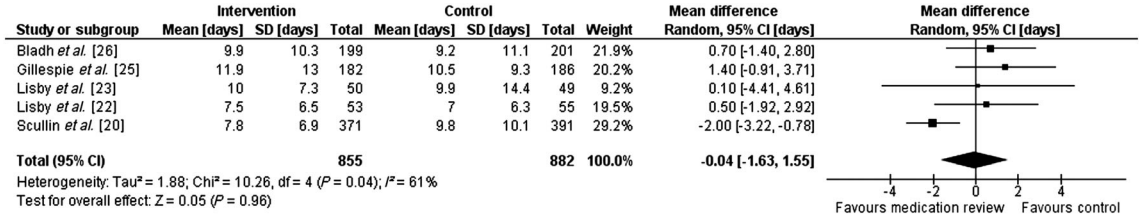

Figure 2

Forest plot of the effect of medication review on the length of admission. Length of stay data from Gillespie exclude patients who died during the index admission.

Length of admission

Six studies reported on the length of hospital admission [20, 22–26]. However, only three reported it as a study outcome [20, 22, 23]. Individual and pooled estimates for length of stay are shown in Figure 2. When pooling data from five studies ($n = 1737$), the average length of stay was reduced by 0.04 days (95% CI −1.63, 1.55, $P = 0.96$) [20, 22, 23, 25, 26]. There was substantial statistical heterogeneity ($I^2 = 61.0\%$, Cochran Q = 10.6, $P = 0.03$).

Mortality

Six studies reported data on mortality [20–23, 25, 26]. However, only four analyzed it as an outcome [21–23, 25] and only three randomized trials reported or released 3 month data for pooling ($n = 607$) [22, 23, 25]. Individual and pooled estimates are shown in Figure 3. The pooled odds ratio for mortality was 1.09 with medication review (95% CI 0.69, 1.72, $P = 0.71$), with low statistical heterogeneity ($I^2 = 0\%$, Cochran Q = 0.6, $P = 0.75$). Two studies not included in the meta-analysis because of missing 3 month data, reported no difference in mortality at 12 months, with Scullin *et al.* ($n = 762$) reporting 18.1% *vs.* 19.8% mortality [20] and Spinewine *et al.* ($n = 186$) reporting 22.1% *vs.* 30.1% in the intervention *vs.* control groups, respectively [21].

Re-admissions

Six studies reported data on re-admissions [20–25], two of which were not randomized [21, 24]. We pooled data from the three randomized studies for which 3 month outcomes were reported or released ($n = 607$) [22, 23, 25]. The pooled odds ratio for re-admissions was 1.15 (95% CI 0.81, 1.63,$P = 0.44$) and is shown in Figure 3. Statistical heterogeneity of the pooled estimate was low ($I^2 = 0\%$,

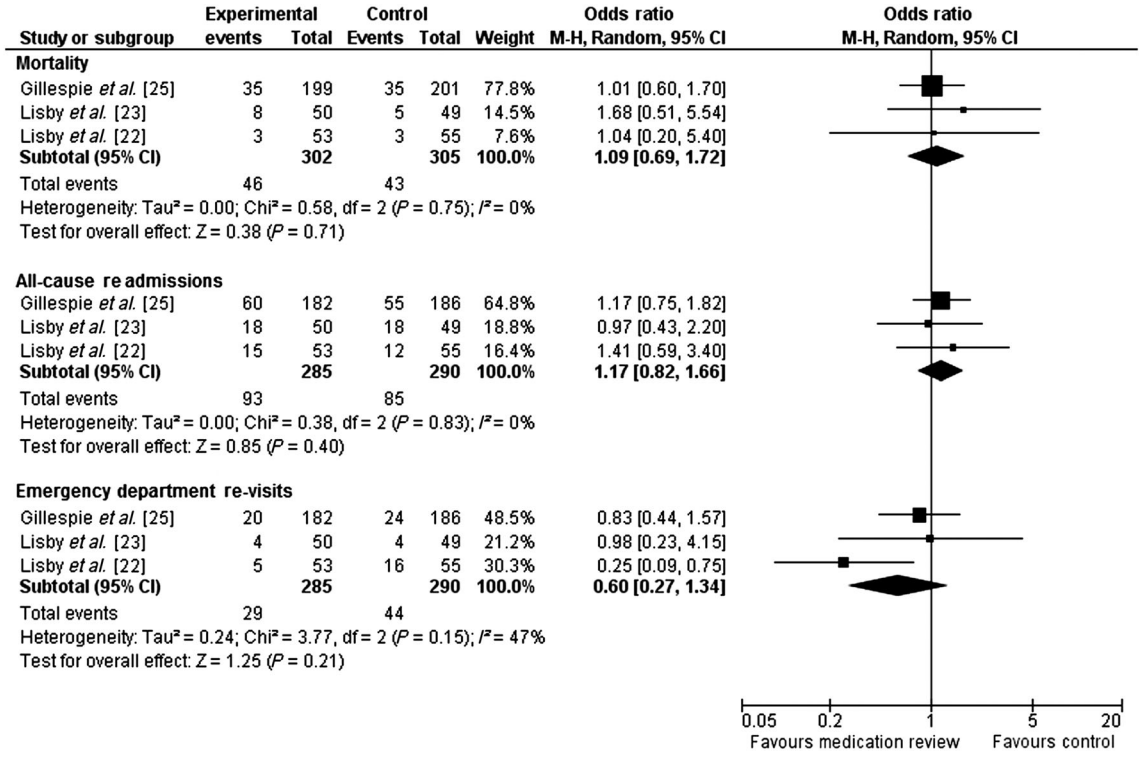

Figure 3

Forest plot of the effect of medication review on 3 month mortality, 3 month all cause re-admissions and 3 month emergency department revisits. Gillespie data obtained from the study authors include all randomized patients.

Cochran Q = 0.38, $P = 0.83$). However, the largest randomized trial ($n = 762$) not included in the meta-analysis because of missing data, reported a significant decrease in re-admissions at 12 months (40.9% *vs*. 49.3%, $P = 0.03$) [20]. One non-randomized study ($n = 452$) reported a reduced odds of being re-admitted at 3 months (OR 0.63, 95% CI 0.42, 0.94) [24], while the other reported no difference [21].

Emergency department revisits

Four studies reported data on emergency department revisits [21–23, 25], of which three were randomized [22, 23, 25]. The individual and pooled estimates from the three randomized studies ($n = 607$) are shown in Figure 3 [22, 23, 25]. The odds ratio for emergency department revisits was 0.60 (95% CI 0.27, 1.32, $P = 0.20$) with medication review [22, 23, 25]. Statistical heterogeneity was substantial, but not statistically significant ($I^2 = 46.3\%$, Cochran Q = 3.73, $P = 0.16$). The fourth (non-randomized) study reported a non-statistically significant reduction in emergency department revisits: 7.9% *vs*. 12.0% ($P = 0.45$) [21].

Discussion

This systematic review on in-hospital pharmacist-led medication review did not identify an effect on the length of hospital admission, mortality or re-admissions. Our pooled estimates on emergency department revisits was consistent with a 40% reduction, but was not statistically significant. However, limitations in the available evidence, including the number, size and quality of available studies precluded us from concluding that no effect exists.

Recent reviews on a variety medication review interventions have reported beneficial effects on outcomes related to process, including medication errors and the numbers of prescribed medications [10–13]. While their effect on process outcomes is promising, medication review interventions incur substantial cost, and warrant rigorous evaluation on objective and sustained patient-oriented outcomes to ensure optimal health value for expenditure. Evidence should guide implementation strategies to ensure that qualified healthcare personnel target patient groups who are most likely to benefit and deliver effective components of the intervention.

Only one previous quantitative systematic review has examined the relationship between in-hospital medication review and patient outcomes [13]. Christensen *et al*. pooled the results of studies involving physician- and pharmacist-led medication review, making it difficult to isolate the effects of interventions by pharmacists [13, 27]. They excluded non-randomized studies, and did not report its effect on the length of hospital admission, a crucial outcome measure of in-hospital medication review in an era marked by hospital crowding and bed shortages. Finally, the authors extrapolated 12 month outcomes from 3 and 6 month outcomes for three of four pooled studies, while little is known about the magnitude, duration and attenuation of any effect that medication review may have on these outcomes. It is possible that the effect of medication review is attenuated over time, and that Christensen *et al*. may have overestimated its effect by combining outcomes from 3, 6 and 12 month observation periods. Thus, our goal was to summarize the available evidence based on observed outcomes and primary data obtained from study authors, while including the results of non-randomized studies and reporting its effect on the length of admission.

Our review demonstrates an inconsistent effect on the length of admission. Four of five studies involving just over one thousand subjects reported no effect [22, 23, 25, 26], while the remaining study of nearly 800 patients found a large decrease in the length of admission [20]. Patients were younger in this study, suggesting that an effect in younger patients may be negated by no effect in the frail elderly whose length of stay may be determined by factors not amenable to medication review such as waiting for long term care placement. In this study, personnel delivering the interventions received dedicated training, delivered the intervention at each stage of the patients' hospital journey, and participated in discharge planning and dispensing. The latter aspects may have influenced the duration of admissions, by facilitating patient discharges. Finally, pharmacists were fully integrated into healthcare teams, and partly enacted their own recommendations [20]. In all other studies pharmacists were unable to enact their recommendations [22, 23, 25, 26], and in three studies, pharmacists had limited contact with patients and physicians, resulting in fewer than 50% of recommendations being adopted [22, 23, 26]. Such differences in the delivery of the interventions could have diluted its effect.

Our review was limited by the quantity and quality of the available evidence. Only few studies have been published on the effect of pharmacist-led medication review in the hospital setting. We do not believe that selection or retrieval bias impacted on our results, as we used an exhaustive search and mitigated publication bias by soliciting data from unpublished trials. The quality of reporting of most studies was modest. Because blinding of patients and personnel to medication review is not feasible, it is essential that future randomized trials incorporate, and clearly disclose, mechanisms to blind the outcome assessments. Finally, our meta-analysis was limited by the variation in the follow-up periods between studies, precluding pooling of data from all randomized trials. Only three studies provided 3 month data on our secondary outcomes [22, 23, 25]. We selected 3 months as being sufficiently long to identify a sustained difference in outcomes, yet short enough to be practical for an interventional trial.

Given the wide confidence intervals of our estimates, the methodological flaws of individual studies, the variation in the medication review interventions studied, and missing data from positive studies that could not contribute to our pooled estimates, we could not reach a conclusive result for or against pharmacist-led medication review. In light of these limitations, it is likely that further high quality randomized trials will contribute to a better understanding of the effects of medication review. Such research is urgently needed to guide the costly and resource intensive implementation of medication review interventions in hospitals, and to inform future hospital accreditation standards to ensure that they are evidence-based.

Competing Interests

All authors have completed the Unified Competing Interest form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare support from a Meetings, Planning and Dissemination Grant from the Canadian Institutes for Health Research for the submitted work [all authors], support from a New Investigator Grant from the Canadian Institutes of Health Research [CMH], no financial relationships with any organization that might have an interest in the submitted work in the previous 3 years and no other relationships or activities that could appear to have influenced the submitted work.

Appendix 1: Medline search strategy

Database: Ovid MEDLINE(R) 1946 to Present with Daily UpdateSearch Strategy:

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1 Pharmacists/ (9895)
2 Pharmacy/ (7782)
3 Pharmacists' Aides/ (491)
4 (pharmacy or pharmacies or pharmacist$).tw. (36734)
5 or/1-4 [28] (43581)

6 drug information services/ or pharmacovigilance/ (3815)
7 Drug Utilization/ or "Drug Utilization Review"/ (18680)
8 drug utili#ation.tw. (1588)
9 brown bag.tw [29].
10 Medication Therapy Management/ (506)
11 ((medicine or medication? or drug? or prescription? or treatment) adj5 (plan$ or manag$ or review?)).mp. (116169)
12 "Referral and Consultation"/ (48373)
13 Medication Reconciliation/ (177)
14 Medical History Taking/ (16187)
15 counseling/ or directive counseling/ (27336)
16 counsel?ing.tw. (51503)
17 (patient? adj3 educat$).tw. (20342)
18 Patient Education as Topic/ (66515)
19 patient compliance/ or medication adherence/ (49036)
20 ((patient? or drug? or medication? or prescription?) adj5 (compl$ or concordance or adherence)).tw. (274674)
21 Pharmaceutical Preparations/ (45327)
22 Drug Prescriptions/ (20940)
23 exp Drug Therapy/ (1016964)
24 Drug Monitoring/ (12853)
25 Drug Combinations/ (56391)
26 Drug Substitution/ (605)
27 drug interactions/ or drug agonism/ or drug partial agonism/ or drug antagonism/ or drug inverse agonism/ or drug synergism/ or food-drug interactions/ or herb-drug interactions/ (134952)
28 drug tolerance/ or tachyphylaxis/ (19568)
29 Substance Withdrawal Syndrome/ (18296)
30 Poisoning/ (19013)
31 drug toxicity/ or drug overdose/ (12743)
32 ((adverse or effect? or manag$ or event? or side effect? or problem? or reaction?) adj5 (drug? or medication? or prescription?)).tw. (142516)
33 Drug Hypersensitivity/ (19944)
34 Medication Errors/ (9624)
35 (Undertreatment adj4 (drug? or Medication?)).tw. (30)
36 "Drug Administration Schedule"/ (80501)
37 ad.fs. [Administration & Dosage] (1040064)
38 "Dose-Response Relationship, Drug"/ (323810)
39 ((drug? or medication? or prescription?) adj3 (selection? or dosage?)).tw. (9371)
40 dosage regimen?.tw. (3845)
41 to.fs. [Toxicity] (305292)
42 de.fs. [Drug Effects] (2281161)
43 ae.fs. [Adverse Effects] (1275664)
44 dt.fs. [Drug Therapy] (1590530)
45 Professional-Patient Relations/ (20269)
46 (patient$ adj20 relation$).tw. (136579)
47 Interprofessional Relations/ (41539)
48 patients/ or inpatients/ (26054)
49 Patient Care Team/ (49487)
50 "Professional Role"/ (7299)
51 treatment outcome/ (559225)
52 td.fs. [trends] (262718)
53 risk management/ (14070)
54 patient care/ (6606)
55 or/6-54 [Medication Review] (6121745)

56 5 and 55 [Pharmacists & Medication Review] (24399)

57 Pharmaceutical Services/ (3940)
58 (pharm$ adj3 (servic$ or care?)).tw. (6500)
59 or/57-58 [29] (9406)

60 emergency medical services/ (29774)
61 emergency service, hospital/ or trauma centers/ (44685)
62 emergency services, psychiatric/ (2037)
63 Admitting Department, Hospital/ (734)
64 exp Hospitals/ (190309)
65 intensive care units/ or burn units/ or coronary care units/ or recovery room/ or respiratory care units/ (38871)
66 hospital?.tw. (634640)
67 (emergency adj3 (department? or room? or centre? or center? or servic$ or ward? or unit?)).tw. (59725)
68 critical care/ or intensive care/ or hospitalization/ or patient admission/ or Patient Readmission/ (123907)
69 or/60-68 [Hospitals] (876066)

70 5 and 55 and 69 [Pharmacists & Medication Review & Hospitals] (6636)
71 59 and 69 [Pharmaceutical Services & Hospitals] (2251)
72 pharmacy service, hospital/ (9529)
73 or/70-72 [Combined Searches] (14418)

74 controlled clinical trial/ or multicenter study/ or randomized controlled trial/ (522825)
75 controlled clinical trials as topic/ or randomized controlled trials as topic/ or multicenter studies as topic/ (97148)
76 74 or 75 (611152)
77 historical article/ or letter/ (1047934)
78 76 not 77 (596906) [MeSH RCT terms]

79 **73** and 78 (626)
80 limit 79 to yr="1990 -Current" (599)
81 limit 80 to English language (557)

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82   80 not 81 [Non-English] (42)

83   randomized controlled trial.pt. (343660)
84   controlled clinical trial.pt. (85469)
85   randomized.ab. (246541)
86   placebo.ab. (136394)
87   Clinical Trials as Topic.sh. (163207)
88   randomly.ab. (176735)
89   trial.ti. (105565)
90   or/83-89 (793530)
91   exp animals/ not humans.sh. (3783744)
92   90 not 91 [Cochrane RCT Filter] (730137)

93   73 and 92 [Combined Searches & Cochrane RCT Filter]
(725)
94   93 not 79 (335)
95   limit 94 to yr="1990 -Current" (270)
96   limit 95 to English language (246)
97   95 not 96 [Non-English] [24]

Note
Combined Searches & MeSH RCTs
81   limit 80 to English language (557)
83   80 not 81 [Non-English] (42)
Combined Searches & Cochrane RCT Filter Minus MeSH RCTs
97   limit 96 to English language (246)
98   96 not 97 [Non-English] [24]
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Appendix 2: List of medical journals and conference proceedings we searched

Medical Journals

Archives of Internal Medicine
Annals of Internal Medicine
The Journal of the American Medical Association
The British Medical Journal
The Canadian Medical Association Journal
BMC Clinical Pharmacology
Pharmacoepidemiology
Drug Safety
The American Journal of Health-System Pharmacy
Annals of Pharmacotherapy
Medical Care
BMC Health Services Research
BMJ Quality and Safety
Basic and Clinical Pharmacology and Toxicology
Clinical Pharmacology and Therapeutics
The British Journal of Clinical Pharmacology
The European Journal of Clinical Pharmacology
The Journal of the American Geriatrics Society
Age and Ageing
The Journal of Population Therapeutics and Clinical Pharmacology

Conference Proceedings

British Pharmaceutical Conference
The UK Clinical Pharmacy Association Conference
Health Services Research and Pharmacy Practice Conference
Pharmacy Care Network Europe Conference
Canadian Association of Health Services and Policy Research Conference
Agency for Healthcare Research and Quality Meeting
International Forum on Safety and Quality in Healthcare
Canadian Society of Hospital Pharmacists Conference
American Society of Health-System Pharmacists Conference
The International Society for Pharmacoepidemiology Conference
European Society of Clinical Pharmacy
European Association of Hospital Pharmacy
Nordic Networking Group of Clinical Pharmacy
International Conference on Emergency Medicine

Appendix 3: Characteristics of included studies

Study	Country	Population	Age (years)	Patients	Outcomes (Primary bold)	Reported results (Intervention *vs.* Control)
Randomized controlled trials						
Bladh *et al*. [26]	Sweden	Internal medicine patients	Median 82	Med review: 199 Control: 201	1. **HRQL**: **Global Health** 2. Mean number PIP/pt 3. Number of drug-related problems	3.0 *vs*. 2.8; $P = 0.08$ 0.34 *vs*. 0.38; $P = 0.67$ Not reported quantitatively
Gillespie *et al*. [25]	Sweden	Geriatric patients on internal medicine wards	Mean 86.6	Med review: 199 Control: 201	1. **ED revisits and re-admissions** 2. Drug-related re-admissions 3. Cost, $ 4.Survival	RR: 0.84 (95% CI 0.72, 0.99) RR: 0.20 (95% CI 0.10, 0.41) −400 (95% CI −4000, 3200) RR: 0.94 (95% CI 0.65, 1.34)
Lisby *et al*. [23]	Denmark	Geriatric patients on internal medicine ward	Mean 78.2*	Med review: 50 Control: 49	1. **Length of admission**, **days** 2. Mean number of re-admissions 3. Mortality 4. Number of contacts with HCP 5. HRQL (EQ-5D)	10 (95% CI 7.9, 12.1) *vs*. 9.9 (95% CI 5.8, 14.2) 0.4 (0.3–0.6) *vs*. 0.5 (0.3–0.7) 16% (95% CI 7, 29) *vs*. 10%(95% CI 3, 22) 8.8 (95% CI 7.2, 10.4) *vs*. 10.5 (95% CI 8.8, 12.3) No statistically significant differences.
Lisby *et al*. [22]	Denmark	Geriatric patients on orthopaedic ward	Mean 80.5*	Med review: 53 Control: 55	1. **Time to physician contact** 2. Length of admission, days 3. Time to re-admission, days 4. Mean number of re-admissions 5. Mean number of ED revisits 6. Mortality	No statistically significant differences. 7.5 (95% CI 5.8, 9.4) *vs*. 7.0 (95% CI 5.3, 8.7) 76 (95% CI 69, 84) *vs*. 78 (95% CI 71, 86) 0.5 (95% CI 0.2, 0.9) *vs*. 0.3 (95% CI 0.1, 0.5) 0.2 (95% CI 0.0, 0.3) *vs*. 0.4 (95% CI 0.2, 0.6), $P = 0.01$ 5.6% (95% CI 1.1, 15.7) *vs*. 5.4 (95% CI 1.1, 15.1)
Scullin *et al*. [20]	Northern Ireland	Patients on medical or surgical wards	Mean 70.1	Med review: 371 Control: 391	1. **Length of admission**, **days** 2. Proportion re-admitted 3. HCP satisfaction 4. Mortality	7.8 (95% CI 7.1, 8.6) *vs*. 9.8 (95% CI 8.8, 10.9) $P = 0.003$ 40.8% *vs*. 49.3%; $P = 0.03$ Not reported quantitatively. 18.1% *vs*. 19.8%, $P = 0.59$
Controlled clinical trials						
Makowsky *et al*. [24]	Canada	Internal medicine and hospitalist patients	Mean 74	Med review: 221† Control: 231	1. **Adherence to indicators** 2. Re-admissions (3 months) 3. Re-admissions (6 months) 4. Length of admission	Difference: 10.4% (95% CI 5.0, 15.7) OR 0.63 (95% CI 0.42, 0.94) OR 0.78 (95% CI 0.53, 1.15) Median ratio: 1.2 (95% CI 1.0, 1.3)
Spinewine *et al*. [21]	Belgium	Geriatric patients	Mean 81.9	Med review: 103 Control: 100	1.**MAI improvement** 2. Mortality 3. Proportion re-admitted 4. Proportion with ED revisits	OR 9.1 (95% CI 4.2, 21.6) 22.5% *vs*. 30.1%, $P = 0.3$ 32.6% *vs*. 33.7%, $P = 1.0$ 7.9% *vs*. 12.0%, $P = 0.45$

CI, confidence intervals; HRQL, health-related quality of life; PIP, potentially inappropriate prescriptions; pt, patient; ED, emergency department; HCP, healthcare provider; RR, risk ratio; OR, odds ratio; MAI, Medication Appropriateness Index. *Mean age in control group. †221 patients in the Makowsky *et al*. study were randomized to the medication review group. However, one patient was excluded post-randomization.

Appendix 4: Characteristics of the medication review interventions in included studies

		BPMH component		Medication review				Communication		
Study	Timing	HCP collecting BPMH	Information sources	Number of pharmacists delivering med review	Education/ experience of involved pharmacist	Ability to enact recommendations independently	Pharmacist integration into team	With patients	With physicians	Additional components
Randomized controlled trials										
Bladh *et al*. [26]	Continuous	NR	Medical record	3	Education NR; None/limited experience in clinical pharmacy)	Unable (41% recommendations adopted)	Partly integrated healthcare team	DC instructions, written medication report	Oral feedback on prescribing, written medica-tion report	HCP education
Gillespie *et al*. [25]	BMPH at admission, med review continuous	Clinical pharma-cist	Not reported	3	Post-graduate training (M.Sc. or courses), ward-based experience	Unable (75% of recommendations adopted)	Participated at rounds as team member	Education, DC counseling, 2-mo post-DC follow-up.	Face-to-face discussion about drug selection, dose, monitoring	HCP education
Lisby *et al*. [23]	Within 24–72 h of admission	Clinical pharma-cist	Pts, GPs, medical and medication records	2	Post-graduate training in clinical pharmacy or pharmacology	Unable (<50% recommendations adopted)	Not integrated	Only for BMPH	Through written notes, letters and fax only	HCP education
Lisby *et al*.[22]	Within 24–72 h of admission	Clinical pharma-cist	Pt, GP, medical and medication records	2	Post-graduate training in clinical pharmacy or pharmacology	Unable (43% recommendations adopted)	Not integrated	Only for BMPH	Through written notes, letters and fax only	HCP education
Scullin *et al*. [20]	Continuous	Clinical pharma-cist	Pt, care provider, GP, med record, community pharmacist	10	Pairs of clinical pharmacists and technicians, training provided	Partly able to enact recommendations	Part of healthcare team	Direct contact with pts for education and DC counseling	Direct, face-to-face contact with team	HCP education, DC instructions, ward stock management
Controlled clinical trials										
Makowsky *et al*. [24]	Continuous	Clinical pharma-cist	Pt	2	Pharmacy residency and prior experience in clinical pharmacy	Unable	Part of health-care team	DC counseling, written summary of changes	Face-to-face contact, bedside rounds partici-pation, GP contact	Med rec, HCP education, contact with community pharmacist
Spinewine *et al*. [21]	Continuous	Clinical pharma-cist	Unclear	1	Post-graduate training	Unable to enact recommendations	Part of health-care team	DC counseling	Direct, face-to-face contact	HCP education, GP contact

NR, not reported; DC, discharge; BPMH, best possible medication history; HCP, healthcare provider; GP, general practitioner; Med rev, medication review; Med rec, medication reconciliation; Pts, patients.

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