

PRT and Multimodal 1

Title: Effects of physical exercise in older adults with reduced physical capacity: Meta-analysis of resistance exercise and multimodal exercise

Running head: PRT and Multimodal

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Abstract

Objective

Older adults with reduced physical capacity are at greater risk of progression to care dependency. Progressive resistance strength exercise and multimodal exercise have been studied to restore reduced physical capacity. To summarize the best evidence of the two exercise regimes, this meta-analysis study appraised randomized controlled trials from published systematic reviews.

Methods

MEDLINE, EMBASE, and the Cochrane Database of Systematic Review and Cochrane Central Register of Controlled Clinical Trials were searched for relevant systematic reviews. Two reviewers independently screened the relevant systematic reviews to identify eligible trials, assessed trial methodological quality, and extracted data. RevMan 5.3 software was used to analyze data on muscle strength, physical functioning, activities of daily living, and falls.

Results

Twenty-three eligible trials were identified from 22 systematic reviews. The mean age of trial participants was 75 years old or above. Almost all multimodal exercise trials included muscle strengthening exercise and balance exercise. Progressive resistance exercise is effective on improving muscle strength of the lower extremity and static standing balance. Multimodal exercise is effective on improving muscle strength of the lower extremity, dynamic standing balance, gait speed and chair stand. Additionally, multimodal exercise is effective on reducing falls. Neither type of exercise was effective on improving activities of daily living.

Conclusion

For older adults with reduced physical capacity, multimodal exercise appears to have a broad effect on improving muscle strength, balance, and physical functioning of the lower extremity, and reducing falls relative to progressive resistance exercise alone.

Keywords: Aged, Exercise, Exercise Therapy, Resistance Training, Muscle Strength, Multimodal Exercise, Review, Falls, Mobility Limitation, Activities of Daily Living

Introduction

Developing and maintaining functional ability that enables older adults to do what they value is essential for healthy aging (World Health Organization, 2015). The makeup of functional ability (e.g., able to climb a flight of stairs) is attributed to intrinsic capacity of the individual (e.g., muscle strength), relevant environmental characteristics (e.g., the bedroom is located on the second floor of the house), and the interaction between the individual and the environmental characteristics (e.g., to access the bedroom on the second floor for rest) (World Health Organization, 2015). As people age, however, one prominent physiological change of the intrinsic capacity is the decline of skeletal muscle mass or muscle strength (Fielding et al., 2011), which is not only a key indicator of frailty (Clegg et al.), but also could result in reduced functional ability (e.g., muscle weakness of the lower extremity increases the difficulty for the older individual to access the 2nd floor bedroom). Multiple comorbidities and inactivity could further accelerate the decline (Kortebein et al., 2007, Brinkley et al., 2009). The loss of muscle mass and strength increases older adults' risk to care dependency and adverse health outcomes, such as mobility limitations, risk of falls, and increased mortality (Moreland et al., 2004, Visser et al., 2005, Landi et al., 2013). The identification of effectiveness interventions to preserve intrinsic capacity in older individuals and reduce late-life disablement is within the realm of rehabilitation professions.

Physical activity, which includes exercise, is a protective factor of disability in older adults (Balzi et al., 2010). The likelihood of developing disability in basic activities of daily living in older adults with medium or high physical activity level is nearly half compared to those with low physical activity level (Tak et al., 2013). Engaging in habitual activities that require contractions of skeletal muscles and increase energy expenditure (e.g., walking, cycling, and sport-related leisure activities) could prevent declining physical capacity in older adults, thereby slowing

down or postpone the progression to disability. For older adults with reduced physical capacity or marked physical limitations, increasing habitual physical activities is encouraged but could be a challenge due to preexisting limited capacity. Physical exercise, which is a structured and planned form of physical activity with the intention to advance fitness or acquired associated health benefits (Caspersen et al., 1985), could be an initial restorative program to improve physical capacity. A large randomized controlled trial conducted in the United States (Lifestyle Interventions and Independence for Elders—LIFE) has shown that a structured physical activity program is more effective on reducing the risk of mobility disability in community-dwelling older adults with physical limitations than a health education program (Pahor et al., 2014).

Progressive resistance strength training (PRT) is a type of structured exercise with a purpose to increase muscle strength based on the principle of overload (Kraemer and Ratamess, 2004). Older adults are able to respond and adapt to PRT by showing training-induced muscle hypertrophy or increased muscle strength (Verdijk et al., 2009, Peterson et al., 2010). Similar results can be observed in older residents in long-term care facilities (Fiatarone et al., 1994), who are one of the most vulnerable populations. Given the strong correlation between muscle strength and late-life disability and robust effects of PRT on physiological outcomes, PRT is generally accepted as an optimal means to enhance and maintain functional ability in older adults (Bean et al., 2004). In contrast to single modal exercise (e.g., PRT), multimodal exercise focuses on the underlying balance, endurance, and muscle strength simultaneously by combining two or more types of exercise. Older adults regardless of age respond to multimodal exercise similarly (Toraman and Şahin, 2004). Research has shown that multimodal exercise as a comprehensive approach to increase physical capacity is effective for fall prevention (Baker et al., 2007, Rose and Hernandez, 2010). Exercise guidelines of physical activity for older adults adopt the regimen of multimodal exercise (Nelson et

al., 2007, Oja and Titze, 2011, Tremblay et al., 2011). Aerobic activities with muscle strengthening activities that involve major muscle groups are normally recommended.

Older adults with reduced physical capacity may not meet the criteria of frailty (Baker et al., 2007), but they experience declined muscle strength, poor balance, mobility limitations, difficulty in activities of daily living, or falls, which increases their risk of progression to late-life disability or becoming care dependent. Studies examined the effects of physical exercise have accumulated after decades of research efforts. A number of systematic reviews have been published, yet the effect varies greatly and the optimal exercise program to the population at risk remains to be determined (Giné-Garriga et al., 2014, de Labra et al., 2015). The goal of this meta-analysis study is to shed light on PRT and multimodal exercise in older adults with reduced physical capacity by reviewing the best evidence available from systematic reviews. The question of this review was “what are the evidence of PRT or multimodal exercise, comparing to no-intervention controls or attentional controls, on improving muscle strength, physical functioning, activities of daily living, and reducing falls in community-dwelling older adults with reduced physical capacity?”

Methods

Literature search and screening

The literature search and screening process consisted of two steps to identify eligible randomized controlled trials from published systematic reviews. The first step was to search electronic databases for potential systematic reviews. MEDLINE, EMBASE, and the Cochrane Database of Systematic Review and Cochrane Central Register of Controlled Clinical Trials were searched in October 2015. An update search was conducted in November 2016. Search terms (resistance training, weight lifting, exercise, exercise therapy, and aged, elderly or senior)

were mapped to the Medical Subject Headings in each database when applicable. Additionally, “systematic review” was used as a search term in the article title to confine the search results.

Two authors independently perused the titles and abstracts to identify relevant systematic reviews. The second step was to search eligible randomized controlled trials from the systematic reviews identified from the first step. Similarly, the two authors perused the study trials included in these systematic reviews. If the authors were uncertain about a particular trial described in the systematic review, full text was retrieved for further review. The screening criteria for potential systematic reviews and randomized controlled trials were based on the predefined PICO term.

Population: community-dwelling, non-demented older adults with reduced physical capacity.

Intervention: PRT or multimodal exercise. PRT is a type of muscle strength training in which an individual exerts an effort against an external resistance that is increased gradually as progress is made. Multimodal exercise combines two or more types of exercise that can be clearly distinguished, including strengthening, balance, stretching, endurance or aerobic exercise, which is not part of warm up or cool down exercise.

Comparison: The comparison was a control group that received no intervention or attention control without any exercise components.

Outcome: Muscle strength of the lower extremity, physical functioning, activities of daily living, and falls.

Specifically, trials were included if 1) the mean age of the trial participants was 60 years or older; 2) participants were community-dwelling older adults with notable or at risk of reduced physical capacity at the time of study recruitment; 3) the research design was a randomized controlled trial; 4) PRT or multimodal exercise was the primary intervention; and 5) one or more

interested outcomes were reported. Trials were excluded if: 1) adults younger than 60 years of age were recruited; 2) participants had cognitive impairments; 3) the trial targeted a specific disease population or applied a single clinical diagnosis as an enrollment criterion (e.g., stroke); 4) the progressive resistance exercise was power training, in which the speed of movement was emphasized; 5) exercises were tai chi, yoga, or water-based; 6) the trial applied a comparative effectiveness research design in which the control group received other type of exercise; and 7) the exercise was combined with supplemental or nutritional intervention. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines was followed to report this study (Moher et al., 2010). The review protocol was not registered.

Assessment of methodological quality

The Cochrane Collaboration's tool for assessing risk of bias in randomized trials was used to evaluate methodological quality (Higgins et al., 2011). Selection bias (random sequence generation and allocation concealment), performance bias (blinding of participants and personnel), detection bias (blinding of outcome assessment), attrition bias (incomplete outcome data), and reporting bias (selective reporting) were rated as low, unclear, or high risk of bias. Two authors individually evaluated the methodological quality of selected trials and sought consensus if discord occurred.

Data extraction

Demographics and characteristics of participants, intervention exercise programs, and interested outcomes at post-intervention were extracted. Data on muscle strength of lower extremity, physical functioning (balance, gait speed, chair stand, Timed Up-and-Go, or overall physical performance), activities of daily living, and fall rates were extracted.

Data analysis

The Cochrane Review Manager software (RevMan 5.3) was used for effect size estimation. For dichotomous outcomes, the rate ratio was calculated. For continuous outcome, the mean difference (MD) was calculated when the unit of measure is similar, or the standardized mean difference (SMD) was calculated when the unit of measure is different.

A minimal of three trials was preferred for pooled effect size calculation. The fixed-effect model was conducted to estimate the pooled effect size across trials. Alternatively, the random-effects model was conducted when significant heterogeneity was detected. Heterogeneity was assessed using the Chi² test (with statistical significance set at $p < 0.10$), and the I² statistic (Higgins et al., 2003).

Results

The initial literature search resulted in 355 records. After reviewing article titles and abstracts and removing duplicates, 22 systematic reviews were relevant to the purpose of this study (Chin A. Paw et al., 2008, Daniels et al., 2008, Orr et al., 2008a, Sherrington et al., 2008a, Liu and Latham Nancy, 2009, Thomas et al., 2010, Howe Tracey et al., 2011, Theou et al., 2011, Chou et al., 2012, Gillespie Lesley et al., 2012, Cadore et al., 2013, El-Khoury et al., 2013, Martin et al., 2013, Martins et al., 2013, Schwenk et al., 2013, Giné-Garriga et al., 2014, Ishigaki et al., 2014, Thiebaud et al., 2014, Burton et al., 2015, de Labra et al., 2015, Hill et al., 2015, Moore et al., 2016). Potential trials from these systematic reviews were then screened, yielding 23 trials. See Figure 1 for the flow chart of trial screening process.

Summary of participants, exercise programs, as well as interested outcomes included in the meta-analysis is presented in Table 1. One trial included two PRT groups with two difference level of exercise guidance (Boshuizen et al., 2005), and the high level of guidance was included in the meta-analysis. One trial included one PRT group and one multimodal exercise group (Buchner et al.,

¹⁹⁹⁷). One trial included two multimodal exercise groups with different exercise combinations (Freiberger et al., 2012), and the group with more exercise combinations was included in the analysis. In total, nine trials compared PRT to no intervention or attentional control (Skelton and McLaughlin, 1996, Buchner et al., 1997, Chandler et al., 1998, Jette et al., 1999, Westhoff et al., 2000, Latham et al., 2003, Miszko et al., 2003, Boshuizen et al., 2005, Lustosa et al., 2011); 15 trials compared multimodal exercise to no intervention or attentional control (Buchner et al., 1997, Rubenstein et al., 2000, Barnett et al., 2003, Nelson et al., 2004, Beyer et al., 2007, Rydwick et al., 2008, Sherrington et al., 2008b, Vestergaard et al., 2008, Haines et al., 2009, Clemson et al., 2010, Giné-Garriga et al., 2010, Villareal et al., 2011, Freiberger et al., 2012, Kim et al., 2012, Kim et al., 2015).

The mean age of participants in most trials was 75 years old or above. Almost every multimodal exercise included muscle strengthening exercise and balance exercise. The exercise frequency was usually two to three times a week. While the trial duration ranged from five weeks to one year, most trials lasted less than six months. If the exercise session took place in a facility, the exercise was supervised or led by research personnel. If the exercise session was at home, an exercise instruction booklet or video was provided to the participant. Home visits or phone calls were conducted to monitor home exercise.

Table 2 shows the results of risk of bias rating. There was a moderate degree of uncertainty about the selection bias among PRT trials and multimodal trials because the description of procedures for random sequence generation and allocation concealment in the text was either missing or insufficient. The risk of performance bias was high because it is difficult to mask participants in exercise studies.

Muscle strength of the lower extremity

Muscle strength of knee extension was the most commonly reported outcome across trials. Leg press was extracted if the muscle strength outcome of knee extension was not available. Figure 2 shows the results of meta-analysis results. Both PRT and multimodal exercise were effective on improving muscle strength of the lower extremity. PRT yielded a slightly larger effect size (SMD = .33) relative to multimodal exercise (SMD = .16)

Physical functioning

Meta-analysis results of physical functioning outcomes are summarized in Table 3.

Balance. The most commonly reported outcomes across trials were one-legged stand and tandem stance, which measure static standing balance. Data of semi-tandem were extracted if tandem stance was not measured. In addition, outcomes of dynamic standing balance measured with step test or tandem walk were analyzed. Other general balance measures, such as Berg Balance Scale, Romberg, and POMI were also included in the analysis. The effect of one-legged stand and dynamic standing balance were not estimated in the PRT trials due to an insufficient number of trials. In short, the effect of PRT on static standing balance was approaching significant ($p = .05$), but on general balance was not significant. Multimodal exercise showed no effect on static standing balance measured by tandem stance and one-legged stand, but was effective on improving dynamic standing balance and overall balance.

Gait speed. Different walking distance or time limit was used to measure gait speed across trials. Effect sizes of maximal gait speed and habitual gait speed were estimated separately. The effect size of maximal speed was not estimated for the PRT trials. The results did not show a significant effect of PRT on habitual gait speed. Multimodal exercise was effective on improving maximal gait speed and habitual gait speed.

Chair stand. Only the multimodal exercise trials were included for this outcome. The performance of chair stand can be timed (e.g., five times chair stand test) or counted (e.g., 30-second chair stand test). The result showed a favorable effect in multimodal exercise.

Timed Up-and-Go. Data on Timed Up-and-Go test were extracted to estimate mobility from standing up from a chair, walk for a short distance, and then return to chair and sit down. The walking distance used in the test varied by trials. No significant effect was found in PRT nor multimodal exercise.

Overall physical functioning. Various instruments were used to assess overall physical functioning, such as the physical function domain of SF-36 and Physical Performance Test. Neither the PRT nor multimodal exercise showed a significant effect.

Activities of daily living

Various self-reported instruments were used to measure ADLs, such as Barthel Index and Gronigen Activity Restriction Scale. PRT did not show a significant effect on improving activities of daily living. Similarly, multimodal exercise did not show a significant effect on improving activities of daily living. See Figure 3.

Falls

The rate of falls was determined by the number of falls during the follow-up period. This outcome was not estimated for the PRT trials. The overall rate ratio in multimodal exercise showed a positive effect on reducing falls. See Figure 4.

Discussion

This study reviewed randomized controlled trials available from existing systematic reviews to synthesize the effects of PRT and multimodal exercise on muscle strength of the lower extremity, physical functioning, activities of daily living, and falls in community-dwelling older adults with reduced physical capacity. More outcomes in multimodal exercise trials than in PRT were available for conducting meta-analysis. PRT was effective on improving muscle strength of the lower extremity and static standing balance. Multimodal exercise was effective on improving muscle strength of the lower extremity, dynamic standing balance, gait speed, and chair stand. Additionally, multimodal exercise was effective on reducing falls. However, neither of the exercise demonstrated a positive effect on improving the outcome of functional mobility nor activities of daily living.

Both PRT and multimodal exercise are effective on improving muscle strength and balance. Specifically, PRT seems more effective on improving muscle strength and static standing balance, while multimodal exercise are more effective on improving dynamic standing balance and gait speed. These findings reflect the specificity of training principle in exercise—which means that the more the exercise closely simulates the actions in a specific motor task or an outcome, the greater the transfer carryover of exercise to performance in that task or outcome (Gamble, 2006). Because muscle strength training exercise is the main component in PRT, and is included in most multimodal exercise trials, both types of exercise are effective on the outcome of muscle strength. Additionally, nearly all multimodal exercise trials included training that requires dynamic balance (e.g., circle turn, tandem walk, and walk over or around small obstacles) (Nelson et al., 2004, Sherrington et al., 2008b), which may explain why the multimodal exercise trials show a significant effect on the dynamic balance but not on the static balance. Muscle strength of the lower extremity is positively associated with static balance (Carter et al., 2002). Although the

literature has suggested that PRT as an isolated intervention does not warrant improved static balance (Orr et al., 2008b), the outcome of static balance in the PRT trials is approaching statistical significance.

Slow walking speed is another feature of frailty in addition to muscle weakness (Clegg et al.). Findings of this study show that multimodal exercise improves gait speed and chair stand, which suggests that multimodal exercise might be effective in reducing frailty. Prior research has identified that aerobic capacity in addition to muscle strength is related to gait speed (Fiser et al., 2010). As several attributes of physical capacities often decline in parallel with age (Saxon et al., 2014), multimodal exercise appears to a better approach to improve physical functioning of the lower extremity in older adults with reduced physical capacity.

Although multimodal exercise shows positive results on various musculoskeletal and physical functioning outcomes, it was not effective on improving functional mobility as measured by the Timed Up and Go (Podsiadlo and Richardson, 1991). The pooled result of Timed Up and Go was estimated from three trials while there were 15 multimodal exercise trials included in this review. The analysis also suggested that a substantial heterogeneity existed among the three trials ($I^2 = 78\%$). To identify the source of heterogeneity would be difficult given the small number of trials. Timed Up and Go is highly correlated with gait speed and balance (Podsiadlo and Richardson, 1991). The information that Timed Up and Go provides, for example predicting falls, is similar to gait speed (Viccaro et al., 2011). Therefore, including the measure in addition to gait speed or balance may be redundant in exercise trials. However, Timed Up and Go is correlated with executive function while the balance measure is not (Herman et al., 2011). Timed Up and Go may be an informative outcome measure of physical functioning for trials that recruit older adults with reduced cognitive ability.

Functional ability is the makeup of physical capacity, environmental characteristics, and the interaction between the two (World Health Organization, 2015). Only improving the physical capacity without addressing the environment may explain why neither PRT nor multimodal exercise yields a significant effect on the outcome of activities of daily living. A multicomponent approach that is tailored and addressed environment modifications at home has shown a greater outcome on the activities of daily living in frail older adults (De Coninck et al., 2017 Online). Another perspective is that preventing functional disability in activities of daily living is a long-term goal of exercise. Despite participants in these trials had shown some degree of reduced physical capacity, their independence in activities of daily living had not yet been severely compromised. Their baseline data suggest very mild to mild-moderate difficulty in activities of daily living. To demonstrate a prominent effect of exercise on maintaining the independence in activity of daily living, a follow up with longer than one-year period is recommended. Finally, the measure of activities of daily living tend to rely on subjective self-reported rating on the level of difficulty or dependence. Literature has shown that older adults overestimate their ability on subjective self-reported rating comparing to objective performance-based rating (Sinoff and Ore, 1997, Shulman et al., 2006), leaving little room for the score to improve. Alternatively, they may inflate the rating at post-test due to response shift (Daltroy et al., 1999), or becoming more aware of their deficits.

This study reviewed trials from published systematic reviews. These scope of literature search in these reviews is overlapped to some degree, which reduces the likelihood of missing significant trials. However, one clear drawback of this approach is that more recent trials on PRT or multimodal exercise could have been missed.

Conclusion

Exercise is a common approach to prevent late-life disability. Although the effects of PRT were not directly compared to multimodal exercise in this review, multimodal exercise shows positive effects on multiple outcomes, including muscle strength, balance, gait speed, chair stand, and falls, which seems to be a well-rounded approach than PRT alone. However, PRT or muscle strengthening exercise is an essential component in multimodal exercise being reviewed. Exercise guidelines for older adults recommend regular aerobic exercise in addition to strength exercise (Nelson et al., 2007, Oja and Titze, 2011, Tremblay et al., 2011). While aerobic exercise is included in half of the multimodal exercise trials, balance exercise is more common than aerobic exercise in these trials. Collectively, a multimodal exercise for older adults with reduced physical capacity needs to include strength exercise and balance exercise as two basic components. Future studies or reviews are needed to support whether a long-term exercise regimen is more effective on improving activities of daily living. Developing sensitive measurements on the activities of daily living for older adults with reduced physical capacity but still reside in the community is also recommended.

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Table 1. Summary of Trial Characteristics.

Author and Publication Year Country	Participants <ul style="list-style-type: none"> ○ Main characteristic of reduced physical capacity ○ Group sample size (gender Male/Female), mean age 	Intervention <ul style="list-style-type: none"> ○ Intervention format/site ○ Intervention duration ○ Intervention frequency ○ Intervention content by group 	Relevant Outcome Measures Included in the Meta-analysis
Progressive Resistance Exercise			
Boshuizen, 2005 Netherlands	<ul style="list-style-type: none"> ○ Knee-extensor strength \leq 87.5 Nm ○ PG <small>high guidance</small> n=24 (0/24), 80 yrs ○ PG <small>medium guidance</small> n=26 (2/24), 79 yrs ○ CG n=22 (2/20), 76 yrs 	<ul style="list-style-type: none"> ○ Combination of home (unsupervised, followed an instruction booklet) and group (supervised in two local welfare centers) ○ 10 weeks ○ 3 times/week, 40 minutes each time ○ PG <small>high guidance</small>: 9 LE exercises using elastic bands (two supervised sessions per week) ○ PG <small>medium guidance</small>: 9 LE exercises using elastic bands (only one supervised session per week) ○ CG: no intervention 	<ul style="list-style-type: none"> ○ Muscle strength of knee extension ○ Balance: Tandem stance ○ Gait speed: 20-meter walk (habitual speed) ○ Timed Up-and-Go ○ ADL: Gronigen Activity Restriction Scale
Buchner, 1997 United States	<ul style="list-style-type: none"> ○ Aged 68-85 yrs with poor balance and weak knee extensor ○ PG n=25 (12/13), 74 yrs ○ CG n=30 (15/15), 75 yrs 	<ul style="list-style-type: none"> ○ Gym-based (supervised) ○ 6 months ○ 3 times/week., 60 minutes each time ○ PG: 2 UE, 5 LE, and one trunk exercises using exercise machines ○ CG: no intervention 	<ul style="list-style-type: none"> ○ Muscle strength of knee extension ○ Balance: Tandem stance ○ Gait speed: 40-meter walk (habitual speed) ○ Overall physical performance: Physical performance of SF-36 ○ ADL: Lawton IADL scale (number of IADLs)

Chandler, 1998 United States	<ul style="list-style-type: none"> ○ Aged 64+ yrs and inability to descend stairs or step over a step without holding the railing ○ PG n=50 (NR), 78 yrs ○ CG n=50 (NR), 78 yrs 	<ul style="list-style-type: none"> ○ Home (supervised) ○ 10 weeks ○ 3 times/week ○ PG: 6 LE exercises with elastic bands or weights ○ CG: no intervention 	<ul style="list-style-type: none"> ○ Muscle strength of knee extension ○ Balance: Functional reach ○ Gait speed: 10-meter walk (habitual speed) ○ Overall physical performance: Physical performance of SF-36
Jette, 1999 United States	<ul style="list-style-type: none"> ○ Aged 60+ yrs and had limitations in at least one of 9 functional areas in a physical function scale ○ PG n=107 (29/78), 75 yrs ○ CG n=108 (19/89), 75yrs 	<ul style="list-style-type: none"> ○ Home (monitored with two home visits and bi-weekly mailed-in exercise logs) ○ 6 months ○ 3 times/week, 35 minutes each time ○ PG: 35-minute video consisted of 11 exercises of UE, LE, and trunk using elastic bands ○ CG: no intervention 	<ul style="list-style-type: none"> ○ Muscle strength of knee extension ○ Balance: Tandem stance ○ Timed Up-and-Go ○ ADL: Physical disability subscale of the Sickness Impact Profile 68
Latham, 2003 New Zealand	<ul style="list-style-type: none"> ○ Aged 65+ yrs and met a frailty clinical screening criteria while hospitalized ○ PG n=120 (54/66), 80 yrs ○ CG n=123 (60/63), 78 yrs 	<ul style="list-style-type: none"> ○ Home (weekly monitored by home visits or phone calls) ○ 10 weeks ○ 3 times/week ○ PG: One LE exercise with ankle weight ○ CG: attention control (received frequency matched telephone calls and home visits to check on recovery after hospitalization) 	<ul style="list-style-type: none"> ○ Muscle strength of knee extension ○ Balance: Berg Balance Test ○ Gait speed: 4-meter walk (habitual speed) ○ Timed Up-and-Go ○ Overall physical performance: Physical performance of SF-36 ○ ADL: Barthel Index
Lustosa, 2011 Brazil	<ul style="list-style-type: none"> ○ Aged 65+ yrs and pre-frail according to the criteria established by Fried et al. ○ PG n=32 (0/32), 72 yrs 	<ul style="list-style-type: none"> ○ Group (supervised) ○ 10 weeks ○ 3 times/week, 60 minutes each time 	<ul style="list-style-type: none"> ○ Muscle strength of knee extension ○ Gait speed: 10-meter walk test (habitual speed) ○ Timed Up-and-Go

	<ul style="list-style-type: none"> ○ CG n=16 (0/16), 72 yrs 	<ul style="list-style-type: none"> ○ PG: LE exercises using ankle weight ○ CG: no intervention 	
<p>Miszko, 2003 United States</p>	<ul style="list-style-type: none"> ○ Aged 65-90 yrs and had leg extensor power that was below average ○ PG n=13 (6/7), 73 yrs ○ CG n=15 (6/9), 72 yrs 	<ul style="list-style-type: none"> ○ Gym-based ○ 16 weeks ○ 3 times/week ○ PG: 4 UE/4 LE & squat exercises with machine ○ CG: attention control (met for an educational presentation three times over the study period) 	<ul style="list-style-type: none"> ○ Muscle strength of leg press ○ Overall physical performance: Continuous Scale Physical Functional Performance
<p>Skelton, 1996 United Kingdom</p>	<ul style="list-style-type: none"> ○ Women aged 75+ yrs with functional or mobility difficulties ○ PG n=10 (0/10), 81_{Median} yrs ○ CG n=10 (0/10), 81_{Median} yrs 	<ul style="list-style-type: none"> ○ Combination of home (unsupervised, followed an illustrated booklet) and class (supervised) ○ 8 weeks ○ 3 times/week, 30-60 minutes each time ○ PG: 2 UE & 4 LE exercises with elastic bands or tin cans ○ CG: no intervention 	<ul style="list-style-type: none"> ○ Muscle strength of knee extension ○ Balance: one-legged stand ○ Timed Up-and-Go
<p>Westhoff, 2000 Netherlands</p>	<ul style="list-style-type: none"> ○ Aged 65+ yrs with knee-extensor strength \leq 87.5Nm ○ PG n=11 (NR), 76 yrs ○ CG n=10 (NR), 78 yrs 	<ul style="list-style-type: none"> ○ Combination of home (unsupervised, followed an exercise booklet) and facility-based (supervised in a community center) ○ 10 weeks ○ 3 times/week, 40 minutes each time ○ PG: 9 LE exercises using elastic bands ○ CG: no intervention 	<ul style="list-style-type: none"> ○ Muscle strength of knee extension ○ Balance: Tandem stance ○ Gait speed: 20-meter walk (habitual speed) ○ Timed Up-and-Go ○ ADL: Gronigen Activity Restriction Scale

Multimodal Exercise

Multimodal Exercise			
<p>Barnett, 2003 Australia</p>	<ul style="list-style-type: none"> ○ Aged 65+ yrs and had ≥ 1 physical performance impairments that are risk factors for falls ○ MG n=83 (25/58), 74 yrs ○ CG n=80 (29/51), 75 yrs 	<ul style="list-style-type: none"> ○ Group in a community setting (supervised) and home (unsupervised) ○ One year ○ 1 time/week, 60 minutes (group); NR (home) ○ MG: balance and coordination, flexibility, aerobic, muscle strengthening, and functional exercises ○ CG: no intervention but received written information about falls prevention. 	<ul style="list-style-type: none"> ○ Muscle strength of knee extension ○ Gait speed: 6-meter walk ○ Chair stand: Five-times chair stand test ○ Overall physical performance: Physical performance of SF-36 ○ Fall: the rate of falls
<p>Beyer, 2007 Denmark</p>	<ul style="list-style-type: none"> ○ Women aged 70-90 yrs with a recent fall history resulted in an emergency room visit ○ MG n=32 (0/32), 79 yrs ○ CG n=33 (0/33), 78 yrs 	<ul style="list-style-type: none"> ○ Group in a gym (supervised) ○ 6 months ○ 2 times/week, 60 minutes each time ○ MG: flexibility, resistance, balance, and stretching exercises ○ CG: no intervention 	<ul style="list-style-type: none"> ○ Muscle strength of knee extension ○ Balance: Berg Balance Scale ○ Gait speed: 30-meter walk (habitual and maximal) ○ Chair stand: Five-times chair stand test (subgroup only)
<p>Buchner, 1997 United States</p>	<ul style="list-style-type: none"> ○ Aged 68-85 yrs with poor balance and weak knee extensor ○ MG n=25 (12/13), 75 yrs ○ CG n=30 (15/15), 75 yrs 	<ul style="list-style-type: none"> ○ Gym-based (supervised) ○ 24-26 weeks ○ 3 times/week, 60 minutes each time ○ MG: aerobic and strength exercises ○ CG: no intervention 	<ul style="list-style-type: none"> ○ Muscle strength of knee extension ○ Balance: Tandem stance and one-legged stand ○ Gait speed: 40-meter walk (habitual speed) ○ Overall physical performance: Physical performance of SF-36 ○ ADL: Lawton IADL scale (Number of IADLs) ○ Fall: the rate of falls

<p>Clemson, 2010 Australia</p>	<ul style="list-style-type: none"> ○ Aged 70+ yrs and had two or more falls or one injurious fall in the past year ○ MG n=16 (7/9), 81 yrs ○ CG n=18 (11/7), 82 yrs 	<ul style="list-style-type: none"> ○ Home (five home visits with two booster visits over a three-month period and two follow-up phone calls) ○ 6 months ○ Exercise was embedded in ADL ○ MG: strength and balance exercises embedded in ADL ○ CG: no intervention 	<ul style="list-style-type: none"> ○ Falls: The rate of falls
<p>Freigberger, 2012 Germany</p>	<ul style="list-style-type: none"> ○ Aged 70+ yrs. and had fallen in the past 6 months or have a fear of falling ○ MG1 n=63 (33/30), 76 yrs ○ MG2 n=64 (41/23), 75 yrs ○ CG n=80 (43/37), 77 yrs 	<ul style="list-style-type: none"> ○ Group (supervised at a university setting) and home (unsupervised) ○ 16 weeks ○ 2 times/week, 60 minutes each time ○ MG1: strength and balance exercises ○ MG2: strength, balance, and endurance exercises ○ CG: no intervention 	<ul style="list-style-type: none"> ○ Balance: Modified Romberg test ○ Gait speed: 10-meter walk (habitual and maximal speed) ○ Chair stand: Five-times chair stand test ○ Timed Up-and-Go ○ Falls: the rate of falls
<p>Giné-Garriga, 2010 Spain</p>	<ul style="list-style-type: none"> ○ Aged 80-90 yrs with self-report difficulty in chair rising or stair climbing ○ MG n=22 (9/13), 84 yrs ○ CG n=19 (7/12), 84 yrs 	<ul style="list-style-type: none"> ○ Group at a primary care facility (supervised) ○ 12 weeks ○ 2 times/week, 45 minutes each time ○ MG: functional circuit training (balance-based activities and lower body strength-based activities) ○ CG: attention control (weekly social meetings) 	<ul style="list-style-type: none"> ○ Muscle strength of quadriceps ○ Balance: Tandem stance and one-legged stand ○ Gait speed: 12-meter walk (habitual and maximal speed) ○ Chair stand: Five-times chair stand test ○ Modified Timed Up-and-Go ○ ADL: Barthel Index
<p>Haines, 2009</p>	<ul style="list-style-type: none"> ○ Aged 65+ yrs with gait 	<ul style="list-style-type: none"> ○ Home (monitored via home 	<ul style="list-style-type: none"> ○ Balance: Balance Outcome

Australia	<p>instability or using a mobility aid</p> <ul style="list-style-type: none"> ○ MG n=19 (5/14), 81 yrs ○ CG n=34 (16/18), 81 yrs 	<p>visits and weekly phone calls)</p> <ul style="list-style-type: none"> ○ 8 weeks ○ As much as possible ○ MG: progressive resistance and balance exercises (Kitchen Table Exercise Program DVD) ○ CG: no intervention 	<p>Measure for Elder Rehabilitation</p> <ul style="list-style-type: none"> ○ Gait speed: 2-minute walk test (maximal speed) ○ ADL: Frenchay Activities Index ○ Fall: the rate of falls
Kim, 2012 Japan	<ul style="list-style-type: none"> ○ Women aged 75+ yrs with sarcopenia ○ MG n=39 (0/39), 79 yrs ○ CG n=39 (0/39), 79 yrs 	<ul style="list-style-type: none"> ○ Facility-based (supervised) in a community setting ○ 3 months ○ 2 times/week, 60 minutes each time ○ MG: strength, balance and gait training exercises ○ CG: attention control (health education class once a month) 	<ul style="list-style-type: none"> ○ Muscle strength of knee extension ○ Gait speed: 11-meter walk (habitual and maximal speed)
Kim, 2015 Japan	<ul style="list-style-type: none"> ○ Frail older women and had unintentional weight loss, grip strength weakness, slow walking speed, exhaustion, and low activity ○ MG n=33, 81 yrs ○ CG n=32, 80 yrs 	<ul style="list-style-type: none"> ○ Group-based ○ 3 months ○ Twice/week, 60 minutes each time ○ PG: moderate intensity progressive resistance strength training, and balance and gait training ○ CG: no intervention 	<ul style="list-style-type: none"> ○ Muscle strength of knee extension ○ Gait speed: 5-meter walk (habitual speed) ○ Timed Up-and-Go
Nelson, 2004 United States	<ul style="list-style-type: none"> ○ Aged 70+ yrs with self-report functional limitations ○ MG n=34 (7/27), 78 yrs. ○ CG n=38 (8/30), 78 yrs. 	<ul style="list-style-type: none"> ○ Home (monitored via home visits) ○ 6 months ○ 3 times/week plus 120 minutes of physical activity each week 	<ul style="list-style-type: none"> ○ Muscle strength of knee extension ○ Balance: Tandem walk, one-legged stand ○ Gait speed: 2-meter walk (maximal speed)

		<ul style="list-style-type: none"> ○ MG: strength and balance exercises, and physical activity ○ CG: attention control (nutrition education with booklets and home visits) 	
<p>Rubenstein, 2000</p> <p>United States</p>	<ul style="list-style-type: none"> ○ Men aged 70+ yrs with one key risk of falls (i.e., leg weakness, impaired gait or balance, previous falls) ○ MG n=31 (31/0), 76 yrs. ○ CG n=28 (28/0), 74 yrs. 	<ul style="list-style-type: none"> ○ Group (supervised at a care center) ○ 12 weeks ○ 3 times/week, 90 minutes each time ○ MG: Strength, endurance/aerobic, and balance exercises ○ CG: no intervention 	<ul style="list-style-type: none"> ○ Muscle strength of knee extension ○ Balance: POMI Balance score and one-legged stand ○ Gait speed: 6-minute walk (convert to m/s, maximal speed) ○ Chair stand: 30-second chair stand test ○ Overall physical performance: Physical performance of SF-36 ○ Falls: the rate of falls
<p>Rydwik, 2008</p> <p>Sweden</p>	<ul style="list-style-type: none"> ○ Aged 75+ yrs who received home services and frail (inactive, weight loss or low body mass index) ○ MG n=23 (12/11), 84 yrs. ○ CG n=23 (7/16), 83 yrs. 	<ul style="list-style-type: none"> ○ Group (supervised) ○ 12 weeks ○ 2 times/week, 60 minutes each time ○ MG: aerobic, strength, and qigong-balance stretching exercise ○ CG: attention control (general physical training advice and diet advice) 	<ul style="list-style-type: none"> ○ Muscle strength of leg press ○ Balance: Step test ○ Gait speed: 10-meter walk (maximal speed) ○ Timed Up-and-Go ○ Chair stand: 30-second chair stand test
<p>Sherrington, 2008</p> <p>Australia</p>	<ul style="list-style-type: none"> ○ Mobility impairments (difficulty in walking, standing up or climbing stairs) ○ MG n=88 (39/49), 73 yrs. ○ CG n=85 (35/40), 76 yrs. 	<ul style="list-style-type: none"> ○ Group (supervised in a hospital setting) ○ 5 weeks ○ 2 times/week, 60 minutes each time and daily home exercise program ○ MG: circuit style exercises (balance and aerobic) 	<ul style="list-style-type: none"> ○ Muscle strength of knee extension ○ Balance: Step test and tandem stance ○ Gait speed: 6-meter walk (maximal speed) ○ Chair stand: Five-times chair stand test

		<ul style="list-style-type: none"> ○ CG: wait list control 	
<p>Vestergaard, 2008</p> <p>Demark</p>	<ul style="list-style-type: none"> ○ Women 75+ yrs who received public home care and unable to walk outdoor without assistance or walking aids ○ MG n=25 (0/25), 75 yrs. ○ CG n=28 (0/28), 76 yrs. 	<ul style="list-style-type: none"> ○ Home (monitored by bi-weekly phone calls) ○ 5 months ○ 3 times/week, 26 minutes each time ○ MG: strength, flexibility and dynamic balance exercises using a video and booklet ○ CG: attention control (bi-weekly phone calls) 	<ul style="list-style-type: none"> ○ Balance: Semi-tandem stance ○ Gait speed: 10-meter walk (maximal speed) ○ Chair stand: Five-times chair stand test ○ Overall physical performance: Physical Performance Test
<p>Villareal, 2011</p> <p>United States</p>	<ul style="list-style-type: none"> ○ Age 65+ yrs with mild to moderate frailty (limited physical performance or difficulty in ADL) ○ MG n=26 (10/16), 70 yrs. ○ CG n=27 (9/18), 69 yrs. 	<ul style="list-style-type: none"> ○ Group (supervised, in a university setting) ○ One year ○ 3 times/week, 90 minutes each time ○ MG: resistance, aerobic, flexibility, and balance exercises ○ CG: attention control (received general information about a healthy diet during monthly visits with the staff) 	<ul style="list-style-type: none"> ○ Balance: one-legged stand ○ Gait speed: 25-feet walk (maximal speed) ○ Overall physical performance: Modified Physical Performance Test ○ ADL: Functional Status Questionnaire
<p>Note. ADL- Activities of daily living. CG- Control group. LE- lower extremity. MG- Multimodal exercise Group. NR- not reported. PG- Progressive resistance exercise group. UE- upper extremity. yrs-years.</p>			

Table 2. Risk of Bias Rating.

	Selection Bias		Performance Bias	Detection Bias	Attrition Bias	Reporting Bias
1 st Author and Publication Year	Random Sequence Generation	Allocation Concealment	Blinding of Participants and Personnel	Blinding of Outcome Assessment	Incomplete Outcome Data	Selective Reporting
Progressive Resistance Exercise						
Bosuizen, 2005	Unclear	Unclear	High	Low	High	Low
Buchner, 1997	Unclear	Unclear	High	Low	Low	Low
Chandler, 1998	Unclear	Unclear	High	Low	Low	Low
Jette, 1999	Low	Unclear	High	Low	Low	Low
Latham, 2003	Low	Unclear	Low	Low	Low	Low
Lustosa, 2011	Low	High	High	Low	Low	Low
Miszko, 2003	Unclear	Unclear	High	Unclear	High	Low
Skelton, 1996	Unclear	Unclear	High	High	Low	Low
Westhoff, 2000	High	Unclear	High	Low	Low	Low
Multimodal Exercise						
Barnett, 2003	Low	Low	Low	Low	Low	Low
Beyer, 2007	Low	Unclear	High	Low	High	Low
Buchner, 1997	Unclear	Unclear	High	Low	Low	Low
Clemson, 2010	Low	Low	High	Low	Low	Low
Freiberger, 2012	Low	Unclear	High	Low	Low	Low

Giné-Garriga, 2010	Low	Unclear	Unclear	Unclear	High	Low
Haines, 2009	Low	Low	High	Low	Low	Low
Kim, 2012	Low	Low	High	Low	Low	Low
Kim, 2015	Low	Unclear	High	Low	Low	Low
Nelson, 2004	High	Unclear	Low	Low	Low	Low
Rubenstein, 2000	Low	Low	High	High	High	Low
Rydwik, 2008	High	Unclear	High	Unclear	High	Low
Sherrington, 2008	Low	Low	High	High	Low	Low
Vestergaard, 2008	High	Unclear	Low	High	Low	Low
Villareal, 2011	High	Unclear	High	Low	Low	Low

Table 3. Summary of Physical Functioning Outcomes by Types of Exercise.

	Progressive Resistance Exercise		Multimodal Exercise	
	# of Comparisons (# of cases)	Pooled effect size (95 % CI)	# of Comparisons (# of cases)	Pooled effect size (95 % CI)
Balance				
Static standing balance: tandem stance	4 (320)	MD = 0.74 (0.00, 1.48)	4 (295)	MD = 2.60 (-0.51, 5.70)
Static standing balance: one-legged stand	-	-	5 (272)	MD = 2.85 (-0.37, 6.07)
Dynamic standing balance	-	-	3 (275)	SMD = 0.46** (0.22, 0.70)
Other balance outcomes	3 (323)	SMD = .10 (-0.39, 0.58)	4 (268)	SMD = 0.37** (0.12, 0.61)
Gait Speed				
Maximal speed	-	-	11 (766)	SMD = 0.31* (0.03, 0.58)
Habitual speed	7 (476)	SMD = 0.08 (-0.11, 0.26)	6 (489)	SMD = 0.50** (0.13, 0.87)
Chair Stand				
	-	-	8 (654)	SMD = -0.26* (-0.50, -0.02)
Timed Up-and-Go				
	6 (536)	SMD = -0.02 (-0.19, 0.15)	3 (214)	SMD = -0.41 (-1.06, 0.24)
Overall Physical Functioning				
	4 (396)	SMD = -0.07 (-0.26, 0.13)	5 (349)	SMD = 0.08 (-0.13, 0.29)

Note. - not estimated. † fixed-effect model. ‡ random-effects model. * $p < .05$. ** $p < .01$

Figure 1. Flow Chart of Trial Selection.

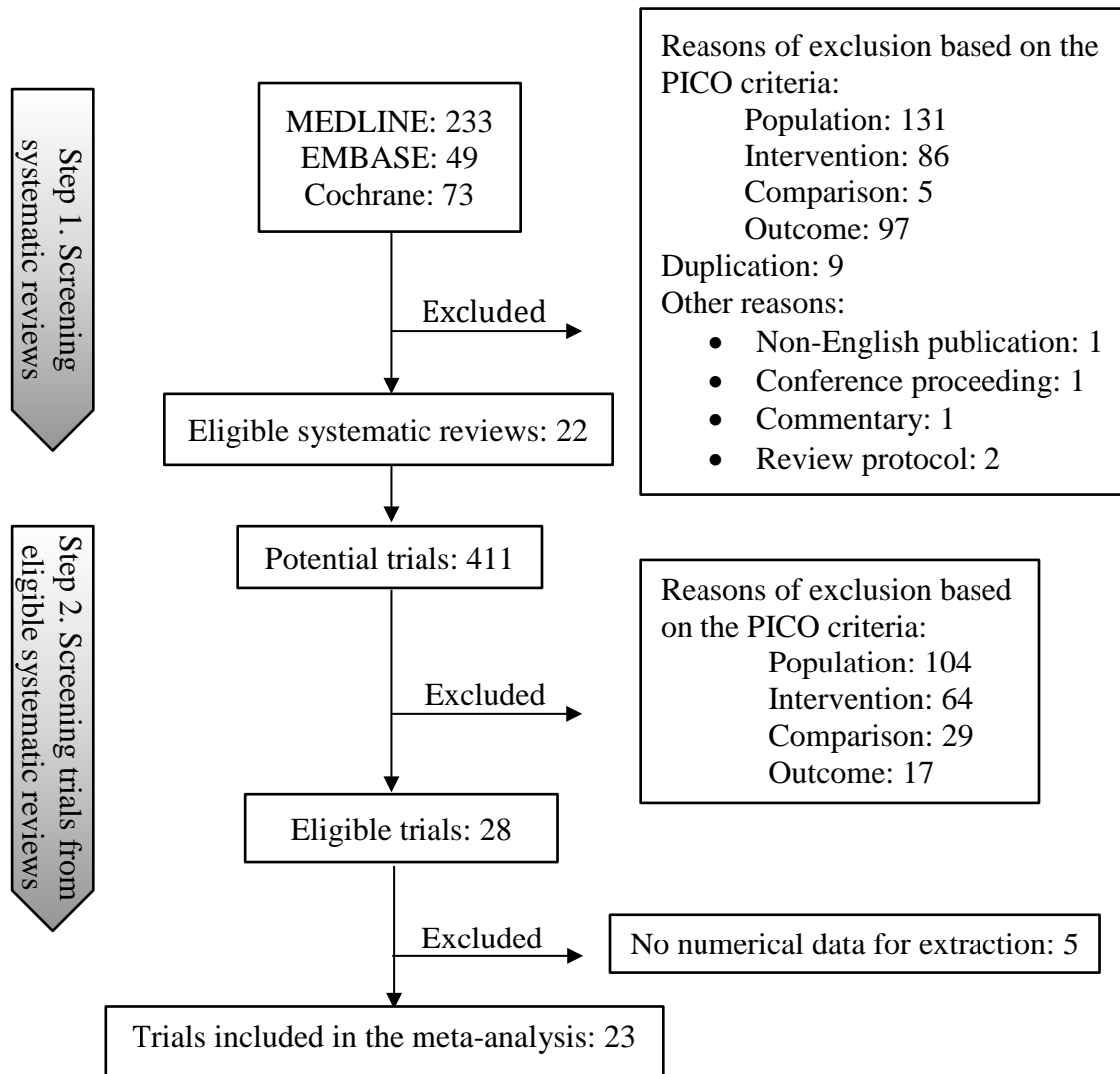


Figure 2. Outcomes of Muscle Strength of the Lower Extremity.

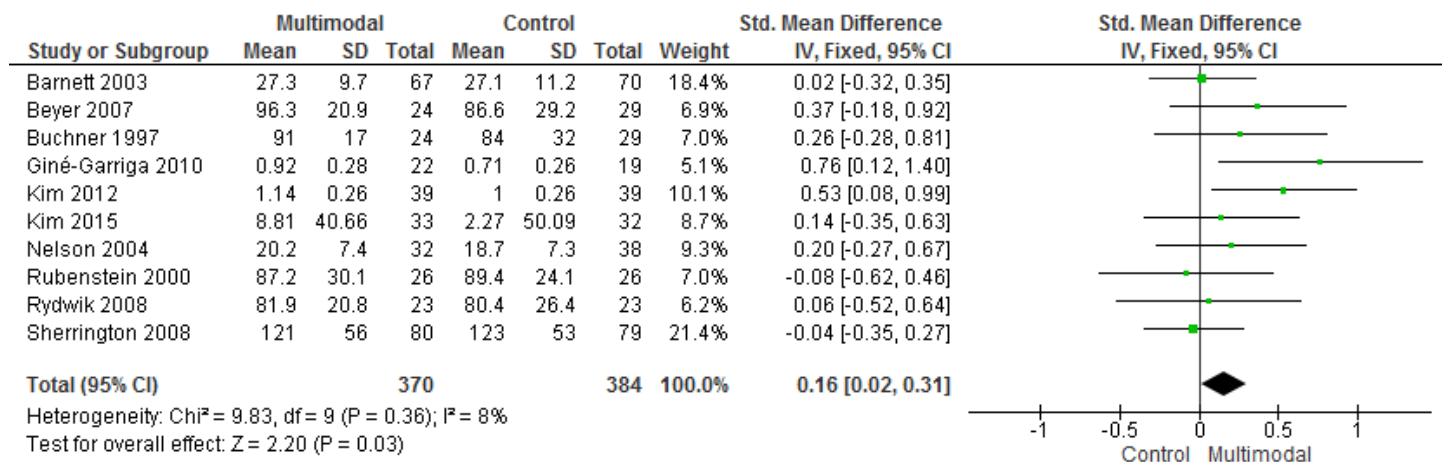
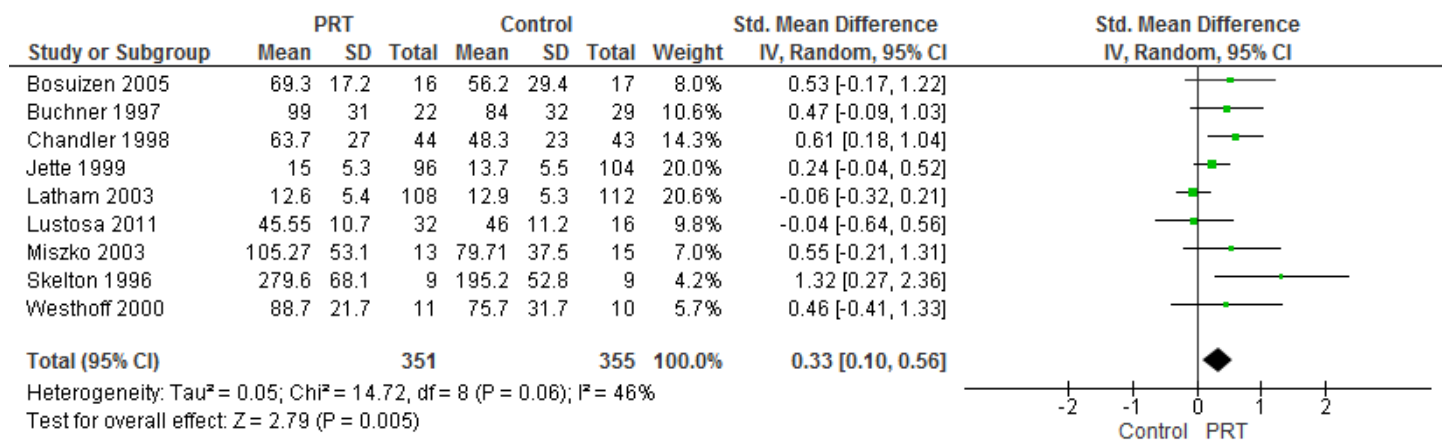


Figure 3. Outcome of Activity of Daily Living

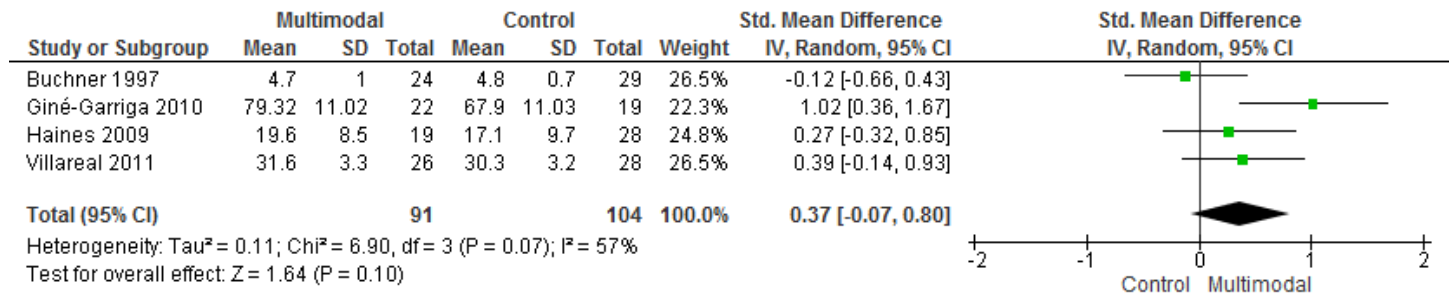
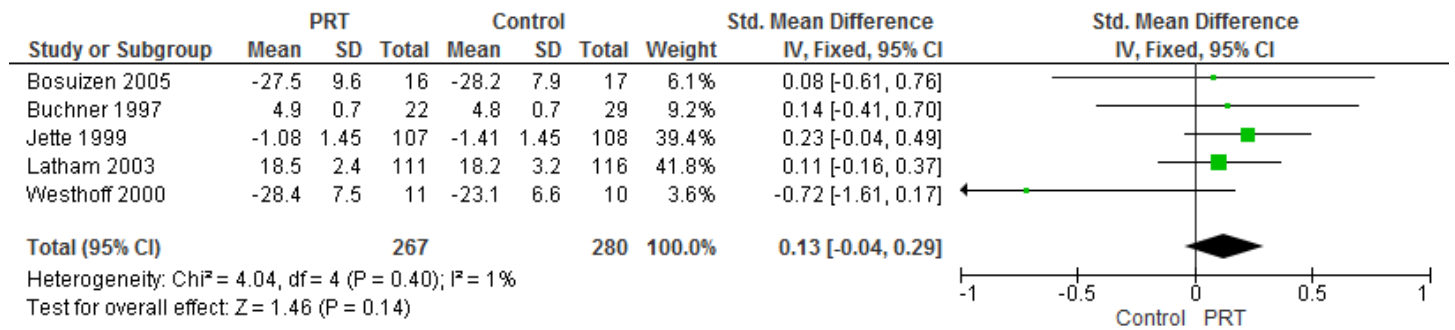
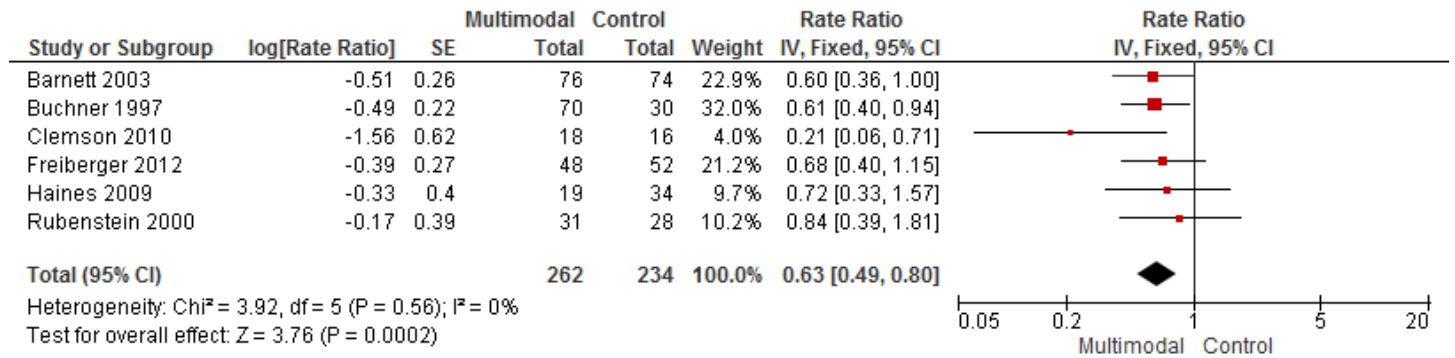


Figure 4. Outcome of Falls Rate





PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2-3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	6
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	6
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	The review was not registered. Stated on page 8
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	6-8
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	6-7
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	6-7
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	6-8
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	8
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	7
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	8
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	9



PRISMA 2009 Checklist

Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	9
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Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	10
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	NA
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	Fig1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	Table 1
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	Table 2
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Fig 2-4
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	Table 3, Fig 2-4 Page 11-13
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	8
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	NA
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	14, 17
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	15-17
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	17
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	1



PRISMA 2009 Checklist

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