The Effect of Therapeutic Exercise Interventions on Physical and Psychosocial Outcomes in Adults Aged 80 Years and Older: A Systematic Review and Meta-Analysis

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This systematic review aimed to evaluate the effects of therapeutic exercise on physical and psychosocial outcomes in community-dwelling adults aged 80 years or older. Databases were searched from inception to July 8, 2020. Randomized controlled trials (RCTs) were screened by two reviewers who extracted data and assessed study quality. Sixteen RCTs (1,660 participants) were included. Compared to nonexercise controls there was no evidence of an effect of exercise on performance based (standardized mean differences: 0.58, 95% confidence interval: [-0.19, 1.36]; I²: 89%; six RCTs; 290 participants; very low-quality evidence) or self-reported physical function (standardized mean differences: 1.35, 95% confidence interval: [-0.78, 3.48]; I²: 96%; three RCTs; 280 participants; very low-quality evidence) at short-medium term follow-up. Four RCTs reporting psychosocial outcomes could not be combined in meta-analysis and reported varying results. Exercise appeared to reduce the risk of mortality during follow-up (risk ratio: 0.47, 95% confidence interval: [0.32, 0.70]; I²: 0.0%; six RCTs; 1,222 participants; low-quality evidence).

Keywords: age 80+, exercise therapy, function, quality of life

The global population is progressively aging. Approximately 3 million people in the United Kingdom were aged 80 years or older in 2018, and this group is projected to increase to almost 6 million by 2043, making it the fastest growing population group (Office for National Statistics, 2018). Adults aged 80 years or older are the least physically active, and have the highest health care expenditure (England., 2018; Manini & Pahor, 2009). More than 85% of people aged 80 years or older in the United Kingdom reside in the community, rather than in nursing homes (Office for National Statistics, 2012). Optimizing physical function, quality of life, and psychosocial outcomes among this group is essential to facilitate ongoing independence.

Therapeutic exercise is participation in physical activity that is planned, structured, repetitive, and purposeful for the improvement or maintenance of a specific health condition (World Health Organization, 2010). The benefits of therapeutic exercise for all adults, and for many age-related conditions such as osteoarthritis and frailty, are well established (fransen et al., 2015; Fransen, McConnell, Hernandez-Molina, & Reichenbach, 2014; Heyn, Johnson, & Kramer, 2008; Silva, Aldoradin-Cabeza, Eslick, Phu, & Duque, 2017). However, adults aged 80 years and older are significantly underrepresented in existing trials, and findings among adults aged in their 60s and 70s cannot necessarily be applied to those aged 80 years or older (Izquierdo, Morley, & Lucia, 2020; Witham et al., 2020).

Adults aged 80 years or older are a more heterogeneous population than younger adults, and these exercise and cognitive function (collerton et al., 2016; Lafortune, Bélard, Bergman, & Ankri, 2009; Santoni et al., 2015). In addition, loss of muscle strength accelerates from 10% to 15% per decade up to the age of 70 years, to 25% to 40% per decade beyond 70 years of age (Goodpaster et al., 2006; Hughes et al., 2001). Adults aged 80 years and older are often excluded from randomized controlled trials (RCTs) of exercise interventions for older adults, and clinically are less likely to be prescribed exercise than younger people (Smith, Collier, Smith, & Mansfield, 2019; Witham et al., 2020). A recent U.K. research priority setting exercise found that health professionals questioned whether exercise would have any impact on the health of people aged 80 years and older, and people aged 80 years or older raised concerns about the safety of exercise for them (James Lind Alliance, 2018).

To our knowledge no systematic reviews have been published evaluating the effects of therapeutic exercise specifically among community-dwelling adults aged 80 years or older. To inform patients, researchers, clinicians, and stakeholders about the effectiveness of therapeutic exercise for this rapidly growing population group a comprehensive review is required. Findings will also provide knowledge that will support the development of a therapeutic exercise intervention for people aged 80 years or older.

The objective of this systematic review was to evaluate the effects of therapeutic exercise interventions on physical function, health-related quality of life, and psychosocial outcomes in community-dwelling adults aged 80 years or older.
Methods

This review is reported according to the Preferred Reporting Items for Systematic Review and Meta-Analyses guidelines (Moher, Liberati, Tetzlaff, & Altman, 2009). The protocol was prospectively registered with the International Prospective Register of Systematic Reviews database (PROSPERO: CRD42020196697).

Search Strategy

The search strategy was developed in consultation with an academic librarian from the University of Oxford. Three components of the search strategy were developed separately (population, exercise, and RCTs), then combined using database-specific truncation terms. Search terms included controlled vocabulary (e.g., MeSH) and free-text terms. We searched the MEDLINE (via OVID), EMBASE (via OVID), and CINAHL (via EBSCOHost) databases from inception to July 8, 2020. No date or language limits were applied. The search strategy for MEDLINE is presented in Supplementary Table S1 (available online), and this was translated to the relevant syntax for each database. Supplementary searches of reference lists of included studies, relevant systematic reviews and the World Health Organization’s International Clinical Trials Registry (http://apps.who.int/trialsearch) were also undertaken.

Study Selection

Randomized controlled trials involving therapeutic exercise for community-dwelling adults aged 80 years or older were eligible. Trials that included younger participants were eligible if the mean age minus 1 SD was 80 years or higher, or if there was clear presentation of results by strata for those aged 80 years or older. Trials with mixed community-dwelling and nursing home populations were eligible if <20% of the population resided in nursing homes, or if results were presented separately for community-dwelling participants. Interventions delivered to participants in inpatient hospital settings were not eligible. We excluded studies that only recruited participants affected by the following conditions: Parkinson’s disease, Huntington’s disease, Alzheimer’s disease, advanced dementia, or stroke. Due to the nature of these neurological conditions, findings in these populations may not be applicable to adults aged 80 years or older without the specific disease. Some individuals with these (and other) health conditions may be included in studies of the general community; these trials were included.

Therapeutic exercise interventions were classified according to the ProFaNE taxonomy: aerobic (aimed at cardiovascular conditioning), resistance (contracting the muscles against external force such as weights, resistance band, or body weight), functional training (utilizing functional activities such as sit to stand as the training stimulus), balance training (challenging specific aspects of the balance systems), gait training (specific correction of walking technique), flexibility (stretching exercises which are practiced and progressed), or 3D (constant movement in a controlled, fluid, repetitive way through all three spatial dimensions, e.g., Tai Chi; Lamb et al., 2011). Interventions that included more than one type of exercise were classified as multicomponent. We included therapeutic exercise interventions with or without additional interventions (e.g., diet or pharmacotherapy) as long as the cointerventions were delivered to both intervention and control groups. We excluded interventions without a structured exercise program (e.g., providing pedometers without an exercise plan). Exercise could be delivered as a group intervention or individually, in an outpatient clinical setting, the participant’s home or a community location (e.g., community center or gym). Interventions could be delivered in-person or via video consultation. Any comparator treatment, including usual care; no treatment; an alternative exercise treatment; pharmacotherapy, education or nutritional interventions were eligible.

Our primary outcomes were measures of physical function (performance-based or self-reported questionnaire) and health-related quality of life indices. Secondary outcomes were measures of psychosocial health (including anxiety, depression, and loneliness), falls, adverse events, and mortality. Trials were eligible if they reported one or more of these outcomes.

Search results were imported into Covidence (Veritas Health Innovation, Melbourne, VIC, Australia, www.covidence.org) for screening. A two-step process was used for screening and selection. In the first step, titles, and abstracts of all identified RCTs were independently screened by two reviewers (PN and VD). Following title and abstract screening, the full text of all potentially eligible articles was retrieved, and each screened independently for final inclusion by the same two reviewers (PN and VD). Disagreements were resolved through discussion, with an adjudicator (SH) available to address any unresolved disagreements.

Data Extraction

Data were extracted independently by two reviewers (PN and VD) using a customized piloted data extraction form in Microsoft Excel (Microsoft Corp., WA, DC, 2019). We extracted the following data:

- Trial design (setting, sample size, inclusion and exclusion criteria, method of recruitment, length of follow-up, number of participants randomized, and number analyzed in the intervention, and comparator groups).
- Characteristics of participants (age, gender, ethnicity, number randomized/analyzed, and dropouts in each arm).
- Type of intervention (experimental/control components). Exercise details: type, supervised/unsupervised, group/individual, duration (weeks), frequency (per week), and intensity (subjective: e.g., self-rated scale or objective: e.g., heart rate monitor).
- Adherence to intervention (method of assessment and reported data).
- Outcomes measured (all time points). We extracted information on differences in outcomes between groups at follow-up only. We categorized follow-up as short-term (≥3 months postrandomization), intermediate term (4–11 months postrandomization), and long term (≥12 months postrandomization). To avoid multiplicity, we selected one outcome measure when multiple outcome measures were reported for the same outcome in a trial. For performance-based physical function we prioritized: (a) the Timed Up and Go Test, (b) Sit to stand test (5× sit to stand or 30-s sit to stand), and (c) Tinetti test. For self-reported physical function we prioritized (a) the Barthel Index and (b) any other self-reported measures of physical function. For health-related quality of life outcomes we prioritized (a) the EuroQol Group 5-Dimension Self-Report Questionnaire, (b) the 36-Item Short Form Survey or the 12-Item Short Form Survey, and (c) any other self-reported health-related quality of life measure. For anxiety symptoms we prioritized (a) the anxiety subscale of the Hospital Anxiety and Depression Scale (anxiety) and (b) any other self-reported anxiety measure. For depression symptoms we prioritized (a) the depression subscale of the Hospital Anxiety and Depression Scale (depression) and (b) any other self-reported depression measure.
• Adverse events, categorized according to the U.S. Food and Drug Administration definition of serious and nonserious (U.S. Food and Drug Administration, 2020), and mortality.

If data were not reported in full in the published manuscript we emailed the corresponding author on two occasions, 1 month apart (if required) requesting the missing data.

Risk of Bias Assessment and Overall Evaluation of the Quality of the Evidence

Two reviewers (PN and VD) independently assessed the risk of bias of each included trial using the Revised Cochrane Risk of Bias Tool 2.0 (RoB 2; Sterne et al., 2019). Any disagreements in assessment between the two reviewers were discussed until consensus was reached.

We assessed the risk of bias for five domains: bias arising from the randomization process or lack of allocation concealment, bias due to deviations from intended interventions, bias due to missing outcome data, bias in measurement of the outcome (blinding), and bias in selection of the reported result. Within each domain, the two reviewers answered one or more signaling questions leading to judgments for each domain as “high risk of bias,” “some concerns,” or “low risk of bias.” The judgments within each domain led to an overall risk of bias judgment (Higgins et al., 2020).

The overall quality of evidence was evaluated using the GRADE (Grading of Recommendations Assessment, Development and Evaluation) approach (Cochrane Handbook for Systematic Reviews of Interventions, 2019). GRADE is a systematic approach to rate the certainty of evidence (high, moderate, low, or very low) across studies for each outcome of interest. Five domains are assessed, including methodological flaws of the included studies, heterogeneity of results across trials, generalizability of the findings to the target population, precision of the estimates, and risk of publication bias.

Data Synthesis

Descriptive characteristics of all included trials were summarized in tables and synthesized in narrative format by outcome. We performed meta-analyses using a random effects model as heterogeneity was expected in participant, intervention, and outcome characteristics. For continuous outcomes measured using the same scale we calculated the mean difference (MD) and for continuous outcomes measured using different scales we calculated the standardized mean differences (SMDs) with 95% confidence intervals (CIs). For binary outcomes we calculated the risk ratio (RR). Statistical heterogeneity across pooled studies was quantified using the $I^2$ statistic (Higgins et al., 2011). Separate meta-analyses were undertaken for studies using nonexercised comparators and trials using a different type of exercise as the comparator. Forest plots were presented by exercise type. Trials with short-medium term follow-up were combined due to the small number of studies, and those with long-term follow-up were analyzed separately. When trials reported multiple time points in one category the longest time point was included in meta-analysis. Meta-analyses were undertaken using Review Manager (Review Manager (RevMan) [Computer program]. Version 5.4, The Cochrane Collaboration, 2020).

Sensitivity Analysis

Where sufficient trials were identified, sensitivity analyses were planned to assess the effects of the exercise interventions excluding trials that included participants younger than 80 years of age; that had one or more “high risk” domains of risk of bias. Meta-regression to explore the impact of trial level characteristics on outcomes was also planned where ≥10 studies provided data for each outcome. Due to the limited number of studies included in each of the meta-analyses, meta-regression was not undertaken.

Results

Study Selection

The literature search identified 5,232 unique citations. Of these, 46 articles progressed to full-text eligibility review. We included 16 RCTs (reported in 20 articles) in narrative analysis, and 10 of these in quantitative analysis (Figure 1).

Characteristics of Included Studies

Characteristics and details of the 16 included RCTs (1,660 participants) are presented in Table 1. Studies were published between 1997 and 2020. Trials were conducted across 13 countries, most commonly in Northern Europe (four studies; Bårdstu et al., 2020; Bechshoft et al., 2017; Hvid et al., 2016; Luukinen et al., 2006; Luukinen et al., 2007) or Australia/New Zealand (three studies; Campbell et al., 1997; Hamdorf & Penhall, 1999; Rosie & Taylor, 2007). Three RCTs were conducted in communities specifically developed for older adults (retirement villages or senior communities where older people lived independently; Bonnefoy et al., 2003; de Bruin & Murer, 2007; Hartshorn, Delage, Field, & Olds, 2002). All other RCTs were conducted with people aged 80 years or older who resided independently in the wider community.

Sample sizes of included RCTs varied widely (range: 26–486). The median sample size was 61. Participants had a median age of 84.2 years (interquartile range: 83.4–86.1 years). The 12 RCTs that recruited both male and female participants included a median of 72.4% females (interquartile range: 61.5–82.9%). Three RCTs recruited only females (Campbell et al., 1997; Hamdorf & Penhall, 1999; Kim et al., 2019), and one RCT included only male participants (Kalapotharakos, Diamantopoulos, & Tokmakidis, 2010).

Risk of Bias

Only one of the included RCTs (Campbell et al., 1997) was deemed low risk of bias overall (Supplementary Table S2 [available online]). Ten of the 16 RCTs (Ansai, Aurichio, Goncalves, & Rebelatto, 2016; Ansai & Rebelatto, 2015; Bårdstu et al., 2020; Bechshoft et al., 2017; Bonnefoy et al., 2003; Gine-Garriga et al., 2010; Hartshorn et al., 2002; Kim et al., 2019; Luukinen et al., 2006; Rosie & Taylor, 2007; Siemonsma et al., 2018) were deemed as “some concerns” and five (Cancela Carral, Pallin, Orbeozgo, & Ayan Perez, 2017; de Bruin & Murer, 2007; Hamdorf & Penhall, 1999; Hvid et al., 2016; Kalapotharakos et al., 2010) were rated as “high” risk. Sources of bias were most commonly Domain 3 (missing outcome data) and Domain 4 (measurement of the outcome).

Intervention and Comparator Groups

The most common type of exercise intervention was multicomponent ($n = 7$, all included resistance training; Ansai et al., 2016; Bonnefoy et al., 2003; Campbell et al., 1997; de Bruin & Murer, 2007; Gine-Garriga et al., 2010; Kim et al., 2019; Luukinen et al., 2006), followed by resistance training ($n = 5$; Bårdstu et al., 2020; Bechshoft et al., 2017; Cancela Carral et al., 2017; Hvid et al., 2016; Kalapotharakos et al., 2010; Perez, 2017; de Bruin & Murer, 2007; Hamdorf & Penhall, 1999; Hvid et al., 2016; Kalapotharakos et al., 2010)
et al., 2010), aerobic exercise ($n=2$; Cancela Carral et al., 2017; Hamdorf & Penhall, 1999), functional training ($n=2$; Rosie & Taylor, 2007; Siemonsma et al., 2018), and 3D exercise ($n=1$; Hartshorn et al., 2002). Intervention duration ranged from 2 weeks (Hartshorn et al., 2002) to 24 months (Campbell, Robertson, Gardner, Norton, & Buchner, 1999; median duration: 12 weeks). Intensity of exercise training was reported in nine of the included RCTs (Ansai et al., 2016; Bårdstu et al., 2020; Bechshoft et al., 2017; Cancela Carral et al., 2017; de Bruin & Murer, 2007; Gine-Garriga et al., 2010; Hamdorf & Penhall, 1999; Hartshorn et al., 2002; Kalapotharakos et al., 2010; Luukinen et al., 2006). Exercise intensities varied, resistance training was most commonly at 70% of one to three repetition maximum, and aerobic exercise was most commonly at 60% of maximum heart rate.

All trials provided partial or total supervision of exercise interventions. Three RCTs included unsupervised home exercises in addition to supervised sessions (Campbell et al., 1997; Luukinen et al., 2006; Rosie & Taylor, 2007). Exercise interventions were delivered in group settings ($n=8$; Bonnefoy et al., 2003; Cancela Carral et al., 2017; de Bruin & Murer, 2007; Gine-Garriga et al., 2010; Hamdorf & Penhall, 1999; Hartshorn et al., 2002; Kalapotharakos et al., 2010; Kim et al., 2019), individually ($n=7$; Ansai et al., 2016; Bårdstu et al., 2020; Bechshoft et al., 2017; Campbell et al., 1997; Hvid et al., 2016; Rosie & Taylor, 2007; Siemonsma et al., 2018), and as a combination of group and individual sessions ($n=1$; Luukinen et al., 2006). Exercise interventions were performed at community health centers or community facilities ($n=9$; Bårdstu et al., 2020; Bonnefoy et al., 2003; Cancela Carral et al., 2017; de Bruin & Murer, 2007; Gine-Garriga et al., 2010; Hamdorf & Penhall, 1999; Hartshorn et al., 2002; Kalapotharakos et al., 2010; Luukinen et al., 2006), in participants’ homes ($n=4$; Bechshoft et al., 2017; Campbell et al., 1997; Rosie & Taylor, 2007; Siemonsma et al., 2018), or at university testing facilities ($n=2$; Ansai et al., 2016; Kim et al., 2019).

Comparator groups varied widely. Nonexercise comparators (13 RCTs) included health education (Gine-Garriga et al., 2010), physical activity counseling (Bårdstu et al., 2020), memory sessions (Bonnefoy et al., 2003), social visits (Campbell et al., 1997), protein supplementation (Bechshoft et al., 2017; Kim et al., 2019), preventative physical therapy (Siemonsma et al., 2018), usual care (Luukinen et al., 2006), and wait list control (Ansai et al., 2016; Hamdorf & Penhall, 1999; Hartshorn et al., 2002; Hvid et al., 2016; Kalapotharakos et al., 2010). Exercise comparator groups were used in five RCTs (Ansai et al., 2016; Cancela Carral et al., 2017; de Bruin & Murer, 2007; Kalapotharakos et al., 2010; Rosie & Taylor, 2007). Two trials compared multicomponent interventions to resistance exercises (Ansai et al., 2016; de Bruin & Murer, 2007), one study used resistance training followed by a detraining period (Kalapotharakos et al., 2010), one trial compared aerobic,
| Study                                      | Country     | Sample size | Inclusion criteria                                                                                                                                                                                                 | Exclusion criteria                                                                                                                                                                                                                             | Mean age (SD) %Women | Exercise intervention type                                      | Exercise intervention frequency/duration | Adherence                                                                                                                                                                                                 | Control intervention | Follow-up time point/s | Outcome/s          |
|-------------------------------------------|-------------|-------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------|---------------------------------------------------------------|-------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------|-----------------------|----------------------|
| Ansai and Rebelatto (2015); Ansai et al. (2016) | Brazil      | 69          | Aged 280 years, community-dwelling, sedentary, and able to walk alone with/without walking aid                                                                                                                         | Any absolute CI to exercise; MMSE score < educational level – 1SD                                                                                                                                  | 82.4 (2.4) 68.1% female | Multicomponent: aerobic, resistance, and balance exercises   | Supervised at university gym Individual                          | 60 min 3×/week 16 weeks                                                                                                                                                                                    | Session attendance Adherent ≥24/48 sessions: 34.7% MT group; and 56.5% RT group | 16 weeks 22 weeks | TUGT motor TUGT cognitive 5× STS GDS Falls                  |
| Bårdstu et al. (2020)                      | Norway      | 110         | Aged 270 years, living at home, and receiving home care due to disabilities                                                                                                                                          | Serious cognitive impairment, physical conditions that could affect testing/training, and any other CI for training                                                                                     | 86.5 (range 80–90) 66% female | Resistance + protein supplement                               | Supervised at local health centers Individual                    | Session attendance Mean: 51%                                                                                                                                                                                 | Physical activity counseling | 4 months 8 months | 5× STS 8 foot up and go Usual gait speed Maximum gait speed Stair climb |
| Bechshøft et al. (2017)                    | Denmark     | 26          | Aged 283 years; living in one suburb of Copenhagen                                                                                                                                                                     | Any CI for training or MRI, unstable cardiac arrhythmia, GOLD 3–4, GFR <30 ml/min, diabetes, severe cognitive impairment, systemic corticosteroid, or anticoagulants for training                                                                                     | 86.9 (3.2) 38% female | Resistance + protein supplement                               | Supervised at home OR in training facilities at local nursing homes Individual | 3 × 12 repetitions increasing to 5 × 6 repetitions 3×/week 12 weeks                                                                                                                                 | Session attendance Mean: 32 ± 1/36 sessions | Protein supplement 12 weeks | 30 s STS Usual gait speed DMMI |
| Bonnefoy et al. (2003)                     | France      | 57          | “Frail older adults;” resident in retirement homes (independent living)                                                                                                                                               | Uncontrolled diseases; dementia, Type 1 diabetes, severe renal insufficiency, long-term corticosteroid therapy, and age <72 years                                                                                       | Exercise 83.0 (1.1) Control 84.0 (1.1) 87.7% female | Multicomponent: resistance and balance and flexibility exercises | Supervised at retirement home Group                             | 60 min 3×/week 9 months                                                                                                                                                                               | Session attendance Mean: 3 months: 70% 9 months: 63% | 3 months 9 months | 5× STS Usual gait speed 6x stair climb                      |
| Campbell et al. (1997, 1999)              | New Zealand | 233         | Women, aged 280 years; able to move around own home, and not receiving physiotherapy                                                                                                                                 | Deemed unsafe to take part by GP                                                                                                                                                                     | Exercise 84.1 (3.3) 100% female 2 years follow-up: 83.9 (3.0) 100% female | Multicomponent: resistance, balance, and functional + walking program | 4× home visits + unsupervised home program Individual            | 30 min 3× week 12 months                                                                                                                                                                               | Exercise diary calendar (monthly) 12 months: 42% completing exercises ≥3×/week | 6 months 12 months 24 months | 5× STS Physical self-maintenance scale Falls               |
| Study                          | Country      | Sample size | Inclusion criteria                                                                 | Exclusion criteria                                                                                   | Mean age (SD) %Women | Exercise intervention type                          | Exercise intervention delivery | Exercise intervention frequency/duration | Adherence | Control intervention | Follow-up time point/s | Outcome/s               |
|-------------------------------|--------------|-------------|-----------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------|----------------------|--------------------------------------------------|-----------------------------------|---------------------------------------|-----------|----------------------|-------------------------|--------------------------|
| Cancela Carral et al. (2017)  | Spain        | 36          | Aged ≥80 years, attending day care centers for older adult, and able to follow simple instructions | Unstable cardiovascular, metabolic, neuromuscular conditions, and any chronic disease that could limit training | 87.91 (4.70) 80.6% female | 1. Aerobic (seated exercises) 2. Resistance (seated exercises) | Supervised at day care centers Group | 45 min 3× week 12 weeks | Session attendance 37/50 attended >80% of the sessions | Joint mobility exercises | 3 months | TINETTI test Barthe Index TUGT |
| de Bruin and Murer (2007)     | Switzerland  | 32          | Aged ≥70 years, resident in senior’s hostel (independent living), and able to walk 6 m | Severe cognitive impairment, rapidly progressive illness, MI, lower extremity fracture within 6/12, insulin-dependent diabetes, and undergoing resistance training | 85.4 (5.4) 91.7% female | Multicomponent: resistance + functional exercises | Supervised at senior’s hostel Group | Resistance: 45 min 2×/week + Function: 30 min 1× week 12 weeks | Session attendance “One participant excluded as they attended only 54% of the sessions” Resistance exercises | 12 weeks | TINETTI test 5× STS |
| Giné-Garriga et al. (2010, 2013) | Spain        | 51          | Aged 80–90 years, classified as frail (physical tests + CES-D or Fried criteria) | Unable to walk, undergoing exercise, severe dementia, stroke, hip fracture, MI, THR, or TKR within 6/12 | 84 (2.9) | Multicomponent: resistance + functional exercises | Supervised at primary care facilities Group | 45 min 2× week 12 weeks | Session attendance 90% completed all 24 exercise sessions | Health education meetings | 12 weeks | 36 weeks | Barthe Index 5× STS Usual gait speed Fast gait speed TUGT motor cognitive SF-12 |
| Hamdorf and Penhall (1999)    | Australia    | 49          | Women, community-dwelling, sedentary, and not functionally impaired | Participating in formal programs or were regularly active; CI or exercise testing (medical screening) | Exercise 82.4 (SEM: 0.66) Control 83.1 (SEM: 0.69) 100% female | Aerobic (walking) | Supervised in community outdoor spaces Group | 5 min in Week 1 to 25 min in Week 22 2× week 6 months | Session attendance Mean: 89.7% | No intervention | 6 months | Philadelphia Geriatric Morale scale |
| Hartshorn et al. (2002)       | United States| 32          | Resident in retirement community | NR | 3D (movement therapy) | Supervised in retirement community Group | 50 min 2×/week 2 weeks | NR | Wait list control | 2 weeks | TINETTI test POMS |

(Ahead of Print)
| Study | Country | Sample size | Sample inclusion criteria | Exclusion criteria | Mean age (SD) | Exercise intervention type | Exercise intervention delivery | Exercise intervention frequency/duration | Adherence | Control intervention | Follow-up time point/s | Outcome/s |
|-------|---------|-------------|---------------------------|--------------------|---------------|--------------------------|-------------------------------|----------------------------------|-----------|----------------------|------------------------|-----------|
| Hvid et al. (2016) | Denmark | 65 | Aged ≥75 years, 3-m usual gait speed <0.90 m/s, and MMSE score >21 | Amputation, major physical impairments, terminal disease, surgery or fractures within 6/12, uncontrolled hypertension (BP > 160/100 mmHg), and severe pain | Exercise 82.3 (1.3) | Resistance (high intensity) | Supervised (location NR) Individual | 12 weeks | Session attendance/ completion 80% of participants attended ≥20/24 sessions and completed ≥80% of each session | No intervention | 12 weeks | Maximum gait speed |
| Kalapotharakos et al. (2010) | Greece | 47 | Men, aged ≥80 years, and independent BDL/IADL | Cognitive impairment; unstable chronic disease that would limit exercise | Resistance 83.4 (2.8) | Resistance | Supervised at older adults public care centre Group | 60 min 2×/week 14 weeks | Session attendance Mean: 8 weeks: 90% 14 weeks: 85% | 1. Resistance + detraining period 2. No intervention | 12 weeks | TUGT 5× STS 6-min walk |
| Kim et al. (Ahead of Print) | Japan | 126 | Aged ≥75 years, community-dwelling, walking speed <1.0 m/s, step width >10 cm, and stride length <100 cm | Severely impaired mobility or unstable cardiac conditions unsafe to exercise | Ex + protein: 82.8 (2.8) Ex + placebo: 83.1 (3.3) Protein: 82.9 (2.9) Placebo: 83.8 (3.3) | Multicomponent: resistance, balance + gait retraining + protein supplement | Supervised at university department Group | 60 min 2× week 12 weeks | NR | 1. Protein supplement 2. Placebo supplement | 12 weeks | TUGT Usual walking speed Grip strength |
| Luukinen et al. (2006, 2007) | Finland | 486 | ≥2 falls in past 12/12, loneliness, poor self-rated health, depression, low cognitive status, impaired vision/hearing/balance, slow walking speed, and difficulty standing from chair | NR | Multicomponent (pragmatic, personalized exercise plan) | Supervised at community centers and/or home based. Group and/or individual | Variable. Home exercises daily. Median duration: 16 months | NR | Routine care | 28 months | ADL score Mobility score Self-reported (verified) falls |
Table 1 (continued)

| Study                              | Country       | Sample size | Inclusion criteria                                                                 | Exclusion criteria                                                                 | Mean age (SD) | Women (%) | Exercise intervention type       | Exercise intervention frequency/duration | Adherence | Control intervention | Follow-up time point/s | Outcome/s |
|------------------------------------|---------------|-------------|-------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------|---------------|------------|-------------------------------|------------------------------------------|------------|----------------------|------------------------|------------|
| Rosie and Taylor (2007)            | New Zealand   | 68          | Aged ≥80 years, able to walk 4 m, sedentary, limited “a lot” in >1 activity in SF-36 PF-10 | Receiving physiotherapy, medically unstable, and any CI for exercise               | 85.2 (3.6)   | 71.2%      | Functional training (repeated STS with biofeedback) | Supervised + unsupervised at home. Individual | Daily 6 weeks | Exercise diary (number of days exercises completed) Mean: 31/42 days 74% | 6 weeks | 30-s STS 15-s step test Usual gait speed LLFDI Falls Efficacy Scale |
| Siemonsma et al. (2018)            | The Netherlands | 155         | Aged ≥75 years, MMSE ≥18, speak Dutch                                               | Admitted to nursing home, life expectancy <3 months, serious psychiatric illness, inability to follow instructions, and current phsyiotherapy | Exercise 84.0 (Q1 79.4; Q3 88.7) 72% female Control 839 (80.2; 86.4) 75% female | Functional training | Supervised at home. Individual | Up to 18 sessions 12 weeks | NR | Preventative physical therapy | 12 weeks | TUGT 5× STS GARS Modified Katz-15 |

Note: ADL = activities of daily living; BDL/IADL = basic activities of daily living / instrumental activities of daily living; CES-D = Center for Epidemiological Studies-Depression; CI = contraindications; Con = control; DMMI = DeMorton Mobility Index; Ex = exercise; GARS = Groningen Activities Restriction Scale; GDS = Geriatric Depression Scale; GFR = glomerular filtration rate; GOLD = Global Initiative for Chronic Obstructive Lung Disease scale; GP = general practitioner; LLFDI = Lower Limb Functional Disability Index; MI = myocardial infarction; MMSE = Mini-Mental State Examination; MRI = magnetic resonance imaging; MT = multicomponent training; NR = not reported; POMS = profile of mood states; RT = resistance training; SF36 PF-10: short form-36 Questionnaire physical function component; STS = sit to stand; THR = total hip replacement; TKR = total knee replacement; TUGT = Timed Up and Go test; BP = blood pressure; SF-12 = 12-Item Short Form Survey; SF-36 = 36-Item Short Form Survey.
resistance and joint mobility exercise interventions (Cancela Carral et al., 2017), and one compared a functional training program to resistance exercises (Rosie & Taylor, 2007). Two RCTs (Ansai et al., 2016; Kalapotharakos et al., 2010) included both nonexercise and exercise comparisons.

Adherence to exercise interventions was measured in three quarters of included RCTs \( (n = 12; \text{Ansai} \ et \ al., \ 2016; \text{Bårdstu} \ et \ al., \ 2020; \text{Bechshoft} \ et \ al., \ 2017; \text{Bonnefoy} \ et \ al., \ 2003; \text{Campbell} \ et \ al., \ 1997; \text{Cancela Carral} \ et \ al., \ 2017; \text{de Bruin} \ & \text{Murer}, \ 2007; \text{Gine-Garriga} \ et \ al., \ 2010; \text{Hamdorf} \ & \text{Penhall}, \ 1999; \text{Hvid} \ et \ al., \ 2016; \text{Kalapotharakos} \ et \ al., \ 2010; \text{Rosie} \ & \text{Taylor}, \ 2007). \) Adherence was most commonly measured by attendance at supervised sessions (10 RCTs; Ansai et al., 2016; Bårdstu et al., 2020; Bechshoft et al., 2017; Bonnefoy et al., 2003; Cancela Carral et al., 2017; de Bruin & Murer, 2007; Gine-Garriga et al., 2010; Hamdorf & Penhall, 1999; Hvid et al., 2016; Kalapotharakos et al., 2010). Adherence to exercise sessions varied widely from 51% to 92% (mean attendance) of the scheduled sessions (Table 1).

### Outcomes

Follow-up periods ranged from 2 weeks to 24 months (median follow-up: 6 months). Physical function was reported in 14 RCTs, of which 13 used performance-based measures (Ansai et al., 2016; Bårdstu et al., 2020; Bechshoft et al., 2017; Bonnefoy et al., 2003; Campbell et al., 1997; Cancela Carral et al., 2017; de Bruin & Murer, 2007; Gine-Garriga et al., 2010; Hamdorf & Penhall, 1999; Hvid et al., 2016; Kalapotharakos et al., 2010; Kim et al., 2019; Rosie & Taylor, 2007; Siemonsma et al., 2018) and five used self-reported measures (Bechshoft et al., 2017; Campbell et al., 1997; Cancela Carral et al., 2017; Luukinen et al., 2006; Rosie & Taylor, 2007). Health-related quality of life was reported in one RCT only (Gine-Garriga, Guerra, & Unnithan, 2013). Psychosocial outcomes (depressive symptoms, morale, or mood) were reported in four RCTs (Ansai & Rebelatto, 2015; Hamdorf & Penhall, 1999; Hartshorn et al., 2002; Luukinen et al., 2006). Falls were reported in four RCTs (Ansai et al., 2016; Campbell et al., 1997; Luukinen et al., 2006; Rosie & Taylor, 2007).

#### Therapeutic exercise compared to nonexercise comparators.

**Performance-based physical function:** Nine RCTs reported on performance-based physical function, most commonly using the Timed Up and Go Test \( (n = 7). \) There was no evidence of a difference in effect between therapeutic exercise and nonexercise comparators on performance-based physical function at short-medium term follow-up (SMD: 0.58, 95% CI \([-0.19, 1.36]\); \(I^2: 89\%\); 6 RCTs; 290 participants; very low-quality evidence; Figure 2). This finding was consistent across exercise types. No data were reported for long-term follow-up.

**Self-reported physical function:** Five RCTs reported self-reported measures of physical function. There was no evidence of a difference in effect between therapeutic exercise and nonexercise comparators on self-reported physical function at short-medium term follow-up (SMD: 1.35, 95% CI \([-0.78, 3.48]\); \(I^2: 96\%\); three RCTs; 280 participants; very low-quality evidence; Figure 3). None of the RCTs included in meta-analysis used the same outcome measure, contributing to the observed high level of heterogeneity. This finding was consistent across exercise types. No data were reported for long-term follow-up.

**Health-related quality of life:** The single RCT that reported health-related quality of life (Gine-Garriga et al., 2013; \(n = 51\)) found statistically significant benefits of a multicomponent exercise intervention compared to a nonexercise control on the physical function subscale of the 12-Item Short Form Survey, and the physical and mental composite scores at both short- and medium-term follow-ups (Table 2).

| Study or subgroup | Control Mean SD Total | Exercise Mean SD Total | Weight | SMD IV, random, [95% CI] | SMD IV, random, [95% CI] |
|-------------------|----------------------|------------------------|--------|--------------------------|--------------------------|
| **1.4.1 Multicomponent exercise** | 28 15.2 12 | 31.1 22.8 22 | 14.5% | \(-0.15 [-0.85, 0.56]\) | \(-0.15 [-0.85, 0.56]\) |
| Ansai et al. (2016) | 41.34 1.42 19 | 35.04 1.32 22 | 11.8% | 4.52 [3.32, 5.72] | 4.52 [3.32, 5.72] |
| Gine-Garriga et al. (2010) | 9.74 2.42 32 | 8.6 2.11 31 | 15.4% | 0.50 [-0.01, 1.00] | 0.50 [-0.01, 1.00] |
| Subtotal [95% CI] | 63 | 75 | 41.7% | 1.55 [-0.50, 3.59] | 1.55 [-0.50, 3.59] |
| Heterogeneity: \(t^2 = 3.09; \chi^2 = 45.23, df = 2 (p < .00001); I^2 = 96\%\) | \(Z = 1.48 (p = .14)\) | \(Z = 1.48 (p = .14)\) |

| **1.4.2 Resistance exercise** | 28 15.2 11 | 28.1 15.3 23 | 14.4% | \(-0.01 [-0.72, 0.71]\) | \(-0.01 [-0.72, 0.71]\) |
| Ansai et al. (2016) | 13.8 3.04 27 | 13.2 2.59 33 | 15.4% | 0.21 [-0.30, 0.72] | 0.21 [-0.30, 0.72] |
| Bårdstu et al. (2020) | \(-11.9\) 2.1 14 | \(-10.8\) 2.3 12 | 14.1% | \(-0.49 [-1.27, 0.30]\) | \(-0.49 [-1.27, 0.30]\) |
| Bechshoft et al. (2017) | 52 | 68 | 43.8% | \(-0.01 [-0.39, 0.38]\) | \(-0.01 [-0.39, 0.38]\) |
| Subtotal [95% CI] | \(Z = .03 (p = .98)\) | \(Z = .03 (p = .98)\) |

| **1.4.3 3D exercise** | \(-18.24\) 5.02 16 | \(-19.38\) 5.51 16 | 14.5% | 0.21 [-0.48, 0.91] | 0.21 [-0.48, 0.91] |
| Hartshorn et al. (2002) | 16 | 16 | 14.5% | 0.21 [-0.48, 0.91] | 0.21 [-0.48, 0.91] |
| Subtotal [95% CI] | \(Z = .59 (p = .55)\) | \(Z = .59 (p = .55)\) |

| Total [95% CI] | 131 | 159 | 100.0% | 0.58 [-0.19, 1.36] | 0.58 [-0.19, 1.36] |
| Heterogeneity: \(t^2 = 0.95; \chi^2 = 54.47, df = 6 (p < .00001); I^2 = 89\%\) | \(Z = 1.47 (p = .14)\) | \(Z = 1.47 (p = .14)\) |
| Test for subgroup differences: \(t^2 = 2.29, df = 2 (p = .32); I^2 = 12.8\%\) | \(Z = 1.47 (p = .14)\) | \(Z = 1.47 (p = .14)\) |

**Figure 2** — Forest plot for the effect of therapeutic exercise compared to a nonexercise comparator group on performance-based physical function. SMD = standardized mean difference; CI = confidence interval.
Papers included in the review on exercise effects on falls were: Bårdstu et al. (2020); Bechshoft et al., 2017; Campbell et al., 1997, 1999; Hamdorf & Penhall, 1999; Hamdorf et al. (2016) reported six nonserious adverse events (mild muscle pain, mild hematoma, and dizziness) in the exercise intervention and none in the nonexercise control group. Mortality data were reported in eight RCTs (n = 1,323; Bårdstu et al., 2020; Bonnefoy et al., 2003; Campbell et al., 1997; Gine-Garriga et al., 2010; Hamdorf & Penhall, 1999; Kim et al., 2019; Luukinen et al., 2006; Siemonsma et al., 2018). Two RCTs reported no deaths in either intervention or control groups (Hamdorf & Penhall, 1999; Kim et al., 2019). Meta-analysis showed evidence that therapeutic exercise may reduce the risk of mortality during follow-up compared to nonexercise comparators (RR: 0.47, 95% CI [0.32, 0.70]; F²: 0.00%; six RCTs; 1,222 participants; low-quality evidence; Figure 4).

**Between-exercise comparisons.** Four RCTs (n = 163; four comparisons) compared aerobic, functional, or multicomponent exercise interventions to resistance exercise comparators. There was no evidence of a difference in effect between therapeutic exercise and resistance exercise comparators on performance-based physical function at short-medium term follow-up (SMD: 0.03, 95% CI [−0.28, 0.33]; four RCTs; 163 participants; F²: 0.00%; low-quality evidence; Figure 5). This finding was consistent across exercise types. No data were reported for long-term follow-up.

**Self-reported physical function.** Two RCTs (n = 193; two comparisons) compared aerobic or functional exercise interventions to resistance exercise comparators. There was no evidence of a difference in effect between therapeutic exercise and resistance exercise comparators on self-reported physical function at short-medium term follow-up (SMD: 0.14, 95% CI [−0.28, 0.55]; two RCTs; 193 participants; F²: 0.00%; low-quality evidence; Figure 6). This finding was consistent across exercise types. No data were reported for long-term follow-up.

**Health-related quality of life.** None of the included RCTs comparing therapeutic exercise to other exercise reported health-related quality of life outcomes.

**Psychosocial outcomes:** One RCT reported psychosocial outcomes (Ansai & Rebelatto, 2015). Ansai and Rebelatto (2015) reported no nonserious adverse events in either intervention or control groups. Ansai et al. (2016) reported six nonserious adverse events (mild muscle pain, mild hematoma, and dizziness) in the exercise intervention and none in the nonexercise control group.
| Study                                      | Outcome used                          | Follow-up time point | Number of participants analyzed | Intervention Mean (SD) | Control Mean (SD) | Mean difference between groups [95% CI] |
|-------------------------------------------|---------------------------------------|----------------------|---------------------------------|------------------------|------------------|---------------------------------------|
| **Health-related quality of life**        |                                       |                      |                                 |                        |                  |                                       |
| Gine-Garriga et al. (2010)                | SF-12 physical function subscale      | Short (12 weeks)     | Intervention: 22 Control: 19    | 40.8 (6.95)            | 28.24 (6.49)     | 12.56 [8.44, 16.68] p < .001          |
|                                           | SF-12 physical composite score        | Medium (36 weeks)    | Intervention: 18 Control: 7     | 40.3 (7.37)            | 29.47 (5.93)     | 10.83 [5.27, 16.39] p = .001          |
|                                           |                                       |                      |                                 |                        |                  |                                       |
|                                           | SF-12 physical function subscale      | Short (12 weeks)     | Intervention: 22 Control: 19    | 35.59 (4.41)           | 29.80 (3.74)     | 5.79 [3.30, 8.28] p < .001           |
|                                           | SF-12 mental composite score          | Medium (36 weeks)    | Intervention: 18 Control: 7     | 36.52 (4.47)           | 29.26 (3.05)     | 7.26 [4.20, 10.32] p = .002          |
|                                           |                                       |                      |                                 |                        |                  |                                       |
| Hartshorn et al. (2002)                   | POMS                                  | Short (2 weeks)      | Intervention: 16 Control: 16    | 20.39 (10.57)          | 20.45 (11.01)    | −0.06 [−7.54, 7.42] p = .002         |
| Luukinen et al. (2006)                    | GDS                                   | Long (28 months)     | Intervention: 144 Control: 150  | Classified as depressed (n [%]): 45 (33) | Classified as depressed (n [%]): 41 (28) |                            |
|                                           | Frequency of feeling lonely           | Long (28 months)     | Intervention: 144 Control: 150  | Classified as lonely (n [%]): 50 (36) | Classified as lonely (n [%]): 57 (39) | NR                                    |
| Study               | Outcome used                              | Follow-up time point | Number of participants analyzed | Intervention group number of falls $n$ (%) | Control group number of falls $n$ (%) | Risk ratio $[95\% \text{ CI}]$ |
|--------------------|-------------------------------------------|----------------------|---------------------------------|------------------------------------------|--------------------------------------|--------------------------------|
| Falls results      |                                           |                      |                                 |                                          |                                      |                                |
| Ansai et al. (2016) | Monthly phone calls                      | Medium (16 weeks)    | Multicomponent: 23 Resistance: 23 Control: 23 Multicomponent: 4 (18.2) Resistance: 8 (34.8) | 8 (34.8) | Multicomponent vs. control 0.50 [0.17, 1.43] Multicomponent vs. resistance 0.50 [0.17, 1.43] Resistance vs. control 1.00 [0.45, 2.21] |
|                    |                                           | Medium (22 weeks)    | Multicomponent: 23 Resistance: 23 Control: 23 Multicomponent: 2 (9.1) Resistance: 1 (4.3) | 5 (25) | Multicomponent vs. control 0.40 [0.09, 1.86] Multicomponent vs. resistance 2.00 [0.19, 20.55] Resistance vs. control 0.20 [0.03, 1.58] |
| Campbell et al. (1997) | Falls calendar and telephone call         | Long (12 months)    | Intervention: 103 Control: 110 Rate (SD): 0.87 (1.29) per year | 88 | 152 Rate (SD): 1.34 (1.94) per year | Reported as hazard ratios First fall: 0.81 [0.56, 1.16] First four falls: 0.68 [0.52, 0.90] Fall resulting in moderate or severe injury: 0.61 [0.39, 0.97] |
| Campbell et al. (1999) | Falls calendar and telephone call         | Long (24 months)    | Intervention: 41 Control: 62 Rate (SD): 0.83 per year | 138 | 220 Rate (SD): 1.19 per year | Reported as hazard ratios All falls: 0.69 [0.49, 0.97] Fall resulting in moderate or severe injury: 0.63 [0.42, 0.95] |
| Luukinen et al. (2007) | Phone calls and medical record confirmation | Bimonthly for 3 years | Intervention: 217 Control: 220 Rate [95\% CI]: 1.15 [1.03, 1.29] per person year Rate [95\% CI]: 1.23 [1.10, 1.37] per person year | 2 | 3 | First 4 falls: 0.88 [0.74, 1.04] All falls: 0.93 [0.80, 1.09] |
| Rosie and Taylor (2007) | Diary and telephone call                  | Short (6 weeks)      | Functional: 34 Resistance: 34 | 2 | 3 | 0.67 [0.12, 3.74] |

**Note.** SF-12 = 12-Item Short Form Survey; GDS = Geriatric Depression Scale; POMS = profile of mood states; CI = confidence interval.
### Figure 4 — Forest plot for the effect of therapeutic exercise compared to a nonexercise comparator group on mortality. CI = confidence interval.

| Study or subgroup | Resistance | Intervention | SMD | SMD |
|-------------------|------------|--------------|-----|-----|
|                   | Mean       | SD           | Total | Mean       | SD           | Total | IV, random, [95% CI] | IV, Random, [95% CI] |
| 2.3.1 Aerobic exercise | -24.18     | 8.36         | 12   | -26.58      | 20.28        | 13    | 15.4%                  | 0.15 [-0.64, 0.93]   |
| Subtotal [95% CI] |            |              | 12   | 15.4%                   | 0.15 [-0.64, 0.93]   |
| Heterogeneity: Not applicable |            |              |      | Test for overall effect: Z = .37 (p = .71) |

### Figure 5 — Forest plot for the effect of therapeutic exercise compared to a resistance exercise comparator group on performance-based physical function. SMD = standardized mean difference; CI = confidence interval.

| Study or subgroup | Resistance | Intervention | SMD | SMD |
|-------------------|------------|--------------|-----|-----|
|                   | Mean       | SD           | Total | Mean       | SD           | Total | IV, random, [95% CI] | IV, Random, [95% CI] |
| 2.3.2 Functional exercise | -5.64      | 4.58         | 34   | -6.39       | 3.5          | 34    | 41.9%                  | 0.18 [-0.29, 0.66]   |
| Subtotal [95% CI] |            |              | 34   | 41.9%                   | 0.18 [-0.29, 0.66]   |
| Heterogeneity: Not applicable |            |              |      | Test for overall effect: Z = .75 (p = .45) |

### Figure 6 — Forest plot for the effect of therapeutic exercise compared to a resistance exercise comparator group on self-reported physical function. SMD = standardized mean difference; CI = confidence interval.

| Study or subgroup | Resistance | Intervention | SMD | SMD |
|-------------------|------------|--------------|-----|-----|
|                   | Mean       | SD           | Total | Mean       | SD           | Total | IV, random, [95% CI] | IV, Random, [95% CI] |
| 2.3.3 Multicomponent exercise | -28.1      | 15.3         | 23   | -28       | 15.2         | 22    | 27.8%                  | -0.01 [-0.59, 0.58]  |
| Subtotal [95% CI] |            |              | 22   | 27.8%                   | -0.01 [-0.59, 0.58]  |
| Heterogeneity: $t^2 = 0.00; \chi^2 = 88; df = 1 (p = .35); I^2 = 0\%$ |            |              |      | Test for overall effect: Z = .71 (p = .47) |
| Total [95% CI] | 82 | 100.0% | 0.03 [-0.28, 0.33] | |
| Heterogeneity: $t^2 = 0.00; \chi^2 = 2.06; df = 3 (p = .56); I^2 = 0\%$ | 82 | 100.0% | 0.03 [-0.28, 0.33] | |
| Test for overall effect: Z = .16 (p = .87) | 82 | 100.0% | 0.03 [-0.28, 0.33] | |
| Test for subgroup differences: $\chi^2 = 1.18; df = 2 (p = .55); I^2 = 0\%$ | 82 | 100.0% | 0.03 [-0.28, 0.33] | |
found no significant differences in scores on the Geriatric Depression Scale at medium-term follow-up between participants who undertook a multicomponent training or resistance training (mean difference: 0.00, 95% CI [−1.55, 1.55]); Table 2).

Falls: One RCT reported falls. Rosie and Taylor (2007) reported no difference in the number of falls short-term between participants who undertook a functional training program and those who completed resistance exercises (RR: 0.67, 95% CI [0.12, 3.74]; Table 2).

Adverse events and mortality: Adverse event data were reported in two RCTs (n = 113; Ansai et al., 2016; Rosie & Taylor, 2007). No serious adverse events were reported. All nonserious adverse events reported were mild muscle pain. Meta-analysis showed no difference in risk of nonserious adverse events between therapeutic exercise and resistance exercise comparators (RR: 0.79, 95% CI [0.40, 1.57]; $F^2$: 0.00%; two RCTs; 113 participants; moderate-quality evidence; Figure 7). Mortality data were reported in one RCT that compared multicomponent exercise to resistance exercise (de Bruin & Murer, 2007). No deaths were reported in either exercise group.

## Overall Evaluation of the Quality of Evidence

The overall quality of the evidence assessed using GRADE, including reasons for downgrading, is summarized in Table 3. The certainty of evidence for all outcomes was downgraded for risk of bias and inconsistency, resulting in low confidence in the effect estimate.

## Discussion

We identified 16 RCTs including 1,660 participants evaluating therapeutic exercise interventions among community-dwelling older adults. Therapeutic exercise interventions varied in their components, and exercise was provided in group and individual formats. The results of our meta-analysis showed that compared to resistance exercise, therapeutic exercise may improve performance-based physical function and self-reported physical function (Figure 7). However, there was no evidence of a difference in the number of falls short-term or mortality between therapeutic exercise groups and resistance exercise groups (Table 3).

### Table 3 Summary of Findings

| Outcome | Risk with nonexposed comparator | Risk with therapeutic exercise | Anticipated absolute effects (SMD) [95% CI] | Relative effect [95% CI] | Number of participants (studies) | Certainty of the evidence (GRADE) |
|---------|---------------------------------|---------------------------------|---------------------------------------------|--------------------------|-------------------------------|-----------------------------------|
| Therapeutic exercise vs. nonexercise comparator | | | | | | |
| Performance-based physical function | — | | 0.58 higher [0.19 lower to 1.36 higher] | — | 290 (six RCTs) | Very low a,b,c |
| Self-reported physical function | — | | 1.35 higher [0.78 lower to 3.48 higher] | — | 280 (three RCTs) | Very low a,b,c |
| Mortality | 55 per 1,000 | 10 per 1,000 | — | 0.47 [0.32, 0.70] | 1,222 (six RCTs) | Low a,b,c |
| Therapeutic exercise vs. resistance exercise comparator | | | | | | |
| Performance-based physical function | — | | 0.03 higher [0.28 lower to 0.33 higher] | — | 163 (four RCTs) | Low a,b,c |
| Self-reported physical function | — | | 0.14 lower [0.55 lower to 0.27 higher] | — | 193 (two RCTs) | Low a,b,c |
| Nonserious adverse events | 246 per 1,000 | 196 per 1,000 | — | 0.79 [0.40, 1.57] | 113 (two RCTs) | Moderate a |

Note. GRADE working group grades of evidence. High certainty: We are very confident that the true effect lies close to that of the estimate of the effect. Moderate certainty: We are moderately confident in the effect estimate. The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different. Low certainty: Our confidence in the effect estimate is limited. The true effect may be substantially different from the estimate of the effect. Very low certainty: We have very little confidence in the effect estimate. The true effect is likely to be substantially different from the estimate of effect. CI = confidence interval; GRADE = Grading of Recommendations, Assessment, Development and Evaluation; RCTs = randomized controlled trials; SF-12 = 12-Item Short Form Survey; SMD = standardized mean difference.

aDowngraded one level for risk of bias (more than one trial at high or unclear risk of bias). bDowngraded one level for inconsistency (considerable statistical heterogeneity in these outcomes that could not be explained by prespecified sensitivity and subgroup analyses). cDowngraded one level for imprecision (relatively broad overall CI).
adults aged 80 years or older. The trials included a range of exercise interventions, most commonly multicomponent or resistance exercise, with most trials using a nonexercise control group.

Due to significant heterogeneity across RCTs, we were only able to conduct a limited meta-analysis. We found no evidence of a difference in effect between therapeutic exercise and nonexercise comparators on performance-based or self-reported physical function at short-medium term follow-up. There was some evidence that therapeutic exercise reduced the risk of mortality during follow-up compared to nonexercise controls. Individual trials reported significant benefits of therapeutic exercise on health-related quality of life, psychosocial outcomes and falls, however these findings have to be considered uncertain as many of these measures were secondary outcomes.

Results in Context

To our knowledge, no systematic reviews have been published evaluating the effects of therapeutic exercise on physical function and psychosocial outcomes among community-dwelling adults aged 80 years or older. The small number of RCTs that were included in our review was unsurprising, given that people aged 80 and over have been deemed “the great forgotten” in clinical studies (Izquierdo et al., 2020).

Our finding of a lack of evidence for the effectiveness of therapeutic exercise interventions on physical function, health-related quality of life, and psychosocial outcomes highlights the gap between the known physiological benefits of exercise and observed clinical benefits in published RCTs. Among the nine included RCTs that reported exercise intensity, both heart rate and resistance intensities were most commonly moderate. We cannot be certain that the therapeutic exercise was sufficient to cause physiological changes needed to improve strength and function. Previous reviews have reported that exercise is commonly prescribed to older adults at an insufficient dose to improve strength and function (Singh, 2002; Steib, Schoene, & Pfeifer, 2010). Future research examining the effects of different dosages of therapeutic exercise is required.

The variation in results of the included RCTs is consistent with a recent systematic review of meta-analyses on exercise interventions in older adults aged 65 or mean age ≥70 (Di Lorito et al., 2021). Di Lorito et al. also found variable results and no significant effects for performance-based physical function (Di Lorito et al., 2021). We noted that health-related quality of life was only measured in one included RCT and psychosocial outcomes were only reported in 25% of included RCTs in our review, a finding also noted by Di Lorito et al. (2021).

Our findings suggest that therapeutic exercise may reduce mortality for community-dwelling adults aged 80 years or older. This is consistent with a recent systematic review and meta-analysis of the safety and effectiveness of long-term exercise interventions among older adults (n = 28,532, mean age 74.2 years), which found that long-term exercise was associated with reduced risk of serious adverse events (including mortality; García-Hermoso et al., 2020). Generally high rates of completion and exercise adherence across the included studies also suggest that exercise interventions are acceptable and feasible for people aged 80 years or older. This supports the similar finding from an earlier systematic review of exercise interventions for frail older people living in the community (Clegg, Barber, Young, Forster, & Illiffe, 2012).

Implications for Clinical Practice

High-quality evidence demonstrating the effectiveness of therapeutic exercise for adults aged 80 years or older is lacking. While future RCTs are undertaken to improve our confidence in the effects of exercise for this population, given that exercise seems safe, it should be recommended in clinical practice. Which type of therapeutic exercise is most beneficial remains unclear, so exercise selection should be based on an individual’s deficits, goals, and preferences.

Implications for Future Research

This systematic review highlights the need for high-quality RCTs evaluating the effects of well-designed therapeutic exercise interventions among community-dwelling adults aged 80 years or older. Identifying how best to facilitate participation of this population in such trials is an important issue. The Innovations in Clinical Trial Design and Delivery for the Under-served project seeks to address this issue, and the resources produced from this work should guide the design of future RCTs (Witham et al., 2020). Future RCTs should assess health-related quality of life, psychosocial outcomes, and cost-effectiveness analyses in addition to physical function, and should include long-term follow-up. Care should also be given to the content of the comparator intervention (Freedland et al., 2019). Variation in comparator interventions may in part explain the inconsistent effects observed in our review.

Given that adults aged 80 years or older are a highly heterogeneous population interventions should be individualized and tailored to the goals and preferences of each participant. Exercise intervention design should be based on behavior change theory, and should include behavior change techniques such as goal setting, motivational strategies, and booster sessions, to optimize exercise uptake and adherence long term (Nicolson et al., 2017).

Strengths and Limitations

The strengths of this review include the comprehensive search, explicit eligibility criteria, duplicate assessment of eligibility, risk of bias assessment, and use of the GRADE approach to rate the overall quality of evidence.

The limitations of our review relate largely to the underlying evidence. First, the heterogeneous nature of the included RCTs reflected the large inconsistency in the effect estimates of the meta-analyses. Second, the sample sizes of included RCTs were generally small, and many included outcomes were secondary. Finally, the quality of evidence for the outcomes of interest was low to very low, suggesting that the true effect may differ from the findings reported in this review.

Conclusions

Results of this systematic review and meta-analysis suggest that evidence for the effectiveness of therapeutic exercise interventions on physical function, health-related quality of life and psychosocial outcomes in community-dwelling adults aged 80 years or older is limited, and of low quality. Therapeutic exercise may reduce mortality in this population. Well-designed RCTs should be a research priority.
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