SYSTEMATIC REVIEW

Efficacy of exercise-based interventions in preventing falls among community-dwelling older persons with cognitive impairment: is there enough evidence? An updated systematic review and meta-analysis

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Abstract

Objective: Exercise prevents falls in the general older population, but evidence is inconclusive for older adults living with cognitive impairment. We performed an updated systematic review and meta-analysis to assess the potential effectiveness of interventions for reducing falls in older persons with cognitive impairment.

Methods: PubMed, EMBASE, CINAHL, Scopus, CENTRAL and PEDro were searched from inception to 10 November 2020. We included randomised controlled trials (RCTs) that evaluated the effects of physical training compared to a control condition (usual care, waitlist, education, placebo control) on reducing falls among community-dwelling older adults with cognitive impairment (i.e. any stage of Alzheimer's disease and related dementias, mild cognitive impairment).

Results: We identified and meta-analysed nine studies, published between 2013 and 2020, that included 12 comparisons (N = 1,411; mean age = 78 years; 56% women). Overall, in comparison to control, interventions produced a statistically significant reduction of approximately 30% in the rate of falls (incidence rate ratio = 0.70; 95% CI, 0.52-0.95). There was significant between-trial heterogeneity ($I^2 = 74\%$), with most trials (n = 6 studies [eight comparisons]) showing no reductions on fall rates. Subgroup analyses showed no differences in the fall rates by trial-level characteristics. Exercise-based interventions had no impact on reducing the number of fallers (relative risk = 1.01; 95% CI, 0.90–1.14). Concerns about risk of bias in these RCTs were noted, and the quality of evidence was rated as low.

Conclusions: The positive statistical findings on reducing fall rate in this meta-analysis were driven by a few studies. Therefore, current evidence is insufficient to inform evidence-based recommendations or treatment decisions for clinical practice. PROSPERO Registration number: CRD42020202094.

Keywords: cognitive function, exercise training, incidental falls, fall prevention, older people, systematic review

Key Points

- Exercise, such as balance or strength training, has been shown to prevent falls in the general older population, but evidence is less compelling and inconclusive for older adults living with cognitive impairment.
- In this systematic review and meta-analysis of published research, exercise-based interventions were found to reduce falls by approximately 30% compared with usual care. Although statistically significant, this finding was primarily driven by a few studies.
- Exercise interventions had no impact on reducing the number of fallers for older adults with cognitive impairment.
- Exercise may have the potential to reduce falls for cognitively impaired, community-dwelling older adults. The current evidence, however, is insufficient to guide clinical practice.

Introduction

Each year, approximately one-third of community-dwelling older adults aged 65 years or older fall [1, 2], with the risk increasing with age [3]. Older adults with cognitive decline perform poorly on balance, gait and dual-task activities [4–8], with cognitive impairment consequently being identified as a major risk factor for falls [9–14]. Studies show that cognitively impaired older adults are between 2 and 5 times more likely to fall compared to cognitively unimpaired or healthy older adults [6, 7] and that at least 50% of older adults with cognitive impairment experience a fall each year [4–6], thus placing this population at greater risk of falls and fall-related injuries.

Many falls among older adults result in serious injury [15], leading to emergency department visits, hospital admissions or death [16, 17] and substantially increasing medical costs [18, 19]. With the prevalence of cognitive decline, including Alzheimer's disease and related dementias (ADRD) [20], expected to increase with the growing ageing population, the incidence of falls among older adults is also expected to accelerate [16]. Identifying ways to effectively mitigate this growing public health problem is increasingly important for individuals, families, health care systems and society.

There is compelling evidence that exercise that focuses on balance and strength training reduces falls among cognitively intact community-dwelling older adults [21-23]. However, evidence drawn from studies having robust designs is lacking for those who experience cognitive impairment. To date, systematic review and meta-analysis studies of exercise interventions involving cognitively impaired, community-dwelling older adults have been sparse. Findings from current review studies are often drawn from a limited number of highquality trials with highly variable study characteristics (e.g. a mix of institutionalised, non-institutionalised, single and multifaceted interventions). These intervention studies have led to conclusions that are inconsistent or inconclusive [24-31]. The paucity of rigorously designed RCTs and the lack of consistency in synthesised evidence have resulted in a lack of findings that can inform evidence-based decision making and clinical practice [24–32].

Recent publication of additional RCTs necessitates the need for timely updates of prior reviews [23, 25, 26, 29]

and synthesis of existing evidence so that clinical practice can be kept current. Accordingly, the aim of this systematic review and meta-analysis is to update and synthesise the evidence drawn from RCTs published up to 2020 on exercisebased interventions. We compare interventions that have control conditions in order to determine the potential effectiveness of exercise-based interventions for preventing falls among community-dwelling older persons with cognitive impairment.

Methods

This study was performed in accordance with the principles outlined in the Cochrane Handbook for Systematic Reviews [33] and was reported using the Preferred Reporting Items for Systematic Review and Meta-Analyses (checklist in eTable 1 in the Appendix) [34]. The study was registered on 31 August 2020, in the International Prospective Register of Systematic Reviews (CRD42020202094).

Eligibility criteria

We searched for all RCTs, including parallel, crossover and clustered designs, that (a) included exercise-based fall prevention interventions (e.g. physical exercise, physical therapy, Tai Ji Quan), (b) were conducted either in community or home settings, (c) targeted community-dwelling older persons (aged ≥ 65 years) with cognitive impairment of any type and (d) included any stage of ADRD (mild to moderate dementia, or Alzheimer's disease) and mild cognitive impairment (MCI) defined by a clinical diagnosis or assessment of an established cognitive evaluation measure. Trials with multiple or combined interventions, such as exercise combined with cognitive training or home fall hazard reduction, were also eligible for inclusion. Eligible control conditions included usual care, waitlist, education and placebo control. An additional requirement for inclusion was that the outcome had to include measures of falls (i.e. number of falls and/or rates of falls, number of fallers). No limits were applied to the language or year.

Literature search

Four independent reviewers (two authors of the paper; two non-author, trained research assistants) performed a

comprehensive literature search in major electronic databases including PubMed, EMBASE, CINAHL, Scopus, Cochrane Central Register of Controlled Trials and PEDro. The full search strategies are described in eTable 2 in the Appendix. The search began in July 2020, with the last search conducted on 10 November 2020.

Search and study selection

The database search was conducted using a mix of keywords and/or terms developed from previous systematic reviews and meta-analyses on falls and fall-related factors in older persons with cognitive impairment [23–29, 35–37]. The search with the predetermined keywords/terms was initially pilot tested, by two independent authors, on PubMed to identify target studies reviewed in the literature (eTable 3 in the Appendix).

Data extraction

The same two authors independently screened titles and abstracts of all article citations identified in the search to ensure that predefined eligibility criteria (target populations, trial design, interventions, comparisons, settings and outcomes) were met. The full text of all relevant articles identified were retrieved and reviewed independently by the same two authors. Using a coding guide informed by the Cochrane data extraction form [33] and other systematic reviews [23–29], we extracted information about research designs, population characteristics, intervention types/comparisons, primary and secondary study outcome measures (i.e. incidence of falls, number of falls), adverse events, attrition rates, intervention effects and length of intervention (eTable 4 in the Appendix).

Risk of bias and quality assessment

The same two authors independently evaluated each study for risk of bias using the Cochrane risk of bias tool (Rob 2) [38, 39], which assesses a study's quality on five dimensions, including bias arising from (a) the randomisation process, (b) deviations from intended interventions, (c) missing outcome data, (d) measurement of the outcome and (e) selection of the reported result. Per the Cochrane guidelines, a trial was judged to be of 'low risk' of bias if the study scored low in all quality domains, of 'some concern' regarding bias if the study was judged to raise some concerns in at least one domain (but not reaching a high level of concern) or of 'high risk' of bias if the study was judged to be of high concern in at least one domain or to generate a lower level of concern in multiple domains.

We also used Grading of Recommendations Assessment, Development and Evaluation (GRADE) [40] to assess the quality of the body of evidence on each individual outcome based on within-study risk of bias (methodological quality), inconsistency of results (i.e. widely differing estimates of the intervention effect in results from different trials), imprecision (studies with few participants and few events that resulted in wide confidence intervals), indirectness of evidence (e.g. an indirect comparison of two interventions or comparison of population, outcome or intervention) and risk of publication bias (when trials with 'negative' findings remain unpublished). Using these criteria, trials are being either 'upgraded' or 'downgraded' for each study outcome. Grades are assigned as 'High' (highly confident that the true effect is similar to the estimated effect), 'Moderate' (the true effect is probably close to the estimated effect), 'Low' (the true effect might be markedly different from the estimated effect) or 'Very Low' (the true effect is probably markedly different from the estimated effect).

Data synthesis and analysis

A pooled effect estimate of a ratio statistic was calculated for (a) incidence rate ratio (IRR) of falls and (b) relative risk ratio of fallers (RR) and their associated 95% confidence intervals (CIs). We used a random-effects model for parameter estimation (i.e. rate ratio, risk ratio) because of the anticipated variation in the type of cognitive impairment and interventions. The results of the meta-analyses were displayed in a forest plot. Between-trial heterogeneity was assessed by examining the I² statistic and forest plots. We also report relative risk reductions (relative to control) in both outcomes as an indication of effect size.

A sensitivity analysis was conducted to assess any changes in estimates due to estimation methods (random- vs. fixedeffects), by sample sizes (<100 versus \geq 100 subjects), and by successively eliminating studies one by one. In the presence of substantial between-trial heterogeneity (i.e. $I^2 \geq 50\%$) [38], meta-regression subgroup analyses were conducted to explore the moderation effect of individual trial-level characteristics of (a) type of impairment (ADRD versus MCI), (b) intervention hours (<45 versus \geq 45 h) [41], (c) intervention delivery (group vs. home interventions) and (d) intervention adherence (<75% versus \geq 75%), with results presented in forest plots. We also examined the small-study effects by visually checking for asymmetry in funnel plots and Egger's test. Details of our analytic approach are presented in eTable 5 in the Appendix.

A two-sided value of P < 0.05 was set as a statistically significant level for all analyses. Analyses were conducted using Stata V.16 software (Stata Corp LLC).

Results

Search results

The search identified 2,038 records. Upon removing duplicates, 1,835 articles were screened. After assessing titles and abstracts, 1,820 records were found to be ineligible. The remaining 15 full-text records were screened in detail for eligibility. Of these, nine individual RCTs [42–50], published between 2013 and 2020, were found to be eligible and included in the final analysis (Figure 1).



Figure 1. Summary of RCTs included in the systematic review and meta-analysis.

Study and Participant Characteristics

Table 1 provides an overview of all included studies (see eTable 6 in the Appendix for details). The nine RCTs had a total of 1,411 participants (mean age = 78 ± 4.1 years, range: 60-93; 56% women), with 841 being randomised into single- or multiple-intervention groups and 570 into control groups. Of the total number of participants randomised, 1,118 (79%) completed their post-intervention assessment. Differences were noted in the areas of (a) type of cognitive impairment (e.g. Alzheimer's dementia, vascular dementia, other types of dementia, MCI), (b) intervention programme delivery (group-based versus home-based), (c) intervention type (physical exercises consisting of endurance, balance, strength and flexibility; combined exercise with cognitive training; exercise with home hazard reduction; and Tai Ji Quan combined with home practice) and (d) intervention duration (range: 6 weeks to 12 months) and frequency (1 session per week to 5 sessions per week).

There was great heterogeneity in the diagnosis methods used to identify study participants and in the level of cognitive impairment across the included trials. The diagnosis approaches involved (a) the use of a standardised neuropsychological measure (e.g. Mini-Mental State Examination, Addenbrooke's Cognitive Examination (ACE), Montreal Cognitive Assessment or Diagnostic and the Statistical Manual of Mental Disorders), (b) a diagnosis performed by a healthcare provider or specialist or (c) a combination of the two methods. Among the nine RCTs, two included patients with Alzheimer Disease [42, 43], two with dementia [46, 47], one with mild to moderate dementia [45], one with mild dementia [44, 48], one with MCI [49] and one with the population defined by a score of <83 on the ACE – II exam or a diagnosis by a clinical specialist [50].

Four studies reported no differences in the number of falls at baseline [44, 47, 49, 50], one reported a greater number of fallers in the exercise group compared to the control group [43] and four did not report any information regarding differences in falls at baseline [42, 45, 46, 48]. Excluding a comparison made between a cognitive training group and a control group [48], a total of 12 comparisons were conducted on the incidence of falls in our meta-analysis. Additional information on trial characteristics can be found in eTable 7 in the Appendix.

Outcome measures

Data on falls, including the number of falls, incidence rate of falls or number of fallers in each study condition, were reported, either as a part of the main outcomes [43–45, 49, 50] or secondary outcomes [46–48] in these trials. Information on falls during the intervention and follow-up period was collected via self-reports, using a monthly falls calendar, from the study participants. Information on falls, however, was inconsistently or incompletely presented across the studies. Six studies reported the number of falls [42, 44, 45, 47–49], three reported the number of falls [43, 45, 47] and four reported the number of fallers [43–45, 50] across intervention conditions.

Table 1. Summary of study characteristics of the nine randomised controlled trials included in the systematic review and meta-analysis

Authors/date/country	Purpose	Population	Sample size	Intervention	Intervention attrition and adherence	Effect on falls
Pitkala et al., 2013, ⁴² Fialand	To assess the effects of long-term exercise on physical function and mobility among older adults with AD	Community-living older persons with ΔD (mean age = 78 years; mean MMSE score = 18)	N = 210, dyads: 70 in each of the three study groups	• Three groups: (1) home-based exercise (1 h twice a week), (2) group-based exercise (1 h twice a week), and (3) usual care	• Atrition: 23% • Adherence: 81%	The two active interventions showed a significantly lower incidence rate in falls compared to usual carte (IRR = 0.44, 95% CI: 0.32-0.56 for home-based reactive relative to usual carter IRR = 0.61, 95% CI: 0.46-0.76 for ortont-based relative to usual carter arte
Suttanon et al., 2013, ⁴³ Australia	To test the feasibility and safety of a home-based exercise intervention for older adults with AD	Community-living older persons with mild to moderate AD (mean age = 81.9 years; mean MMSE score = 21)	N = 40: 19 in home-based exercise group and 21 in control group	 Two groups: (1) home-based exercise (the Orago programme with 4-6 visits by a therapist, with 5 support phone calls) and (2) education control 	• Attrition: 28% • Adherence: 82%	There was no statistically significant difference in faul rates (IRR = 0.997, 95% CI: 0.42–2.39) or number of faillers (47.4% vs 33.3%; RR = 0.42, 95% CI: 0.66–3.06) between study
Wesson et al., 2013, ⁴⁴ Australia	To test the feasibility of a home hazard reduction and exercise fall prevention intervention in older adults with mild dementia	Community-living older persons with mild dementia (mean age = 79.8 years; mean MMSE score = 23.5)	N = 22, dyads: 11 in home intervention group and 11 in usual care group	 Two groups: (1) home strength and balance exercises and home hazard reduction (6 occupational therapy home visits plus 3 phone calls and 5 home visits by a therapist and (2) usual care 	• Artrition: 0.05% • Adherence: 72%	brough There was no significant difference in the incidence rates (IRR = 0.34, 95% CI: 0.06-1.91) or number of fallers (RR = 0.50, 95% CI: 0.11–2.19) between study groups
Zieschang et al., 2013, ⁴⁵ Germany	To examine long-term exercise training effects in older adults with mild to moderate dementia	Primarily community-living persons (84%) with dementia (mean age = 83 years, ±6.8; mean MMSE score = 21.75)	N = 122: 62 in intervention group; 60 in control group	 Two groups: (1) group-tailored intensive and progressive resistance exercises and (2) placebo control 	• Attrition: 25% • Adherence: 93.9%	There was no significant difference in fall rates (IRR = 1.04, 95% CI: 0.81–1.33) or number of fallers (RR = 0.71, 95% CI: 0.39–1.29) between study groups
Lamb et al., 2018, ⁴⁶ United Kingdom	To examine the effect of a moderate- to high-intensity exercise intervention on cognitive impairment in people with mild to moderate dementia	Community-dwelling persons with mild to moderate dementia (mean age = 78 years, ±6.8; mean sMMSE score = 21.8)	N = 494: 329 in intervention group and 165 in usual care group	 Two groups (1) exercise intervention and (2) usual care 	• Attrition: 15% • Adherence: 65%	There was no significant difference in fall rates (IRR = 1.1, 95% CI: 0.8–1.6) between study groups
Nyman et al., 2019, ⁴⁷ United Kingdom	To examine the effect of Tai Chi on balance and preventing falls among people with dementia	Community-dwelling persons with dementia (mean age = 78 years; score of ≥10 on M-ACE)	N = 85, dyads: 42 in Tai Chi group: 43 in control group	 Two groups: (1) Tai Chi, once per week in-class practice supplemented by home practice and home behavioural change techniques, and (2) usual care 	• Attrition: 22% • Adherence: 67%	There was a significant difference in fall rates (IRR = 0.35, 95% CI: 0.15–0.81) between study groups in favour of Tai Chi
Goldberg et al., 2019, ⁴⁸ United Kingdom	To assess the feasibility of a home-based exercise intervention aimed at promoting activity, independence and stability in older persons living with early dementia	Community-dwelling persons diagnosed with mild dementia or MCI (mean age = 76 years, score of 15–25 on MOSE; ar 60-94 on ACE III)	N = 60: 19 in moderate-intensity intervention group; 20 in high-intensity intervention group; and 21 in usual care group	 The groups: (1) moderate-intensity supervision activity intervention, (2) high-intensity supervision activity intervention, and (3) usual care 	 Attrition: 18% Adherence: 66% in high-intensity supervision; 100% in moderare-intensity supervision 	There was no significant difference in fall rates between either intervention group and the usual care group (IRR = 1.20, 95% GT: 0.32–4.50, between moderate-intensity exercise and usual care; IRR = 0.68, 95% GT: 0.16–2.80, between high-intensity exercise and usual care)
Lipardo and Tswang, 2020, ⁴⁹ Philippines	To assess the effects of combined physical and cognitive training on fall rate and risk of falling in older adults with MCI	Community-living older persons with MCI (mean age = 69 years, mean MoCA score = 18)	N = 92: 23 in each of the four study groups	 Four groups: (1) physical training, (2) cognitive training, (3) combined physical and cognitive training, and (4) wait-list control 	 Attrition: 28% Adherence: 85% 	There was no significant difference in fall incidence rate among the study groups (IRR = 0.25, 9.5% CI: 0.20-2.78 for physical training relative to control: IRR = 1.18, 95% CI: 0.36-3.86 for combined physical and coentive training relative to control)
Taylor et al., 2020, ⁵⁰ Australia	To determine the efficacy of a fall prevention intervention in older people with cognitive impairment	Community-living older persons with cognitive impairment (mean age = 82 years; mean M-ACE score = 14; ACE-III = 62)	N = 309: 153 in intervention group and 156 in control group	 Two groups (1) home hazard reduction and home-based exercise intervention and (2) usual care 	• Attention: 21% • Adherence: 67%	There was no statistical difference in fall rates (IRR = 1.05, 95% CI: 0.73–1.15) or number of fallers (RR = 1.10, 95% CI: 0.91–1.33) between study groups
^a Information on falls is ascertai Montreal Cognitive Assessment	ned through each study or other t MMSE: Mini-Mental State Eva	systematic reviews. ACE: Addenl luation sMMSE: standardised Mi	brooke's Cognitive Examination ini-Mental State Evaluation IRR:	M-ACE: Mini ACE AD: Alzhein Incidence rate ratio RR: Risk rat	ner's disease MCI: Mild io CI: Confidence inter	cognitive impairment MoCA: ⁄al

Efficacy of exercise-based interventions in preventing falls



Figure 2. Risk of bias assessments for the nine randomised controlled trials included in the systematic review and meta-analysis. Note: Per these guidelines, a trial was judged to be of 'low risk' of bias if the study scored low in all quality domains, of 'some concern' regarding bias if the study was judged to raise some concerns in at least one domain (but not reaching a high level of concern), and 'high risk' of bias if the study was judged to be of high concern in at least one domain or to generate a lower level of concern in multiple domains.

Adverse events

Six studies reported no major (serious) adverse events (e.g. serious injuries, hospitalisation, death) related to the intervention [43–45, 47–49]. One study did not report adverse events [42]. Of the studies that provided adverse events reports, two indicated some minor complaints from participants (e.g. pain or discomfort during initiation to new exercise [43] or muscle stiffness, joint pain or dizziness [44]) and two reported some adverse events but did not provide specifics [47, 48]. In one trial [45], an adverse event was reported by 7% of those in the intervention group, with 25 adverse events and four serious adverse events documented. In another trial, a total of four falls were reported being associated with the intervention [50].

Risk of bias

Applying the Rob 2 tool, overall, eight trials (89%) were judged as having 'some concerns' on risk of bias (Figure 2). This is a reflection of the fact that for eight trials (89%) the domain 'Deviations from intended interventions' was graded consistently as 'some concerns'. This notable weakness mainly reflected the fact that these trials were singleblind in design, with bias potentially introduced by the inability to blind study participants and interventionists. All other sources of bias in these nine trials were shown to be acceptable except for two trials (22%) which reported blinding that was partially broken during follow-up assessment [47, 48].

Quality assessment using GRADE ratings

The quality of evidence was assessed using GRADE ratings for each of the study outcomes in the included RCTs. The outcomes are presented in Table 2. The rate of falls outcome was downgraded by two levels due to 'risk of bias', 'inconsistency' and 'imprecision' of the resulting findings. The outcome on the number of fallers also showed low quality and therefore was downgraded by two levels for serious risk of bias (for a lack of blinding of outcome assessors and study participants) and imprecision in results (i.e. concerns over the results that are derived from only a handful of small studies or wide 95% CI with no effect). Overall, the quality of evidence for both falls outcomes was rated low.

Intervention to reduce the incidence of falls

The pooled effect of intervention from the nine RCTs on the incidence of falls between the intervention groups versus control groups, expressed as a fall rate ratio, was 0.70 (95% CI, 0.52 to 0.95, $I^2 = 74\%$, 12 comparisons) (Figure 3.a),

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atient pop	ılation: comn nmunities	nunity-dwelling	older adults v	vith cognitive in	mpairment					
nterventior	1: exercise-base	ed interventions								
Comparisor	: usual care									
rimary	Risk of	Inconsistenc	y ^b Indirectness	Imprecision ^c	Other con-	Anticipated absolute		Relative effect	No. of patients	Certainty of
Jutcome	$bias^a$				siderations ^d	effects (95% CI)		(95% CI) ^f	(studies)	evidence (GRADE)
						Risk with control	Risk with intervention ^e			
ncidence	serious	serious	not serious	serious	none	500 per 1,000	350 fewer per 1,000 person/years (260	IRR 0.70	1,411	
of falls						person/years	fewer to 475 more)	(0.52 to 0.95)	(9 RCTs)	Low
Vumber of	serious	not serious	not serious	serious	none	425 per 1,000	429 per 1,000	RR 1.01	1,411	
allers						person	(383 to 484)	(0.90 to 1.14)	(9 RCTs)	Low

effect, (c) plausible confounding, and (d) dose response gradient. "The risk in the intervention group (and its associated 95% CI) is based on the estimated risk in the usual care group and the relative effect of the intervention (and its associated 95% confidence interval). Based on nine studies with 12 comparisons GRADE Working Group grades of evidence High certainty: authors are highly confident that the true effect is similar to the The estimated effect Moderate certainty: authors believe that the true effect is probably close to the estimated effect Low certainty: The true effect might be markedly different from the estimated effect is probably close to the estimated effect Low certainty: fallers.

Efficacy of exercise-based interventions in preventing falls

indicating a significant reduction (approximately 30%) in fall rates favouring exercise-based interventions. As can been seen, only four comparisons (group-based and home-based exercise interventions, and a mix of group and home Tai Ji Quan practice) involving three trials [42, 45, 47] contributed significantly to the overall effectiveness of exercise in reducing the number of falls among older persons with ADRD. Eight comparisons involving six RCTs [43, 44, 46, 48–50] showed no significant reductions. In an unplanned analysis, removing the four comparisons with significant rate ratios resulted in a non-significant pooled estimate on IRR (1.02, 95% CI, 0.85 to 1.51, $I^2 = 0\%$, eight comparisons).

Intervention to reduce the number of fallers

The pooled effect of these exercise-based interventions [42-50] on the number of fallers between the intervention groups and the control groups, expressed as fall risk ratio, was 1.01 (95% CI, 0.90 to 1.14; $I^2 = 0\%$; 12 comparisons), which was not statistically significant (P = 0.86; Figure 3.b). It was observed that none of the 12 comparisons from nine individual studies contributed to the reduction in the number of

Sensitivity and subgroup analyses

There were no major changes in the pooled effect size estimates on rate and risk ratios using the random- or fixedeffects modelling methods (IRR_{fixed} = 0.68, 95% CI, 0.60 to 0.78, $I^2 = 74\%$, P = 0.001; $RR_{fixed} = 1.10$, 95% CI, 0.91 to 1.33, $I^2 = 0\%$, P = 0.83). There was no statistical difference (P = 0.98) in the fall rate estimate by study sample sizes (i.e. <100 versus >100). In addition, by successively eliminating studies one by one, there was no noticeable change in the interpretation of the pooled IRR and risk ratio estimates (eFigure 1.a and 1.b in the Appendix).

Subgroup meta-regression analyses showed no differences in effect-size estimates in the fall rates by the study-level characteristics evaluated (i.e. type of delivery, type of cognitive impairment, total intervention hours or adherence rates) (eTable 8 in the Appendix). In the absence of substantial between-trial variability ($I^2 = 0\%$) on the number of fallers outcome, no subgroup analyses were performed.

Small-study effects

rue effect is probably markedly different from the estimated effect

Visual inspection of funnel (scatter) plots (eFigure 2.a and 2.b in the Appendix) of the intervention effect estimates suggested an asymmetry appearance on incidence of falls but not on the number of fallers. Egger's test for funnel plot asymmetry on each outcome, however, was not significant (P = 0.69 for incidence of falls, P = 0.20 for number of fallers).

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a Study		Rate Ratio with 95% CI	Weigh (%)
Pitkala et al. (2013). Group exercise vs. control		0.61 [0.45, 0.81]	12.95
Pitkala et al. (2013). Home exercise vs. control		0.44 [0.33, 0.59]	12.80
Suttanon et al. (2013). Home exercise vs. control		1.00 [0.42, 2.37]	6.57
Wesson et al. (2013). Strength/balance/home safety vs. control		0.34 [0.12, 0.98]	5.16
Zieschang et al. (2017). Intensive motor training vs. control		0.97 [0.71, 1.33]	12.69
Lamb et al. (2018). Aerobic/strength exercise vs. control		- 1.10 [0.78, 1.56]	12.28
Nyman et al. (2019). Tai Chi/home practice vs. control		0.35 [0.24, 0.51]	12.00
Goldberg et al. (2019). High intensity exercise vs. control	- 0	→1.20 [0.34, 4.25]	4.03
Goldberg et al. (2019). Moderate intensity exercise vs. control		0.68 [0.18, 2.53]	3.80
Lipardo & Tsang (2020). Physical training vs. control		→1.18 [0.22, 6.43]	2.54
Lipardo & Tsang (2020). Combined physical & cognitive vs. contro	a	→0.75 [0.17, 3.34]	3.11
Taylor et al. (2020). Exercise & home hazard reduction vs. control		1.05 [0.73, 1.51]	12.09
Overall			
Heterogeneity: $\tau^2 = 0.16$, $I^2 = 73.81\%$, $H^2 = 3.82$			
Test of $\theta_i = \theta_i$: Q(11) = 42.51, p = 0.00	Favors Intervention No	Effect	
Test of $\theta = 0$: $z = -2.31$, $p = 0.02$			
	0.10 0.50 Effect size (Rate Ratio	3.00	

Random-effects REML model

b	Inte	rvention	С	ontrol	Risk Ratio Weight
Study	Events	No events	Events	No events	with 95% CI (%)
Pitkala et al. (2013). Group exercise vs. control	29	41	17	18	0.85 [0.55, 1.32] 7.33
Pitkala et al. (2013). Home exercise vs. control	27	43	18	17	0.75 [0.48, 1.16] 7.43
Suttanon et al. (2013). Home exercise vs. control	9	10	7	14	→ 1.42 [0.66, 3.06] 2.41
Wesson et al. (2013). Strength/balance/home safety vs. control	2	9	4	7	• 0.50 [0.11, 2.19] 0.65
Zieschang et al. (2017). Intensive exercise vs. control	26	36	30	30	0.84 [0.57, 1.24] 9.48
Lamb et al. (2018). Aerobic/strength vs. control	131	198	60	105	
Nyman et al. (2019). Tai Chi/home practice vs. control	17	25	17	26	<u> </u>
Goldberg et al. (2019). High intensity supervision vs. control	4	16	3	8	0.73 [0.20, 2.70] 0.84
Goldberg et al. (2019). Moderate intensity supervision vs. control	3	16	2	8	→ 0.79 [0.16, 3.98] 0.54
Lipardo & Tsang (2020). Physical training vs. control	5	18	3	9	● 0.87 [0.25, 3.03] 0.91
Lipardo & Tsang (2020). Combined physical/cognitive training vs. control	4	19	2	9	→ 0.96 [0.21, 4.45] 0.60
Taylor et al. (2020). Exercise plus home inspection vs. control	94	59	87	69	1.10 [0.91, 1.33] 40.25
Overall					♦ 1.01 [0.90, 1.14]
Heterogeneity: T ² = 0.00, I ² = 0.00%, H ² = 1.00					
Test of $\theta_i = \theta_j$: Q(11) = 6.49, p = 0.84					Favors Intervention No Effect
Test of $\theta = 0$: $z = 0.18$, $p = 0.86$					
				0.	10 0.50 3.00 Effect size (Risk Ratio)

Random-effects REML model

Figure 3. The effects of exercise interventions compared to control conditions on reductions of falls and fallers among older persons with cognitive impairment: A meta-analysis. Figure 3.a. The effect on reducing the incidence of falls. Figure 3.b. The effects on reducing the number of fallers.

Discussion

Our meta-analyses showed that exercise-based interventions, compared to usual care, reduced the rate of falls by approximately 30% among community-living older persons with cognitive impairment. There was significant heterogeneity between trials, but we found no evidence that the effects of interventions on reducing falls were moderated by trial or intervention characteristics such as study sample sizes, type of impairment, intervention hours, intervention delivery style or adherence. Results showed a non-significant effect of exercise-based interventions on reducing the number of fallers in this high-risk population.

Our risk assessment indicated some concern regarding overall risk of bias in the included studies, with bias primarily being in the areas of blinding of participants (including dyads), interventionists or study outcome assessors that would be necessary to ensure unbiased ascertainment of outcomes. While masking assessors to intervention allocation is important in clinical trials, blinding participants, particularly in trials that involve dyads, is highly challenging, if not impossible, due to the nature of the intervention, and this issue is inherent in many behavioural and dyadic interventions.

The meta-analyses provide encouraging preliminary results with regard to the therapeutic potential of exercisebased interventions in reducing the incidence of falls. However, these findings should be interpreted with caution because (a) 8 of the 12 comparisons from the nine included trials were non-significant, (b) most of the studies (56%) involved small samples (of fewer than 100 subjects) and had a short intervention duration that lasted less than 6 months (56%) and (c) as shown in our quality of evidence assessment using the GRADE, evidence from meta-analyses of the included trials was of low quality.

Our study involves a larger number of studies than any of the previous systematic reviews and meta-analyses, which included studies ranging in number from one to three [23, 25, 26, 29]. However, even with the additional number of studies included in our study, the overall strength of reduction in fall rates remains less robust than what has been previously reported. For example, in the most recent metaanalysis that involved subgroup analyses of older adults with cognitive impairment (of any type), exercise interventions were shown to reduce the rate of falls by 45% (pooled RR = 0.55, 95% CI 0.37 to 0.83 based on three studies) [23]. Indeed, by removing early studies with significant reductions in fall rates, we showed that recent published studies contributed little to the efficacy of exercise in lowering fall rates in this population. On the number of fallers, an early metaanalysis showed that, among community-living older adults with dementia or cognitive impairment, exercise reduced the risk of being a faller by 32% (pooled RR = 0.68, 95% CI 0.55 to 0.85 based on two studies) [29]. Overall, the weaker reductions on fall rates and non-significant reductions on number of fallers in our study highlight uncertainty of the clinical significance of evidence.

It is clear from the current evidence that exercise interventions designed for older persons with cognitive impairment, including ADRD and MCI, are feasible and can be implemented in either group or home settings. Moreover, it seems that involving caregivers of persons with cognitive impairment in these programmes provides greater motivation and improves adherence, as evidenced by the relatively low attrition rates across the dyad studies. Consistent with exercises designed for general older adult populations, common exercises that focus on strength and balance, including Tai Ji Quan [21, 47], have been shown to also be safe for older persons with cognitive impairment, given the low incidence of major adverse effects.

There are some caveats associated with the exercise interventions included in our study. First, many of the studies were often blended with other interventions, such as regular phone support [43, 44, 50], or had multiple components (e.g. exercise integrated with cognitive training, supplemental instructional booklets, home safety inspections or practice) [44, 47, 49]. Second, six of the nine interventions in our review were delivered by a healthcare professional (i.e. a physiotherapist or an occupational therapist) [42-44, 48–50], making them less generalizable in under-resourced community settings. Third, some of the trials [42, 44, 47, 48] involved patient-caregiver dyads, making them a caregiversupported intervention. These factors should be taken into account in the design and implementation of exercise-based interventions for an older population with cognitive impairments, especially when the interventions depend on the use of locally available resources.

The trials included in our review also varied in terms of exercise parameters, such as duration, frequency, intensity and mode of exercise and delivery. For example, not all interventions met the minimum of 3 h per week of exercise for participants or the 50 h of training recommended in guidelines [23, 41]. Intervention deliveries were mixed with other supplemental components, which makes it challenging to tease out the source of the true effect of the intervention. Our meta-regression subgroup analyses also failed to show any differences between home-based and group-based interventions, or any differences involving training variables based on duration and frequency. Current evidence on fall prevention in the general community suggests that a single exercise intervention that includes >3 h/week of exercise involving a high challenge to balance may have greater fall prevention benefits than other types of interventions [23]. The lack of clear evidence on the efficacy of homebased versus group-based interventions and the inconsistent adherence to guidelines make it difficult to provide clinicians with recommendations for implementing community fall prevention programmes for cognitively impaired older adults.

In all the studies included in our meta-analysis, falls were ascertained through self-reports, a common method of recording falls information in the falls prevention field. Such an approach has been criticised for being subject to recall bias, which may impact the drawing of inferences from the findings in our study. In addition, falls data ascertainment varies significantly across the included studies, making it challenging to assess the full impact of exercise interventions on falls in the study population. Thus, it is necessary to standardise falls outcome data collection and report key outcome information, including data on number of falls, number of fallers/recurrent fallers, fall rate per person-time in relation to follow-up and time to first fall, so that it can be utilised to facilitate data synthesis and meta-analysis [51].

Exercise can be effective in preventing and reducing falls in the general older population [21–23]. Results from our review and others [24, 27, 30] suggest a promising benefit for those living with cognitive impairment, but the small number of rigorously designed, high-quality RCTs limits both the impact and broad applicability of these findings in clinical practice. Additionally, consistent with other reports [24, 27, 30, 31], our review shows that studies of exercisebased interventions (a) primarily have been feasibility studies, (b) used small samples and end-points that were not statistically powered, (c) lacked an active control group and long-term follow-up and (d) were not tailored to address the therapeutic needs facing older adults who have cognitive impairment and experience frequent falls.

To date, conclusions drawn from systematic review and meta-analysis studies, and from systematic reviews of reviews, have varied. Their results range from promising [26, 29] to conflicting [24, 27, 30]. Findings from our analyses incorporating the most recent additions to the literature also highlight the paucity of relevant research and lack of substantial data that support the efficacy of group- or homebased exercise interventions for older persons with cognitive impairment. Our updated review and other reviews [24, 29, 30] suggest that significant gaps remain. This is not surprising given that current clinical and public health guidelines and recommendations for falls prevention among community-living older persons [52] do not explicitly include a cognitively impaired population that is at high risk for falling.

Limitations

First, the number of studies involving cognitively impaired community-dwelling older adults remains very limited compared to the large quantity of research conducted using a general population of older adults [23]. Therefore, our metaanalyses may be underpowered and the results may have limited broad generalizability. Second, we did not consider trials that were conducted in other settings such as nursing care facilities [35] and hospitals [53] because of the high level of supervision in these settings.

Conclusions

Exercise-based interventions show promise in reducing falls among community-dwelling older adults with cognitive impairment. However, the statistical significance of this meta-analysis supporting this contention is primarily driven by a small number of studies, which calls into question the clinical significance. Although available evidence remains insufficient to inform recommendations for clinical and community practice, findings from our study should serve as an incentive for additional research to clarify the relationship between exercise and falls prevention among this high-risk population.

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