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SYSTEMATIC REVIEW

# Safety and Effectiveness of Long-Term Exercise Interventions in Older Adults: A Systematic Review and Meta-analysis of Randomized Controlled Trials

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## Abstract

**Background** Physical exercise is beneficial to reduce the risk of several conditions associated with advanced age, but to our knowledge, no previous study has examined the association of long-term exercise interventions (≥ 1 year) with the occurrence of dropouts due to health issues and mortality, or the effectiveness of physical exercise versus usual primary care interventions on health-related outcomes in older adults (≥ 65 years old).

**Objective** To analyze the safety and effectiveness of long-term exercise interventions in older adults.

**Methods** We conducted a systematic review with meta-analysis examining the association of long-term exercise interventions (≥ 1 year) with dropouts from the corresponding study due to health issues and mortality (primary endpoint), and the effects of these interventions on health-related outcomes (falls and fall-associated injuries, fractures, physical function, quality of life, and cognition) (secondary endpoints).

**Results** Ninety-three RCTs and six secondary studies met the inclusion criteria and were included in the analyses ($n = 28{,}523$ participants, mean age 74.2 years). No differences were found between the exercise and control groups for the risk of dropouts due to health issues (RR = 1.05, 95% CI 0.95–1.17) or mortality (RR = 0.93, 95% CI 0.83–1.04), although a lower mortality risk was observed in the former group when separately analyzing clinical populations (RR = 0.67, 95% CI 0.48–0.95). Exercise significantly reduced the number of falls and fall-associated injuries, and improved physical function and cognition. These results seemed independent of participants' baseline characteristics (age, physical function, and cognitive status) and exercise frequency.

**Conclusions** Long-term exercise training does not overall influence the risk of dropouts due to health issues or mortality in older adults, and results in a reduced mortality risk in clinical populations. Moreover, exercise reduces the number of falls and fall-associated injuries, and improves physical function and cognition in this population.

## 1 Introduction

The growing prevalence of physical inactivity among older adults represents an important public health problem in light of global population aging [1, 2]. For instance, only 27–44% of older U.S. adults meet international physical activity recommendations (≥ 150 min per week of moderate-to-vigorous physical activity) [3]. In this respect, regular exercise has multi-system anti-aging effects [4], and can attenuate the deleterious effects of inactivity while increasing healthy lifespan [5].

Recent systematic reviews and meta-analyses have concluded that physical exercise is beneficial to reduce the risk of several conditions associated with an advanced age, such as frailty [6], cognitive decline [7], low muscle power, or poor functional capacity [8]. There is also evidence that exercise intervention programs can prevent falls in older people with minor concomitant adverse effects [9–11]. To the best of our knowledge, however, no study has specifically analyzed the risk of dropouts from an exercise program due to health issues (adverse events, medical problems) in older persons, or the effect of this type of intervention on risk of

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**Key Points**

Long-term exercise does not influence the risk of dropouts due to health issues or mortality in older adults and results in a reduced mortality risk in clinical populations.

Exercise reduces the number of falls and fall-associated injuries and improves physical function and cognition in this population.

Long-term exercise training interventions are an effective and beneficial strategy in older adults for the prevention falls and fall-associated injuries and improvement of physical function and cognition.

mortality, with both outcomes being indicators of the safety and practical applicability of this type of lifestyle intervention in this population segment. It also remains to be determined whether the type of participant (age, health status) or intervention influences the risk of dropouts or mortality.

It was, therefore, the aim of our study to systematically review and meta-analyze (i) the association of long-term exercise programs (≥ 1 year) with dropouts due to health issues and risk of mortality in older adults (primary endpoints), and (ii) the effects of this type of intervention on health-related outcomes, including physical function, cognition status, health-related quality of life, risk of hospitalization, falls and fall-associated injuries, and fractures (secondary endpoints).

## 2 Methods

### 2.1 Protocol and Registration

This study followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement checklist [12] and is registered in the International Prospective Register of Systematic Reviews (PROSPERO) (Registration number: CRD42020139614) (Electronic Supplementary Material Appendix S1).

### 2.2 Information Sources and Search

Searches in PubMed, Cochrane Controlled Trials Registry, and SPORTDiscus combined with manual searches of existing literature were done from inception to September 16, 2019. The search strategy applied is available in Electronic Supplementary Material Appendix S2. In addition, the reference list of each of the included studies was reviewed to find potential studies that could be used in this review.

### 2.3 Eligibility Criteria and Study Selection

The criteria for a study to be included in the systematic review were the following: (i) adults aged ≥ 65 years assessed at baseline; (ii) a randomized controlled trial (RCT) design, where the control group received usual care combined or not with a nutritional or educational intervention, but no structured physical exercise intervention; (iii) the study assessed the occurrence of dropouts due to health issues and/or mortality; and (iv) the exercise intervention lasted ≥ 1 year. Regarding exercise programs, no restrictions were made in terms of combination or not with a concomitant nutritional intervention, supervision or structure (e.g., supervised group based, unsupervised home based or a combination thereof), setting (e.g., community dwellers or institutionalized), or exercise modality, frequency or intensity (i.e., whether focusing only on either muscle strength [‘resistance’] or aerobic exercises, including multicomponent exercise training [combined aerobic, muscle strength, and balance exercises], or using Tai Chi). However, when the study included a nutritional intervention (e.g., health education), both the control and exercise groups had to participate in this intervention.

We excluded those studies with the following characteristics: (i) the exercise intervention was not well defined; (ii) included subjects aged < 65 years; and (iii) did not include a control (non-exercise) group for comparison. Titles, abstracts and full texts were assessed for eligibility independently by two authors (AG-H and RR-V) for potential inclusion. If necessary, a third researcher (MI) was consulted. Finally, only those papers written in the English language were included.

### 2.4 Data Collection Process

For each study, the following data were extracted (i) first author’s last name; (ii) year of publication; (iii) country; (iv) study setting; (v) sample size, participants’ characteristics and mean age; and (vi) characteristics of the exercise (exercise modality, frequency, and duration) and control intervention.

### 2.5 Endpoints

Primary endpoints were dropouts (defined as the number of randomized participants having no post-intervention measurements available due to health issues [medical problems, adverse events]), and mortality. Secondary endpoints were the following: physical function, cognition status, health-related quality of life, risk of hospitalization (inpatient hospitalization ≥ 24 h), falls (people who fell at least once) and fall-associated injuries, and fractures (number of people who sustained a fracture). When there was insufficient information, the corresponding author of the study in question was contacted.

### 2.6 Risk of Bias of Individual Studies

The risk of bias was evaluated using the Physiotherapy Evidence Database (PEDro) criteria [13], using an 11-item scale designed for measuring the methodological quality of RCT.

### 2.7 Statistical Analyses

All analyses were carried out using Comprehensive Meta-analysis Software (2nd version, Biostat; Englewood, NJ, USA) to calculate (i) the risk ratio (RR) for dichotomous outcomes, that is, dropouts due to health issues, mortality, hospitalization, falls, and fractures; or (ii) the standardized mean difference (SMD) for continuous data (i.e., physical function parameters, cognition and health-related quality of life parameters) [14]. The RR or SMD of each parameter (from baseline to follow-up) between groups [15] was calculated and pooled using a random-effects model (DerSimonian–Laird approach). For continuous outcomes, the pooled effect size for SMD was classified as small ($0 \leq SMD \leq 0.50$), moderate ($0.50 < SMD \leq 0.80$) or large ($SMD > 0.80$) [16].

The percentage of total variation across studies due to heterogeneity (Cochran's Q test) was used to calculate the $I^2$ statistic [17], considering $I^2$ values < 25%, 25–75%, and > 75% as indicators of small, moderate, and high heterogeneity, respectively [18]. Each study was removed once from the model to analyze its individual influence on the overall results. Egger's regression tests and funnel plots were performed to detect small study effects and possible publication bias [19]. Data were pooled if outcomes were reported in at least 10 studies, because the power of the tests for funnel plot asymmetry is too low to distinguish chance from real asymmetry when fewer studies are evaluated [14].

When possible, a subgroup analysis for the primary endpoint was conducted taking into account the following potential moderators: type of exercise intervention, participants' health status (apparently healthy vs clinical population), intervention structure (supervised group based, unsupervised home based, or a combination thereof), primary mode of exercise intervention (muscle strength [or 'resistance']-based, aerobic-based, multicomponent exercise training, or Tai Chi), study setting (community dwellers *vs* institutionalized), and risk of bias (PEDro Scale score < 7 or ≥ 7) [10]. Additionally, random-effects meta-regression analyses were used to evaluate the influence of age, physical function and cognition characteristics at baseline and the frequency of exercise (number of sessions per week) in the primary endpoints (dropouts due to health issues, and risk of mortality).

## 3 Results

### 3.1 Study Selection

From the retrieved articles, 93 RCTs [1, 20–111] and 6 [112–117] secondary studies met the inclusion criteria and were included in the analyses (with secondary studies being only included to pool the secondary outcomes) (Fig. 1). However, due to missing data, we have included only 90 RCTs in the quantity analysis (meta-analysis).

### 3.2 Study Characteristics

The characteristics of the included studies are summarized in Electronic Supplementary Material Table S1. The final analysis included 28,523 participants (mean age 74.2 years). Most studies included apparently healthy older adults, but 25 RCTs were conducted in clinical populations (i.e., individuals with cancer [$n = 3$ studies], mild cognitive impairment, Parkinson, Alzheimer or dementia [$n = 11$], or cardiorespiratory [$n = 4$], renal [$n = 1$], musculoskeletal [n = 3], or metabolic [$n = 3$] disease). Participants enrolled in the different studies were predominantly from the U.S. ($n = 23$ articles), with other studies from Australia ($n = 15$), Belgium ($n = 2$), Brazil ($n = 2$), Canada ($n = 5$), Chile ($n = 2$), Denmark ($n = 2$), Finland ($n = 8$), France ($n = 3$), Germany ($n = 5$), Hong Kong ($n = 4$), Hungary ($n = 2$), Japan (n = 2), The Netherlands ($n = 1$), New Zealand ($n = 4$), South Korea ($n = 1$), Spain ($n = 2$), Sweden ($n = 2$), Taiwan ($n = 1$), Thailand ($n = 2$), or the UK ($n = 5$). Most studies included men and women except four [78, 81, 90, 118] that included only men, and 19 studies with women only [30, 33, 34, 42, 44, 49, 61, 62, 68, 69, 72, 83, 88, 89, 93, 95, 99, 103, 108]. Sample sizes across studies ranged from 20 [23, 56] to 6420 [54] participants.

The primary mode of exercise intervention was multicomponent exercise training ($n = 47$), followed by muscle strength ($n = 24$) and aerobic training (e.g., walking, dancing) (n = 19), and Tai Chi ($n = 4$). Most studies used group-based supervised exercise training alone ($n = 56$) or combined with home-based unsupervised training ($n = 21$). The duration of the interventions ranged from 52 (in most studies) to 208 [85] weeks, and training frequency ranged from 1 to 7 sessions per week, with a duration of 10–90 min per session. Most control groups were instructed to maintain usual activity levels with or without an additional non-exercise intervention (e.g., health education, social visits, or telephone calls).

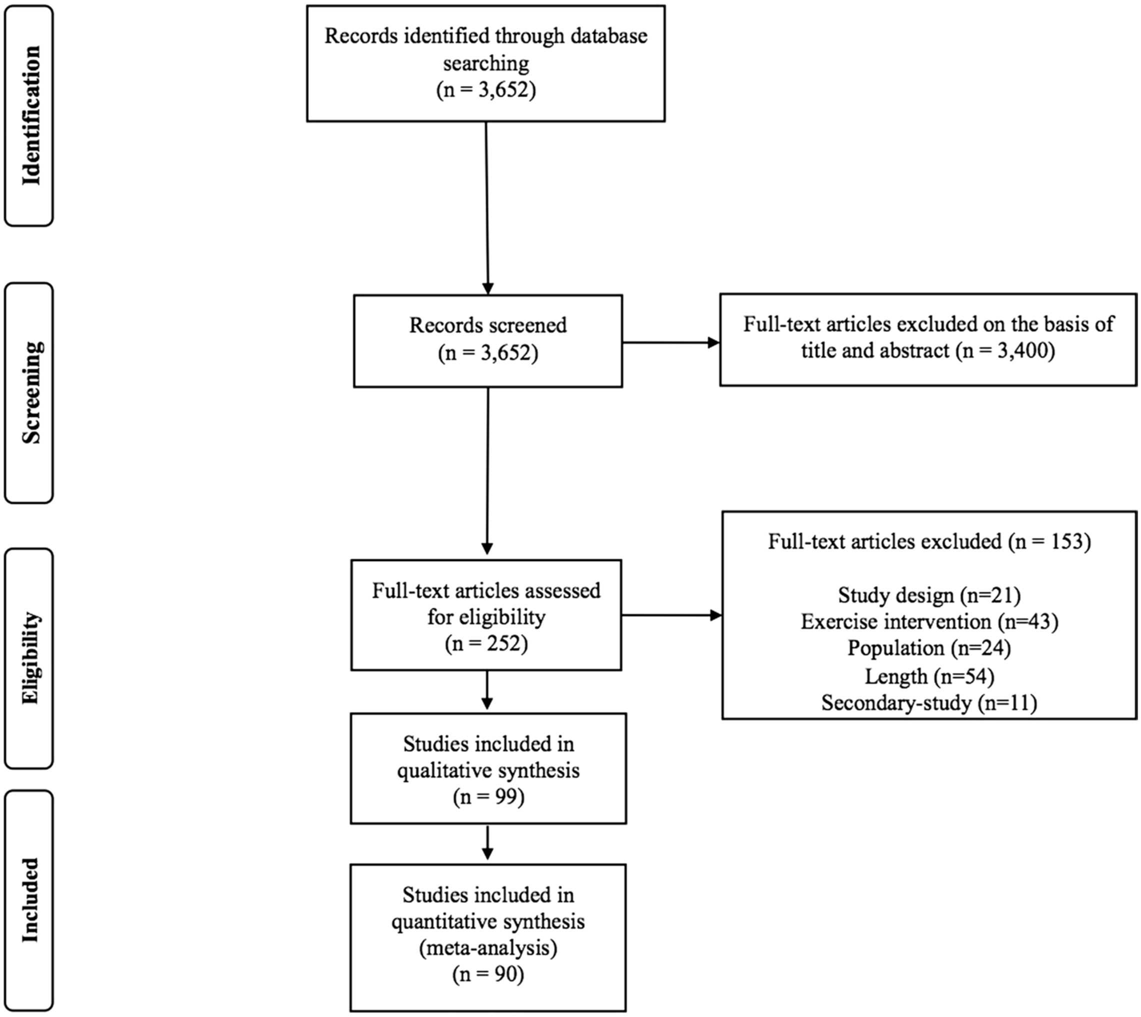


**Fig. 1** PRISMA flow diagram

### 3.3 Risk of Bias Within Studies

The average total score was 6.1 with a range of 1–8. Thirty-six studies scored 7 or higher. Low scores corresponded to studies that failed to conceal allocation (40.2%), or to blind subjects (0%), or had researchers in charge of endpoint assessment and/or exercise supervision (1.0%) (Electronic Supplementary Material Table S2).

### 3.4 Synthesis of Results

#### 3.4.1 Primary Endpoints

*Dropouts due to health issues* Forty-nine studies provided information on dropouts due to medical problems for 21,292 participants. Overall, 16.9% (1638 older adults) and 19.0% (2207 older adults) of participants dropped out of the corresponding study due to health issues in the exercise and control group, respectively (Electronic Supplementary Material Table S3). Exercise and control groups did not differ in terms of dropouts due to medical problems (RR = 1.05, 95% confidence interval [CI] 0.95–1.17), with low heterogeneity for this result ($I^2 = 14.07\%$).

All subgroup analyses provided similar results independent of the study setting, type of exercise training, or risk of bias (Table 1). The meta-regression analyses showed that participants' age, physical function or cognition at baseline, or exercise frequency (number of exercise sessions per week) was not related to risk of mortality ($\beta = -0.13$–$0.03$) (Table 2 and Electronic Supplementary Material Figure S1–S5).

There was no evidence of publication bias in the analysis of dropouts due to medical problems ($p = 0.618$), and the results remained the same in the sensitivity analysis. The funnel plot is presented in Electronic Supplementary Material Figure S6.

*Mortality* Fifty-six RCTs provided information on death for 26,017 participants. Of these, 19 reported no deaths during the trial [26, 28, 36, 38, 44, 48, 49, 55, 56, 78, 79, 81, 86, 92, 93, 103, 107, 108, 119]. Exercise intervention had no effects on mortality (RR = 0.93, 95% CI 0.83–1.04), with low heterogeneity between studies ($I^2$ = 0%). Specifically, 5.5% (664 older adults) and 5.8% (820 older adults) of participants died in the exercise and control groups, respectively (Electronic Supplementary Material Table S3). All subgroup analyses provided similar results (Table 1), except for the analysis restricted to clinical populations, which showed that exercise significantly ($p$ = 0.024) reduced the risk of mortality (RR = 0.67, 95% CI 0.48–0.95; $I^2$ = 0%) (Table 1).

**Table 1** Association of long-term exercise interventions with primary endpoints (i.e., dropouts due to health issues, and mortality). Sensitivity analyses as a function of participant's characteristics, exercise type, study setting and risk of bias are also shown

| | *n* | RR | 95%CI | *p* value | $I^2$ | Egger's *p* |
|---|---|---|---|---|---|---|
| Dropouts due to health issues | | | | | | |
| Overall | 49 | 1.05 | 0.95–1.17 | 0.338 | 14.07 | 0.618 |
| Characteristics of older adults | | | | | | |
| Clinical population | 16 | 0.82 | 0.61–1.11 | 0.212 | 0 | 0.902 |
| Apparently healthy | 37 | 1.07 | 0.94–1.22 | 0.308 | 30.63 | 0.357 |
| Type of exercise training | | | | | | |
| Multicomponent | 26 | 1.03 | 0.92–1.17 | 0.580 | 20.25 | 0.676 |
| Strength | 13 | 0.85 | 0.62–1.15 | 0.297 | 0 | 0.943 |
| Aerobic | 8 | – | | | | |
| Tai Chi | 2 | – | | | | |
| Intervention structure | | | | | | |
| Home based | 11 | 0.97 | 0.59–1.61 | 0.918 | 60.59 | 0.434 |
| Group based | 27 | 1.05 | 0.99–1.12 | 0.102 | 0 | 0.559 |
| Home and group based | 11 | 1.07 | 0.97–1.19 | 0.181 | 0 | 0.564 |
| Study setting | | | | | | |
| Community dwellers | 42 | 1.05 | 0.89–1.23 | 0.564 | 25.34 | 0.981 |
| Institutionalized | 6 | – | | | | |
| Risk of bias | | | | | | |
| PEDro score < 7 | 24 | 1.06 | 0.98–1.14 | 0.101 | 3.27 | 0.455 |
| PEDro score ≥ 7 | 24 | 1.01 | 0.78–1.30 | 0.941 | 28.30 | 0.550 |
| Mortality | | | | | | |
| Overall | 56 | 0.93 | 0.83–1.04 | 0.182 | 0 | 0.097 |
| Characteristics of older adults | | | | | | |
| Clinical population | 16 | 0.67 | 0.48–0.95 | **0.024** | 0 | 0.512 |
| Apparently healthy | 39 | 0.96 | 0.87–1.06 | 0.441 | 0 | 0.514 |
| Type of exercise training | | | | | | |
| Multicomponent | 33 | 0.95 | 0.85–1.06 | 0.376 | 0 | 0.002 |
| Strength | 12 | 1.02 | 0.75–1.40 | 0.933 | 6.56 | 0.075 |
| Aerobic | 7 | – | | | | |
| Tai Chi | 3 | – | | | | |
| Intervention structure | | | | | | |
| Home based | 13 | 1.07 | 0.83–1.39 | 0.604 | 2.89 | 0.869 |
| Group based | 33 | 0.95 | 0.84–1.07 | 0.400 | 0 | 0.030 |
| Home and group based | 9 | – | | | | |
| Study setting | | | | | | |
| Community dwellers | 48 | 0.91 | 0.81–1.01 | 0.082 | 0 | 0.075 |
| Institutionalized | 7 | – | | | | |
| Risk of bias | | | | | | |
| PEDro score < 7 | 24 | 0.95 | 0.85–1.06 | 0.347 | 2.91 | 0.410 |
| PEDro score ≥ 7 | 31 | 0.86 | 0.67–1.10 | 0.240 | 0 | 0.072 |

*CI* confidence interval, *PEDro* Physiotherapy Evidence Database, *RR* risk ratio

Significant *p* values are in bold

The meta-regression analyses showed that neither age nor physical function nor cognition at baseline was associated with risk of mortality ($\beta = -0.20$– 0.09) (Table 2 and Electronic Supplementary Material Figure S7–S11).

There was no evidence of publication bias in the analysis of mortality ($p = 0.097$), and the results remained the same in the sensitivity analysis. The funnel plot is presented in Electronic Supplementary Material Figure S12.

#### 3.4.2 Secondary Endpoints

The secondary endpoint measures (which were pooled when there were ≥ 10 studies per endpoint) were: physical function (assessed with balance tests, gait speed, knee-extension strength, timed get-up-and-go test, sit-to-stand test, and the short physical fitness battery [SPPB]), cognition status (assessed with the mini-mental state examination [MMSE]), health-related quality of life (assessed with the Short Form Health Survey [SF]-36 or SF-12), and risk of hospitalization, falls, fall-associated injuries, and fractures.

Compared with the control group, exercise interventions were associated with a significantly lower number of falls and fall-associated injuries, as well as with improvements in all analyzed physical function parameters (balance, gait speed knee-extension strength, SPPB, sit-to-stand and timed get-up-and-go tests) and cognition (MMSE) (Table 3). The forest plots are shown in Electronic Supplementary Material Figure S13–S25.

Finally, Fig. 2 illustrates how long-term physical exercise programs are safe and effective among older adults.

**Table 2** Meta-regression analysis of the association between participants' age, physical function and cognition at baseline with the primary endpoints

| | *n* | *β* | 95% CI | *p* |
|---|---|---|---|---|
| Dropouts due to health issues | | | | |
| Age | 49 | −0.01 | −0.00 to 0.01 | 0.758 |
| SPPB | 16 | 0.03 | −0.03 to 0.10 | 0.308 |
| Gait speed | 22 | −0.13 | −1.51 to 1.25 | 0.858 |
| Cognition (MMSE) | 15 | −0.01 | −0.05 to 0.05 | 0.915 |
| Frequency per week | 43 | −0.01 | −0.08 to 0.04 | 0.508 |
| Mortality | | | | |
| Age | 56 | 0.01 | −0.01 to 0.02 | 0.112 |
| SPPB | 15 | 0.09 | −0.21 to 0.39 | 0.553 |
| Gait speed | 22 | −0.20 | −1.43 to 1.03 | 0.749 |
| Cognition (MMSE) | 23 | −0.01 | −0.05 to 0.03 | 0.683 |
| Frequency per week | 49 | 0.03 | −0.05 to 0.12 | 0.450 |

*MMSE* mini-mental state examination, *SPPB* short physical fitness battery

## 4 Discussion

The present meta-analysis found that long-term (≥ 1 year) exercise training interventions in older adults do not cause more dropouts due to health issues and do not affect mortality compared with a control (usual care) group. Similar results were found for risk of hospitalization and fractures. Importantly, however, these types of interventions are associated with a lower risk of falls and fall-induced injuries, and with improvements in muscle strength, balance, physical function, and cognition. Moreover, a lower risk of mortality was found in a separate analysis for patient populations only. Therefore, long-term physical exercise is overall safe and effective in older adults, and its benefits appear to be independent of participants' age, physical function or cognition status at baseline.

To determine the safety of exercise training, we registered the number of dropouts per group due to health issues, and the pooled analysis suggests that physical exercise does not increase the risk of dropouts compared with the control group, and thus, compliance to this type of intervention does not seem to be compromised by health issues related to the intervention itself. In the same line, a recent systematic review reported only minor harms of exercise interventions aiming at preventing falls in community-dwelling older adults [11]. Therefore, our results, together with the aforementioned study [11], suggest that, beyond its practical benefits, exercise does not cause more harm among older adults than maintaining usual activity levels or usual care. Similar to the conclusions of our review, recent meta-analyses have reported that long-term exercise training does not increase the overall risk of mortality in older adults [9, 11]. The magnitude of the association for the risk of mortality in our review in patients and healthy individuals combined (56 RCTs, RR = 0.93, 95% CI 0.83–1.04) is in general agreement with the results reported by Barreto et al. [9] (RR = 0.96, 95% CI 0.85–1.09) and Guirguis-Blakeet al. [11] (RR = 0.96, 95% CI 0.79–1.17). In line with recent research [9], the risk of mortality in the general population of older adults is unlikely to be affected by exercise interventions alone. However, an important finding of our review is that long-term exercise decreases mortality risk specifically in clinical populations of older adults (16 RCTs; RR = 0.67, 95% CI 0.48–0.95). In this respect, a recent population-based cohort study reported significantly lower risk of mortality if becoming physically active among middle-aged and older patients with cardiovascular disease and cancer, which reinforces the role of physical exercise as a core therapeutic element for treating prevalent diseases [120].

Subgroup analyses revealed that type of physical exercise training, setting of the study, and risk of bias do not appear to influence the effect of exercise on the primary endpoint; that

**Table 3** Association of long-term exercise interventions with secondary endpoints (i.e., adverse events, hospitalization, cognition, health-related quality of life and physical function parameters)

| | n | RR/SMD | 95% CI | p | $I^2$ | Egger's p |
|---|---|---|---|---|---|---|
| Adverse events and hospitalization | | | | | | |
| Number of falls | 44 | *0.89* | *0.83–0.96* | **0.002** | 69.57 | 0.674 |
| Fall-associated injuries | 16 | *0.78* | *0.67–0.92* | **0.003** | 46.67 | 0.309 |
| Fractures | 24 | *0.94* | *0.80–1.11* | 0.490 | 0 | 0.376 |
| Hospitalization | 12 | *1.04* | *0.97–1.11* | 0.217 | 19.17 | 0.439 |
| Cognition | | | | | | |
| MMSE | 10 | 0.24 | 0.05–0.42 | **0.011** | 68.52 | 0.028 |
| Health-Related Quality of Life | | | | | | |
| Physical functioning (SF-36 or SF-12) | 12 | 0.03 | − 0.03–0.10 | 0.336 | 46.00 | 0.635 |
| Mental health (SF-36 or SF-12) | 12 | 0.05 | − 0.01–0.11 | 0.124 | 27.99 | 0.615 |
| Physical function parameters | | | | | | |
| Balance | 21 | 0.31 | 0.21–0.42 | **< 0.001** | 54.95 | 0.058 |
| Gait speed | 19 | 0.13 | 0.03–0.23 | **0.008** | 46.60 | 0.932 |
| Knee-extension strength | 15 | 0.28 | 0.13– 0.44 | **< 0.001** | 72.89 | 0.012 |
| SPPB | 10 | 0.16 | 0.01–0.30 | **0.040** | 70.97 | 0.587 |
| Sit to stand | 15 | − 0.27 | − 0.38 to − 0.17 | **< 0.001** | 44.42 | 0.133 |
| Timed up and Go | 18 | − 0.20 | − 0.34 to − 0.06 | **0.005** | 74.64 | 0.501 |

*CI* confidence interval, *MMSE* mini-mental state examination, *SF-12* 12-Item Short Form Survey, *SF-36* 36-Item Short Form Survey, *SPPB* short physical fitness battery

Non-italicized entries = Standardized Mean Difference values; italicized entries = Risk Ratio values

Significant *p* values are in bold

is, dropouts due to medical problems and mortality. We also evaluated the influence of age, cognition, physical function and exercise frequency on these results. With regard to age, although one could expect a priori that older participants are at greater risk of having adverse events when enrolling in an exercise program, this hypothesis was not corroborated by our results. In this respect, Hewitt et al. [41] showed a lower risk of dropouts due to health issues (RR = 0.35, 95% CI 0.15–0.91) in the exercise group, in individuals with low physical function level (SPPB score < 9) [121]. However, the results of the present meta-regression analysis should be interpreted with caution because the low number of studies might have affected the results.

With regard to secondary endpoints, our findings corroborate the results of a recent meta-analysis showing that exercise decreased the risk of falls and fall-associated injuries [9], and similar results were reported by Guirguis-Blake et al. for the US Preventive Services Task Force [11]. Thus, there seems to be compelling evidence to support the positive effects of exercise against fall-related outcomes in older adults. Furthermore, our review extends this literature by examining, for the first time, the association of long-term exercise training with several health outcomes in an elderly population, showing significant improvements in physical function and cognition parameters, and providing further support to the notion that regular exercise is necessary for healthy aging and offers multi-systemic health benefits [122].

Some limitations of our review should be acknowledged. First, health issues were recorded through dropouts and we cannot determine whether they were directly associated with physical exercise. In this regard, however, most RCTs reported only minor harms associated with exercise interventions. Second, the included RCTs were heterogeneous with respect to exercise training protocols and study population (healthy vs clinical population); however, we performed subgroup analyses to account for heterogeneity among studies. Third, most of the analyzed studies included community-dwelling older adults, and the small number of studies with institutionalized elderly people ($n = 9$) prevented us from performing a separate subgroup analysis, thereby limiting the generalizability of our results. On the other hand, a main strength of our meta-analysis is that it is, to our knowledge, the first to determine both the safety and effectiveness of long-term physical exercise interventions among older adults. Our meta-analysis provides an update and extension of the evidence reported in an earlier reviews [9], including more studies and other health outcomes. Furthermore, according to the Cochrane Handbook, and to avoid publication bias, we pooled only the results of those outcomes that were reported by at least 10 studies [14], thereby avoiding any loss of statistical power.

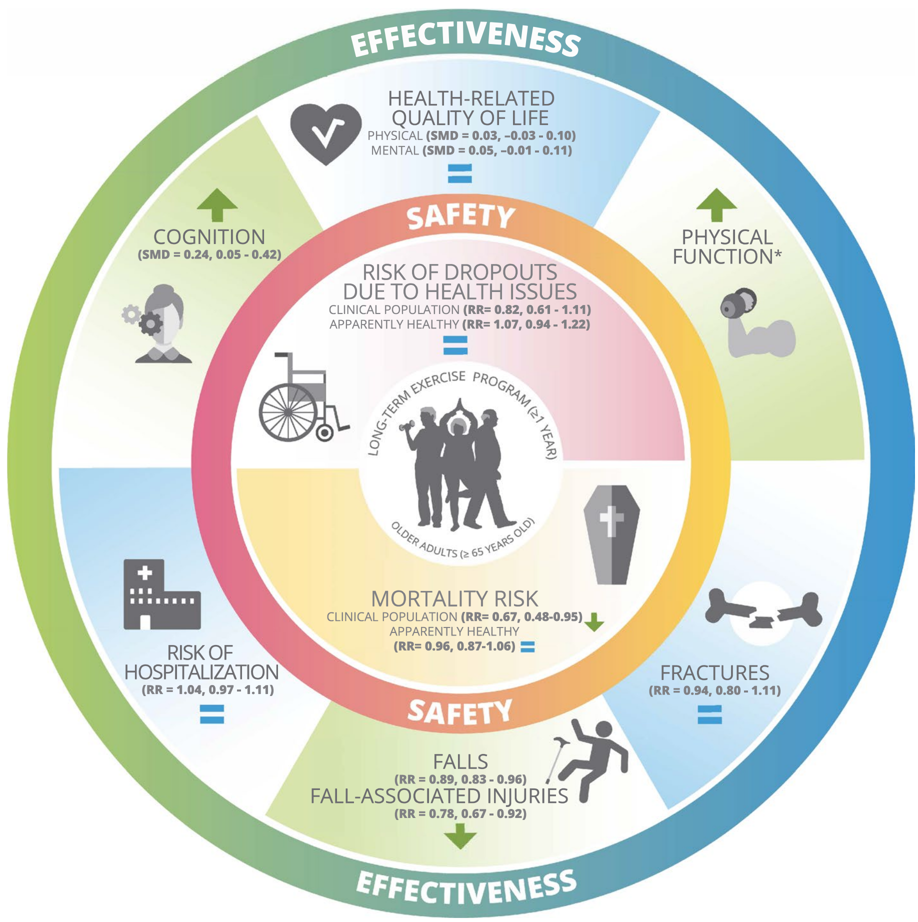


**Fig. 2** This figure illustrates how long-term physical exercise programs are safe and effective among older adults. Green arrows represent significant results and blue equal signs depict non-negative effects. Numbers in brackets represent data results for each parameter. *RR* risk ratio, *SMD* standardized mean difference. *The results are shown in Table 3

## 5 Conclusion

Compared with usual care, long-term (≥ 1 year) exercise training interventions in older adults do not increase the risk of dropouts due to health issues, mortality, hospitalization, or fractures, but do decrease the risk of falls and fall-associated injuries and mortality (although the latter only in clinical populations), while improving physical function and cognition. Therefore, health care professionals have an important role to play in reducing the prevalence of inactivity and fostering regular exercise among older adults.

**Data Availability Statement** The data that support the findings of this review are available on request from the corresponding author (Mikel Izquierdo).

## Compliance with Ethical Standards

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**Conflicts of Interest** Antonio García-Hermoso, Robinson Ramirez-Vélez, Mikel López Sáez de Asteasu, Nicolás Martínez-Velilla, Fabricio Zambom-Ferraresi, Pedro Valenzuela, Alejandro Lucia and Mikel Izquierdo declare that they have no conflicts of interest relevant to the content of this review.

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