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Comparisons of Interventions for Preventing Falls in Older Adults
A Systematic Review and Meta-analysis

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IMPORTANCE Falls result in substantial burden for patients and health care systems, and given the aging of the population worldwide, the incidence of falls continues to rise.

OBJECTIVE To assess the potential effectiveness of interventions for preventing falls.

DATA SOURCES MEDLINE, Embase, Cochrane Central Register of Controlled Trials, and Ageline databases from inception until April 2017. Reference lists of included studies were scanned.

STUDY SELECTION Randomized clinical trials (RCTs) of fall-prevention interventions for participants aged 65 years and older.

DATA EXTRACTION AND SYNTHESIS Pairs of reviewers independently screened the studies, abstracted data, and appraised risk of bias. Pairwise meta-analysis and network meta-analysis were conducted.

MAIN OUTCOMES AND MEASURES Injurious falls and fall-related hospitalizations.

RESULTS A total of 283 RCTs (159 910 participants; mean age, 78.1 years; 74% women) were included after screening of 10 650 titles and abstracts and 1210 full-text articles. Network meta-analysis (including 54 RCTs, 41 596 participants, 39 interventions plus usual care) suggested that the following interventions, when compared with usual care, were associated with reductions in injurious falls: exercise (odds ratio [OR], 0.51 [95% CI, 0.33 to 0.79]; absolute risk difference [ARD], −0.67 [95% CI, −1.10 to −0.24]); combined exercise and vision assessment and treatment (OR, 0.17 [95% CI, 0.07 to 0.38]; ARD, −1.79 [95% CI, −2.63 to −0.96]); combined exercise, vision assessment and treatment, and environmental assessment and modification (OR, 0.30 [95% CI, 0.13 to 0.70]; ARD, −1.19 [95% CI, −2.04 to −0.35]); and combined clinic-level quality improvement strategies (eg, case management), multifactorial assessment and treatment (eg, comprehensive geriatric assessment), calcium supplementation, and vitamin D supplementation (OR, 0.12 [95% CI, 0.03 to 0.55]; ARD, −2.08 [95% CI, −3.56 to −0.60]). Pairwise meta-analyses for fall-related hospitalizations (2 RCTs; 516 participants) showed no significant association between combined clinic- and patient-level quality improvement strategies and multifactorial assessment and treatment relative to usual care (OR, 0.78 [95% CI, 0.33 to 1.81]).

CONCLUSIONS AND RELEVANCE Exercise alone and various combinations of interventions were associated with lower risk of injurious falls compared with usual care. Choice of fall-prevention intervention may depend on patient and caregiver values and preferences.

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Data from the National Institute on Aging showed that the 2-year prevalence of falls among individuals aged 65 years or older was 36% in 2010.[1] Falls cause a substantial burden to patients and health care systems.[2-4] In 2012, the cost of falls to Medicare was $31 billion.[5] Not only can falls result in serious injury or death,[6,7] but older adults who experience falls also report increased anxiety and depression and reduced quality of life.[8,9] Given the aging of the population worldwide, the incidence of falls is expected to continue rising.[5] As such, preventing falls among older persons is increasingly important for health care systems.

Previous randomized clinical trials (RCTs) and systematic reviews have selectively examined fall-prevention programs.[10-13] However, directly comparing more than 2 interventions using conventional meta-analysis has major limitations. The key elements of an effective fall-prevention program remain unclear, which has hampered implementation of effective interventions. Furthermore, a network meta-analysis ranking all available fall-prevention interventions and their combinations has not been conducted. Therefore, a systematic review and network meta-analysis on all available fall-prevention interventions for older people were conducted.

Key Points

Question What types of fall-prevention programs may be effective for reducing injurious falls in older people?

Findings In a network meta-analysis including 54 studies and 41 596 participants, exercise (odds ratio [OR], 0.51), combined exercise, vision assessment and treatment, and environmental assessment and modification (OR, 0.30), combined exercise, and vision assessment and treatment (OR, 0.17), and combined clinic-level quality-improvement strategies, multifactorial assessment and treatment, calcium supplementation, and vitamin D supplementation (OR, 0.12) were significantly associated with reductions in injurious falls.

Meaning The analysis identified combinations of interventions likely to be more effective than usual care for preventing injurious falls.

Methods

Protocol
The systematic review protocol was developed using guidance from the Preferred Reporting Items for Systematic Review and Meta-analysis Protocols (PRISMA-P) statement,[14] registered in PROSPERO (CRD42013004151), and published.[15] Because the methods were reported previously, they are described only briefly here. The PRISMA-network meta-analysis extension[16] was used to report results.

Eligibility Criteria
All types of RCTs (eg, cluster, crossover) examining fall-prevention interventions (whether single or multifactorial) for adults aged 65 years or older in all settings (eg, community, acute care) were included. Potential comparators were usual care, other fall-prevention interventions, and placebo.

Outcomes
The primary outcomes were the numbers of injurious falls and fall-related hospitalizations. The secondary outcomes were rate of falls, number of fallers, number of fall-related emergency department visits, number of fall-related physician visits, number of fractures, costs (eg, to the health care system), number of intervention-related harms (eg, muscle soreness from exercise), and quality of life. Quality of life was measured with the SF-12 or SF-36 physical and mental summary component measures (range, 0-100) or the EuroQol-5D VAS (range, 0-100), where 0 indicates maximum disability, and 100 indicates no disability.[17-19]

Data Sources
MEDLINE, Embase, Cochrane Central Register of Controlled Trials, and Ageline databases were searched from inception until December 1, 2015 (see protocol for search strategy[15]). Reference lists of included RCTs and relevant reviews were scanned for additional RCTs. Study authors were contacted for unpublished studies or additional data. An updated search was conducted on April 19, 2017, which involved screening, abstraction, and risk-of-bias appraisal by 2 reviewers, working independently without additional reference scanning or author contact regarding conference abstracts, trial protocols, or non-English articles for any studies identified in the update.

Study Selection
After pilot-testing eligibility criteria for citations and full-text articles, screening was conducted independently by pairs of reviewers. Conflicts were resolved by a third reviewer.

Data Abstraction
Data abstraction was completed by independent pairs of reviewers after pilot-testing of the data abstraction form. Conflicts were resolved by a third reviewer. Interventions were coded independently by a clinician (S.E.S.) and a methodologist (A.C.T.) using a preestablished coding guide (eTable 1 in the Supplement). Included interventions were classified into the following broad categories: basic falls risk assessment, calcium supplementation, cognitive behavioral therapy, devices, diet modification, electromagnetic field therapy and whole-body vibration, environmental assessment and modification, exercise, floor modifications, multifactorial assessment and treatment, osteoporosis medications, podiatry assessment and treatment, quality improvement strategies, social engagement, surgery, vision assessment and treatment, and vitamin D supplementation. Quality improvement strategies were focused on increasing use of research in practice and were classified at the health system, clinic and clinician, and patient levels (**Box 1** and **Table 1**).[20]

Box 1. Components of Quality Improvement Strategies Classified by Level of Implementation

Clinic Level
Quality improvement initiatives targeting the clinic or care team include case management, team changes, electronic patient registries, facilitated relay of information to clinicians, continuous quality improvement, audit and feedback, staff education, and clinician reminders

Patient Level
Quality improvement initiatives targeting the patient include promotion of self-management, patient education, patient reminders, and motivational interviewing

Health System Level
Quality improvement initiatives targeting the health system include interventions with positive or negative financial incentives directed at clinicians (eg, linked to adherence to some process of care or achievement of some target outcome), positive or negative financial incentives directed at patients, or system-wide changes in reimbursement systems

Risk-of-Bias Appraisal

The Cochrane Effective Practice and Organisation of Care (EPOC) Group's risk-of-bias tool was used to appraise included studies.[21] This appraisal was conducted by pairs of independent reviewers, with conflicts resolved by a third reviewer. Small study effects were assessed for each outcome (when >10 RCTs were available) using the comparison-adjusted funnel plot and the *netfunnel* command (Stata 13.0)[22] with a fixed meta-analysis model and ordering treatments from most to least effective according to clinical insight.

Data Synthesis and Analysis

Across all outcomes, pairwise random-effects meta-analysis was conducted. Effect estimates are reported as odds ratios (ORs) for dichotomous outcomes and mean differences for continuous outcomes. Studies reporting dichotomous outcomes with zero events across all groups were included in the systematic review, but excluded from analysis. Studies reporting continuous outcomes with the average effect estimate but not reporting the associated measure of variance (eg, standard deviation) were included in the analysis, with standard errors imputed when feasible.[23,24]

Random-effects network meta-analyses were conducted for connected networks of included RCTs when more than 10 RCTs were available and the number of RCTs was greater than the number of intervention nodes. To surmount small study effects,[25] smaller trials (n <100 participants) were excluded from analysis. Across all outcomes for which network meta-analysis was possible, the transitivity and consistency assumptions were assessed a priori.[26-28] In both network meta-analysis and inconsistency models, common within-network, between-study variance across intervention comparisons was assumed because the treatments included in each network of trials were mostly nonpharmacological. Subgroup and sensitivity network meta-analyses were conducted for the primary outcome with consideration of potential treatment effect modifiers. Interventions were ranked using P scores[29] and presented in a rank-heat plot.[30] For each network meta-analysis, the overall risk for the control group (considering usual care as the control) of the included studies was calculated via the variance-stabilizing Freeman-Tukey double arcsine approach.[31] A random-effects pairwise meta-analysis was applied using inverse variance weights, and to facilitate interpretation, summary group risks were back-transformed to the initial scale. All network meta-analyses and consistency assessments were conducted with R software (version 3.3.3)[32] using the netmeta package.[33] Results were summarized using effect estimates (ORs or mean differences) and their associated 95% CIs. Overall ORs, derived from each network meta-analysis, were transformed to risk differences to allow judgment of the clinical importance of statistically significant results.[34] Analysis details are provided in eMethods in the Supplement.

Table 1. Components of Interventions to Prevent Falls

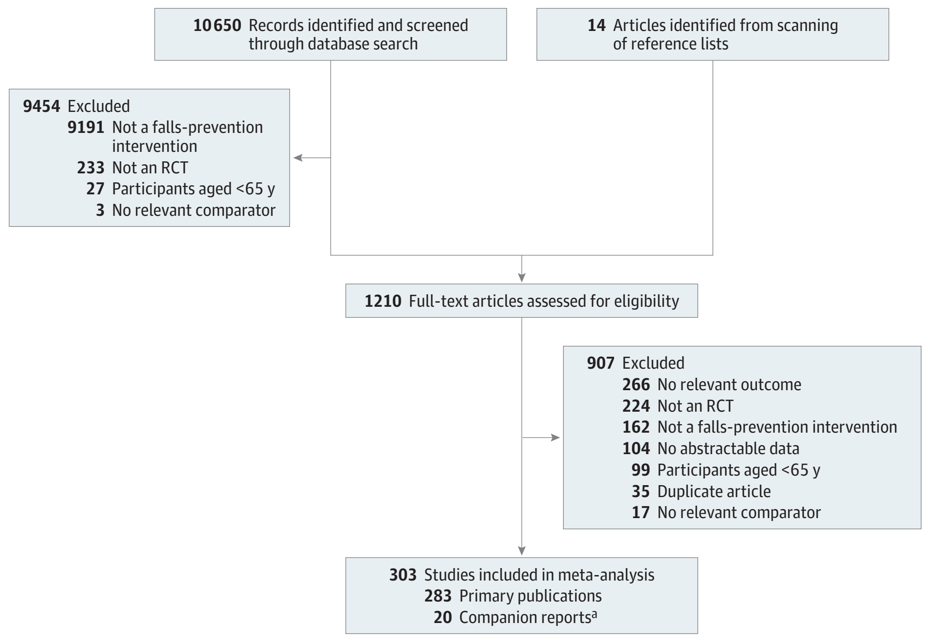
Intervention Component	Abbreviation
Basic falls risk assessment	bf
Calcium	ca
Cognitive behavioral therapy	cb
Clinic-level quality improvement	cl-qi
Comprehensive podiatry assessment and treatment	cp
Device—alarm	de-al
Device—hip protector	de-hp
Device—orthosis	de-or
Dietary modifcations	di
Environmental assessment and modification	ea
Electromagnetic field therapy and whole-body vibration	em + wb
Exercise	ex
Flooring	fl
Lavender	la
Multifactorial assessment and treatment	mf
Osteoporosis treatment	op-tx
Patient-level quality improvement	pa-qi
Social engagement	so
Surgery—cataract	su-ey
Surgery—hip	su-hi
Surgery—pacemaker	su-pm
Health system-level quality improvement	sy-qi
Usual care	uc
Vision assessment and treatment	va
Vitamin D	vi-d

Results

Study Selection

A total of 10 650 titles and abstracts and subsequently 1210 full-text articles were screened (**Figure 1**). Across all outcomes, 283 RCTs and 20 companion reports were

Figure 1. Study Flow From Literature Search



RCT indicates randomized clinical trial.

[a] If multiple publications reported data from the same trial (eg, reporting results at 1-year vs 2-year follow-up), the first was identified as the primary publication and any additional publications were referred to as companion reports to avoid double counting data from the same trial.

Table 2. Summary of Patient Characteristics

Characteristic	No. (%) of Randomized Clinical Trials (N = 283)
Age, mean, y	
64-73.9	56 (19.8)
74-83.9	155 (54.8)
≥84	36 (12.7)
Not reported	36 (12.7)
% Women	
0-49.9	20 (7.1)
50-100	248 (87.6)
Not reported	15 (5.3)
History of falls	
All	60 (21.2)
Mixed	169 (59.7)
None	0
Not reported	54 (19.1)
No. of medications taken[a]	
0-4	56 (19.8)
≥5	55 (19.4)
Not reported	172 (60.8)

[a] Refers to the reported mean or median number of medications taken by patients—not necessarily the number of medications taken daily.

included (citations in eReferences in the Supplement), with a total of 159 910 participants (mean age 78.1 years; 74% women). Two included studies were available only as conference abstracts,[35,36] and 14 other studies were identified by scanning reference lists of included studies and relevant reviews.[37-50]

Author Contact

Fifty-four authors were contacted, and responses were received from 35 (response rate, 65%), which allowed inclusion of 2 additional studies.

Study and Participant Characteristics

For 155 of the RCTs (54.8%), the mean age of participants was between 74 and 84 years (**Table 2**; eTable 2 in the Supplement). In 248 of the RCTs (87.6%), at least 50% of the participants were women. One hundred sixty-nine RCTs (59.7%) included a mixture of individuals with and without a history of falls. The number of medications taken was not reported in 172 RCTs (60.8%).

Two hundred fifty-five of the RCTs (90.1%) were published in 2001 or later, and the studies were conducted in Europe (121 [42.8%]), Australia or New Zealand (66 [23.3%]), and other regions (**Table 3**; eTable 3 in the Supplement). The setting for 142 studies (50.2%) was at home, 75 were in a clinic ([26.5%]), and 72 were in the community (25.4%), with some studies including multiple settings. One hundred and fifty-one RCTs (53.4%) had an intervention duration of 26 weeks or less, and 223 of the studies (78.8%) had a duration (ie, from recruitment to the end of follow-up) of 1 year or less.

Risk of Bias

Most RCTs had a low risk of bias for random sequence generation (187 [66.1%]), similar baseline outcome measures (212 [74.9%]), similar baseline characteristics (238 [84.1%]), incomplete outcome data (221 (78.1%]), blinding (267 [94.3%]), and other components of bias (171 [60.4%]) (eTable 4 and eFigure 1 in the Supplement). However, a high proportion had unclear risk of bias for allocation concealment

(145 [51.2%]), contamination (190 [67.1%]), and selective outcome reporting (183 [64.7%]). All comparison-adjusted funnel plots suggested no evidence of publication bias (eFigure 2 in the Supplement).

Statistical Analysis

The design-by-treatment interaction model showed no evidence of significant inconsistency across the network meta-analysis (eTable 5 in the Supplement). Because of the large number of results from the analysis, the overall results for each outcome are presented and focus on statistically significant intervention effects relative to usual care for network meta-analyses (summarized in **Box 2**). The results from all statistically significant treatment comparisons are available in eTable 5 in the Supplement, and the results from all analyses are posted on the Open Science Framework.[50] P scores were used to summarize results for the primary outcome, and all results are presented in eTable 6, eTable 7, and eTable 8 in the Supplement. The rank-heat plot, presented in eFigure 3 in the Supplement, indicates that exercise is likely the most effective intervention in terms of numbers of fallers, injurious falls, fractures, and hip fractures.

Injurious Falls

Network meta-analysis for the primary outcome of injurious falls included 54 RCTs (41 596 participants) with 39 interventions plus usual care (**Figure 2**). The event rate for injurious falls in the usual care group was 0.34 (95% CI, 0.24 to 0.44). Across all 780 network meta-analysis comparisons, 101 (12.9%) were statistically significant (eTable 5 in the Supplement). The following 4 interventions were associated with a reduced risk of injurious falls relative to usual care:

- Exercise (OR, 0.51 [95% CI, 0.33 to 0.79]; absolute risk difference [ARD], −0.67 [95% CI, −1.10 to −0.24])
- Combined exercise and vision assessment and treatment (OR, 0.17 [95% CI, 0.07 to 0.38]; ARD, −1.79 [95% CI, −2.63 to −0.96])
- Combined exercise, vision assessment and treatment, and environmental assessment and modification (OR, 0.30 [95% CI, 0.13 to 0.70]; ARD, −1.19 [95% CI, −2.04 to −0.35])
- Combined clinic-level quality improvement strategies, multifactorial assessment and treatment, calcium supplementation, and vitamin D supplementation (OR, 0.12 [95% CI, 0.03 to 0.55]; ARD, −2.08 [95% CI, −3.56 to −0.60])

The remaining 35 single or multifactorial interventions were not significantly associated with the risk of injurious falls relative to usual care. According to the P score results, combined exercise and vision assessment and treatment was probably the most effective intervention (97% likelihood) to reduce injurious falls.

The results of subgroup analyses are summarized in **Table 4**. For the 37 RCTs that had less than 75% women (20 354 participants), which examined 27 treatments plus usual care, the network meta-analysis results were consistent with the main analysis. For the 44 RCTs with duration of 12 months or less (32 890 participants; examined 28 interventions plus usual care), the network meta-analysis results

Table 3. Summary of Study Characteristics

Study Characteristic	No. (%) of RCTs (N = 283)
Year of publication	
1990-1995	10 (3.5)
1996-2000	18 (6.4)
2001-2005	66 (23.3)
2006-2010	77 (27.2)
2011-2015	87 (30.7)
2016-2017	25 (8.8)
Continent[a]	
Europe	121 (42.8)
Australia/New Zealand	66 (23.3)
North America	47 (16.6)
Asia	43 (15.2)
South America	4 (1.4)
Multicontinent	2 (0.7)
Study design	
Parallel RCT	243 (85.9)
Cluster RCT	40 (14.1)
Site	
Multicenter	155 (54.8)
Single center	127 (44.9)
Not reported	1 (0.4)
Settings[b]	
Home	142 (50.2)
Clinic	75 (26.5)
Community	72 (25.4)
Hospital	51 (18.0)
Long-term care facility	39 (13.8)
Retirement home	28 (9.9)
Not reported	9 (3.2)
Sample size (No. of patients)	
Parallel RCTs	
20-99	65 (23.0)
100-299	90 (31.8)
300-999	68 (24.0)
1000-9440	20 (7.1)
Cluster RCTs	
68-500	21 (7.4)
501-1500	11 (3.9)
1501-5500	6 (2.1)
5501-10 558	2 (0.7)
No. of clusters, median (IQR)	17 (8.00-25.00)
Duration of Intervention, wk	
<1-26	151 (53.4)
27-52	72 (25.4)
53-78	11 (3.9)
79-104	13 (4.6)
105-260	17 (6.0)
Not reported	19 (6.7)

Abbreviations: IQR, interquartile range; RCT, randomized clinical trial.

[a] Continent refers to where the study was conducted; if not reported explicitly, the location of the first author's institution was used as a proxy.

[b] The number of RCTs exceeds 283 and percents total more than 100% because some studies involved multiple settings.

Box 2. Interventions Associated With Reduction of Outcome Compared With Usual Care in Network Meta-analysis

Outcomes

Number of Injurious Falls

Exercise

Combined exercise and vision assessment and treatment

Combined exercise, vision assessment and treatment, and environmental assessment and modification

Combined clinic-level quality improvement strategies, multifactorial assessment and treatment, calcium supplementation, and vitamin D supplementation

Number of Fallers

Exercise

Combined exercise, patient-level quality improvement strategies, clinic-level quality improvement strategies, and multifactorial assessment and treatment

Combined exercise, patient-level quality improvement strategies, hip protectors, and environmental assessment and modification

Combined patient-level quality improvement strategies, clinic-level quality improvement strategies, dietary modifications, calcium supplementation, and vitamin D supplementation

Combined orthotics and exercise

Number of Fractures

Combined osteoporosis treatment, calcium supplementation, and vitamin D supplementation

Number of Hip Fractures

Combined osteoporosis treatment, calcium supplementation, and vitamin D supplementation

were consistent with the main analysis for the interventions of exercise vs usual care and combined clinic-level quality improvement strategies, multifactorial assessment and treatment, calcium supplementation, and vitamin D supplementation vs usual care; the remaining 2 significant comparisons from the main analysis (combined exercise and vision assessment and treatment vs usual care; combined exercise, vision assessment and treatment, and environmental assessment and modification vs usual care) were no longer included in the network. Network meta-analysis was conducted for the 32 RCTs with participants who were younger than 80 years old (24 869 participants), which examined 26 interventions plus usual care. Compared with the main analysis, the same interventions were associated with a reduced risk of injurious falls except for the combination of clinic-level quality improvement strategies, multifactorial assessment and treatment, calcium supplementation, and vitamin D supplementation, which was no longer in the network. This finding was consistent in another network meta-analysis involving the 40 RCTs (37 010 participants) for people with a mixed fall history (ie, some had fallen previously and some had not), which examined 34 interventions plus usual care. A network meta-analysis restricted to 11 RCTs involving 3830 patients who had fallen previously and examining 9 interventions plus usual care found that the combination of clinic-level quality improvement strategies, multifactorial assessment and treatment, calcium supplementation, and vitamin D supplementation was associated with fewer injurious falls than usual care (OR, 0.12 [95% CI, 0.04 to 0.44]; ARD, −2.08 [95% CI, −3.34 to −0.83]), while the remaining 3 comparisons (exercise vs usual care; combined exercise and vision assessment and treatment vs usual care; combined exercise, vision assessment and treatment, and environmental assessment and modification vs usual care) were no longer in the network. Sensitivity analysis was conducted restricting the network meta-analysis to 24 RCTs with a low risk of contamination bias (26 969 participants; 19 interventions plus usual care); no intervention was associated with a lower risk of injurious falls compared with usual care (eg, exercise vs usual care, OR, 0.59 [95% CI, 0.29 to 1.18]; ARD, −0.53 [95% CI, −1.23 to 0.17]), and 3 of the significant comparisons from the main analysis were no longer in the network (combined exercise and vision assessment and treatment vs usual care; combined exercise, vision assessment and treatment, and environmental assessment and modification vs usual care; combined clinic-level quality improvement strategies, multifactorial assessment and treatment, calcium supplementation, and vitamin D supplementation vs usual care).

Overall, each of the 4 interventions that was associated with better outcomes than usual care in the main analysis was also associated with fewer injurious falls in 2 or more of the additional analyses, although in some cases, an additional analysis was not feasible for a particular subgroup.

Hospitalizations

For the primary outcome of fall-related hospitalizations, 20 RCTs (24 531 participants) with 25 interventions plus usual care were included. Two pairwise meta-analyses were possible across all comparisons (eTable 9 in the Supplement). There were no significant associations with hospitalizations for combined clinic-level quality improvement strategies, patient-level quality improvement strategies, and multifactorial assessment and treatment relative to usual care (2 RCTs [516 participants]; OR, 0.78 [95% CI, 0.33 to 1.81]; ARD, −0.03 [−0.10 to 0.093]) or for combined patient-level quality improvement strategies and exercise relative to exercise alone (2 RCTs [2126 participants]; OR, 1.12 [95% CI, 0.38 to 3.25]; ARD, 0.02 [−0.09 to 0.22]).

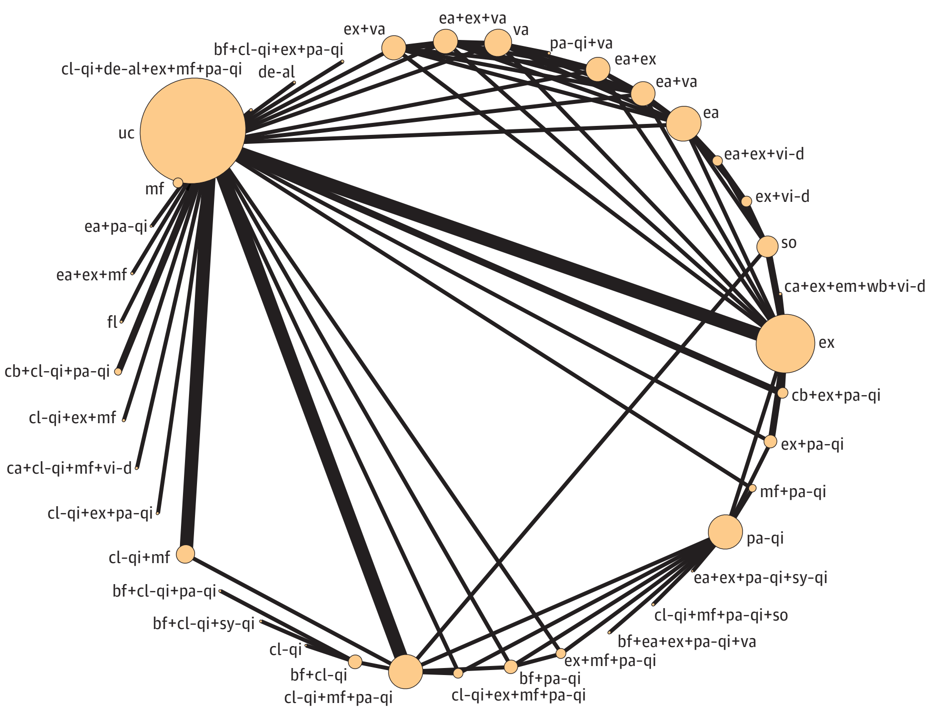
Emergency Department Visits

Eleven RCTs (2956 participants) with 12 interventions plus usual care reported on emergency department visits. Only 1 pairwise meta-analysis (2 RCTs; 499 participants) was possible across all comparisons (eTable 9 in the Supplement). There was no significant association with emergency department visits for multifactorial assessment and treatment relative to usual care (OR, 1.24 [95% CI, 0.86 to 1.77]; ARD, 0.04 [−0.03 to 0.13]).

Outpatient Physician Visits

Twenty-one RCTs (17 193 participants) with 32 interventions plus usual care reported on physician visits. Only 1 pairwise meta-analysis (2 RCTs; 681 participants) was possible across all treatment comparisons (eTable 9 in the Supplement). There was no significant association with outpatient

Figure 2. Network Geometry for Injurious Falls



Network geometry for 54 randomized clinical trials (41 596 patients). Each treatment node indicates an intervention and is weighted according to the number of patients who received the particular intervention. Each edge (line connecting the nodes) is weighted according to the number of studies and directly compares the treatments it connects. See Table 1 for expansions of treatment abbreviations. The coding guide, which provides a description of each intervention component, can be found in eTable 1 of the Supplement.

physician visits for exercise relative to usual care (OR, 0.62 [95% CI, 0.32 to 1.18]; ARD, −0.10 [−0.19 to 0.04]).

Number of Fallers

Network meta-analysis for the outcome of number of fallers included 158 RCTs, 107 300 participants, and 77 interventions plus usual care (**Figure 3**). One RCT (0.6%) with 31 participants (0.03%) was excluded from the network meta-analysis because it had zero events across all groups. The event rate for falls in the usual care group was 0.38 (95% CI, 0.33 to 0.43). Across all 3003 network meta-analysis comparisons, 200 (6.7%) were statistically significant (eTable 5 in the Supplement). Of these, 5 interventions were associated with a lower risk of patients experiencing a fall relative to usual care:

- Exercise (OR, 0.83 [95% CI, 0.70 to 0.99]; ARD, −0.19 [95% CI, −0.36 to −0.01])
- Combined exercise, patient-level quality improvement strategies, clinic-level quality improvement strategies, and multifactorial assessment and treatment (OR, 0.68 [95% CI, 0.49 to 0.94]; ARD, −0.39 [95% CI, −0.72 to 0.06])
- Combined exercise, patient-level quality improvement strategies, hip protectors, and environmental assessment and modification (OR, 0.53 [95% CI, 0.29 to 0.97]; ARD, −0.63 [95% CI, −1.22 to −0.03])
- Combined patient-level quality improvement strategies, clinic-level quality improvement strategies, dietary modifications, calcium supplementation, and vitamin D supplementation (OR, 0.36 [95% CI, 0.14 to 0.93]; ARD, −1.03 [95% CI, −1.99 to −0.08])
- Combined orthotics and exercise (OR, 0.22 [95% CI, 0.07 to 0.67]; ARD, −1.54 [95% CI, −2.67 to −0.40])

The remaining interventions were not significantly associated with a lower risk of falls than usual care. One intervention (combined exercise, patient-level quality improvement strategies, and social engagement) was associated with a higher risk that patients would experience falls relative to usual care (OR, 5.13 [95% CI, 2.14 to 12.30]; ARD, 1.63 [95% CI, 0.76 to 2.51]).

Fractures

Network meta-analysis for the outcome of fractures included 68 RCTs, 86 491 participants, and 43 interventions plus usual care (**Figure 4**). The event rate for fractures in the usual care group was 0.07 (95% CI, 0.05 to 0.10). Across all 946 network meta-analysis comparisons, 45 (4.8%) were statistically significant (eTable 5 in the Supplement). Of these, 1 intervention (combined osteoporosis treatment (eg, bisphosphonates), calcium supplementation, and vitamin D supplementation) was associated with a lower risk of fractures relative to usual care (OR, 0.22 [95% CI, 0.09 to 0.54]; ARD, −1.51 [95% CI, −2.41 to −0.62]). The remaining 42 interventions were not significantly associated with a lower risk of fractures than usual care.

Hip Fractures

Network meta-analysis for the outcome of hip fractures included 39 RCTs, 52 281 participants, and 23 interventions plus usual care (Figure 4). Four RCTs (9.1%) with 1877 participants (3.5%) were excluded from the network meta-analysis because they had zero events across all groups. The event rate for hip fractures in the usual care group was 0.03 (95% CI, 0.02 to 0.04). Across all 276 network meta-analysis

Table 4. Subgroup Analyses of Network Meta-analysis for Injurious Falls Outcome

Comparison by Subgroup	Studies, No.	Patients, No.	Proportion With Event (95% CI)		Odds Ratio (95% CI)	Absolute Mean Difference in Proportions (95% CI)[a]
			Intervention	Control		
Exercise vs Usual Care						
Overall analysis					0.51 (0.33 to 0.79)	
Participants <75% women	37	20 354	0.36 (0.16 to 0.59)	0.41 (0.29 to 0.53)	0.49 (0.31 to 0.78)	−0.71 (−1.17 to −0.25)
Study duration ≤12 mo	44	32 890	0.30 (0.13 to 0.52)	0.33 (0.22 to 0.44)	0.48 (0.29 to 0.80)	−0.72 (−1.23 to −0.22)
Age <80 y of age	32	24 869	0.25 (0.08 to 0.48)	0.35 (0.19 to 0.53)	0.44 (0.26 to 0.75)	−0.81 (−1.35 to −0.28)
Mixed history of falling[b]	40	37 010	0.36 (0.16 to 0.59)	0.37 (0.25 to 0.49)	0.49 (0.30 to 0.82)	−0.71 (−1.22 to −0.20)
History of falling only[c]	11	3830	0.16 (0.07 to 0.27)	0.24 (0.07 to 0.47)	0.90 (0.24 to 3.30)	−0.11 (−1.41 to 1.19)
Low risk of contamination bias	24	26 969	0.40 (0.00 to 0.96)	0.26 (0.15 to 0.37)	0.59 (0.29 to 1.18)	−0.53 (−1.23 to 0.17)
Combined Exercise and Vision Assessment and Treatment vs Usual Care						
Overall analysis					0.17 (0.07 to 0.38)	
Participants <75% women	37	20 354	0.51 (0.42 to 0.59)	0.41 (0.29 to 0.53)	0.16 (0.07 to 0.39)	−1.82 (−2.68 to −0.95)
Study duration ≤12 mo	44	32 890	NA	0.33 (0.22 to 0.44)	NA	
Age <80 y of age	32	24 869	0.51 (0.42 to 0.59)	0.35 (0.19 to 0.53)	0.17 (0.07 to 0.43)	−1.76 (−2.66 to −0.85)
Mixed history of falling[b]	40	37 010	0.51 (0.42 to 0.59)	0.37 (0.25 to 0.49)	0.16 (0.06 to 0.42)	−1.82 (−2.77 to −0.86)
History of falling only[c]	11	3830	NA	0.24 (0.07 to 0.47)	NA	
Low risk of contamination bias	24	26 969	NA	0.26 (0.15 to 0.37)	NA	
Combined Exercise, Vision Assessment and Treatment, and Environmental Assessment and Modification vs Usual Care						
Overall analysis					0.30 (0.13 to 0.70)	
Participants <75% women	37	20 354	0.65 (0.57 to 0.73)	0.41 (0.29 to 0.53)	0.30 (0.12 to 0.71)	−0.22 (−2.09 to −0.35)
Study duration ≤12 mo	44	32 890	NA	0.33 (0.22 to 0.44)	NA	
Age <80 y of age	32	24 869	0.65 (0.57 to 0.73)	0.35 (0.19 to 0.53)	0.31 (0.13 to 0.78)	−1.16 (−2.07 to −0.24)
Mixed history of falling[b]	40	37 010	0.65 (0.57 to 0.73)	0.37 (0.25 to 0.49)	0.30 (0.11 to 0.78)	−1.22 (−2.18 to −0.25)
History of falling only[c]	11	3830	NA	0.24 (0.07 to 0.47)	NA	
Low risk of contamination bias	24	26 969	NA	0.26 (0.15 to 0.37)	NA	
Combined Clinic-Level Quality Improvement Strategies, Multifactorial Assessment and Treatment, Calcium Supplementation, and Vitamin D Supplementation vs Usual Care						
Overall analysis					0.12 (0.03 to 0.55)	
Participants <75% women	37	20 354	0.03 (0.00 to 0.07)	0.41 (0.29 to 0.53)	0.12 (0.03 to 0.56)	−2.08 (−3.58 to −0.58)
Study duration ≤12 mo	44	32 890	0.03 (0.00 to 0.07)	0.33 (0.22 to 0.44)	0.12 (0.03 to 0.54)	−2.08 (−3.56 to −0.61)
Age <80 y of age	32	24 869	NA	0.349 (0.191 to 0.527)	NA	
Mixed history of falling[b]	40	37 010	NA	0.37 (0.25 to 0.49)	NA	
History of falling only[c]	11	3830	0.03 (0.00 to 0.07)	0.24 (0.07 to 0.47)	0.12 (0.04 to 0.44)	−2.08 (−3.34 to −0.83)
Low risk of contamination bias	24	26 969	NA	0.26 (0.15 to 0.37)	NA	

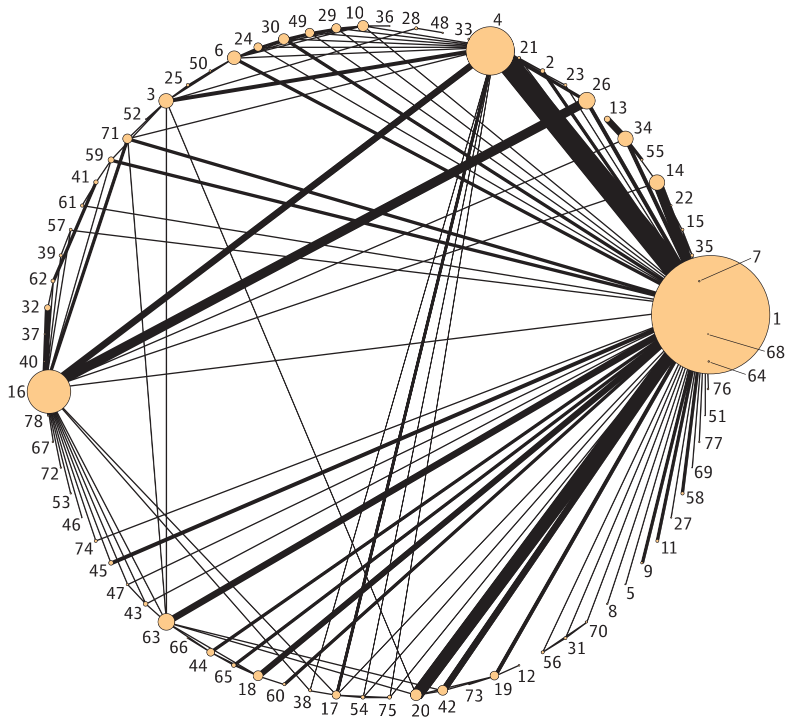
Abbreviations: NA, not applicable.

[a] Odds ratios derived from each network meta-analysis were transformed to risk differences using established methods.[34]

[b] Studies that included participants regardless of whether they had fallen in the past or not.

[c] Studies that only included participants who had fallen in the past.

Figure 3. Network Geometry for Fallers



Order Code	Treatment Abbreviation	Order Code	Treatment Abbreviation
1	uc	40	cl-qi+de-hp
2	di	41	cl-qi+pa-qi
3	so	42	cl-qi+mf
4	ex	43	bf+pa-qi
5	em+wb	44	bf+cl-qi
6	ea	45	mf+pa-qi
7	fl	46	ex+pa-qi+so
8	de-al	47	ex+mf+pa-qi
9	de-hp	48	ex+mf+sy-qi
10	va	49	ea+ex+va
11	su-ey	50	ea+ex+vi-d
12	su-PM	51	ea+ex+mf
13	ca	52	ea+mf+sy-qi
14	vi-d	53	cp+de-ft+pa-qi
15	op-tx	54	ca+di+vi-d
16	pa-qi	55	ca+op-tx+vi-d
17	cb	56	ca+pa-qi+vi-d
18	cl-qi	57	cb+ex+pa-qi
19	bf	58	cb+cl-qi+pa-qi
20	mf	59	cl-qi+ex+pa-qi
21	di+ex	60	cl-qi+ex+mf
22	di+vi-d	61	cl-qi+ea+pa-qi
23	ex+so	62	cl-qi+de-hp+pa-qi
24	ex+va	63	cl-qi+mf+pa-qi
25	ex+vi-d	64	bf+ex+pa-qi
26	ex+pa-qi	65	bf+cl-qi+pa-qi
27	ex+sy-qi	66	bf+cl-qi+sy-qi
28	ex+mf	67	ea+ex+pa-qi+sy-qi
29	ea+ex	68	de-hp+ea+ex+pa-qi
30	ea+va	69	ca+cl-qi+mf+vi-d
31	ea+pa-qi	70	ca+ea+pa-qi+vi-d
32	de-hp+pa-qi	71	cl-qi+ex+mf+pa-qi
33	de-or+ex	72	cl-qi+mf+pa-qi+so
34	ca+vi-d	73	bf+cp+ex+pa-qi
35	op-tx+vi-d	74	bf+cl-qi+ex+pa-qi
36	pa-qi+va	75	ca+cb+di+ex+vi-d
37	pa-qi+vi-d	76	ca+cl-qi+di+pa-qi+vi-d
38	cb+ex	77	cl-qi+de-al+ex+mf+pa-qi
39	cb+pa-qi	78	bf+ea+ex+pa-qi+va

Network geometry for 158 randomized clinical trials (107 300 patients). Each treatment node indicates an intervention and is weighted according to the number of patients who received the particular intervention. Each edge (line connecting the nodes) is weighted according to the number of studies and directly compares the treatments it connects. See Table 1 for expansions of treatment abbreviations. The coding guide, which provides a description of each intervention component, can be found in eTable 1 of the Supplement.

comparisons, 9 (3.3%) were statistically significant (eTable 5 in the Supplement). Of these, 1 intervention (combined osteoporosis treatment, calcium supplementation, and vitamin D supplementation) was associated with a lower risk of hip fracture relative to usual care (OR, 0.18 [95% CI, 0.05 to 0.62]; ARD, −1.70 [95% CI, −2.92 to −0.48]). An additional 22 interventions were not significantly associated with a lower risk of hip fractures than usual care.

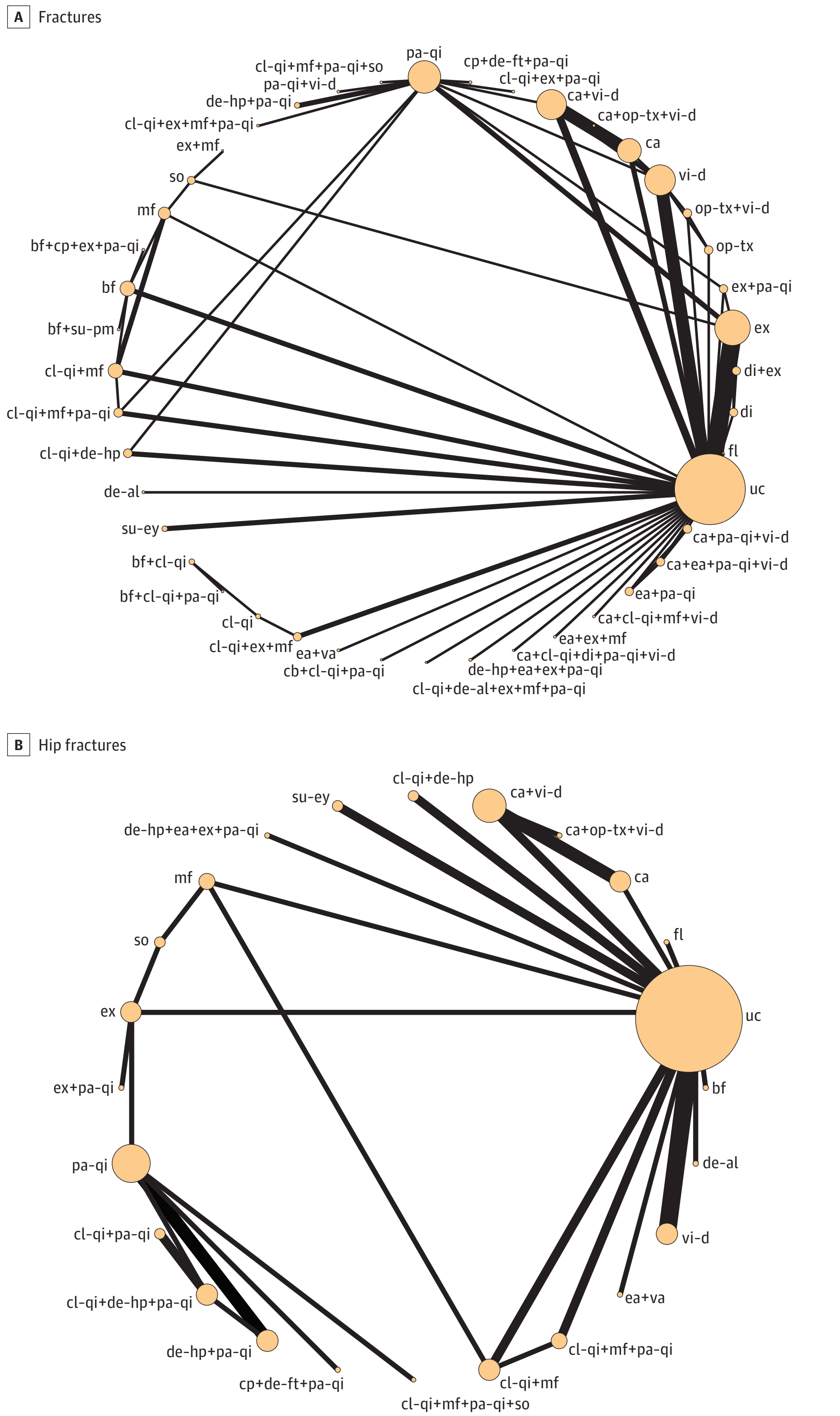
Quality of Life

Although 32 RCTs (18 521 participants) provided data on quality-of-life measures (eTable 10 in the Supplement), only 2 pairwise meta-analyses were possible (eTable 9 in the Supplement). Exercise was not significantly associated with improvement in quality of life as measured by the SF-36 or SF-12 physical component summary score compared with usual care (mean difference, −0.06 [95% CI, −0.90 to 0.77]; 2 RCTs; 1206 participants). Similar results were obtained for the SF-36 or SF-12 mental component summary score (mean difference, 0.29 [95% CI, −1.00 to 1.58]; 2 RCTs; 1206 participants).

Harms

Fifty-seven of the RCTs (24 558 participants) reported no intervention-related harmful events in any study group, and another 62 RCTs (39 596 participants) reported 1 or more harms (eTable 11 in the Supplement). Only 2 pairwise meta-analyses were possible (eTable 9 in the Supplement). Exercise was not significantly associated with an increased risk of muscle soreness compared with usual care (OR, 4.97 [95% CI, 0.35 to 70.38]; ARD, 0.13 [95% CI, −0.02 to 0.70]; 2 RCTs; 1021 participants). Supplementation with calcium and vitamin D was not significantly associated with an increased risk of gastrointestinal harm compared with usual care (OR, 1.05 [95% CI, 0.52 to 2.09]; ARD, 0.001 [95% CI, −0.01 to 0.03]; 2 RCTs; 3853 participants).

Figure 4. Network Geometry for Fractures and Hip Fractures



A, Network geometry for 68 randomized clinical trials (86 491 patients). B, Network geometry for 39 randomized clinical trials (52 281 patients). Each treatment node indicates an intervention and is weighted according to the number of patients who received the particular intervention. Each edge (line connecting the nodes) is weighted according to the number of studies and directly compares the treatments it connects. See Table 1 for expansions of treatment abbreviations. The coding guide, which provides a description of each intervention component, can be found in eTable 1 of the Supplement.

Discussion

Exercise alone and various combinations of interventions were associated with lower risk of injurious falls compared with usual care. Choice of intervention may depend on patient and caregiver values and preferences. Combinations of interventions, including exercise, vision assessment and treatment, environmental assessment and modification, multifactorial assessment and treatment, and vitamin D supplementation were associated with preventing injurious falls compared with usual care. The combination of exercise and vision assessment and treatment was probably the intervention most strongly associated with reduction in injurious falls.

These results suggest that encouraging patients to exercise, undergo a vision assessment, and consider osteoporosis therapy (for those at risk), given the potential impact of these interventions in preventing injurious falls. Other combinations of interventions to consider include exercise, patient-level and clinic-level quality improvement strategies, multifactorial assessment and treatment; exercise, patient-level quality improvement strategies, hip protectors, and environmental assessment and modification; and orthotics and exercise in patients at risk for falls. The results suggest focusing on implementing patient-level quality improvement strategies (eg, patient education and patient reminders) and clinic-level quality improvement interventions (eg, audit and feedback) to increase uptake of this evidence. The results also suggest that calcium and vitamin D supplementation may decrease fractures, as may osteoporosis therapy plus calcium and vitamin D supplementation. However, the results indicate the need for a tailored approach; subgroup analyses showed that the combination of exercise, environmental assessment and modification, and multifactorial assessment and treatment was associated with an increased risk of injurious falls among patients who had fallen previously. In addition, the combination of exercise, patient-level quality improvement strategies, and social engagement was associated with increased fall risk. Exercise may increase fall risk in some individuals because these people become more mobile as their strength increases; patients can be made aware of this situation, but any cautionary advice must be balanced with the need to improve mobility and avoid deconditioning. This finding also raises the issue of the type of exercise to recommend, such as exercise focused on enhancing balance.[52] Health care managers might consider the use of clinic-level quality improvement strategies, such as clinician reminders and audit and feedback, to increase uptake of multifactorial assessment and treatment and of vitamin D supplementation to reduce injurious falls. As well, for patients in long-term care settings, hip protectors, environmental assessment and modification, exercise, and patient-level quality improvement strategies are potential options to reduce falls.

A 2015 systematic review and network meta-analysis examining vision and risk factor interventions to prevent falls included 7 RCTs with 2723 participants; interventions combining vision assessment and treatment and multifactorial assessment and treatment were found to be the most effective.[53] The current systematic review was much larger (with an additional 276 RCTs and 157 187 participants; eReferences in the Supplement) and includes information on the effectiveness of quality improvement strategies and multifactorial assessment and treatment. Although the authors of a systematic review on exercise[54] did not conduct network meta-analysis, their results were similar to those reported here, which suggests that exercise might be associated with decreased falls in older adults, but the type of exercise should be tailored to the individual.

The authors of RCTs included in this review could have improved their studies by conducting adequate allocation concealment (which is possible in any RCT), ensuring that results were not influenced by contamination bias, and reporting all outcomes. Most RCTs were completed within 6 months, but longer-term follow-up and confirmation of the sustainability of these interventions are required. In addition, few studies were conducted in the acute care setting, despite falls in hospitals often being considered during hospital accreditation processes.

Strengths of the review process include reviewers working in pairs across all levels of screening, data abstraction, and risk-of-bias appraisal; cleaning of the data by a third reviewer; and following the guidance of the International Society for Pharmacoeconomics and Outcomes Research in conducting statistical analyses.[55]

This study had several limitations. The published protocol included both the falls rate and costs as secondary outcomes. However, because few studies reported these outcomes consistently, these outcomes could not be analyzed directly; rather, data for falls rates were converted to number of falls. As well, another outcome, quality of life, as measured by SF-12 or SF-36 summary component measures or EuroQol-5D, was added.[17-19] Some of the planned subgroup analyses and sensitivity analyses were not conducted because of insufficient data. Although the point estimate was similar to the overall OR, the results were no longer statistically significant for the injurious falls network meta-analysis when only studies with a low risk of contamination bias were included. However, because most of the studies (67%) were assessed as having an unclear risk of contamination bias, the power of this sensitivity analysis was limited by the lower number of studies that could be included. This limitation suggests that improvements in reporting are required. Most network meta-analyses included numerous interventions, with sparse data for the treatment comparisons; additional analyses, using the models suggested by Welton et al[56] and Caldwell and Welton[57] to account for sparseness, could be conducted in the future. Scanning the reference lists of 32 additional studies from the updated search and inclusion of an unpublished conference abstract[58] and a non-English paper[59] were not possible. Because of the large number of comparisons in the network meta-analyses, multiplicity may have elevated the rate of false positives in the statistically significant results (type I error).[60,61] Although P scores are based on the treatment effect estimates and their associated CIs, it is recommended that the P score values be interpreted along with the network meta-analysis point estimates and their precision.[29]

Conclusions

Exercise alone and various combined interventions were associated with lower risk of injurious falls compared with usual care. Choice of intervention may depend on patient and caregiver values and preferences.

ARTICLE INFORMATION

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