Medication Review in Preventing Older Adults' Fall-Related Injury: a Systematic Review & Meta-Analysis

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ABSTRACT

Background

Medication review is essential in managing adverse drug reactions and improving drug safety in older adults. This systematic review evaluated medication review's role as a single intervention or combined with other interventions in preventing fall-related injuries in older adults.

Methods

Electronic databases search was conducted in PubMed, EMBASE, Scopus, and CINAHL. Two reviewers screened titles and abstracts, reviewed full texts, and performed data extraction and risk of bias assessment. Meta-analyses were conducted on studies with similar participants, interventions, outcomes or settings.

Results

Fourteen randomized, controlled studies were included. The pooled results indicated that medication review as a stand-alone intervention was effective in preventing fall-related injuries in community-dwelling older adults (Risk Difference [RD] = -0.06, 95% CI: [-0.11, -0.00], I^2 = 61%, p = .04). Medication review also had a positive impact on decreasing the risk of fall-related fractures (RD = -0.02, 95% CI: [-0.04, -0.01], I^2 = 0%, p = .01).

Discussion

This systematic review and meta-analysis has demonstrated that medication review is effective in preventing fall-related injuries in general, and fractures specifically, in community-dwelling older adults. Future investigations focusing on the process of performing medication review will further inform fall-related injury prevention for older adults.

Key words: medication review, falls, fall-related injuries, prevention, older adults

INTRODUCTION

Significance of injury in later life cannot be underestimated, especially in light of worldwide anticipated increase in number of older adults. Recent forecast indicates that from 2025 to 2050 the global population of older adults will double to 1.6 billion.(1) About 30% of community-dwelling older adults fall each year and among these fallers, 30–50% of falls lead to minor injuries such as bruises or lacerations, while 5–10% of falls result in serious injuries such as wrist or hip fractures, or traumatic brain injury (TBI).(2-7) Fall-related injuries can have adverse consequences such as disability, reduced independence and mobility, a fear of falling, increased likelihood of admission to long-term care facilities, and higher risk of death.(8,9) Fall-related injuries also pose substantial economic burden to an individual and the health-care system.(10,11)

Older adults are the largest consumers of prescription medications worldwide.(12,13) The reduction of hepatic and renal functions, together with increased total body fat, predispose older adults to medication side effects, such as drug–drug and drug–disease interactions, that could lead to the increased risk of falls, injuries, hospital admissions, and diminished quality of life.(14-18) Therefore, medication review is an essential process in preventing unintended fall-related consequences while managing chronic comorbidities in older adults.(19,20,21) Medication review is defined as "a structured evaluation of patient's medicines with the aim of optimizing medicines use and improving health outcomes".(22) A number of randomized trials, systematic reviews, and meta-analyses have examined the effectiveness of medication review in reducing the mortality,(19,23,24-28) hospital admissions and health-care use,(19,23,24-27,29-31) preventing falls,(3,28,31) and improving quality of life(19,27,31) in older adults. However, no study reported positive impact of medication review on enhancing quality of life or reducing mortality of patients. Conflicting results were reported on hospital admissions

reduction and ADR (Adverse Drug Responses) alleviation. In this review "fall-related injury" is a specific outcome, with focus on "injury" not the fall. To date, no systematic review focused specifically on examining the effectiveness of medication review in fall-related injury prevention.

This aim of this study was to summarize the evidence on the effectiveness of medication review, as either a single intervention or a component included in multifactorial interventions, on preventing fall-related injuries in older adults.

METHODS

This systematic review and meta-analysis were registered with PROSPERO on 28th April, 2020 (Registration number: CRD42020161567) and followed Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) recommendation[32] (see Appendix A). Electronic database searches were conducted in PubMed, CINAHL, EMBASE, and Scopus using a combination of keywords, controlled vocabulary terms, and free-text terms with various substitution forms for the three search themes—"medication review", "fall-related injuries" and "older adults". For "fall-related injuries", different types of injuries were included, such as sprains and strains, dislocations, perforations, lacerations, penetrations, and fractures. Injuries of different body parts included head, teeth, neck, shoulder, arm, hand, abdominal, hip, leg, foot, tendon, soft tissue, spinal cord, and vascular system injuries. Hospitalizations and episodes of seeking medical treatment in clinical facilities were also included as possible indications of fall-related injuries. Adults 65 years of age or older were eligible participants, defined by the term "older adults" and its synonyms specifically identified in titles and abstracts. An example of a detailed search strategy for PubMed is provided in Appendix B.

Only patient-randomized controlled trials and cluster-randomized controlled trials of older adults living in the community, long-term care facilities, and hospitals were included in this review. Studies were also taken into consideration if the mean age was greater than 65 years. Medication review had to be a single intervention or one component of a multi-factorial intervention for prevention of fall-related injuries in older adults. The comparison was defined as usual care. Injuries, hospitalizations, and episodes of seeking medical treatment in clinical facilities due to falls were defined as outcomes.

After removal of duplicates, two reviewers (YM and WM) independently screened titles and abstracts using the Covidence online software (https://www.covidence.org) to determine if the studies met the inclusion criteria. Studies without full text and those not published in the English language were excluded. Two reviewers (YM and WM) extracted details of included studies independently, using a specially designed data extraction form. The information extracted from the included studies included the authors, year of publication, study design, participants, settings, definition of fall and fall-related injuries, interventions, definition of medication reviews, comparisons, outcome measures, length of follow-up, sample size calculation, statistical analysis methods, and main results. Four authors were contacted by email to obtain missing information or clarifications.[33-36] Salminen *et al*.[35] provided information on the mean age of the participants, and Sjöberg and Wallerstedt[36] provided information on the calculation of the sample size. No response was received from the other two authors.

All selected studies were assessed by two reviewers (YM and WM) for risk of bias using the Cochrane Collaboration's tool for assessing risk of bias in randomized trials.[37] The two reviewers also applied four additional criteria designed by Cochrane Effective Practice and Organization of Care Group.[38] For each domain, the reviewers independently made judgements on whether the studies were at low, high or unclear risk of bias, and recorded them in individual tables.

Meta-analysis was performed using Review Manager 5.3 (RevMan 5.3; Cochrane Collaboration/Cochrane Training, London UK). The Inverse Variance method and Random-Effect Model were used to calculate Risk Differences (RDs) between the intervention and control group. Random effects approach was chosen because it could statistically adjust to some extent for the heterogeneity among studies.[39] Sources of heterogeneity were explored by a priori subgroup analyses. Subgroup analysis was conducted according to (1) different injury types, (e.g., operationally defined as fall-related injuries, fractures or hospital admissions due to falls), (2) different interventions (e.g., medication review as a single intervention or included in a multifactorial fall prevention program), and (3) participants, (e.g., low risk vs. high risk of falling). Sensitivity analysis was performed for pooled results based on the risk of bias. A funnel plot was created for the estimated RDs of 11 community-based studies.

RESULTS

Characteristics of Included Studies

The search of EMBASE, PubMed, CINAHL, and Scopus produced 479, 437, 146, and 829 citations, respectively. Among 1,891 citations, 134 were duplicates and 1,740 articles were excluded during screening of the titles and abstracts, leaving 17 studies for the full-text screening. Three studies were excluded because they lacked detailed descriptions of the medication review. Finally, 14 studies were included in this systematic review (Figure. 1).

The characteristics of included studies are summarized in Table 1. Seven studies were patient-randomized controlled trials and seven were cluster-randomized controlled trials. Four studies were conducted in the UK,[40-43] three in Sweden,[33,36,44] two in Finland,[35,45] two in Australia,[34,46] and one each in US,[47] the Netherlands,[48] and Singapore.[49] Eleven studies[34-36,40,41,43,45-49] involved community-dwelling older adults, one study hospital patients,[42] and two studies long-term care homes residents.[33,44] Sample size ranged from 186 to 3,384 participants. Eight studies used fall-related injuries as outcomes,[34,40,42,44-47,49] two studies used fractures,[33,36] two studies used fall-related hospitalization,[41,43] and two

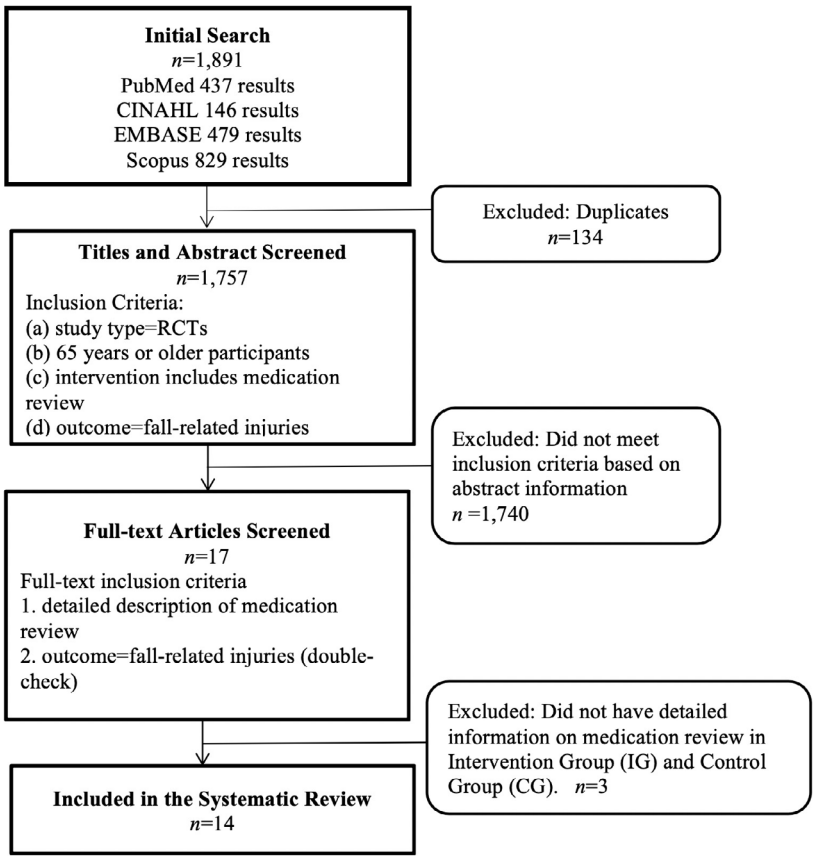

FIGURE 1. Fourteen studies were included in this systematic review

used falls requiring medical treatment, general practitioner-consultations or emergency department (ED) visits.[35,48]

Detailed information on medication review performed in each study is summarized in Table 2. Four studies[34,36,47,48] used medication review as a single intervention, while ten studies assessed the effect of medication review as a part of multifactorial interventions to prevent fall-related injuries.[33,35,40-46,49] In six studies, a physician reviewed the prescription medications used by the patients and made the final decision on whether to change the regimen.[33,34,41,42,44,45] In three studies, geriatricians reviewed the medication regimen and forwarded their suggestions to participants' family physicians for decision-making.[35,36,40] There were two studies in which pharmacists, geriatricians, and physicians collaborated on medication reviews.[46,48] In two studies, nurses or physiotherapists reviewed medication use according to strict pre-planned strategies,[43,49] while Blalock *et al*.[47] used pharmacists to review the patients' medications. In all studies, reduction or cancellation in the medication regimens were decided by physicians. Researchers in 12 studies performed only one systematic medication review. Sjöberg and Wallerstedt[36] performed three medication reviews over a 12-month period, and Palvanen *et al*.[45] conducted a second medication review for patients at sixth months during a 12-months follow-up period. Twelve studies had a 12-month follow-up period, while Salmimen *et al*.[35] followed patients for 36 months, and Matchar *et al*.[49] followed patients for nine months. Six studies focused on participants with high risk of falling or fall-related injuries.[35,40,43,45,47,48] The risk in these studies was determined by previous fall history, taking more than four medications or taking more than one CNS-active drug.

Risk of Bias in Included Studies

Figure 2 and Figure 3 summarized the risk of bias in the 14 included studies. On average, studies had five (range 2-6) out of 11 domains in the low risk of bias. Most studies had low risk of bias on randomization and allocation concealment. Due to the nature of medication review, it was not practical to blind participants or personnel in such studies. The two reviewers judged all the studies to have high risk of performance bias. The authors of seven studies[40-42,45-47,49] were able to blind the outcome assessors, resulting in low detection bias. Six studies were found to have high risk of bias on the reliability of the outcome measurement because the fall-related injuries were self-reported by patients.[34,40,41,43,47,49] Remaining studies had low bias in reliability of outcome measurement, as they confirmed injuries by physicians,[33,44] through medical records,[36,45] hospital's Health and Safety Department,[42] health centre, hospital registers[35] or health service use.[46,48] Only two studies[47,48] had published research protocols and reported all the outcomes stated in the method section, so they were judged to have low risk of reporting bias.

Intervention Effect

Four studies reported positive results,[33,34,45,49] while the remaining 10 studies did not find that medication review as a single intervention or a part of multifactorial interventions was effective in preventing fall-related injuries in older adults.

0Jensen *et al*.[33] detected 145 injuries in 691 falls among 362 older adults who lived in nine residential care facilities in Sweden. The adjusted odds ratio (aOR) for having a femoral fracture was 0.23 (95% CI: 0.06-0.94). Pit *et al*.[34] found that, after adjustment for clustering effect, there was significant reduction in fall-related injuries (aOR=0.56, 95% CI: 0.32-0.96) and other consequences that needed medical attention (aOR=0.46, 95% CI: 0.30-0.70) in the intervention group by the end of 12-month follow-up. Palvanen *et al*.[45] reported that fall-induced injury risk ratio (RR) was significantly deceased (0.74 with 95% CI: 0.61-0.89, p = .002) in the intervention group (i.e., multifactorial fall prevention program), compared to older adults with usual care. The aOR for fall-related medical attention was 0.46 (95% CI: 0.30-0.70) in the intervention group. Matchar *et al*.[49] showed that the relative risk of injurious falls in the intervention group was 0.56 (95% CI: 0.32-0.98, p = .041). They also completed a sub-group analysis on patients with 0–1 critical comorbidity vs. patients with two or more comorbidities and concluded that the intervention was more effective in patients without major comorbidities.

Meta-Analyses

Pooled results from 11 studies conducted with community-dwelling participants produced 714 fall-related injuries in the intervention group and 913 in the control group.[34-36,40-42,45-49] The meta-analysis showed that the risk difference of -0.07 (95% CI: -0.11 to -0.02, p = .007, heterogeneity: χ^2 = 47.30, df = 10 (p < .00001); I^2 = 79%) was significantly different in favour of the intervention group (see Figure 4).

Results of five studies in which fall-related fractures were outcomes[33,36,41,43,45] were pooled together, and the heterogeneity was low χ^2 = 2.30, df = 4, p = .68; I^2 = 0%). The pooled results favored the intervention group slightly with the RD=-0.02 (95% CI: -0.04 to -0.01, p = .01; Figure 5).

Results of four studies using medication review as a single intervention[34,36,47,48] were pooled together and the heterogeneity was low (χ^2 = 5.13, df = 3, p = .16, I^2 = 41%). They suggested that, compared with usual care, medication review alone can lower the risk of fall-related injuries in community-dwelling older adults (RD = -0.07, 95% CI: -0.11 to -0.02, p = .008; Figure 6).

The pooled results of two studies which used hospital admission due to falls as an outcome[41,43] indicated low heterogeneity (Figure 7), but were inconclusive to show if the intervention group had lower risk of fall-related admissions, compared to the control group (RD = -0.03, 95% CI: -0.09 to 0.02, p = .23).

Sensitivity analysis was performed for three studies[45,46,49] with low risks of bias which focused on fall-related injuries in community-dwelling adults. When pooled, there was high heterogeneity (Figure 8), but the intervention group had a significantly lowered risk of fall-related injuries, compared with the control group, with RD = -0.16 (95% CI: -0.23 to -0.08, p < .0001).

TABLE 1.
Summary of the characteristics of included studies

Author (Year)	*Country*	*Settings*	*No. of Pts (IG/CG)*	*Calculated SS (IG/CG)*	*Mean age ±SD (IG/CG)*	*Fall-related Outcome*
Jensen[33] (2002)	Sweden	LTC	181/181	N/A	82.2±7.5/83.9±5.8	Femoral fracture
Jensen[44] (2003)	Sweden	LTC	181/181	N/A	82.2±7.5/83.9±5.8	Fall-related injuries
Healey[42] (2004)	UK	Hospital	1,525/1,859	1,500/1,500	81.4/81.2	Fall Injury
Davison[41] (2005)	UK	Community	159/154	176/176	77.0±7.0/77.0±7.0	Hospital admission
Pit[34] (2007)	Australia	Community	452/397	398/398	N/A	Fall injury
Salminen[35] (2009)	Finland	Community	293/298	229/229	73.4±6.0/73.5±6.3	Falls requiring treatment
Spice[43] (2009)	UK	Community	141/162	172/172	81.0±6.6/83.0±6.6	Hospital admission
Conroy[40] (2010)	UK	Community	183/181	200/200	78.4±5.6/79.1±5.7	Injurious falls
Blalock[47] (2010)	USA	Community	93/93	95/95	75.5±7.0/74.1±6.8	Injurious falls
Sjöberg[36] (2013)	Sweden	Community	100/100	100/100	84.0±6.9/85.0±7.3	Fractures
Palvanen[45] (2014)	Finland	Community	661/653	1,600/1,600	77.5±5.6/77.7±6.7	Fall-induced injuries
Boyé[48] (2016)	Netherland	Community	319/293	310/310	76.5±7.2/76.4±7.4	Falls requiring GP or ED visits
Mikolaizak[46] (2017)	Australia	Community	111/110	117/117	83.9±6.9/82.8±7.5	Injurious falls
Matchar[49] (2017)	Singapore	Community	177/177	165/165	78.2±6.9/77.4±7.2	Injurious Falls

No. = number; Pts = participants; SD = standard deviation; SS = sample size; IG = intervention group; CG = control group; N/A = not available; GP = general practitioner; ED = Emergency Department.

The funnel plot (Figure 9) showed asymmetry, indicating the existence of either publication bias or heterogeneity. A thorough examination on the literatures did not disclose other unpublished peer-reviewed studies, so the publication bias was regarded as of low risk. The heterogeneity could be explained by variation in population size, the different ways of performing medication reviews and different outcomes (such as fall-related fractures, fall-related hospitalizations, and fall-related injuries that required medical consultations).

DISCUSSION

In this systematic review and meta-analysis, medication review, either as a single intervention or a part of multi-factorial

TABLE 2.
Summary of medication review characteristics of included studies

Author (Year)	*Design*	*HCP Involvement*	*Patient-I*	*No. of R*	*HCP Training*	*Follow-up (months)*	*Study Inclusion Criteria*
Jensen[33] (2002)	M	R: physician D: physician	No	1	Yes	12	1. ≥65 years; 2. Living in nursing homes
Jensen[44] (2003)	M	R: physician D: physician	No	1	Yes	12	1. ≥65 years; 2. Living in nursing homes
Healey[42] (2004)	M	R: physician D: physician	No	1	No	12	1. ≥65 years; 2. Received care in hospital wards and community units
Davison[41] (2005)	M	D: physician R: physician	No	1	No	12	1. ≥65 years; 2. Presenting to A&E with a fall or fall-related injury; 3. Community-dwelling
Pit[34] (2007)	S	D: physician R: physician	No	1	Yes	12	1. ≥65 years; 2. Community-dwelling
Salminen[35] (2009)	M	R: geriatrician D: physician	Yes	1	No	36	1. ≥65 years; 2. At least one fall during the previous year; 3. MMSE ≥17; 4. Able to walk for 10 min; 5. Living at home
Spice[43] (2009)	M	R: nurse D: physician	No	1	No	12	1. ≥65 years; 2. ≥2 falls in the preceding year; 3. Living in community
Conroy[40] (2010)	M	R: geriatrician D: physician	No	1	No	12	1. ≥70 years; 2. ≥1 fall in the previous year or ≥2 of other falls risk factors; 3. Living in community
Blalock[47] (2010)	S	R: pharmacist D: physician	Yes	1	No	12	1. ≥65 years; 2. ≥1 falls preceding 1. ≥65 years; 2. ≥1 falls preceding randomization; 3. Taking ≥4 prescription or ≥1 CNS-active medications; 4. Living in community
Sjöberg[36] (2013)	S	R: geriatrician D: physician	No	3	Yes	12	1. ≥65 years; 2. Undergone surgery for a hip fracture
Palvanen[45] (2014)	M	R: physician D: physician	No	2	Yes	12	1. ≥70 years; 2. Increased risk for falling or fall-induced injuries; 3. Living in community
Boyé[48] (2016)	S	R: geriatrician-pharmacist-physician D: physician	No	1	No	12	1. ≥65 years; 2. Attended the ED due to a fall; 3. ≥1 FRIDs for ≥2 weeks prior to a fall; 4. MMSE ≥21; 5. Able to walk independently; 6. Living in community
Mikolaizak[46] (2017)	M	R: pharmacist-geriatrician D: pharmacist-physician	No	1	No	12	1. ≥65 years; 2. Received a fall-related emergency response from paramedics; 3. Living in community
Matchar[49] (2017)	M	R: PT D: physician	No	1	No	9	1. ≥65 years; 2. Seen in the ED for a fall or fall-related injury; 3. Able to perform Three-Step Command Test; 4. Discharged or admitted to hospital but able to recover within 1 month; 5. Community-dwelling

HCP = Health Care Professional; Patient-I = patient involvement; R = medication review; S = medication review as single intervention; M = medication review was one of the components in a multi-factorial intervention; D = decision on medication change; PT = physiotherapist.

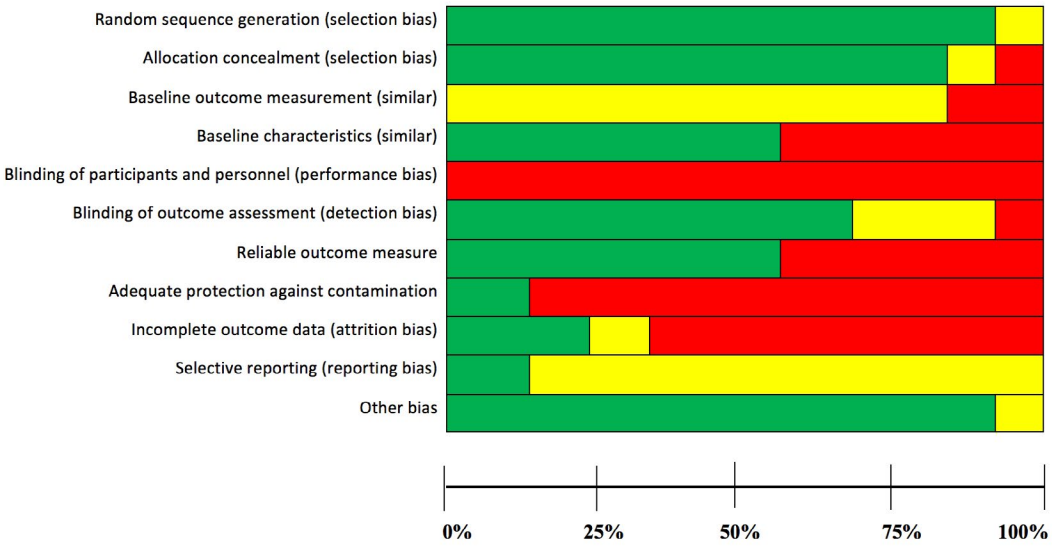

FIGURE 2. Risk of bias summary graph: each risk of bias item presented as percentage across all included studies

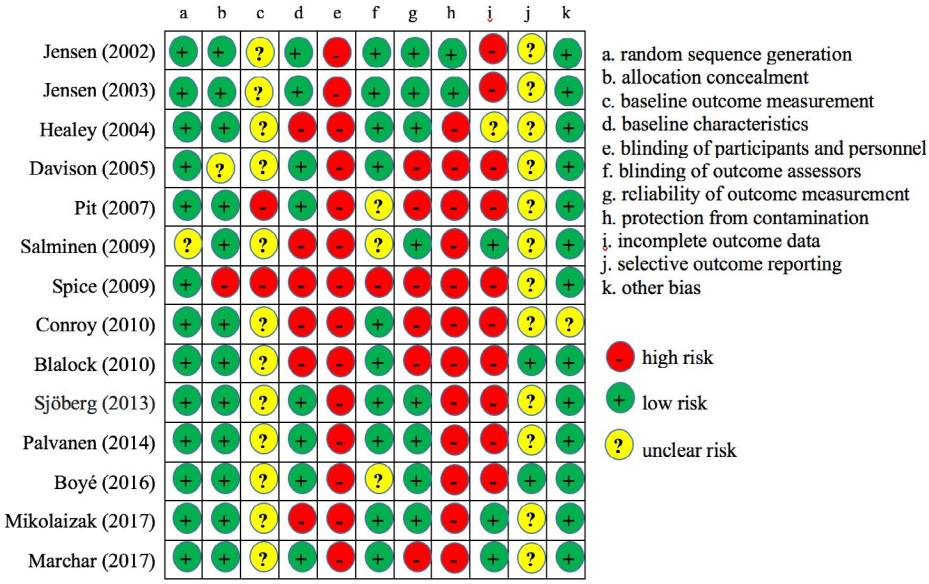

FIGURE 3. Risk of bias summary: each risk of bias item for each included study

fall prevention program, was found to be effective in preventing fall-related injuries and fall-related fractures in community-dwelling older adults. Moreover, a beneficial effect of medication review as the sole intervention was found in reducing fall-related risk of injuries. However, the review was not conclusive on whether medication review was effective in reducing fall-related hospital admissions in older-adults. To the authors' knowledge, this is the first systematic review exploring the effectiveness of medication review in preventing fall-related injuries in older adults. The results suggest that improvement in prevention of fall-related injuries can be achieved by the delivery of medication reviews in community-dwelling older adults.

In 2011, the American Geriatrics Society and British Geriatrics Society Clinical Practice Guideline for Prevention of Falls in Older Persons identified strong evidence to support withdrawal of psychotropic medication for older adults.[21] The Registered Nurses' Association of Ontario (RNAO) falls prevention guidelines also recommended conducting medication review or referring to appropriate health-care provider to reduce, gradually withdraw or discontinue medications that are associated with falling,[50] but their evidence was obtained from expert opinion or committee reports. The findings presented here provide further evidence on the positive role of medication review in preventing fall-related injuries in older adults, thus supporting prominent practice guidelines recommendations.

The results of the meta-analysis indicated high heterogeneity among the included studies. Several factors can explain this variation. First, there is a lack of standardized process on how to perform a medication review. Various tools are available

to health-care professionals to optimize patients' medication, prevent inappropriate prescribing, and minimize adverse drug reactions and polypharmacy. Examples are the Screening Tool of Older Person's Prescriptions (STOPP) and Screening Tool to Alert doctors to Right Treatment (START),[51] Beers criteria,[52] Medication Appropriate Index,[53] and Drug Burden Index.[54] However, none of these tools is all-inclusive to be regarded as a gold standard. In such context, the performance of medication review is greatly based on the personal assessment and judgement built on pharmacists' or physicians' knowledge of medications, comprehensive understanding of patients' clinical information, and efficient communication and cooperation between health-care providers.[55] Secondly, researchers in different studies designed their patient selection criteria to optimize detection of intervention effects. Seven studies chose older adults with high risk of falling, with the assumption that this group could benefit the most from medication review.

The strengths of this review include the methodological rigor, detailed, and comprehensive search strategies, strict inclusion and exclusion criteria, a high inter-rater agreement between the two reviewers when screening the titles and abstracts, a strict requirement for a detailed description of the medication review process to facilitate comparison between trials, and acceptably low risk of bias of included studies, thus producing convincible results.

Several limitations are associated with this systematic review and meta-analysis. Inclusion of only studies published in English language resulted in exclusion of 44 non-English

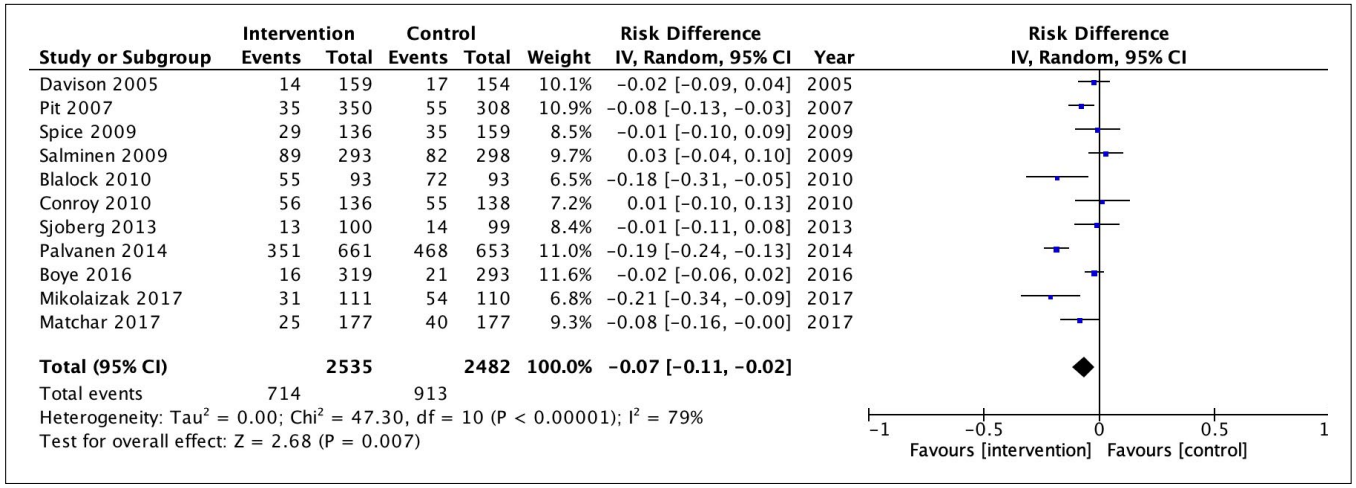

FIGURE 4. Risk of difference in community-dwelling participants

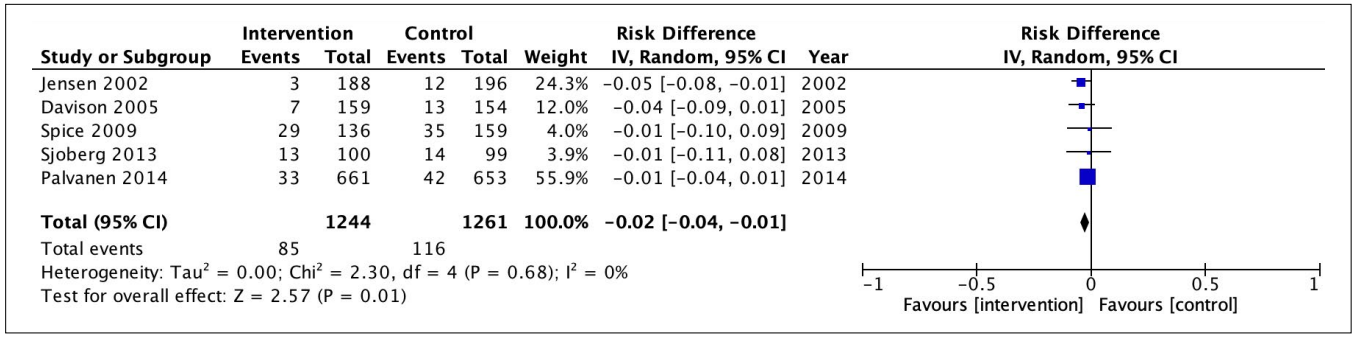

FIGURE 5. Results of five studies of fall-related fractures

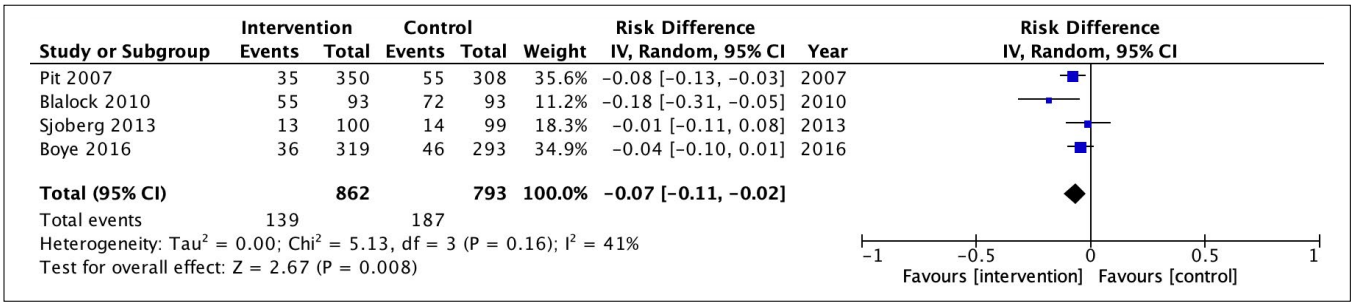

FIGURE 6. Results of four studies using medication review as a single intervention

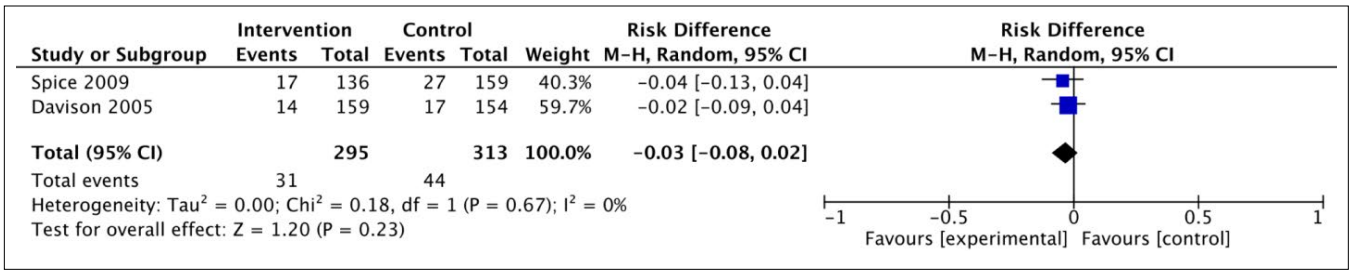

FIGURE 7. Pooled results from two studies investigating effects of medication review on fall-related hospital admissions in community-dwelling older adults

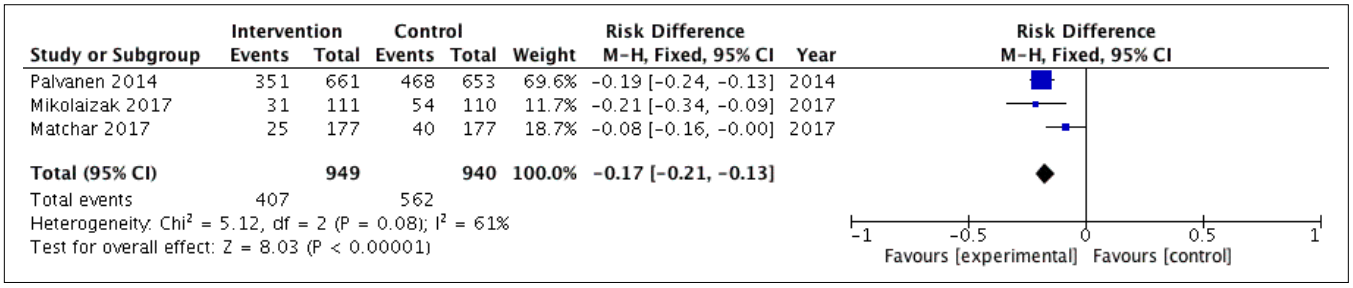

FIGURE 8. Pooled results from three studies with low risk of bias investigating effects of medications review on fall-related injuries in community-dwelling older adults

studies during the titles and abstracts screening. A close examination of translated abstracts revealed that these studies would not meet other inclusion criteria; hence, it is unlikely that their exclusion would have impacted the study findings. Due to the nature of the studies, where the blinding of participants and intervention providers was impractical, the risk of performance bias was high. This has the potential to undermine the results of this review, but statistically significant associations noted in the meta-analyses point to at least conservative estimates of the intervention effect. Next, although only four studies used medication review as the single intervention for fall-related injury prevention, they all demonstrated a positive effect. For the remaining 10 studies, where medication review was a part of multifactorial fall prevention programs, even when a positive effect was detected, it could not be ascribed solely to the medication review. Finally, contamination of the control group could not be avoided, because medication reviews have become a widespread part of the usual geriatric care.

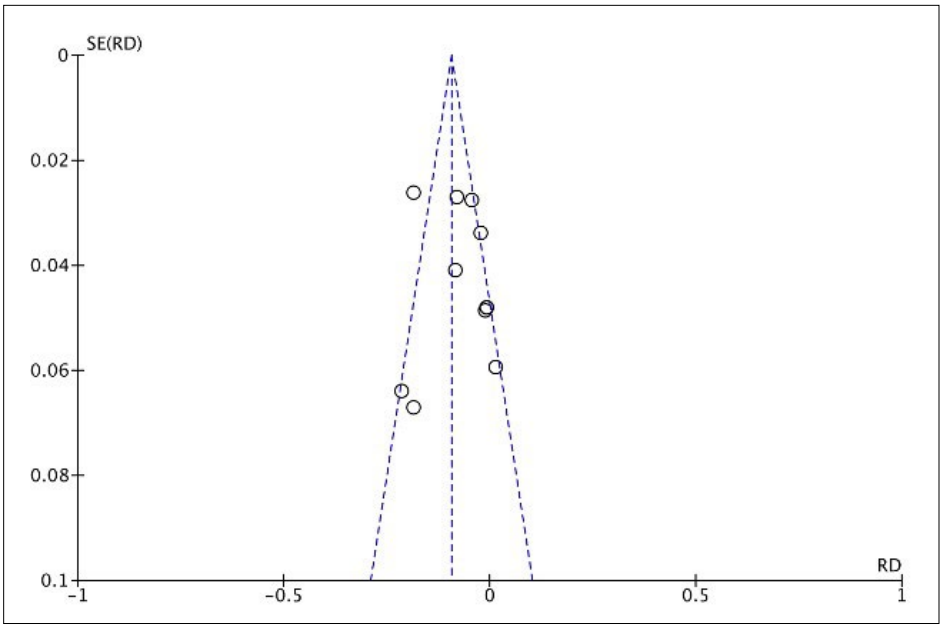

FIGURE 9. Funnel plot of 11 studies including community-dwelling participants

CONCLUSION

This systematic review and meta-analysis summarized evidence from 14 randomized controlled studies to identify the effectiveness of medication review, either as a single intervention or combined in multi-factorial fall prevention programs, on preventing fall-related injuries in older adults. Despite differences between included studies, medication review was found to be effective in preventing fall-related injuries and specifically fall-related fractures in community-dwelling older adults. Building on these positive findings, future research should explore the optimal process for conducting medication reviews, the eligibility criteria for—and frequency of—medication reviews, the cooperation between pharmacists and physicians, and compliance to recommendations resulting from medication review. This will contribute to a better fall-related injury prevention for older adults.

CONFLICT OF INTEREST DISCLOSURES

The authors declare that no conflicts of interest exist.

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APPENDIX A. PRISMA 2009 CHECKLIST

Section/Topic		*Checklist Item*	*Reported on Page #*
		Title	
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
		Abstract	
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
		Introduction	
Rationale	3	Describe the rationale for the review in the context of what is already known.	3-4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	4
		Methods	
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	4
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	4-5
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	4
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	4, App. B
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	Fig. 1
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	5
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	5
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	5
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	5
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	5
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	5
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	6
		Results	
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	Fig. 1 and page 6
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	Tables 1 & 2

APPENDIX A. PRISMA 2009 CHECKLIST (continued)

Section/Topic		*Checklist Item*	*Reported on Page #*
		Results continued	
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	Figs. 2, 3
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Table 2, Figs. 4, 5, 6
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	Figs. 4, 5, 6
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	N/A
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	Figs. 4, 7, 8
		Discussion	
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	10
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	11-12
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	12
		Funding	
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	1

APPENDIX B. SEARCH STRATEGY FOR PUBMED: FULL SEARCH TERMS

((((((((((((“seniors”[Title/Abstract]) OR “senior citizen”[Title/Abstract]) OR “senior citizens”[Title/Abstract]) OR “older people”[Title/Abstract]) OR “old people”[Title/Abstract]) OR “old person”[Title/Abstract]) OR “old persons”[Title/Abstract]) OR “older adults”[Title/Abstract]) OR “elderly”[Title/Abstract]) OR “geriatric”[Title/Abstract]) OR “aged”[Title/Abstract])) AND (((((“accidental falls”) OR ((“fall” OR “falls”))) OR falling) OR “accidental fall”))) AND ((((((((((((((((((((((((((((“Wo unds and Injuries”[Majr]) AND “Abdominal Injuries”[Mesh]) AND “Amputation, Traumatic”[Mesh]) OR “Arm Injuries”[Mesh]) OR “Back Injuries”[Mesh]) OR “Spinal Injuries”[Mesh]) OR “Fractures, Bone”[Mesh]) OR “Fractures, Cartilage”[Mesh]) OR “Hand Injuries”[Mesh]) AND “Hip Injuries”[Mesh]) OR “Joint Dislocations”[Mesh]) OR “Lacerations”[Mesh]) OR “Leg Injuries”[Mesh]) OR “Multiple Trauma”[Mesh]) OR “Nasal Septal Perforation”[Mesh]) OR “Neck Injuries”[Mesh]) OR “Rupture”[Mesh]) OR “Shoulder Injuries”[Mesh]) OR “Soft Tissue Injuries”[Mesh]) OR “Spinal Cord Injuries”[Mesh]) OR “Sprains and Strains”[Mesh]) OR “Tendon Injuries”[Mesh]) OR “Thoracic Injuries”[Mesh]) OR “Tooth Injuries”[Mesh]) OR “Trauma, Nervous System”[Mesh]) OR “Vascular System Injuries”[Mesh]) OR “Wounds, Nonpenetrating”[Mesh]) OR “Wounds, Penetrating”[Mesh])) OR ((“fall-related injury” OR “fall-related injuries” OR “fall related injury” OR “fall related injuries”))) OR (“fall related hospitalization” OR “fall-related hospitalization”)))) AND ((((((((((((((((((((((((((((((“pharmaceutical services”) OR (“Pharmaceutical Services”[Mesh] OR “Pharmaceutical Services, Online”[Mesh] OR “Community Pharmacy Services”[Mesh] OR “Pharmacy Service, Hospital”[Mesh])) OR “medication therapy management”) OR ((“Medication Therapy Management/classification”[Majr] OR “Medication Therapy Management/legislation and jurisprudence”[Majr] OR “Medication Therapy Management/organization and administration”[Majr] OR “Medication Therapy Management/standards”[Majr] OR “Medication Therapy Management/statistics and numerical data”[Majr] OR “Medication Therapy Management/trends”[Majr] OR “Medication Therapy Management/utilization”[Majr]))) OR “drug utilization review”) OR “Drug Utilization Review”[Mesh]) OR ((((((((((((((((“pharmacist review”) OR “pharmacist reviews”) OR “pharmacist intervention”) OR “pharmacist interventions”) OR “pharmacist program”) OR “pharmacist programs”) OR “pharmacist assessment”) OR “pharmacist assessments”)

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"pharmacologists' programs") OR "pharmacologists' program") OR "pharmacologists' assessment") OR "pharmacologists' assessments") OR "pharmacologists' consult") OR "pharmacologists' consults") OR "pharmacologists' evaluation") OR "pharmacologists' evaluations") OR "pharmacologists' counselling") OR "pharmacologists' care")) OR "pharmacologists' consultation") OR "pharmacologists' consultations"))