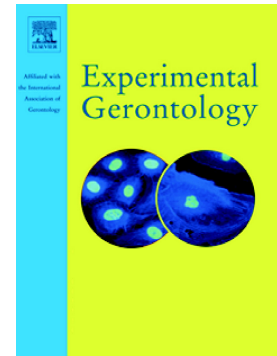


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Effects of resistance training concentric velocity on older adults' functional capacity: A systematic review and meta-analysis of randomised trials

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**EFFECTS OF RESISTANCE TRAINING CONCENTRIC VELOCITY ON OLDER
ADULTS' FUNCTIONAL CAPACITY: A SYSTEMATIC REVIEW AND META-
ANALYSIS OF RANDOMISED TRIALS**

Running title: Resistance training velocity and functional capacity

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ABSTRACT

Reduced levels of functional capacity in older adults are related to lower quality of life, frailty, and sarcopenia, and can increase risks of falling, fractures and hospitalisation. Resistance training is an effective method to attenuate age-related functional declines. Based on the findings that muscle power and explosive strength are strongly associated with functional performance in older adults, it has been suggested that fast-intended-velocity resistance training may elicit greater improvements in functional capacity when compared to moderate-velocity resistance training. However, currently, there is no high-quality systematic review and meta-analysis supporting this assertion. The present study compared the magnitude of functional capacity improvements following resistance training performed with fast-intentional velocity versus moderate velocity. Pubmed, Scopus, and Web of Science databases were searched from inception to January 2019. The following eligibility criteria for selecting studies was adopted: Participants aged ≥ 60 years; resistance training based intervention for lower limbs performed solely with slow to moderate concentric velocity (≥ 2 s for each concentric phase) or solely with the intention of maximising velocity (i.e., as fast as possible); and at least one functional test for lower limbs, with pre- and post-intervention measurements. When studies employed multiple functional tests, a single (pooled) standardised mean difference was calculated and presented as combined functional capacity. In addition, functional tests were grouped accordingly to their specificity for the sub-groups meta-analyses. Fifteen studies were selected (high quality, $n=3$; and pre-registered, $n=2$). The results presented heterogeneity and small-studies publication bias, leading to a biased advantage for fast-intended-velocity resistance training (95% CI=0.18, 0.65; $I^2=45\%$). Short physical performance battery indicated an advantage for fast-intended-velocity resistance training (95% CI=0.10, 0.94; $I^2=0\%$). There was no difference for timed up and go (95% CI=-0.07, 0.94; $I^2=48\%$), 30-s chair stand (95% CI=-0.24, 1.39; $I^2=71\%$), 5-times chair stand (95% CI=-1.63, 1.27; $I^2=57\%$) stair climb

(95%CI=-1.89, 2.81; $I^2=0\%$), short walk (95%CI=-0.99, 0.96; $I^2=21\%$) and long walk (95%CI=-0.59, 1.00; $I^2=0\%$). These results suggest that there is inconclusive evidence to support the superiority of fast-intended-velocity resistance training to improve functional capacity when compared to moderate-velocity resistance training. These results may have been influenced by the lack of high-quality and pre-registered studies, high heterogeneity, and small-studies publication bias.

PROSPERO registration number: CRD42019122251

Key words: Ageing; Function; Sarcopenia; Elderly; Concentric velocity; Strength training.

1. INTRODUCTION

The ability to perform distinct daily living and work physical activities, such as walking, chair standing and stair climbing, (i.e. functional capacity) (da Silva et al., 2018) is considerably decreased during human aging as a consequence of several neuromuscular impairments (Orssatto et al., 2018; World Health Organization, 2015). Reduced levels of functional capacity in older adults are related to lower quality of life (Öztürk et al., 2011), frailty (Podsiadlo and Richardson, 1991), sarcopenia (Cruz-Jentoft et al., 2018), and can increase risk of falling (Moreira et al., 2018), fractures (Kärkkäinen et al., 2008) and hospitalisation (Cawthon et al., 2009). This is of particular relevance given the growing elderly population, which creates an increased economic burden on healthcare systems (Heinrich et al., 2010). Thus, effective interventions for maintenance or improvements in functional capacity during aging have a significant impact with personal, societal and economic outcomes.

Resistance training is an effective intervention to improve functional capacity in the elderly (Borde et al., 2015; Byrne et al., 2016; Csapo and Alegre, 2015; Fiatarone et al., 1990; Orssatto et al., 2019; Skelton et al., 1995; Steib et al., 2010; Tschopp et al., 2011). This type of exercise is characterised by sets of repeated muscle contractions against an external load, interspersed by rest intervals (Kraemer et al., 2017; Ratamess et al., 2009). The velocity at which the muscle shortens during each contraction (concentric action) can directly influence motor unit recruitment patterns (Desmedt and Godaux, 1977). While the size principle of motor unit recruitment appears to be maintained motor unit recruitment thresholds are diminished, and discharge rates are increased as the rates of force development increase (Budinggen and Freund, 1976; Del Vecchio et al., 2019; Desmedt and Godaux, 1977, 1978; Tanji and Kato, 1973). These recruitment patterns may influence training adaptations. For example, training with the intention to perform the concentric portion of each repetition as rapidly as possible has been proven effective for power improvement (Straight et al., 2015), and muscular power

is related to functional performance in older adults (Byrne et al., 2016). Thus, it has been suggested that resistance training with the intention to lift as fast as possible might induce greater functional performance improvements in the elderly than slow to moderate velocity training.

Some reviews have attempted to investigate the potential superiority of fast-intended velocity versus moderate-velocity resistance training on functional performance improvement, but their methods suffer from some limitations (Byrne et al., 2016; Orsatto et al., 2019; Steib et al., 2010; Tschopp et al., 2011). In summary, findings of the previous two meta-analyses are limited by the small number of studies included in the statistical analyses ($n \leq 3$ (Steib et al., 2010), and $n \leq 6$ (Tschopp et al., 2011)) that is naturally due to the date when the searches were performed (~10 years ago). This limits meta-analysis power, heterogeneity, and limits the interpretation of publication bias. Factors, such as the inclusion of studies from the same clinical trial (Steib et al., 2010; Tschopp et al., 2011), inadequate method for risk of bias assessment (Tschopp et al., 2011), and lack of pre-registration of clinical trials (Steib et al., 2010; Tschopp et al., 2011) contributes to their weakness. In addition, non-systematic review and selection of studies without fast-intended- vs moderate-velocity resistance training comparison results in potential bias (Orsatto et al., 2019). Furthermore, subjective exploration of data, without conducting meta-analyses (Byrne et al., 2016; Orsatto et al., 2019) does not provide quantitative statistical information. Consequently, current data supporting the hypothetical advantage of resistance training with fast-intended concentric velocities in older persons are unclear.

Given the volume of new research published since the most recent meta-analyses (Tschopp et al., 2011), it is now possible to conduct analyses with increased power and this allows for the analysis of specific or different functional capacity tests. Furthermore, by taking into consideration methodological limitations observed in previously mentioned studies,

conducting a proper meta-analysis should provide more robust evidence about the topic. Therefore, the aim of this systematic review and meta-analysis was to compare the magnitude of functional capacity improvements following fast-intended velocity vs. moderate-velocity resistance training for lower-limbs in older adults. It was hypothesised that performing fast-intended velocity training would result in greater improvements in functional capacity tests than moderate-velocity resistance training.

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2. MATERIAL AND METHODS

This study was registered at International Prospective Register of Systematic Reviews (PROSPERO: CRD42019122251).

2.1. Search strategy

A systematic literature search was undertaken in the PUBMED, SCOPUS, and Web of Science databases in January 2019. In summary, adopted terms were separated by four categories: 1) aging, 2) training type, 3) contraction velocity, and 4) functional capacity tests. Search details are depicted in Appendix A. The reference lists of the selected studies were screened for additional studies. Figure 1 illustrates the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) flow diagram (Moher et al., 2009).

2.2. Eligibility criteria

Study inclusion was decided by consensus between first and second authors. In case of disagreement on the inclusion of an article, the last author was consulted. Inclusion criteria were defined according to the Population, Intervention, Comparison, Outcome, and Study design (PICOS) approach (Liberati et al., 2009). Population: participants aged ≥ 60 years; Intervention: resistance training based intervention for lower limbs; Comparator: resistance training performed with moderate concentric velocity (duration of concentric phase ≥ 2 s), versus training performed with the intention of maximising concentric velocity (i.e., as fast as possible); Outcome: at least one functional test for lower limbs, with pre- and post-intervention measurements; Study design: randomised trials. In addition, the Physiotherapy Evidence Database (PEDro) criteria for inclusion of clinical trials was adopted: 1) the trials should

involve comparison of at least two interventions; 2) at least one of the interventions being evaluated must be currently part of physiotherapy practice; 3) the interventions should be applied to participants who are representative of those to whom the intervention might be applied in the course of physiotherapy practice; 4) the trial should involve random allocation; 5) the reference should not be an abstract and should be published in a peer-reviewed journal.

Exclusion criteria were defined as follows: 1) did not clearly describe the concentric and eccentric velocity; 2) did not compare at least one group performing fast-intended velocity resistance training to at least one group performing moderate-velocity resistance training; 3) moderate-velocity resistance training groups adopted a training intensity lower than fast-velocity group; 4) did not employ an external load equal to or greater than 60% of 1-RM (or Borg scale ≥ 13) as recommended by the American College of Sports Medicine for older adults (Ratamess et al., 2009) in any phase during the intervention period for the moderate-velocity resistance training groups; 5) did not report results adequately without accessibility to the data by alternative manners (e.g., contacting authors); 6) employed a pilot study design; 7) included cognitively limited participants that would impair the proper performance of exercises technique; 8) examined of the effects of combined training methods (i.e. fast-intended- and moderate-velocity resistance training) with different concentric velocity within the same group (e.g. mixed session periodization (Bezerra et al., 2018)); 9) employed intentional overload during eccentric contraction (i.e., eccentrically-biased training), since this could influence functional capacity changes (Raj et al., 2012). In addition, when different published reports were derived from the same trial, those with the shorter intervention periods were excluded to reduce the unit-of-analysis problem (Higgins and Green, 2008).

2.3. Data extraction

The sample (size and age) and exercise intervention characteristics (i.e., types of training, duration, frequency, intensity, volume (sets and repetitions), rest interval, concentric and eccentric velocity, lower limbs exercises, and functional tests adopted, for each group were extracted.

The means and standard deviations (SD) or standard error of the outcome measurements (functional capacity tests) were extracted for fast-intended and moderate-velocity resistance training conditions. When presented in graphs figures, data was extracted with Web Plot Digitizer (version 4.1). When the standard error was reported, it was transformed to SD by multiplying the standard error by the square root of the sample size.

Measures of functional capacity were grouped according to their characteristics for meta-analysis, as follows: Timed up and go, short physical performance battery, 30-s chair stand, 5 times chair stand, short walk (≤ 10 m walk) performed with intention of maximum velocity, long walk (400 m or 6 min walk). Functional tests adopted in only one study did not appear in the subgroups meta-analysis. Balance tests and flexibility tests were not analysed.

2.4. Quality assessment

Methodological study quality was assessed using the PEDro scale (Maher et al., 2003). This scale includes 11 items for rating randomised clinical trials on a scale from 0 to 10 (low- to high-quality) (the first item is not included in the rating). The cut-off score for high-quality studies is ≥ 6 points. Scores were obtained from the PEDro database and were therefore scored by independently, avoiding any potential bias of the authors. When a study was not available on the PEDro database, the first and second authors independently rated the risk of bias. The

disagreement was resolved by consensus with the last author. In addition, articles were screened to identify if clinical trial pre-registration was conducted.

2.5. Statistical analysis

First, absolute changes in functional capacity were calculated with an Excel spreadsheet (version 2016, Microsoft), for both groups from the difference between final and baseline means. Change SD was calculated with equation 1 (Higgins and Green, 2008). Since the correlation coefficient (r) between baseline and final measures was not reported by most studies, a conservative estimate ($r = 0.7$) was employed (Khoury et al., 2013).

$$\text{Equation 1: Change SD} = \sqrt{\text{Baseline SD}^2 + \text{Final SD}^2 - (2 \times r \times \text{Baseline SD} \times \text{Final SD})}$$

RStudio (Version 1.0.153) was used for meta-analysis, heterogeneity analysis, Egger's test and trim-and-fill procedures, and forest and funnel plots production. Meta-analysis was undertaken pooling the studies' standardised mean differences, with the inverse variance method, random effects (Hartung-Knapp adjustment), and Sidik-Jonkman estimator for τ^2 (Sidik and Jonkman, 2007). Heterogeneity was assessed by visual inspection of forest plots and using X^2 test for heterogeneity ($\alpha = 0.1$), and described inconsistency between trials using I^2 statistic ($I^2 = 0 - 40\%$, might not be important; $30 - 60\%$, may represent moderate heterogeneity; $50 - 90\%$, may represent substantial heterogeneity; and $75 - 100\%$, considerable heterogeneity) (Deeks et al., 2008; Higgins and Green, 2008). A funnel plot and Egger's regression test (Egger et al., 1997) was performed in the analysis with more than 10 studies to assess publication bias. When Egger's test was significant, the trim-and-fill procedure was adopted to estimate an actual effect size without the influence of potential publication bias (Duval and Tweedie, 2000). Meta-analyses were performed for combined and specific functional tests. Combined functional tests were determined by pooling the standardised mean

difference (inverse variance and random effect) of all the lower limbs' functional tests from the each study. Specific functional tests were analysed in sub-groups according to test type: a) timed up and go, b) short physical performance battery, c) 30-s chair stand, d) 5 times chair stand, e) stair climb, f) short walk, and g) long walk. An α of 5% was adopted for all meta-analyses. In addition, an independent samples Student's t-test (2-tailed) was employed to compare participants' dropout during the intervention period for fast-intended-velocity and moderate-velocity groups ($\alpha = 5\%$).

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3. RESULTS

3.1. Summary of findings

A PRISMA flow diagram of the article search, showing included and excluded studies, is shown in Figure 1. The search retrieved 4752 studies, with 840 excluded after duplicate removal and a further 3883 were excluded after the title and abstract reading. After reading 29 full-text articles, 14 were excluded (see Appendix B for a list of excluded studies), and fifteen studies were considered eligible for the qualitative synthesis (Balachandran et al., 2014; Bean et al., 2009; Bottaro et al., 2007; Correa et al., 2012; Englund et al., 2017; Gray et al., 2018; Henwood et al., 2008; Lopes et al., 2016; Marsh et al., 2009; Miszko et al., 2003; Ramírez-Campillo et al., 2014; Richardson et al., 2019; Tiggemann et al., 2016; Yoon et al., 2017; Zech et al., 2012). Gray et al., (2018) was not included in the meta-analyses.

** Figure 1 near here **

3.2. Methodological Quality

Bias assessment revealed a mean PEDro score of 4.5 ± 1.1 points for the selected studies. Three studies achieved the cut-off score for high quality (≥ 6), while 12 did not. The allocation concealment, participant, therapist, and assessor blinding, >15% participant drop out during intervention, and the lack of intention-to-treat analysis were the quality items that most studies failed to achieve or report, resulting in a low overall rating. All selected trials adopted a randomised design. Only two studies (Bean et al., 2009; Zech et al., 2012) pre-registered their clinical trials (NCT00158119 and NCT00783159) (Table 1).

3.3. Studies characteristics

Six studies were conducted in the USA, four in Brazil, and one each in Australia, Chile, United Kingdom, Korea, and Germany. Fifteen included studies resulted in a total n of 593 (n = 304 for fast-intended-velocity resistance training, and n = 289 for moderate-velocity resistance training). Mean age ranged from 64.4 to 81.6 years. Short physical performance battery test was assessed in 7 studies, timed up and go in 8, 30-s chair stand in 6, 5-times chair stand in 3, short walk tests in 3, long walk in 4, stair climb in 2. Refer to table 1 for intervention methods, description of the functional tests adopted for each study and other study characteristics.

One study did not report the detailed time course of the participants' selection and exclusion (Correa et al., 2012). Fast-intended-velocity resistance training groups had $22.5 \pm 12.7\%$, and moderate-velocity resistance training groups had $20.1 \pm 14.1\%$ participant drop-out during the experimental period, without statistical difference between groups ($p = 0.63$) (Table 1). Only two studies reported injury-related dropouts (fast, n = 3; and moderate, n = 1) (Bean et al., 2009; Zech et al., 2012).

Correa et al. (2012) compared two groups that trained with fast-intended-velocity resistance training with one group of moderate-velocity resistance training. Therefore, in this meta-analysis, each fast-intended-velocity group was compared to the moderate-velocity group, in which sample size was divided by two with the intention of reducing the unit-of-analysis problem (Higgins and Green, 2008). Richardson et al. (2019) compared two different frequencies for two groups of fast intended velocity and two of moderate velocity. The comparison was conducted between groups with the same training frequency.

** Table 1 here **

3.4. Training Characteristics

Table 2 details the studies' training characteristics. Training frequency ranged from 1 to 3 sessions per week and was matched between fast-intended- and moderate-velocity resistance training groups for all studies. Training duration comparing both types of training ranged from 6 to 36 weeks. Seven studies adopted a similar training load (%1RM) for fast-intended- and moderate-velocity groups (Bean et al., 2009; Bottaro et al., 2007; Correa et al., 2012; Englund et al., 2017; Marsh et al., 2009; Tiggemann et al., 2016; Zech et al., 2012) and eight adopted higher load (%1RM) for moderate-velocity resistance training (Balachandran et al., 2014; Gray et al., 2018; Henwood et al., 2008; Lopes et al., 2016; Miszko et al., 2003; Ramírez-Campillo et al., 2014; Richardson et al., 2019; Yoon et al., 2017). Sets per exercise ranged from 2 to 4, and this was matched between groups for 14 studies and except for Lopes et al., (2016). Repetitions per set ranged from 6 to 15, where eleven studies adopted the same repetitions per set between groups (Balachandran et al., 2014; Bottaro et al., 2007; Correa et al., 2012; Englund et al., 2017; Gray et al., 2018; Henwood et al., 2008; Marsh et al., 2009; Miszko et al., 2003; Ramírez-Campillo et al., 2014; Tiggemann et al., 2016; Zech et al., 2012), two adopted more repetitions for fast-intended-velocity groups (Richardson et al., 2019; Yoon et al., 2017) and one adopted more repetitions for moderate-velocity group (Lopes et al., 2016). One study did not clearly report the number of repetitions performed for the fast-intended-velocity group (Bean et al., 2009). Rest interval between sets and exercises ranged from 60 to 180 s, except in one study that performed circuit training for the fast-intended-velocity group, alternating upper- and lower-limbs exercises, without rest between exercises (Balachandran et al., 2014). This was the only study in which the rest interval differed between groups. Concentric velocity was performed as fast as possible for all fast-intended-velocity groups and ranged from 2 to 4 s for the moderate-velocity groups.

** Table 2 here **

3.5. Studies or data not included on meta-analysis

Gray et al. (2018) only reported the data for the complete training period (48 weeks), which combined moderate (first 24 weeks) and fast-intended velocities (last 24 weeks) for the high-velocity training group. Attempts to contact the authors to obtain mean and SD for all the testing phases were not successful. Thus, it was not possible to include this study results in the meta-analyses. Data from functional tests assessed in only one study were not included in subgroups meta-analysis. Miszko et al. (2003) was the only one that used the Continuous Scale Physical Functional Performance test, while only Henwood et al. (2008) conducted the usual and backward gait velocity tests. Two studies were not included in the short physical performance battery subgroup meta-analysis due to the following reasons: Richardson et al. (2019) adopted Short Physical Performance Battery balance test and participants achieved maximal score (12 points) in baseline and post-intervention measurements. In Englund et al. (2017), post-intervention short physical performance battery test achieved maximal score (12 points) for both fast-intended-velocity and moderate-velocity groups. Therefore, it was not possible to ensure if the further increases in functional performance occurred.

3.6. Effects of concentric velocity during resistance training on functional capacity

Meta-analysis including the 14 studies combining different functional capacity tests indicated that fast-intended-velocity resistance training improvements may be superior compared to moderate-velocity resistance training for general functional capacity improvements in older persons ($p = 0.0024$; Figure 2A). For subgroups analysis, fast-intended-velocity resistance training improvements was superior versus moderate-velocity resistance training for short physical performance battery ($p = 0.026$; Figure 2C). On the other hand, the

effects of fast-intended-velocity and moderate-velocity resistance training were not statistically different on timed up and go ($p = 0.079$ Figure 2B), 30-s chair stand tests ($p = 0.136$; Figure 3A), 5-times chair stand ($p = 0.644$; Figure 3B), stair climb ($p = 0.243$; Figure 3C), short walk ($p = 0.952$; Figure 3D), or long walk ($p = 0.243$; Figure 3E) data.

** Figure 2 here **

** Figure 3 here **

3.7.Heterogeneity of results

X^2 statistics indicate that combined functional tests, 30-s chair stand and 5-times chair stand subgroups analyses presented statistically significant heterogeneity (Figures 2A, 3A, and 3B, respectively). I^2 statistics indicate that combined functional tests and 5-times chair stand analyses presented moderate heterogeneity (Figure 2A and 3B, respectively), and 30-s chair stand subgroup presented substantial heterogeneity (Figures 2B and 3A, respectively).

For the combined functional tests analysis, significant Egger's test of the intercept (Intercept = 1.872; 95%CI = 0.23, 3.51; $p = 0.045$) indicates that there is funnel plot asymmetry (Figure 4A). The trim-and-fill procedure identified and trimmed five studies (Balachandran et al., 2014; Bottaro et al., 2007; Correa et al., 2012; Lopes et al., 2016; Miszko et al., 2003), which resulted in a bias-corrected estimated standardised mean effect of 0.23 ($p = 0.092$; 95%CI = -0.042, 0.501). This suggests that publication bias may have resulted in overestimated effects of this meta-analysis (Figure 4B).

** Figure 4 here **

4. DISCUSSION

4.1. Summary of main results

The systematic literature search identified 15 studies, which allowed the meta-analyses comparing the combined functional tests of all studies and different sub-groups of specific tests, with stronger power than previous studies (Steib et al., 2010; Tschopp et al., 2011). The main findings suggest a lack of good-quality and pre-registered studies comparing fast-intended versus moderate-velocity resistance training. These analyses revealed moderate-to-substantial levels of heterogeneity, a wide range of predictive interval, and small-studies publication bias for most of the performed meta-analyses. Therefore, the advantages toward fast-intended-velocity resistance training, as observed in the meta-analysis for combined functional tests, and short physical performance battery are unclear and should be interpreted with caution. In addition, fast-intended and moderate-velocity resistance training presented similar improvements for timed up and go, 30-s chair stand, 5-times chair stand, stair climb, and short and long walk tests.

4.2. Agreements and disagreements with other reviews

There are a number of important methodological differences between the present study and previous reviews. For example, none of the previous systematic reviews was pre-registered, which is fundamental for transparency and the avoidance of bias (e.g. selective data reporting and statistical analysis).

In the current study, the adoption of pre-published PEDro scores minimised bias in the assessment of risk of bias. However, three recent studies had not yet been scored in the PEDro database and these were evaluated by us. Tschopp et al. (2011) assessed the risk of bias without a proper instrument, and used their own subjective criteria to determine bias. The authors

considered only allocation sequence, concealment of allocation, blinding of assessors and adequacy of analyses. Steib et al. (2010) adopted the van Tulder et al., (2003) scale, and the authors ranked study bias. Byrne et al. (2016) assessed the risk of bias with Cochrane Collaboration's tool for assessing the risk of bias on two domains (i.e. random sequence generation and blinding of outcome assessment) (Higgins and Green, 2008), while Orssatto et al. (2019) did not assess the risk of bias.

The current search retrieved 15 studies, while Tschopp et al. (2011) and Steib et al. (2010) selected only 7 and 3, respectively. Tschopp et al. (2011) therefore conducted a limited analysis combining different functional capacity tests ($n = 6$), and grouping timed up and go, 400-m walk, treadmill walking speed, and timed 2.4 m ($n=4$) tests. Steib et al. (2010) grouped chair rise ($n = 3$), stair climbing ($n = 2$), walking speed ($n = 2$) and timed up and go tests ($n = 1$). The small number of included studies reduced the statistical power of these meta-analyses and did not allow an appropriate analysis of heterogeneity and small studies effect/publication bias. One major limitation of Steib et al. (2010) was the inclusion of two studies from the same clinical trial (Henwood and Taaffe, 2006, 2008), which results in analysis bias. The larger number of studies included in the present systematic review allowed the grouping of functional tests in seven categories according to their characteristics.

4.3. Quality of the evidence, pre-registration, heterogeneity, and publication bias

Most of the included studies (12/15) did not achieve the PEDro scale's high-quality cut-off point (≥ 6), indicating a high risk of bias. Due to the nature of the interventions comparing fast-intended-velocity versus moderate-velocity resistance training, blinding of participants and therapists is not feasible. Furthermore, most of the studies failed to employ concealed participant allocation, blinding of assessors and intention-to-treat analysis.

Only two of the included studies pre-registered their clinical trials (Bean et al., 2009; Zech et al., 2012). Prospective registration of clinical trials increases transparency by reporting study's purpose, recruitment status, design, eligibility criteria, locations and primary and secondary outcomes before the study commencement (Zarin et al., 2011). This prevents selective reporting of the outcomes that are derived after the trial is completed. The current requirement for prospective pre-registration of clinical trials has been associated with an increase in the number of clinical trials reporting null results (Kaplan and Irvin, 2015). Interestingly, the two pre-registered studies (Bean et al., 2009; Zech et al., 2012) are among the three high-quality studies (Bean et al., 2009; Richardson et al., 2019; Zech et al., 2012), and these two studies reported smaller benefits in favour of fast-intended-velocity training than most of the low-quality, non-pre-registered studies (see figures 2 and 3). This suggests that low-quality non-registered studies might have biased the present findings to the benefit of fast-intended-velocity resistance training.

There were moderate to substantial levels of heterogeneity between studies for combined functional tests, timed up and go, 30-s chair stand, and 5-times chair stand. High heterogeneity may indicate that there are no real benefits of high-intended-velocity training over moderate-velocity training (Higgins and Green, 2008; Rücker et al., 2008). Furthermore, all the variables showed a prediction interval crossing the zero line, suggesting the possibility that future studies could favour moderate velocity resistance training.

The funnel plot graph asymmetry for combined functional tests (Figure 4) showed the potential that the current study had been unable to identify some small-studies with negative findings. The non-significant and lower bias-corrected standardised mean difference after trim-and-fill, indicates that advantages for fast-intended-velocity resistance training were potentially overestimated as a consequence of small-studies publication bias.

4.4. Potential biases in the review process and data analyses

The current study minimised multiple publication bias by excluding articles originated from the same clinical trial (Higgins and Green, 2008). Henwood et al. (2008) published data from the first 8 weeks of training (Henwood and Taaffe, 2006) and from a detraining and retraining period (Henwood and Taaffe, 2008). Zech et al. (2012) performed a clinical trial with a duration of 36 weeks but published data from the first 12 weeks in another manuscript (Drey et al., 2012). Therefore, these articles were excluded.

Balance and flexibility tests were not included in the review and meta-analysis. Despite studies considering balance as a functional capacity, it was considered as a very specific ability that may influence functional capacity and not as an assessment of functional capacity per se.

Henwood et al. (2008) performed three different walking tests (i.e., usual velocity, fast velocity, and backward). It was decided to adopt only fast velocity gait because of the similarity to other studies that evaluated this outcome (Ramírez-Campillo et al., 2014; Zech et al., 2012).

Balachandran et al. (2014) adopted circuit-based resistance training for the fast-intended-velocity group and not for the moderate-velocity group. Circuit training could potentially result in greater fatigue levels, attenuating functional capacity improvements observed in the fast-velocity group. However, the authors attempted to reduce fatigue by alternating lower- and upper-limb exercises, and by giving 60-120-s rest after each completed circuit. In addition, the standardised mean difference favoured the fast-intended-velocity group (Figure 2), and the training volume was equalised between groups. Also, it has been shown that fatigue levels during resistance training do not affect functional capacity improvements when training volume is equalised (Teodoro et al., 2019). Finally, although the authors acknowledge that the design of the study reported by Balachandran et al. (2014) in which fast-intended-

velocity circuit training was compared with non-circuit training for moderate velocity, differed methodologically from the other included studies, removal of that study from the combined functional capacity tests analysis did not result in significant changes to the current findings (standardised mean difference = 0.395; 95% CI = 0.148 – 0.643; $p = 0.0046$; $I^2 = 47\%$).

4.5. Implications for practice

The current findings suggest that in an elderly population, resistance training velocity or intended velocity may not be an influential factor when the outcomes are measures of functional capacity. However, functional capacity is not the only outcome that can be affected following resistance training. Therefore, when prescribing resistance training methods for older adults, potential acute (e.g., cardiovascular, metabolic, and neuromuscular demands) (Machado et al., 2019; Miyamoto et al., 2017; Orssatto et al., 2018) and chronic effects (e.g., increases in muscle mass, force and power) (Borde et al., 2015; Byrne et al., 2016; Guizelini et al., 2018; Orssatto et al., 2019; Steib et al., 2010; Straight et al., 2015; Tschopp et al., 2011) should also be considered. For example, fast-intended-velocity resistance training seems superior for power improvements in older adults (Byrne et al., 2016; Straight et al., 2015), but similar improvements are observed for strength (Steib et al., 2010; Tschopp et al., 2011). However, it remains unclear if the hypertrophic response of skeletal muscle are influenced by different resistance training velocities in older adults.

4.6. Implications for research

The low methodological quality of the selected studies may have biased the apparent advantage of fast-intended-velocity resistance training. Therefore, future high-quality randomised controlled trials are needed. These should attend to all the possible items of PEDro

score and be pre-registered. Such trials could additionally compare the effectiveness of fast-versus moderate-velocity resistance training on specific daily living activities, especially for the tasks that have been less explored in the literature to date (e.g. stair climb – ascent and descent, short and long walk velocity).

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5. CONCLUSIONS

Based on the available data, the findings suggesting that fast-intended-velocity resistance training might cause superior improvements when compared to moderate-velocity resistance training are inconclusive. The lack of high-quality and pre-registered studies, the level of heterogeneity, a wide range of predictive interval and small-studies publication bias could have influenced the results that favour fast-intended-velocity over moderate-velocity resistance training. More high-quality studies should be developed to provide evidence that is more robust and clarify the effects of concentric velocity during resistance training in older persons.

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Figure captions

Figure 1. PRISMA flow diagram for the systematic review.

Figure 2. Forest plot presenting standardised mean difference and 95% confidence intervals from studies reporting fast-intended-velocity versus moderate-velocity resistance-training-induced changes in A) combined functional capacity tests; B) timed up and go test; C) Short Physical Performance Battery test in older persons. PI, predictive interval; CI, confidence interval. Red, low-quality study (PEDro score <6); Green, high-quality study (PEDro score ≥ 6).

Figure 3. Forest plot reflecting standardised mean difference and 95% confidence intervals from the studies reporting fast-intended-velocity versus moderate-velocity resistance-training-induced changes in A) 30-s chair stand test; B) 5-times chair stand test; C) stair climb test; D) short walk test; D) long walk test in older persons. PI, predictive interval; CI, confidence interval; LF, low training frequency; HF, high training frequency; PT, power training group; RS, rapid strength group. Red, low-quality study (PEDro score <6); Green, high-quality study (PEDro score ≥ 6).

Figure 4. Funnel plot relating the 15 studies' effect sizes to the inverse of their standard error. A) Before, and B) After trim-and-Fill procedures. Grey scatter dots, studies included in the meta-analysis; White scatter dots, imputed studies mirrored for each trimmed study to reach funnel plot symmetry. Figure A: Note an asymmetry influenced by five studies. Figure B: After trim-and-fill, five studies were imputed, and the funnel plot then achieved symmetry and effect size reduced (dotted vertical line) compared to figure A.

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Table 1. Selected studies' characteristics

Reference	Country	Intervention method	Age	Health status	Initial n	Final n	Subjects exclusion (%)	Lower limbs functional capacity tests	PE Dro scores (0-10)	Pre-registered?
Balachandran et al. (2014)	USA	High-speed circuit	71.6 ±7.8	Sarcopenic obese	11	8	3 (27.3)	SPPB*	5	No
		Strength/Hypertrophy	71.0 ±8.2		10	9	1 (10)			
Bean et al. (2009)	USA	inVEST	74.7 ±6.8	With mobility limitations but able to climb a flight of stairs independently or using a device	72	59	13 (18.1)	SPPB	6	Yes
		NIA	76.1 ±6.9		66	58	8 (12.1)			
Bottaro et al. (2007)	Brazil	Power training	66.6 ±5.8	Apparently healthy	12	11	1 (8.3)	TUG, and 30sCR	4	No
		Traditional resistance training	66.3 ±4.8		12	9	3 (25)			
Correa et al. (2012)	Brazil	Power	67±5	Apparently healthy	13		-	30sCR	4	No
		Rapid strength			14		-			
		Traditional			14		-			
		Control			17		-			
Englund et al. (2017)	USA	High velocity resistance training	64.5 ±2.4	Apparently healthy	13	13	0 (0)	SPPB and TUG	3	No
		Low velocity	65.1 ±6.7		13	13	0 (0)			

		resistance training								
Gray et al. (2018)	USA	High-velocity	81.6 ±5.9	Apparently healthy	34	20	14 (41.2)	TUG, and 30sCR	4 [#]	No
		Low-velocity	81.0 ±5.5		41	25	16 (39.0)			
		Active control	81.3 ±5.3		24	8	16 (66.7)			
Henwood et al. (2008)	Australia	High-velocity	71.2 ±5.7	Apparently healthy	23	19	4 (17.4)	Floor rise to standing, stair climb, gait (usual, fast and backwards), 5xCR, and 400m walk	4	No
		Strength training	69.6 ±4.8		22	19	3 (13.6)			
		Control	69.3 ±3.9		22	15	7 (31.8)			
Lopes et al. (2016)	Brazil	Power-training	67±7.4	Apparently healthy and able to perform daily life activities without assistance	20	12	8 (40)	6 min walk, TUG, and 30sCR	4 [#]	No
		Strength-training	69±7.3		20	14	6 (30)			
		Control	65±3.1		15	11	4 (26.7)			
	USA	Power training	76.8 ±6.4		15	12	3 (20)	SPPB	4	No

Marsh et al. (2009)		Strength training	74.6 ±5.4	Apparently healthy	15	11	4 (26.7)			
		Wait-list control	74.4 ±5.2		15	13	2 (13.3)			
Miszko et al. (2003)	USA	Power-training	72.3 ±6.7	Low level of physical function	18	11	7 (38.9)	CS-PFP	3	No
		Strength-training	72.8 ±5.4		17	13	4 (23.5)			
		Control	72.4 ±7.2		15	15	0 (0)			
Ramirez-Campillo et al. (2014)	Chile	High-speed resistance training	66.3 ±3.7	Apparently healthy	20	15	5 (25)	10 m walk, TUG, and 30sCR	4	No
		Low-speed resistance training	68.7 ±6.4		20	15	5 (25)			
		Control	66.7 ±4.9		20	20	0 (0)			
Richardson et al. (2019)	United Kingdom	High-velocity, low load, once-weekly	66±5	Apparently healthy	11	10	1 (9.1)	TUG, and 30sCR, 6 min walk, SPPB (balance)	6 [#]	No
		High-velocity, low load, twice-weekly	67±4		11	10	1 (9.1)			
		Low-velocity, high load, once-weekly	67±6		10	10	0 (0)			
		Low-velocity, high load, twice-weekly	66±6		11	10	1 (9.1)			

		Control	65±5		11	10	1 (9.1)			
Tiggemann et al. (2016)	Brazil	Power training	64.4 ±4.0	Apparently healthy	15	12	3 (20)	Stair climb, TUG, and 5xCR	4	No
		Traditional resistance training	65.6 ±5.3		15	13	2 (13.3)			
Yoon et al. (2017)	Korea	High-speed power training	75.0 ±3.5	Mild cognitive impairment and able to walk without a walking aid	20	14	6 (30)	SPPB, and TUG	4	No
		Low-speed strength training	76.0 ±3.9		19	9	10 (52.6)			
		Control	78.0 ±2.8		19	7	12 (63.2)			
Zech et al. (2012)	Germany	Muscle power training	77.4 ±6.2	Pre-frail	24	16	8 (33.3)	SPPB (gait, chair rise)	7	Yes
		Muscle strength training	77.8 ±6.1		23	18	5 (21.7)			
		Control	78.0 ±1.0		22	20	2 (9.1)			

Method, named equal as in the respective studies; SPPB, Short Physical Performance battery; inVEST, weighted vest training; NIA, National Institute on Aging's strength training program; TUG, timed up and go; 30sCR, 30 s chair rise; 5xCR, 5 times chair rise; CP, conditioning period; CS-PFP, Continuous Scale Physical Functional Performance; *Adapted version; #Scored by the present study's authors.

Table 2. Training characteristics.

Reference	Intervention method	Lower-limbs' exercises	Training method	Supervision	Duration	Frequency	Intensity	Sets /exercise	Reps per set	Rest (s)	Conc vel	Ecc vel
Balachandran et al. (2014)	High-speed circuit	Leg press Leg curl Hip adduction Hip adduction Calf raise (Pneumatic exercise machines, Keiser A420, Keiser Sports Health Equipment, Fresno, CA)	Circuit training Alternate lower and upper limb exercise	The training was supervised by a minimum of two trainers.	15	2	50% - 80% 1RM (based on optimal loads for power outputs on specific machine)	3	10-12	60-120s after each circuit completion	AFA P	2s
	Strength/Hypertrophy	Equipment, Fresno, CA)	Split resistance training				70% 1RM			60-120s		
Bean et al. (2009)	inVEST	Weighted chair rise Toe raises Dorsiflexion Unilateral stance Step ups Stair climbing exercise	Emphasize a task-specific movement pattern rather than the	Maintenance of safe positioning, posture, and form was provided	16	3	RPE 11-16	2	When RPE ≥ 17 or heart rate $\geq 85\%$ of age-predicted	NR	AFA P	3s

			isolation of a specific muscle group.	by reinforcement from the trainer during exercise.					maximum			
	NIA	National Institute on Aging's strength training program with free weights	Focuses on isolating specific muscle groups using barbells or ankle weights						10		3s	3s
Bottaro et al. (2007)	Power training	Horizontal leg press Knee extension Knee flexion Technogym®, Biomedical line, Gambettola, Italy.	Split resistance training	NR	10	2	40% 1RM (sessions 1-2) 50% 1RM (sessions 3-4) 60% 1RM (subsequent sessions)	3	8-10	90s	AFA P	2-3s
	Traditional resistance training										2-3s	2-3s

Correa et al. (2012)	Rapid strength	Knee extension Knee flexion Lateral box jump. (Plated weights machine and box).	Split resistance training and plyometric training	NR	CP6+6	2	10–12 RM (first 3 weeks) 8–10 RM (first 3 weeks) Box heights were 10, 20 and 30 cm, increased every two weeks.	3 sets (first 3 weeks) 4 sets (last 3 weeks)	8 - 12	120s	AFA P	2s
	Power	Leg press Knee extension Knee flexion (Plated weights machine)	Split resistance training				10–12 RM (weeks 7–9) 8–10 RM (weeks 10–12)				AFA P	2s
	Traditional										2s	2s
Englund et al. (2017)	High velocity resistance training	Knee extensions Isokinetic dynamometer (Biodex Medical)	Split resistance training	NR	6	3	Maximal contraction	3	8	180s	240°/s.	-
	Low velocity										75°/s.	-

	resistance training	Systems, Shirley, NY)										
Gray et al. (2018)	High-velocity	Standing knee curl, Heel raises, Chair stand or Half lunge (Community setting, using free weight resistance)	Split resistance training. Trained at a low velocity at for 24 weeks before transitioning to high-velocity for the remaining 24 weeks.	Each exercise session was supervised by a member of the research team for increased safety as well as to document attendance and compliance	CP24+ 24	2	80% 1RM for 24 weeks and 50% 1RM for the remaining 24 weeks.	3	10	NR	AFA P	2s
	Low-velocity		Split resistance training.				80% 1RM					2s
Henwood et al. (2008)	High-velocity	Leg press, Leg curl Leg extension (Extek Pty Ltd, Brisbane, Qld, Australia).	Split resistance training.	Direct supervision by an exercise instructor to ensure safety and	CP2+2 2	2	45% (set 1), 60% (set 2) and 75% (set 3) 1RM	3	8 (third set of each exercise until failure.	60s	AFA P	3s

	Strength training			the maintenance of the exercise protocols.			75% 1RM				3s	3s
Lopes et al. (2016)	Power-training	Horizontal leg press, Knee extension, Knee flexion, Plantar Flexion Abductor Adductor Resistance training equipment (Nakagym)	Split resistance training	Direct supervision of an exercise instructor to ensure safety and maintenance of the exercise protocol.	12	3	40% 1RM Increases of 6%–8% every 2 weeks until 80% 1RM	3 - 4	6 - 8	180 s	AFA P	~2 s
	Strength-training						60% 1RM with increases when the last set repetitions were greater than 8	3	8		~2 s	~2 s
Marsh et al. (2009)	Power training	Leg press Knee extensors (Keiser pneumatic-	Split resistance training	Supervised by two ACSM–certified interventio	12	3	70% 1RM	3	8 to 10	NR	AFA P	2-3 s
	Strength training										2-3 s	2-3 s

		resistance machines)		nists. Participants attended a one-on-one orientation session								
Miszko et al. (2003)	Power-training	Leg press, Leg extension, Seated leg curl, Jump squats, Plantar flexion (Keiser Inc., Fresno, CA)	Split resistance training	NR	16	3	40% 1RM	3	6 - 8	NR	AFA P	2 s
	Strength-training						50-70% 1RM (weeks 1-8) 80% 1RM (weeks 9-16)				4 s	Slow and controlled
Ramirez-Campillo et al. (2014)	High-speed resistance training	Leg press, Prone Leg curl, Leg extension	Split resistance training	Direct supervision of an exercise instructor to ensure safety and the maintenance of the exercise protocol.	12	3	45% (set 1), 60% (set 2) and 75% (set 3) 1RM	3	8	60 s	AFA P	3s
	Low-speed resistance training						75% 1 RM				3 s	3 s
	High-velocity, low load,	Leg press, Calf raise, Leg extension,	Split resistance	NR	10	1	40% 1 RM	3	14	90-180 s	AFA P	3s

Richardson et al. (2018)	once-weekly	Leg curl (Cybex resistance training equipment)	e training																
	High-velocity, low load, twice-weekly												2					AFA P	3 s
	Low-velocity, high load, once-weekly												1	80% 1 RM	7	2 s	3 s		
	Low-velocity, high load, twice-weekly												2			2 s	3 s		
Tiggeman et al. (2016)	Power training	Leg press, Knee extension, Leg curl	Split resistance training	All training sessions were supervised by at least two trained technicians	10	2	RPE ranged between 13 and 18	2 - 3	8 - 15	120 s	AFA P	2 s							
	Traditional resistance training	Machines with weight columns (Ajustfitness, Caxias do Sul, Brazil).									2 s	2 s							
	High-speed	No exercise description.	Split resistance		12	2	Green elastic	2 - 3	12 - 15	60 - 120 s	AFA P	2 s							

Yoon et al. (2017)	power training	Authors stated that Exercise program followed the ACSM guidelines (Elastic bands training)	e training	Participants were supervised by a qualified Instructor for proper velocity and technique			bands (tension very low). RPE 12–13.					
	Low-speed strength training											
Zech et al. (2012)	Muscle power training	Hip Extension and flexion while standing, Hip adduction/abduction while standing Tip-toe raises Chair rise ('Bodyspider' resistance training machine)	Split resistance training	Trained instructors supervised all standardized training sessions	36	2	Borg's RPE 10–12 in the first weeks. The intensity increased every fortnight up to RPE 16	2	15 (initial weeks) to 6 (final weeks)	120 s	AFA	2 - 3 s
	Muscle strength training										2 - 3 s	2 - 3 s

1RM, 1-repetition maximum; RPE, rating of perceived exertion; AFAP, as fast as possible; NR, not reported; CP, conditioning period; Con, concentric; Ecc, eccentric; Vel, velocity; ACSM, American College of Sports Medicine.

HIGHLIGHTS

- We compared functional changes after fast- vs moderate-velocity resistance training;
- Out of the 15 selected studies only 3 were high-quality and 2 were pre-registered;
- Small-studies publication bias and significant heterogeneity were observed;
- The current data suggesting an advantage of fast-velocity training are inconclusive.

Journal Pre-proof

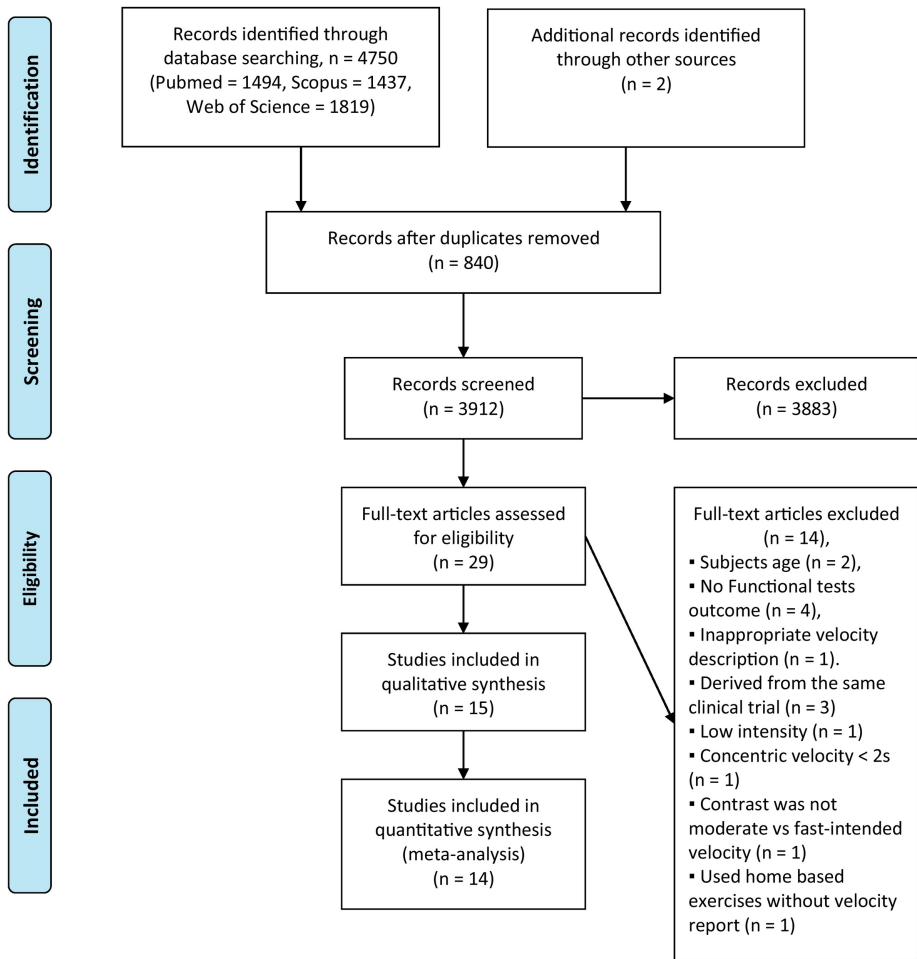
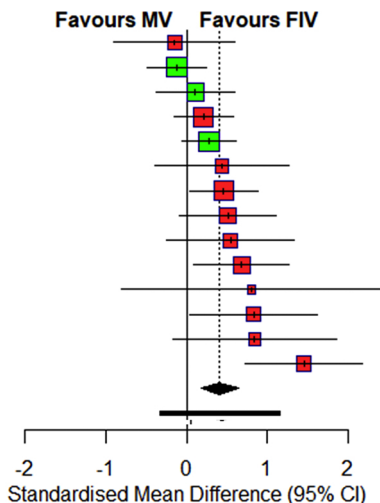


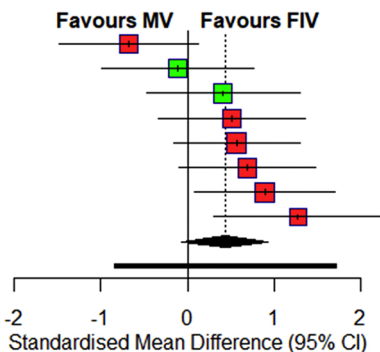
Figure 1

A

Source	SMD (95% CI)
Tiggemann et al. 2016	-0.15 [-0.90; 0.60]
Richardson et al. 2019	-0.12 [-0.48; 0.24]
Zech et al. 2012	0.11 [-0.37; 0.59]
Henwood et al. 2008	0.21 [-0.15; 0.57]
Bean et al. 2009	0.28 [-0.05; 0.61]
Marsh et al. 2009	0.44 [-0.39; 1.27]
Ramirez-Campillo et al. 2014	0.46 [0.04; 0.88]
Yoon et al. 2017	0.51 [-0.09; 1.11]
Englund et al. 2017	0.54 [-0.24; 1.32]
Miszko et al. 2003	0.68 [0.09; 1.27]
Correa et al. 2012	0.80 [-0.81; 2.41]
Lopes et al. 2016	0.83 [0.05; 1.61]
Balachandran et al. 2014	0.84 [-0.17; 1.85]
Bottaro et al. 2007	1.45 [0.73; 2.17]
Total	0.41 [0.18; 0.65]
95% PI	[-0.33; 1.16]
Heterogeneity: $\chi^2_{13} = 23.46$ ($P = .04$), $I^2 = 45\%$	

**B**

Source	SMD (95% CI)
Tiggemann et al. 2016	-0.68 [-1.49; 0.13]
Richardson et al. 2019 (LF)	-0.11 [-0.99; 0.76]
Richardson et al. 2019 (HF)	0.41 [-0.47; 1.30]
Yoon et al. 2017	0.51 [-0.34; 1.36]
Ramirez-Campillo et al. 2014	0.57 [-0.16; 1.30]
Englund et al. 2017	0.69 [-0.10; 1.48]
Lopes et al. 2016	0.90 [0.09; 1.71]
Bottaro et al. 2007	1.28 [0.31; 2.25]
Total	0.43 [-0.07; 0.94]
95% PI	[-0.84; 1.71]
Heterogeneity: $\chi^2_7 = 13.51$ ($P = .06$), $I^2 = 48\%$	

**C**

Source	SMD (95% CI)
Bean et al. 2009	0.28 [-0.05; 0.62]
Marsh et al. 2009	0.44 [-0.39; 1.27]
Yoon et al. 2017	0.52 [-0.33; 1.38]
Balachandran et al. 2014	0.84 [-0.15; 1.84]
Zech et al. 2012	1.15 [0.23; 2.06]
Total	0.52 [0.10; 0.94]
95% PI	[-0.33; 1.37]
Heterogeneity: $\chi^2_4 = 3.83$ ($P = .43$), $I^2 = 0\%$	

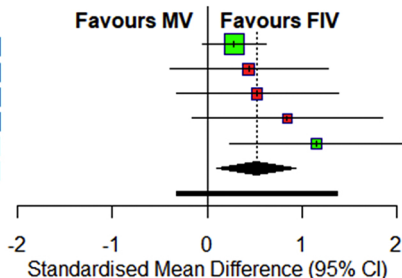
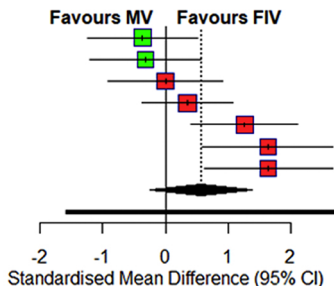


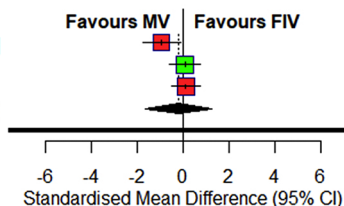
Figure 2

A

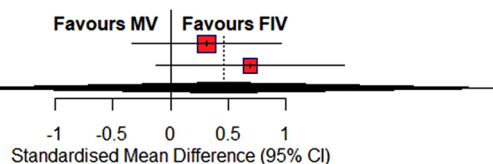
Source	SMD (95% CI)
Richardson et al. 2019(LF)	-0.37 [-1.25; 0.52]
Richardson et al. 2019 (HF)	-0.32 [-1.20; 0.56]
Correa et al. 2012 (PT)	0.00 [-0.92; 0.92]
Ramirez-Campillo et al. 2014	0.35 [-0.37; 1.07]
Lopes et al. 2016	1.26 [0.42; 2.11]
Correa et al. 2012 (RS)	1.64 [0.59; 2.68]
Bottaro et al. 2007	1.65 [0.62; 2.68]
Total	0.58 [-0.24; 1.39]
95% PI	[-1.59; 2.74]
Heterogeneity: $\chi^2_6 = 20.76$ ($P < .01$), $I^2 = 71\%$	

**B**

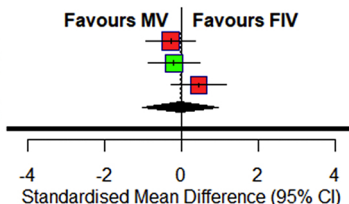
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Tiggemann et al. 2016	-0.92 [-1.75; -0.09]
Zech et al. 2012	0.11 [-0.57; 0.78]
Henwood et al. 2008	0.15 [-0.49; 0.78]
Total	-0.18 [-1.63; 1.27]
95% PI	[-7.56; 7.19]
Heterogeneity: $\chi^2_2 = 4.70$ ($P = .10$), $I^2 = 57\%$	

**C**

Source	SMD (95% CI)
Henwood et al. 2008	0.31 [-0.33; 0.95]
Tiggemann et al. 2016	0.69 [-0.12; 1.50]
Total	0.46 [-1.89; 2.81]
Heterogeneity: $\chi^2_1 = 0.52$ ($P = .47$), $I^2 = 0\%$	

**D**

Source	SMD (95% CI)
Henwood et al. 2008	-0.26 [-0.90; 0.38]
Zech et al. 2012	-0.19 [-0.86; 0.49]
Ramirez-Campillo et al. 2014	0.47 [-0.26; 1.19]
Total	-0.02 [-0.99; 0.96]
95% PI	[-4.51; 4.48]
Heterogeneity: $\chi^2_2 = 2.52$ ($P = .28$), $I^2 = 21\%$	

**E**

Source	SMD (95% CI)
Richardson et al. 2019 (LF)	-0.24 [-1.12; 0.64]
Richardson et al. 2019 (HF)	0.03 [-0.85; 0.90]
Lopes et al. 2016	0.08 [-0.69; 0.85]
Tiggemann et al. 2016	0.29 [-0.50; 1.08]
Henwood et al. 2008	0.64 [-0.02; 1.29]
Total	0.21 [-0.21; 0.63]
95% PI	[-0.59; 1.00]
Heterogeneity: $\chi^2_4 = 2.96$ ($P = .56$), $I^2 = 0\%$	

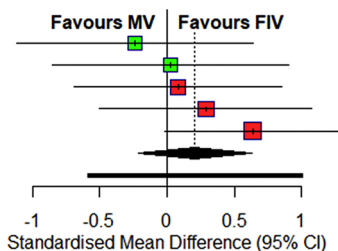


Figure 3

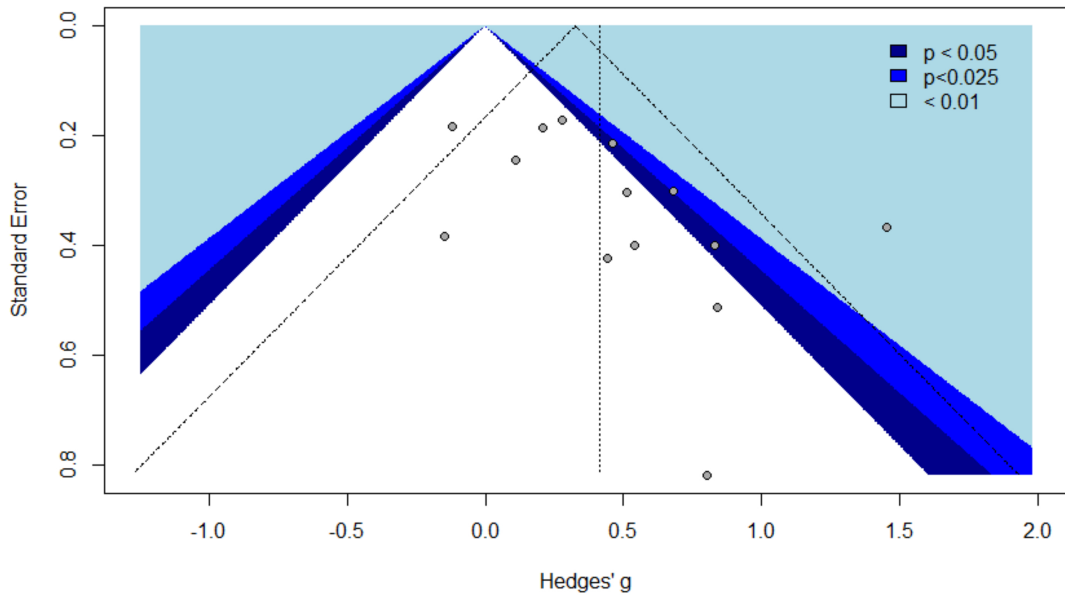
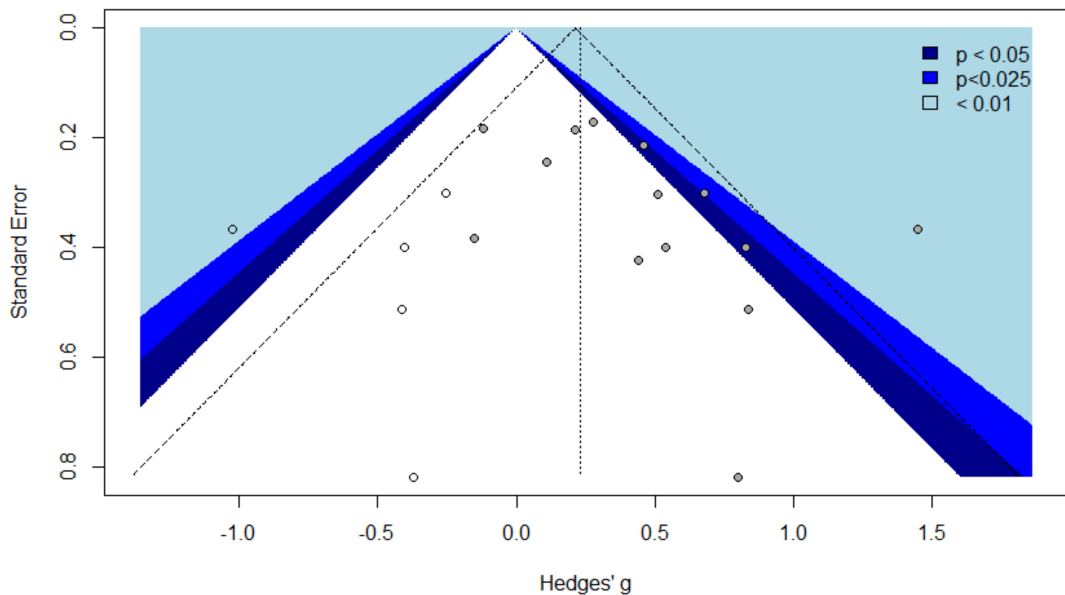
A**B**

Figure 4