Advancing age is not associated with greater exercise-induced muscle damage: A systematic review, meta-analysis, and meta-regression.

John F.T. Fernandes[1*], Laura J. Wilson[2], Amelia F. Dingley[3], Andrew N. Hearn[4], Kelsie O. Johnson[5], Kirsty M. Hicks[6,7], Craig Twist[5], Lawrence D. Hayes[8]

[1]School of Sport and Health Sciences, Cardiff Metropolitan University, Cardiff, UK
[2]London Sport Institute, Middlesex University, London, UK
[3]Department of Life Sciences, Brunel University, London, UK
[4]Department of HE Sport, Hartpury University, Hartpury, UK
[5]Research Institute of Sport and Exercise Sciences, Liverpool John Moores University, Liverpool, UK
[6]Department of Sport, Exercise and Rehabilitation, Northumbria University, Newcastle, UK
[7]Washington Spirit, District of Columbia, Washington, USA
[8]Lancaster Medical School, Lancaster University, Lancaster, UK

*Corresponding author
Dr John Fernandes
School of Sport and Health Sciences
Cardiff Metropolitan University
Cardiff
CF23 6XD

Advancing age is not associated with greater exercise-induced muscle damage: A systematic review, meta-analysis, and meta-regression.

Abstract

Objective: The aim of this paper was to undertake a PRISMA-accordant meta-analysis comparing exercise-induced muscle damage (EIMD) in older and younger adults. Methods: Google Scholar, PubMed and Sport Discus were searched in June 2023 for the terms “ageing” OR “age” OR “middle-aged” OR “old” OR “older” OR “elderly” OR “masters” OR “veteran” AND “muscle damage” OR “exercise-induced muscle damage” OR “exercise-induced muscle injury” OR “contraction-induced injury” OR “muscle soreness” OR “delayed onset muscle soreness” OR “creatine kinase”. From 1092 originally identified titles, 36 studies were included which had an exercise component comparing a younger against an older group. The outcome variables of EIMD were muscle function, muscle soreness, and creatine kinase (CK). A meta-analysis was conducted on change to EIMD after exercise in older vs younger adults using standardised mean difference (SMD) and an inverse-variance random effects model. Results: Change after 24 and 72 hours, and peak change, in muscle function was not different between old and young (SMD range = -0.16 to -0.35). Muscle soreness was greater in younger than older adults for all comparisons (SMD range= -0.34 to -0.62). CK was greater in younger than older adults at 24 hours (SMD= -0.32), as was peak change (SMD= -0.32). A relationship between sex and peak muscle function change was evident for males (SMD= -0.45), but not females (SMD= -0.44). All other meta-regression were non-significant. Conclusion: Advancing age is not associated with greater symptoms of EIMD. Implications: Older adults can pursue regular physical activity without concern for experiencing greater EIMD.

Key words

Muscle function; muscle soreness; creatine kinase; eccentric exercise; fatigue; recovery; meta-analysis

Key points

1. Exercise-induced muscle damage (EIMD) can negatively affect sport and exercise performance and reduce adherence to exercise.
2. Older adults exhibit smaller post-exercise increases in muscle soreness and creatine kinase, and similar muscle function decrements, compared to their younger counterparts.
3. Those working with older adults should use these data to inform the planning and programming of physical activity, and to improve exercise adherence.

Introduction

Between 2017 and 2050, the number of people aged over 60 years is expected to double, and to triple by 2100 (United Nations, 2017). Improvements in medical care, a greater appreciation for longevity, and a decline in the leading causes of mortality contribute to the ageing population (Baker & Tang, 2010). The ageing population has driven interest in 'successful' ageing (Elliott, Hayes, Hughes, & Burtscher, 2020; Geard, Reaburn, Rebar, & Dionigi, 2017; Hayes, Burtscher, & Elliott, 2022), which comprises physical, psychological, social, and cognitive domains (Garai et al., 2021; Stenbäck et al., 2019; Steptoe et al., 2015; Urtamo et al., 2019). Whilst ageing is associated with reduced muscle strength and power (Dodds et al., 2014; Fernandes et al., 2018b, 2018a, 2019, 2021), alterations in body compositions (Fernandes et al., 2018a; Lexell et al., 1988) and declines in aerobic fitness (Tanaka & Seals, 2008; Valenzuela et al., 2020; Yasar et al., 2021), physical activity, changes in appetite-related hormones (Johnson et al., 2020) and exercise can offset and ameliorate these declines (Cruz-Jentoft et al., 2014; Hayes, Elliott, et al., 2021; Hayes et al., 2020; Hayes, Herbert, et al., 2021a, 2021b; Herbert et al., 2021a, 2021b; Johnson et al., 2021; Sellami et al., 2017; Yasar et al., 2023; Zouhal et al., 2022). Therefore, physical activity is core to successful ageing, and as such is included in national and international health guidelines (Izquierdo et al., 2021).

Despite the benefits of physical activity, an acute consequence is exercise-induced muscle damage (EIMD), particularly if the mode or intensity is novel, includes eccentric muscle contractions, or is of high volume (Fernandes et al., 2023; Owens et al., 2018; Reaburn & Fernandes, 2023; Wilson et al., 2018, 2019). According to the "popping-sarcomere hypothesis" (Morgan & Proske, 2004), increased stress per myofiber during eccentric contractions causes non-uniform lengthening whereby weaker sarcomeres extend beyond their myofilament overlap and fail to re-interdigitate (Hyldahl & Hubal, 2014; Morgan & Proske, 2004). Thereafter, disruptions to calcium homeostasis leads to excitation–contraction uncoupling and a prolonged loss of muscle strength and other associated symptoms (Damas et al., 2016; Hyldahl & Hubal, 2014; Morgan & Proske, 2004). Regardless of age, EIMD manifests as reductions in muscle function (e.g. strength and power), increased muscle soreness and pain, and intramuscular enzymes 'leaking' into circulation (e.g. creatine kinase; CK). Typically, these symptoms peak between 24 and 48 hours after the initial bout of physical activity and are recovered (i.e. returned to baseline) by seven days (Damas et al., 2016; Hyldahl & Hubal, 2014; Reaburn & Fernandes, 2023; Wilson et al., 2018, 2019). These symptoms are highly individualised, not synchronous (Damas et al., 2016; Hubal et al., 2007; Machado & Willardson, 2010) and appear to differ between sexes (e.g. (Kendall & Eston, 2002)) and exercising limb (e.g. (Chen et al., 2011)).

Ageing is associated with a reduction in muscle protein synthesis in response to exercise (Kumar et al., 2009) and protein ingestion (Cuthbertson, 2004), reductions in satellite cell count (Ballak et al., 2015), and impaired proliferation of existing satellite cells (Pietrangelo et al., 2009). Theoretically, this would result in an impaired ability to activate regenerative pathways and repair muscle damage. Although it has previously been reported that older adults display greater symptoms of EIMD after aerobic (Easthope et al., 2010) and intermittent activity (Borges et al., 2018), a recent review of 11 studies suggested alterations in muscle function, muscle soreness/pain, and CK after resistance exercise-induced muscle damage are comparable between older and younger males (Fernandes, Lamb, Norris, et al., 2020). This could indicate that the exercise modality might influence the EIMD response between age-groups.

Divergent EIMD responses between ages remains an important and contentious consideration in exercise and health science (Fernandes et al., 2023; Fernandes et al., 2020; Hayes et al., 2023). For example, EIMD symptoms are likely to reduce physical activity adherence and could result in discontinuation (Farias-Junior et al., 2019). Given the benefit of physical activity to health outcomes (Ashton et al., 2020; Sprung et al., 2013), strategies that maintain exercise adherence in older adults remain fundamental, including programming of physical activity. Though recommendations have been provided for resistance EIMD (Fernandes, Lamb, Norris, et al., 2020), none have been provided for other exercise modalities (e.g., aerobic exercise). If EIMD symptoms increase with age, then it is also important to develop an understanding of the influence of sex and the exercising limb. Such information can guide practitioners working with adults to appropriately plan and programme physical activity regimes and recovery strategies.

Recent work has meta-analysed indirect symptoms of EIMD in youths compared to young adults (Fernandes et al., 2023) but there is a need to establish how these symptoms differ across the adult lifespan. Despite the interest in EIMD across the adult lifespan, there was no meta-analysis to provide pooled analysis of published studies to date. Therefore, the aim of this investigation was to conduct meta-analyses on the effect of a single exercise bout on muscle function, muscle soreness/pain and CK between two different adult age groups. A secondary aim was to investigate study characteristics (exercise modality, sex, and involved limb) and whether this influenced the effect of age on EIMD markers.

Methods

This systematic review with meta-analysis was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines (Page et al., 2021). The literature search was performed by three authors with the data extraction and verification performed by two authors.

Information sources

On the 15th June 2023 a systematic search, with no date restrictions, was performed on Google Scholar, PubMed and Sport Discus.

Search strategy

Only peer-reviewed articles written in English were considered. Using Boolean logic combinations of the following search terms were used; “ageing” OR “age” OR “middle-aged” OR “old” OR “older” OR “elderly” OR “masters” OR “veteran” AND “muscle damage” OR “exercise-induced muscle damage” OR “exercise-induced muscle injury” OR “contraction-induced injury” OR “muscle soreness” OR “delayed onset muscle soreness” OR “creatine kinase”. When selecting studies for inclusion, all relevant article titles were reviewed before an examination of article abstracts and, then, full published articles. After the formal systematic searches, additional searches of the reference lists were conducted. The search process is outlined in Figure 1.

INSERT FIGURE 1 HERE

Eligibility criteria

The following criteria were used to determine the eligibility of studies for the meta-analysis using the PICO framework (Participants [P], Intervention [I], Comparator [C], Outcomes [O]: P) An older adult human group and a younger comparison, I) An acute exercise bout without provision of a recovery aid (e.g., cold-water immersion), C) An older versus younger comparison O) Measure of muscle function (e.g., strength, power), muscle soreness/pain, or CK beyond ≥ 24 hours.

Selection process, data collection process, and data items

Data extraction was conducted independently by two reviewers (JFTF and LJW) using a standardised Microsoft Excel form. Any disagreement between both reviewers was discussed in a consensus meeting, and unresolved items were addressed by a third independent reviewer for resolution (LJH). Where data were not numerically reported, and only visualised, authors were contacted. In the case of authors not responding (up to 6 weeks response time was allowed), ImageJ software was used to manually extract data from figures (Schneider et al., 2012). Data were extracted on baseline and post-EIMD measures of muscle strength, muscle soreness/pain, and CK. Anthropometric and physical activity characteristics of the participants, as well as the exercise bout were also extracted. As there is no consensus for what is deemed a ‘young’ and ‘old’ adult (Fernandes et al., 2020) the age comparisons are based upon the criteria set in each individual study. The EIMD bout was categorised as resistance (i.e. exercise performed against an external load) or aerobic (i.e. continuous and rhythmic movement of the body for a sustained period) in nature. Muscle function data from Fell et al. (2008) was only presented for the whole groups, thus only the muscle soreness data was extracted. Similarly, CK data from Lavender and Nosaka (2006) could not be accurately extracted, so only muscle function and soreness data were extracted from this study. In both cases the data were excluded from analysis. The 24 hours standard deviation data for CK in Lavendar and Nosaka (2006) could not be extracted. Therefore, results are presented with the standard deviations values at 48 hours and with the removal of these data. Importantly, the results were identical and did not affect the main analysis. Any data reported as standard error were converted to standard deviation for analysis. As differences at baseline were expected between youths and adults for muscle strength, the peak percentage change from baseline was entered for analysis. Where standard deviation of the change was not reported (merely pre- and post-EIMD SDs), the standard deviation of the change was calculated thusly:

$$SD\ of\ the\ change = \sqrt{(a^2 + b^2)} - (2correl. \times a \times b)$$

Equation 1. a = baseline SD; b = peak SD; and correl. = the Pearson’s correlation between baseline and 24h post-EIMD muscle strength (r = 0.94) in Fernandes et al. (2020).

One study (Lavender & Nosaka, 2007) included multiple age group comparisons (e.g., younger adults versus both middle-aged and old adults) and both were included for analysis. Previous work (Kadlec et al., 2022) has raised concerns that including multiple groups from the same study within a meta-analysis could ignore the within-study correlation. However, the differences in biometric characteristics of the groups (see Table 2) in Lavender and Nosaka (2007) indicate distinct physical and physiological differences which warrant their inclusion. Trivisonno et al. (2021) analysed data from both upper- and lower-body. As the upper- and lower-body respond differently to EIMD (Chen et al., 2011; Jamurtas et al., 2005; Saka et al., 2009), and under-go differing sarcopenic (i.e., loss of muscle mass) and dynapenic (i.e., loss of muscle strength) responses (e.g. (Abe et al., 2011; Fernandes et al., 2018a)) both data were included in the meta-analysis. As per the suggestion of Kadlec et al. (2022) multiple variables were not included in the same analysis, e.g. both concentric and isometric strength into the muscle strength analysis.

Analysis and interpretation of results

Jamovi (version 2.3.0.0, MAJOR package) was used to conduct the meta-analyses. Means and standard deviations of baseline and post-exercise markers of EIMD were used to calculate the standardised mean difference (SMD). Standardised mean difference expressed the intervention effect within each study using a restricted maximum-likelihood model estimate (Langan et al., 2017). An inverse-variance random effects model for meta-analyses allocated a proportionate weight to trials based on the standard error and accounted for heterogeneity between studies (Deeks et al., 2019). Effect sizes are reported as SMD and 95% confidence intervals (CIs). The following qualitative criteria were used to interpret the SMD; 0.2 = trivial; 0.2–0.59 = small, 0.6–1.19 = moderate, 1.2–1.99 = large, 2.0–3.99 = very large, > 4.0 = extremely large (Hopkins et al., 2009). To assess the degree of heterogeneity amongst the included studies, the I^2 statistic was employed. This represents the proportion of effects that are due to heterogeneity as opposed to chance (Liberati et al., 2009). Low, moderate, and high heterogeneity correspond to I^2 values of 25, 50, and 80%, respectively. Random-effects meta-regressions tested the influence of sex (i.e. female or male), the involved limb segment (i.e. upper- or lower-limb) and the exercise type (i.e., resistance or aerobic) on the SMD. Studies which included a mixed sex sample ($k = 6$) or did not state the sex of their sample ($k = 1$) or used plyometric exercise ($k = 1$) were not included in the regression analysis.

Quality assessment and risk of bias assessment

The quality of the included studies was determined using the National Institute of Health's Quality Assessment Tool for Before-After (pre-post) Studies with No Control Group (National Health Lung and Blood Institute, 2023). The assessment tool analyses the following domains 1) study question was clearly stated; 2) eligibility was prespecified and clearly described; 3) study subjects were representative of those who would be of interest; 4) eligible subjects were enrolled; 5) sample size was sufficiently large; 6) intervention was clearly described and evenly applied to subjects; 7) outcome measures prespecified, clearly defined, valid, reliable; 8) assessors were blind to the intervention/outcomes; 9) subject attrition was less than 20%; 10) statistical measures assessed pre to post changes; 11) outcome measures were taken multiple times; 12) statistical analysis took into account group level data. Two reviewers conducted the quality assessment independently with any disputes settled by a third reviewer.

Results

Study selection

Results from the three database searches identified 1092 articles, 121 of which were duplicates (Figure 1). A total of 650 articles were removed after the screening of abstracts, leaving 321 articles available for full text inspection. After manual screening of reference lists and review articles 10 studies were added. One study (Manfredi et al., 1991) reported CK values relative to creatinine, which no other study did. As this is not typical within the EIMD literature the study was removed. Therefore, data was retrieved from all 36 studies identified for analysis.

Study characteristics

The NIH Quality Assessment Tool resulted in a mean score of 9.2 ± 0.5. Individual assessments can be found in Table 1, with study characteristics found in Table 2. On completion of data pooling, 38 comparisons (from 36 individual studies) were included in the analysis; 29 included a marker of muscle function, 23 included a marker of muscle soreness and 26 measured CK. A total of 389 younger adults and 390 older adults were included in the meta-analysis. As Easthope et al. (2010) did not include the sex of participants, the number of males and females is unknown. However, 6 comparisons include females only, 25 males only and 6 both female and male. Nine comparisons investigated EIMD in the upper-limb, with the remaining 29 reporting on EIMD in the upper-limbs.

INSERT TABLES 1 AND 2 HERE

The effect of advancing age on muscle function after an exercise bout

EIMD as determined by muscle function per age group at 24, 48, 72 hour, and peak comparisons changes are displayed in Figure 2. There were no differences between age groups at 24 (SMD = -0.28; 95% CI = -0.63, 0.08; Z = -1.54; *P* = 0.124), 48 (SMD = -0.35; 95% CI = -0.71, 0.01; Z = -1.89; *P* = 0.059), or 72 hours (SMD = -0.16; 95% CI = -0.69, 0.38; Z = -0.58; *P* = 0.561), or for the peak change (SMD = -0.26; 95% CI = -0.59, 0.08; Z = -1.50; *P* = 0.132). Heterogeneity was moderate to high which justified the use of a random effects model (I^2= 74 to 83%). No publication bias was detected for 48 and 72 hours comparisons. For 24 hour and peak comparisons 2 and 4 studies, respectively, needed to be removed to negate publication bias according to the Trim and Fill method (Rothstein et al., 2005). The removal of Lavender and Nosaka (2006) and Lavender and Nosaka (2007) (which fell outside of the funnel) for the 24 hours comparison removed the publication bias but did not alter the interpretation (SMD = -0.15; 95% CI = -0.46, 0.16; Z = -0.952; *P* = 0.341). The removal of four studies (Arroyo et al., 2017; Gorianovas et al., 2013; Lavender & Nosaka, 2006, 2007) that fell outside the funnel for peak comparison resulted in a similar observation as the original analysis (SMD = -0.04; 95% CI = -0.29, 0.22; Z = -0.278; *P* = 0.781) and removed the publication bias. We also noted that the study by Ploutz-Synder et al. (2001) was an outlier as it repeatedly fell outside the funnel plot. The removal of the study at 24 hours (SMD = -0.36; 95% CI = -0.67, -0.05; 0.14; Z = -2.25; *P* = 0.024) and for peak alterations (SMD = -0.33; 95%

CI = -0.63, 0.02; Z = -2.10; *P* = 0.036) achieved a Trim and Fill statistic of 0 in both cases and indicated greater losses in muscle function in the younger than older group.

INSERT FIGURE 2 HERE

The effect of advancing age on muscle soreness after an exercise bout

EIMD as determined by muscle soreness for 24, 48, 72 hour and peak alterations are displayed in Figure 3. Muscle soreness was smaller in older adults than their younger counterparts at 24 (SMD = -0.61; 95% CI = -0.81, -0.41; Z = -6.04; *P* < 0.001), 48 (SMD = -0.34; 95% CI = -0.63, -0.06; Z = -2.34; *P* = 0.019) and 72 hours (SMD = -0.62; 95% CI = -0.98, -0.26; Z = -3.38; *P* < 0.001) and at its peak value (SMD = -0.42; 95% CI = -0.67, -0.18; Z = -3.40; *P* < 0.001). Heterogeneity was low for the 24-hour comparison (I^2= 77%), but moderate for all other comparisons (I^2= 46 to 57%). For all analyses the Trim and Fill method suggested no publication bias.

INSERT FIGURE 3 HERE

The effect of advancing age on creatine kinase after an exercise bout

EIMD as determined by CK for 24, 48, 72 hour and peak concentrations are displayed in Figure 4. Creatine kinase at 24 hours after exercise (SMD = -0.28; 95% CI = -0.63, -0.08; Z = -2.54; *P* = 0.011) and for peak magnitude (SMD = -0.26; 95% CI = -0.59, 0.08; Z = -2.56; *P* = 0.010) was smaller in older than younger adults. Differences between groups at 48 (SMD = -0.35; 95% CI = -0.71, 0.01; Z = -1.29; *P* = 0.197) and 72 (SMD = -0.16; 95% CI = -0.69, 0.38; Z = -1.78; *P* = 0.076) hours did not reach the *P* < 0.05 level. Heterogeneity was moderate for all comparisons (I^2= 46 to 52%), justifying the use of a random effect model. For 24 and 72 hours and peak analysis the Trim and Fill method suggested that no studies needed to be removed to reduce publication bias. According to the 48 hours comparison Trim and Fill statistic three studies needed to be removed; the removal of eradication of publication bias (removal of Borges et al. (2018), Gorianovas et al. (2013) and Nikolaidis et al. (2013)) did not alter interpretation (SMD = -0.02; 95% CI = -0.27, 0.23; Z = -0.177; *P* = 0.859). Therefore, we are confident results from the initial meta-analysis are robust against the analysis decisions.

INSERT FIGURE 4 HERE

Meta-regressions

A random effects meta-regression revealed a significant relationship between sex and SMD (coefficient estimate = -0.12; 95% CI = -2.30, -1.14; *P* = 0.027), but no relationship of limb involved (coefficient estimate = 0.09; 95% CI = -0.68, 0.86; *P* = 0.817), or exercise type (coefficient estimate = 0.34; 95% CI = -0.39, 1.07; *P* = 0.367). A random effects meta-regression examined the effects of limb involved (coefficient estimate = 0.40; 95% CI = -0.12, 0.93; P = 0.131), sex (coefficient estimate = -0.72; 95% CI = -0.91, 0.43; *P* = 0.475), and exercise type (coefficient estimate = 0.07; 95% CI = -0.69, 0.56; *P* = 0.828) on muscle soreness SMD and indicated no relationship. Similarly, the relationships between limb involved (coefficient estimate = -0.21; 95% CI = -0.91, 0.49; *P* = 0.554), sex (coefficient estimate = -0.23; 95% CI = -0.42, 0.88; *P* = 0.491), and exercise type (coefficient estimate = -0.14; 95% CI = -0.63, 0.36; *P* = 0.587) on CK SMD were not significant. Subgroup analysis can be found in Table 3.

INSERT TABLE 3 HERE

Sensitivity analysis

A *post-hoc* sensitivity analysis was performed by individually removing these comparisons from the main analysis. For muscle function, the removal of the Lavender and Nosaka's (2007) middle-aged versus young (SMD = -0.25; *P* = 0.161), Lavender and Nosaka (2007) old versus young (SMD = -0.20; *P* = 0.218), Trivisonno et al. (2021) upper-limb (SMD = -0.26; *P* = 0.149) and finally Trivisonno et al. (2021) lower-limb (SMD = -0.27; *P* = 0.138) resulted in similar SMDs as the original analysis (SMD = -0.26; *P* = 0.132). For muscle soreness, the removal of Trivisonno et al. (2021) upper-limb (SMD = 0.42; *P* = 0.001) and Trivisonno et al. (2021) lower-limb (SMD = 0.42; *P* = 0.001) did not change the interpretation of the original analysis (SMD = 0.42; *P* < 0.001). The results of this sensitively check justifies the inclusion of these comparisons in the main analysis.

Discussion

This was the first study to 1) meta-analyse and systematically review the effect of age on markers of EIMD and 2) determine if sex, exercising limb and exercise modality moderated findings. Our results indicate that 1) muscle soreness is smaller in *older* compared to younger individuals after muscle damaging exercise, 2) *older* individuals present lower peak CK values, and lower values acutely (i.e., at 24 hours after exercise) compared to younger individuals, 3) there are no differences in muscle function responses between older and younger adult age groups 4) in the moderator analysis, sex affected muscle function SMD only. These data show that ageing is not associated with greater EIMD and should provide encouragement to those looking to increase physical activity habits in older adults.

Whilst some of the mechanisms which underpin ageing holistically suggest greater EIMD and impaired recovery (i.e., reduced muscle protein synthesis rates (Cuthbertson, 2004; Kumar et al., 2009), satellite cell count and proliferation (Ballak et al., 2015; Pietrangelo et al., 2009) in older adults, this is not reflected in the EIMD studies' findings. Indeed, the present investigation reveals there were no differences in acute strength decrements with advancing age. The lack of agreement between mechanistic and empirical EIMD findings might be explained, in part, by changes in skeletal muscle fatigability with age. Systematic reviews and meta-analyses have reported that older adults can experience greater muscular fatigue during dynamic contractions than younger adults (Christie et al., 2011; Krüger et al., 2018). Given all studies in this meta-analysis used dynamic contractions to initiate muscle damage, it is possible that older adults exhibit a reduced absolute load (e.g. work, force, torque, power), despite working at the same relative load, thereby reducing tissue damage compared younger individuals. Increases in cross linking, collagen content and advanced glycation end products with age can increase muscle stiffness (Haus et al., 2007; Kjær, 2004; Olson et al., 2021). Conversely, tendon degradation with ageing; could cause a decline in stiffness (Narici & Maganaris, 2007). Regardless, it is plausible that these changes result in altered dynamic stiffness during the eccentric component, thus improving the sarcomeres' ability to withstand lengthening.

Although there was no difference between the older and younger adults for muscle function changes after muscle-damaging exercise, there was a small effect of sex. SMDs were similar, but only the male comparison was significant, indicating a difference between older and younger males but not females. For a given protocol, even after accounting for fat free mass, men perform more work, are subjected to greater loads, and experience greater muscle damage than women (Heavens et al., 2014). Additionally, oestrogen is thought to have a protective effect against skeletal muscle damage (Kendall & Eston, 2002). Oestrogen exhibits a high antioxidant capacity which could attenuate metabolic damage; cell membrane stabilising properties that could protect the structural integrity of muscle fibre units; and a gene regulatory effect that might inhibit the inflammatory response after muscle damage (Kendall & Eston, 2002; Hayes et al., 2024). Although the processes underpinning muscle damage are complex, it is possible that one, or a combination, of these factors could play a role in the reduction of muscle damage, and the maintenance of muscle function in females. Given this pronounced disparity in sex responses, it might be that the age effect reported herein is diminished in females. Another consideration is the role of tendon stiffness, and the potential 'mechanical buffer' this can provide during eccentric contractions (Hicks et al., 2016). Males exhibit greater patella tendon stiffness than females, and this results in greater vastus lateralis fascicle lengthening and potential structural damage in males during eccentric contractions (Hicks et al., 2013). However, when examining sex differences in fascicle lengthening, tendon properties and the impact on function, Hicks and colleagues (Hicks et al., 2016) reported no differences between sexes for knee extension torque loss after EIMD. Another important factor is that age associated losses in muscle mass might also influence sex effects between younger and older individuals. The aetiology of skeletal muscle mass loss is complex, and factors such as declining anabolic hormone concentrations, nutritional deficiencies, chronic inflammation, insulin resistance and a reduction in physical activity have all been implicated (Abe et al., 2011). Several large-scale studies (Abe et al., 2011; Gallagher et al., 1997; Janssen et al., 2014) report that despite greater muscle mass in males compared to females at all ages, muscle mass loss with age was greater in men than in women. This could explain the sex-related disparity in age effects between the older and younger adults in that women maintain a greater proportion of their lean mass as they age, whereas older males will experience a much greater mechanical load per muscle fibre unit than their younger counterparts for a given protocol due to sarcopenic changes. The considerable heterogeneity in participant cohorts might have further confounded any potential age-effect in females. Some studies reported menstrual cycle phase information and whether older females were post-menopausal (Romero-Parra et al., 2021) others included oral contraceptive users (Conceição et al., 2012), or simply reported chronological age (Ploutz-Snyder et al., 2001). Lastly, four studies compared female muscle function changes, and 19 male muscle function changes. Given the female and male SMDs were similar, despite differences in significance, it is possible that this comparison was underpowered.

Increases in muscle soreness are because of the complex interaction of damage to the muscle structure and connective tissue, disrupted calcium homeostasis, sensitization of nociceptors from inflammatory cell infiltrates, and reductions in range of motion (Hyldahl & Hubal, 2014; Jamurtas et al., 2005; Nogueira et al., 2014; Nosaka et al., 2002). Our findings indicate that muscle soreness was small to moderately lower for older than younger adults from 24 to 72 hours post-exercise and that the previously stated mechanisms were less severe in older than younger adults. Ageing leads to increased collagen concentrations in skeletal muscle connective tissues (Haus et al., 2007) which can stiffen both the muscle and connective tissue. In the same way that muscle undergoes an adaptation to EIMD, ageing might cause mechanical changes which improve dynamic and passive muscle stiffness (Hyldahl et al., 2017; McHugh, 2003). These age-related changes might offer some protection against structural damage and resultant soreness because of an improvement in dissipating myofibrillar stresses (Lapier et al., 1995). This is an important finding as muscle soreness can have negative effects on physical activity adherence, particularly for older individuals who perceive typical EIMD and soreness responses as causing ‘more harm than good’ (Hayes, Stevenson, Sayer, Granic, & Hurst, 2023; Schutzer & Graves, 2004). Moreover, recent work has indicated the need to educate older adults on the post-exercise symptoms of soreness (Hurst et al., 2022). Thus, the message to older adults should be a positive one, in that muscle soreness is not worse than when they were younger or at least not worse than for their younger counterparts. Importantly, the peak magnitude of soreness experienced was not affected by sex, involved limb, or exercise type. The finding that there was no difference in soreness responses between males and females after EIMD, irrespective of exercise limb or type, is a novel addition to the literature. Thus, older adults can engage in physical activity that might induce muscle damage irrespective of their sex, the involved limb or exercise type, without fear of an 'increased' soreness response compared to younger individuals. Practically, this finding should provide encouragement to older adults and practitioners/clinicians working with those older populations who need to engage in physical activity.

CK at 24 h after exercise, and at peak magnitude was smaller in older than younger adults. EIMD increases membrane permeability and causes muscle proteins to leak into the blood (Sorichter et al., 1999). However, CK demonstrates a poor temporal relationship with muscle function, a high intra- and interindividual variability (Damas et al., 2016; Fridén & Lieber, 2001), and most likely reflects only the occurrence of tissue damage rather than the magnitude (Fernandes, Lamb, Norris, et al., 2020; Owens et al., 2018). These data suggest that older adults exhibit less structural damage than their younger counterparts after muscle damaging exercise. It is plausible that many of the mechanisms mentioned above (e.g., changes in tissue stiffness) would explain the lower CK leakage in older adults. Nonetheless, CK demonstrates high interindividual variability, and there are differential responses between 'high' and 'low' responders (Clarkson & Dedrick, 1988). Thus, it is unsurprising that there was no effect of sex, involved limb, or exercise type on peak CK perturbations. Whilst these findings are important to report given the prevalence of CK as a marker to indicate the presence of muscle tissue damage, readers should interpret these data cautiously when other markers offer a more valid assessment of the EIMD magnitude.

Whilst this study provides new insight into EIMD responses across the adult lifespan, it also highlights key areas for future research. Much like sport and exercise science research in general (Cowley et al., 2021), there remains a paucity of literature examining female responses to EIMD (Hayes et al., 2023). Such observations are likely to reflect the patriarchal nature of sport and exercise research (Caven et al., 2020; O'Malley & Greenwood, 2018). Previous work has suggested that there are sex-specific differences in the symptoms of EIMD (Hyldahl & Hubal, 2014), meaning future work should ensure that women are benefitting from the same quality and quantity of research on the topic (Cowley et al., 2021). Researchers must now improve equity in the literature and future studies must consider the cyclical (i.e., menstrual cycle), exogenous (i.e., oral contraceptives) and age-related (i.e., menopause) changes in female sex hormones on EIMD between age groups (Hayes et al., 2023). With more older athletes and increased interest in ‘successful ageing’, further studies investigating the efficacy of recovery strategies in older individuals are also warranted. Though some symptoms of EIMD are attenuated with ageing, older adults still experience muscle damage. Moreover, the implications of reduced muscle strength, and muscle soreness, after muscle-damaging exercise could have more severe negative consequences for older adults than their younger counterparts (e.g. increasing fall risk). Therefore, improved understanding of recovery strategies in older populations might increase exercise adherence and long-term health benefits. Thirdly, there appears to be a perception that ageing is associated with greater EIMD, particularly muscle soreness (Fernandes, Lamb, Norris, et al., 2020; Reaburn & Fernandes, 2023), although this is not reflected in the intervention studies presented here. Therefore, future studies should seek to both understand why older adults perceive muscle damage to be greater and establish methods to effectively disseminate the current evidence. This would be particularly useful for those using physical activity to improve their health. If future research in older adults is concerned with lifelong physical activity, it would be useful if this was reflected in the muscle damaging protocols employed (Hayes et al., 2024). For example, using protocols that mirror activities of daily living will provide benchmarks from which to investigate damage and recovery responses, rather than those solely designed to induce greater magnitudes of muscle damage. Lastly, one of the emergent themes here was that older adults might experience less muscle damage because the external load during exercise is less, due to dynapenia and age-related increases in exercise fatigue. A study which standardises the external load during muscle-damaging exercise or investigates the recovery from a set force decrement between age groups would help determine the extent to which external load is mediating muscle damage and recovery between age groups.

The studies included within this manuscript compared two different age groups, rather than investigating ageing directly. Readers should therefore be aware of the cross-sectional nature of the studies included. Whilst this could provide a direction for future research, conducting studies over the course of ~20+ years is challenging. We did not utilise age thresholds because of differences in chronological and biological age (Balcombe & Sinclair, 2001) and the changing nature of terms such as ‘middle-aged’ or ‘old’ (Orimo et al., 2006). Moreover, as this study sought to examine the effects of advancing age (i.e. and older group compared to a younger group) on EIMD responses, it was not deemed necessary to define specific age category thresholds for included studies. However, future studies may seek to clarify the definitions of different age groups and determine the effects of EIMD on distinct age groups.

Conclusion

The findings from this meta-analysis suggest advancing age is not associated with greater muscle damage and a prolonged recovery from EIMD. Indeed, we demonstrated that there were no differences in muscle function changes between older and younger adults, but that older adults exhibited smaller increases in muscle soreness and CK after exercise. Generally, there did not appear to be any effect of sex, involved limb, or exercise type on the observed results. These findings indicate that older adults can, and should, pursue regular physical activity without concerns for experiencing greater EIMD compared to younger counterparts. Given a lack of female participants included in the pooled analysis for all EIMD markers, future research should focus on understanding EIMD and recovery responses in older females. These findings should provide confidence to older adults engaging in physical activity and those practitioners and clinicians who work with them.

Disclosure of interests

There are no conflicts of interest.

References

Abe, T., Sakamaki, M., Yasuda, T., Bemben, M. G., Kondo, M., Kawakami, Y., & Fukunaga, T. (2011). Age-related, site-specific muscle loss in 1507 Japanese men and women aged 20 to 95 years. *Journal of Sports Science and Medicine*, *10*(1), 145–150.

Arnett, M. G., Hyslop, R., Dennehy, C. A., & Scheider, C. M. (2000). Age-Related Variations of Serum CK and CK MB Response in Females. *Canadian Journal of Applied Physiology*, *25*(6), 419–429.

Arroyo, E., Wells, A. J., Gordon, J. A., Varanoske, A. N., Gepner, Y., Coker, N. A., Church, D. D., Fukuda, D. H., Stout, J. R., & Hoffman, J. R. (2017). Tumor necrosis factor-alpha and soluble TNF-alpha receptor responses in young vs. middle-aged males following eccentric exercise. *Experimental Gerontology*, *100*(September), 28–35.

Ashton, R. E., Tew, G. A., Aning, J. J., Gilbert, S. E., Lewis, L., & Saxton, J. M. (2020). Effects of short-term, medium-term and long-term resistance exercise training on cardiometabolic health outcomes in adults: Systematic review with meta-analysis. In *British Journal of Sports Medicine* (Vol. 54, Issue 6, pp. 341–348). BMJ Publishing Group. https://doi.org/10.1136/bjsports-2017-098970

Baker, A. B., & Tang, Y. Q. (2010). Aging performance for masters records in athletics, swimming, rowing, cycling, triathlon, and weightlifting. *Experimental Aging Research*, *36*(4), 453–477.

Balcombe, N. R., & Sinclair, A. (2001). Ageing: Definitions, mechanisms and the magnitude of the problem. *Best Practice and Research in Clinical Gastroenterology*, *15*(6), 835–849.

Ballak, S. B., Jaspers, R. T., Deldicque, L., Chalil, S., Peters, E. L., de Haan, A., & Degens, H. (2015). Blunted hypertrophic response in old mouse muscle is associated with a lower satellite cell density and is not alleviated by resveratrol. *Experimental Gerontology*, *62*, 23–31. https://doi.org/10.1016/j.exger.2014.12.020

Borges, N. R., Reaburn, P. R., Doering, T. M., Argus, C. K., & Driller, M. W. (2018). Age-related changes in physical and perceptual markers of recovery following high-intensity interval cycle exercise. *Experimental Aging Research*, *44*(4), 338–349. https://doi.org/10.1080/0361073X.2018.1477361

Borges, N., Reaburn, P., Argus, C., & Driller, M. (2015). The effect of age on muscle strength recovery following an anaerobic exercise stimulus. *Journal of Science and Medicine in Sport*, *19*(2015), e103. https://doi.org/10.1016/j.jsams.2015.12.379

Buford, T. W., MacNeil, R. G., Clough, L. G., Dirain, M., Sandesara, B., Pahor, M., Manini, T. M., & Leeuwenburgh, C. (2014). Active muscle regeneration following eccentric contraction-induced injury is similar between healthy young and older adults. *Journal of Applied Physiology*, *116*(11), 1481–1490.

Cannon, J. G., Fiatarone, M. A., Fielding, R. A., & Evans, W. J. (1994). *Aging and stress-induced changes in complement activation and neutrophil mobilization*. www.physiology.org/journal/jappl

Caven, E. J. G., Bryan, T. J. E., Dingley, A. F., Drury, B., Garcia-Ramos, A., Perez-Castilla, A., Arede, J., & Fernandes, J. F. T. (2020). Group versus individualised minimum velocity thresholds in the prediction of maximal strength in trained female athletes. *International Journal of Environmental Research and Public Health*, *17*(21), 1–10.

Chapman, D. W., Newton, M., McGuigan, M. R., & Nosaka, K. (2008). Comparison between old and young men for responses to fast velocity maximal lengthening contractions of the elbow flexors. *European Journal of Applied Physiology*, *104*(3), 531–539.

Chen, T. C., Lin, K. Y., Chen, H. L., Lin, M. J., & Nosaka, K. (2011). Comparison in eccentric exercise-induced muscle damage among four limb muscles. *European Journal of Applied Physiology*, *111*(2), 211–223.

Christie, A., Snook, E. M., & Kent-Braun, J. A. (2011). Systematic review and meta-analysis of skeletal muscle fatigue in old age. *Medicine and Science in Sports and Exercise*, *43*(4), 568–577. https://doi.org/10.1249/MSS.0b013e3181f9b1c4

Clarkson, P. M., & Dedrick, M. E. (1988). Exercise-induced muscle damage, repair, and adaptation in old and young subjects. *Journal of Gerontology*, *43*(4), 91–96.

Conceição, M. S., Libardi, C. A., Nogueira, F. R. D., Bonganha, V., Gáspari, A. F., Chacon-Mikahil, M. P. T., Cavaglieri, C. R., & Madruga, V. A. (2012). Effects of eccentric exercise on systemic concentrations of pro- and anti-inflammatory cytokines and prostaglandin (E2): Comparison between young and postmenopausal women. *European Journal of Applied Physiology*, *112*(9), 3205–3213. https://doi.org/10.1007/s00421-011-2292-6

Cowley, E. S., Olenick, A. A., McNulty, K. L., & Ross, E. Z. (2021). "Invisible Sportswomen": The sex data gap in sport and exercise science research. *Women in Sport and Physical Activity Journal*, *29*(2), 146–151. https://doi.org/10.1123/WSPAJ.2021-0028

Cruz-Jentoft, A. J., Landi, F., Schneider, S. M., Zuniga, C., Arai, H., Boirie, Y., Chen, L.-K., Fielding, R. A., Martin, F. C., Michel, J.-P., Sieber, C., Stout, J. R., Studenski, S. A., Vellas, B., Woo, J., Zamboni, M., & Cederholm, T. (2014). Prevalence of and interventions for sarcopenia in ageing adults: a systematic review. Report of the International Sarcopenia Initiative (EWGSOP and IWGS). *Age and Ageing*, *43*(6), 748–759. https://doi.org/10.1093/ageing/afu115

Cuthbertson, D. (2004). Anabolic signaling deficits underlie amino acid resistance of wasting, aging muscle. *The FASEB Journal*, *22*(1), 1–22. https://doi.org/10.1096/fj.04-2640fje

Damas, F., Nosaka, K., Libardi, C. A., Chen, T. C., & Ugrinowitsch, C. (2016). Susceptibility to exercise-induced muscle damage : A cluster analysis with a large sample. *International Journal of Sports Medicine*, *37*(8), 633–640.

Dedrick, M. E., & Clarkson, P. M. (1990). The effects of eccentric exercise on motor performance in young and older women. *European Journal of Applied Physiology*, *60*, 183–186.

Deeks, J. J., Higgins, J. P., & Altman, D. G. (2019). Analysing data and undertaking meta-analyses. In *Cochrane Handbook for Systematic Reviews of Interventions* (pp. 241–284). Wiley. https://doi.org/10.1002/9781119536604.ch10

Dodds, R. M., Syddall, H. E., Cooper, R., Benzeval, M., Deary, I. J., Dennison, E. M., Der, G., Gale, C. R., Inskip, H. M., Jagger, C., Kirkwood, T. B., Lawlor, D. A., Robinson, S. M., Starr, J. M., Steptoe, A., Tilling, K., Kuh, D., Cooper, C., & Sayer, A. A. (2014). Grip Strength across the Life Course: Normative Data from Twelve British Studies. *PLoS ONE*, *9*(12), e113637. https://doi.org/10.1371/journal.pone.0113637

Doering, T. M., Jenkins, D. G., Reaburn, P. R., Borges, N. R., Hohmann, E., & Phillips, S. M. (2016). Lower Integrated Muscle Protein Synthesis in Masters Compared with Younger Athletes. *Medicine and Science in Sports and Exercise*, *48*(8), 1613–1618. https://doi.org/10.1249/MSS.0000000000000935

Easthope, C. S., Hausswirth, C., Louis, J., Lepers, R., Vercruyssen, F., & Brisswalter, J. (2010). Effects of a trail running competition on muscular performance and efficiency in well-trained young and master athletes. *European Journal of Applied Physiology*, *110*(6), 1107–1116. https://doi.org/10.1007/s00421-010-1597-1

Elliott, B. T., Hayes, L. D., Hughes, D. C., & Burtscher, M. (2020). Editorial: Exercise as a Countermeasure to Human Aging. In *Frontiers in Physiology* (Vol. 11). Frontiers Media S.A. https://doi.org/10.3389/fphys.2020.00883

Farias-Junior, L. F., Browne, R. A. V., Freire, Y. A., Oliveira-Dantas, F. F., Lemos, T. M. A. M., Galvão-Coelho, N. L., Hardcastle, S. J., Okano, A. H., Aoki, M. S., & Costa, E. C. (2019). Psychological responses, muscle damage, inflammation, and delayed onset muscle soreness to high-intensity interval and moderate-intensity continuous exercise in overweight men. *Physiology and Behavior*, *199*, 200–209. https://doi.org/10.1016/j.physbeh.2018.11.028

Fell, J., Haseler, L., Gaffney, P., Reaburn, P., & Harrison, G. (2006). Performance during consecutive days of laboratory time-trials in young and veteran cyclists. *Journal of Sports Medicine and Physical Fitness*, *46*(3), 395–402.

Fell, J., Reaburn, P., & Harrison, G. J. (2008). Altered perception and report of fatigue and recovery in veteran athletes. *Journal of Sports Medicine and Physical Fitness*, *48*(2), 272–277.

Fernandes, J. F. T., Dingley, A. F., Garcia-Ramos, A., Perez-Castilla, A., Tufano, J. J., & Twist, C. (2021). Prediction of one repetition maximum using reference minimum velocity threshold values in young and middle-aged resistance-trained males. *Behavioral Sciences*, *11*(5). https://doi.org/10.3390/bs11050071

Fernandes, J. F. T., Hayes, L. D., Dingley, A. F., Moeskops, S., Oliver, J. L., Arede, J., Twist, C., & Wilson, L. J. (2023). Youths Are Less Susceptible to Exercise-Induced Muscle Damage Than Adults: A Systematic Review With Meta-Analysis. *Pediatric Exercise Science*, 1–12. https://doi.org/10.1123/pes.2023-0108

Fernandes, J. F. T., Lamb, K. L., Norris, J. P., Moran, J., Drury, B., Borges, N. R., & Twist, C. (2020). Aging and recovery after resistance-exercise-induced muscle damage: Current evidence and implications for future research. *Journal of Aging and Physical Activity*, 1–8.

Fernandes, J. F. T., Lamb, K. L., & Twist, C. (2018a). A comparison of load-velocity and load-power relationships between well-trained young and middle-aged males during three popular resistance exercises. *Journal of Strength and Conditioning Research*, *32*(5), 1440–1447.

Fernandes, J. F. T., Lamb, K. L., & Twist, C. (2018b). Internal loads, but not external loads and fatigue, are similar in young and middle-aged resistance-trained males during high volume squatting exercise. *Journal of Functional Morphology and Kinesiology*, *3*(3), 45.

Fernandes, J. F. T., Lamb, K. L., & Twist, C. (2020). Low body fat does not influence recovery after muscle-damaging lower-limb plyometrics in young male team sport athletes. *Journal of Functional Morphology and Kinesiology*, *5*(4), 79.

Fernandes, J. F. T., Lamb, K. L., & Twist, Craig. (2019). Exercise-induced muscle damage and recovery in young and middle-aged males with different resistance training experience. *Sports*, *7*(6), 132.

Fridén, J., & Lieber, R. L. (2001). Serum creatine kinase level is a poor predictor of muscle function after injury. *Scandinavian Journal of Medicine and Science in Sports*, *11*(2), 126–127.

Gallagher, D., Visser, M., De Meersman, R. E., Sepu, D., Baumgartner, R. N., Pierson, R. N., Harris, T., Heymsfield, S. B., Sepú lveda, D., Baumgart-ner, R. N., & Heymsfield Appendicular, S. B. (1997). Appendicular skeletal muscle mass: effects of age, gender, and ethnicity. *Journal of Applied Physiology*, *83*(1), 229–239. http://www.jap.org

Garai, K., Adam, Z., Herczeg, R., Banfai, K., Gyebrovszki, A., Gyenesei, A., Pongracz, J. E., Wilhelm, M., & Kvell, K. (2021). Physical Activity as a Preventive Lifestyle Intervention Acts Through Specific Exosomal miRNA Species—Evidence From Human Short- and Long-Term Pilot Studies. *Frontiers in Physiology*, *12*. https://doi.org/10.3389/fphys.2021.658218

Geard, D., Reaburn, P. R. J., Rebar, A. L., & Dionigi, R. A. (2017). Masters athletes: Exemplars of successful aging? In *Journal of Aging and Physical Activity* (Vol. 25, Issue 3, pp. 490–500). Human Kinetics Publishers Inc. https://doi.org/10.1123/japa.2016-0050

Gordon III, J., Hoffman, J. R., Arroyo, E., Varanoske, A., Coker, N., Gepner, Y., Wells, A., Stout, J., & Fukuda, D. (2017). Comparisons in the recovery response from resistance exercise between young and middle-aged men. *Journal of Strength and Conditioning Research*, *31*(12), 3454–3462.

Gorianovas, G., Skurvydas, A., Streckis, V., Brazaitis, M., Kamandulis, S., & McHugh, M. P. (2013). Repeated bout effect was more expressed in young adult males than in elderly males and boys. *BioMed Research International*, *2013*. https://doi.org/10.1155/2013/218970

Hamada, K., Vannier, E., Sacheck, J. M., Witsell, A. L., & Roubenoff, R. (2005). Senescence of human skeletal muscle impairs the local inflammatory cytokine response to acute eccentric exercise. *The FASEB Journal*, *19*(2), 264–266. https://doi.org/10.1096/fj.03-1286fje

Haus, J. M., Carrithers, J. A., Trappe, S. W., & Trappe, T. A. (2007). Collagen, cross-linking, and advanced glycation end products in aging human skeletal muscle. *Journal of Applied Physiology (Bethesda, Md.: 1985)*, *47306*(6), 2068–2076. https://doi.org/10.1152/japplphysiol.00670.2007.

Hayashi, K., Leary, M. E., Roy, S. J., Laosiripisan, J., Pasha, E. P., & Tanaka, H. (2019). Recovery from Strenuous Downhill Running in Young and Older Physically Active Adults. *International Journal of Sports Medicine*, *40*(11), 696–703. https://doi.org/10.1055/a-0951-0017

Hayes, E. J., Hurst, C., Granic, A., Sayer, A. A., & Stevenson, E. (2024). Challenges in Conducting Exercise Recovery Studies in Older Adults and Considerations for Future Research: Findings from a Nutritional Intervention Study. *Geriatrics*, *9*(5), 116. https://doi.org/10.3390/geriatrics9050116

Hayes, E. J., Stevenson, E., Sayer, A. A., Granic, A., & Hurst, C. (2023). Recovery from Resistance Exercise in Older Adults: A Systematic Scoping Review. In *Sports Medicine - Open* (Vol. 9, Issue 1). Springer Science and Business Media Deutschland GmbH. https://doi.org/10.1186/s40798-023-00597-1

Hayes, L. D., Burtscher, M., & Elliott, B. T. (2022). Editorial: Exercise as a Countermeasure to Human Aging, Volume II. In *Frontiers in Materials* (Vol. 13). Frontiers Media S.A. https://doi.org/10.3389/fphys.2022.878983

Hayes, L. D., Elliott, B. T., Yasar, Z., Bampouras, T. M., Sculthorpe, N. F., Sanal-Hayes, N. E. M., & Hurst, C. (2021). High Intensity Interval Training (HIIT) as a Potential Countermeasure for Phenotypic Characteristics of Sarcopenia: A Scoping Review. In *Frontiers in Physiology* (Vol. 12). Frontiers Media S.A. https://doi.org/10.3389/fphys.2021.715044

Hayes, L. D., Herbert, P., Sculthorpe, N. F., & Grace, F. M. (2021a). Short-Term and Lifelong Exercise Training Lowers Inflammatory Mediators in Older Men. *Frontiers in Physiology*, *12*. https://doi.org/10.3389/fphys.2021.702248

Hayes, L. D., Herbert, P., Sculthorpe, N. F., & Grace, F. M. (2021b). Short-Term and Lifelong Exercise Training Lowers Inflammatory Mediators in Older Men. *Frontiers in Physiology*, *12*. https://doi.org/10.3389/fphys.2021.702248

Hayes, L. D., Herbert, P., Sculthorpe, N., & Grace, F. (2020). High intensity interval training (HIIT) produces small improvements in fasting glucose, insulin, and insulin resistance in sedentary older men but not masters athletes. *Experimental Gerontology*, *140*. https://doi.org/10.1016/j.exger.2020.111074

Heavens, K. R., Szivak, T. K., Hooper, D. R., Dunn-Lewis, C., Comstock, B. A., Flanagan, S. D., Looney, D. P., Kupchak, B. R., Maresh, C. M., Volek, J. S., & Kraemer, W. J. (2014). The effects of high intensity short rest resistance exercise on muscle damage markers in men and women. *Journal of Strength and Conditioning Research*, *28*(4), 1041–1049.

Heckel, Z., Atlasz, T., Tékus, É., Kőszegi, T., Laczkó, J., & Váczi, M. (2019). Monitoring exercise-induced muscle damage indicators and myoelectric activity during two weeks of knee extensor exercise training in young and old men. *PLoS ONE*, *14*(11), 1–16.

Herbert, P., Hayes, L. D., Beaumont, A. J., Grace, F. M., & Sculthorpe, N. F. (2021a). Six weeks of high intensity interval training (HIIT) facilitates a four year preservation of aerobic capacity in sedentary older males: A reunion study. *Experimental Gerontology*, *150*. https://doi.org/10.1016/j.exger.2021.111373

Herbert, P., Hayes, L. D., Beaumont, A. J., Grace, F. M., & Sculthorpe, N. F. (2021b). Six weeks of high intensity interval training (HIIT) facilitates a four year preservation of aerobic capacity in sedentary older males: A reunion study. *Experimental Gerontology*, *150*. https://doi.org/10.1016/j.exger.2021.111373

Hicks, K. M., Onambélé, G. L., Winwood, K., & Morse, C. I. (2016). Muscle Damage following Maximal Eccentric Knee Extensions in Males and Females. *PLoS ONE*, *11*(3). https://doi.org/10.1371/journal.pone.0150848

Hicks, K. M., Onambele-Pearson, G. L., Winwood, K., & Morse, C. I. (2013). Gender differences in fascicular lengthening during eccentric contractions: The role of the patella tendon stiffness. *Acta Physiologica*, *209*(3), 235–244. https://doi.org/10.1111/apha.12159

Hopkins, W. G., Marshall, S. W., Batterham, A. M., & Hanin, J. (2009). Progressive statistics for studies in sports medicine and exercise science. *Medicine and Science in Sports and Exercise*, *41*(1), 3–12.

Hubal, M. J., Rubinstein, S. R., & Clarkson, P. M. (2007). Mechanisms of variability in strength loss after muscle-lengthening actions. *Medicine and Science in Sports and Exercise*, *39*(3), 461–468.

Hurst, C., Robinson, S. M., Witham, M. D., Dodds, R. M., Granic, A., Buckland, C., De Biase, S., Finnegan, S., Rochester, L., Skelton, D. A., & Sayer, A. A. (2022). Resistance exercise as a treatment for sarcopenia: Prescription and delivery. In *Age and Ageing* (Vol. 51, Issue 2). Oxford University Press. https://doi.org/10.1093/ageing/afac003

Hyldahl, R. D., Chen, T. C., & Nosaka, K. (2017). Mechanisms and mediators of the skeletal muscle repeated bout effect. *Exercise and Sport Sciences Reviews*, *45*(1), 24–33.

Hyldahl, R. D., & Hubal, M. J. (2014). Lengthening our perspective: Morphological, cellular, and molecular responses to eccentric exercise. *Muscle and Nerve*, *49*(2), 155–170.

Izquierdo, M., Merchant, R. A., Morley, J. E., Anker, S. D., Aprahamian, I., Arai, H., Aubertin-Leheudre, M., Bernabei, R., Cadore, E. L., Cesari, M., Chen, L. K., de Souto Barreto, P., Duque, G., Ferrucci, L., Fielding, R. A., García-Hermoso, A., Gutiérrez-Robledo, L. M., Harridge, S. D. R., Kirk, B., … Singh, M. F. (2021). International Exercise Recommendations in Older Adults (ICFSR): Expert Consensus Guidelines. *Journal of Nutrition, Health and Aging*, *25*(7), 824–853. https://doi.org/10.1007/s12603-021-1665-8

Jamurtas, A. Z., Theocharis, V., Tofas, T., Tsiokanos, A., Yfanti, C., Paschalis, V., Koutedakis, Y., & Nosaka, K. (2005). Comparison between leg and arm eccentric exercises of the same relative intensity on indices of muscle damage. *European Journal of Applied Physiology*, *95*, 179–185. https://doi.org/10.1007/s00421-005-1345-0

Janssen, I., Heymsfield, S. B., Wang, Z., Ross, R., Kung, T. A., Cederna, P. S., Meulen, J. H. Van Der, Urbanchek, M. G., Kuzon, M., Faulkner, J. A., Biol, J. G. A., Med, S., Morton, D., Rankin, P., Kent, L., & Dysinger, W. (2014). *Skeletal muscle mass and distribution in 468 men and women aged 18 − 88 yr Skeletal muscle mass and distribution in 468 men and women aged 18 – 88 yr*. 81–88.

Jastrzębski, Z., Zychowska, M., Radzimiński, Ł., Konieczna, A., & Kortas, J. (2015). Damage to liver and skeletal muscles in marathon runners during a 100 km run with regard to age and running speed. *Journal of Human Kinetics*, *45*(1), 93–102. https://doi.org/10.1515/hukin-2015-0010

Johnson, K. O., Mistry, N., Holliday, A., & Ispoglou, T. (2021). The effects of an acute resistance exercise bout on appetite and energy intake in healthy older adults. *Appetite*, *164*. https://doi.org/10.1016/j.appet.2021.105271

Johnson, K. O., Shannon, O. M., Matu, J., Holliday, A., Ispoglou, T., & Deighton, K. (2020). Differences in circulating appetite-related hormone concentrations between younger and older adults: a systematic review and meta-analysis. In *Aging Clinical and Experimental Research* (Vol. 32, Issue 7, pp. 1233–1244). Springer. https://doi.org/10.1007/s40520-019-01292-6

Kadlec, D., Sainani, K. L., & Nimphius, S. (2022). With great power comes great responsibility: Common errors in meta-analyses and meta-regressions in strength and conditioning research. In *Sports Medicine* (Vol. 53, Issue 2, pp. 313–325). Springer Science and Business Media Deutschland GmbH. https://doi.org/10.1007/s40279-022-01766-0

Kendall, B., & Eston, R. (2002). Exercise-Induced Muscle Damage and the Potential Protective Role of Estrogen. *Sports Medicine*, *32*(2), 103–123.

Kjær, M. (2004). Role of Extracellular Matrix in Adaptation of Tendon and Skeletal Muscle to Mechanical Loading. In *Physiological Reviews* (Vol. 84, Issue 2, pp. 649–698). https://doi.org/10.1152/physrev.00031.2003

Krüger, R. L., Aboodarda, S. J., Samozino, P., Rice, C. L., & Millet, G. Y. (2018). Isometric versus Dynamic Measurements of Fatigue: Does Age Matter? A Meta-analysis. *Medicine and Science in Sports and Exercise*, *50*(10), 2132–2144. https://doi.org/10.1249/MSS.0000000000001666

Kumar, V., Selby, A., Rankin, D., Patel, R., Atherton, P., Hildebrandt, W., Williams, J., Smith, K., Seynnes, O., Hiscock, N., & Rennie, M. J. (2009). Age-related differences in the dose-response relationship of muscle protein synthesis to resistance exercise in young and old men. *Journal of Physiology*, *587*(1), 211–217. https://doi.org/10.1113/jphysiol.2008.164483

Kyriakidou, Y., Cooper, I., Kraev, I., Lange, S., & Elliott, B. T. (2021). Preliminary Investigations Into the Effect of Exercise-Induced Muscle Damage on Systemic Extracellular Vesicle Release in Trained Younger and Older Men. *Frontiers in Physiology*, *12*. https://doi.org/10.3389/fphys.2021.723931

Langan, D., Higgins, J. P. T., & Simmonds, M. (2017). Comparative performance of heterogeneity variance estimators in meta-analysis: a review of simulation studies. *Research Synthesis Methods*, *8*(2), 181–198.

Lapier, T., Burton, H. W., Almon, R., Cerny, F., & Kinney, T. (1995). Alterations in intramuscular connective tissue after limb casting affect contraction-induced muscle injury. *Journal of Applied Physiology*, *78*(3), 1065–1069. www.physiology.org/journal/jappl

Lavender, A. P., & Nosaka, K. (2006). Comparison between old and young men for changes in makers of muscle damage following voluntary eccentric exercise of the elbow flexors. *Applied Physiology, Nutrition, and Metabolism*, *31*(3), 218–225.

Lavender, A. P., & Nosaka, K. (2007). Fluctuations of isometric force after eccentric exercise of the elbow flexors of young, middle-aged, and old men. *European Journal of Applied Physiology*, *100*(2), 161–167.

Lavender, A. P., & Nosaka, K. (2008). Changes in markers of muscle damage of middle-aged and young men following eccentric exercise of the elbow flexors. *Journal of Science and Medicine in Sport*, *11*(2), 124–131.

Lexell, J., Taylor, C. C., & Sjöström, M. (1988). What is the cause of the ageing atrophy?. Total number, size and proportion of different fiber types studied in whole vastus lateralis muscle from 15- to 83-year-old men. *Journal of the Neurological Sciences*, *84*(2–3), 275–294.

Liberati, A., Altman, D. G., Tetzlaff, J., Mulrow, C., Gøtzsche, P. C., Ioannidis, J. P. A., Clarke, M., Devereaux, P. J., Kleijnen, J., & Moher, D. (2009). The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: Explanation and elaboration. *Journal of Clinical Epidemiology*, *62*(10), e1–e34. https://doi.org/10.1016/j.jclinepi.2009.06.006

Machado, M., & Willardson, J. M. (2010). Short recovery augments magnitude of muscle damage in high responders. *Medicine and Science in Sports and Exercise*, *42*(7), 1370–1374.

Manfredi, T. G., Fielding, R. A., O'Reilly, K., Meredith, C. N., Lee, Y., & Evans, W. J. (1991). Plasma creatine kinase actiivty and eimd in older men. *Medicine and Science in Sports and Exercise*, *23*(9), 1028–1034.

Markus, I., Constantini, K., Goldstein, N., Amedi, R., Bornstein, Y., Stolkovsky, Y., Vidal, M., Lev-Ari, S., Balaban, R., Leibou, S., Blumenfeld-Katzir, T., Ben-Eliezer, N., Peled, D., Assaf, Y., Jensen, D., Constantini, N., Dubnov-Raz, G., Halperin, I., & Gepner, Y. (2022). Age Differences in Recovery Rate Following an Aerobic-Based Exercise Protocol Inducing Muscle Damage Among Amateur, Male Athletes. *Frontiers in Physiology*, *13*. https://doi.org/10.3389/fphys.2022.916924

Martin, T. G., Pata, R. W., D'Addario, J., Yuknis, L., Kingston, R., & Feinn, R. (2015). Impact of age on haematological markers pre- and post-marathon running. *Journal of Sports Sciences*, *33*(19), 1988–1997.

McHugh, M. P. (2003). Recent advances in the understanding of the repeated bout effect: The protective effect against muscle damage from a single bout of eccentric exercise. *Scandinavian Journal of Medicine and Science in Sports*, *13*(2), 88–97.

Morgan, D. L., & Proske, U. (2004). Popping sarcomere hypothesis explains stretch-induced muscle damage. *Clinical and Experimental Pharmacology and Physiology*, *31*(8), 541–545.

Narici, M. V, & Maganaris, C. N. (2007). Plasticity of the Muscle-Tendon Complex With Disuse and Aging. In *Rev* (Vol. 35, Issue 3). www.acsm-essr.org

National Health Lung and Blood Institute. (2023, March). *Study quality assessment tools*. Https://Www.Nhlbi.Nih.Gov/Health-Topics/Study-Quality-Assessment-Tools.

Nikolaidis, M. (2017). The effects of resistance exercise on muscle damage, position sense, and blood redox status in young and elderly individuals. *Geriatrics*, *2*(4), 20.

Nikolaidis, M., Kyparos, A., Spanou, C., Paschalis, V., Theodorou, A. A., Panayiotou, G., Grivas, G. V., Zafeiridis, A., Dipla, K., & Vrabas, I. S. (2013). Aging is not a barrier to muscle and redox adaptations: Applying the repeated eccentric exercise model. *Experimental Gerontology*, *48*(8), 734–743.

Nogueira, F. R. D., Libardi, C. A., Nosaka, K., Vechin, F. C., Cavaglieri, C. R., & Chacon-Mikahil, M. P. T. (2014). Comparison in responses to maximal eccentric exercise between elbow flexors and knee extensors of older adults. *Journal of Science and Medicine in Sport*, *17*(1), 91–95.

Nosaka, K., Newton, M., & Sacco, P. (2002). Delayed-onset muscle soreness does not reflect the magnitude of eccentric exercise-induced muscle damage. *Scandinavian Journal of Medicine and Science in Sports*, *12*(6), 337–346.

Olson, L. C., Redden, J. T., Schwartz, Z., Cohen, D. J., & McClure, M. J. (2021). Advanced glycation end-products in skeletal muscle aging. In *Bioengineering* (Vol. 8, Issue 11). MDPI. https://doi.org/10.3390/bioengineering8110168

O'Malley, L. M., & Greenwood, S. (2018). Female coaches in strength and conditioning - why so few? *Strength and Conditioning Journal*, *40*(6), 40–48.

Orimo, H., Ito, H., Suzuki, T., Araki, A., Hosoi, T., & Sawabe, M. (2006). Reviewing the definition of elderly. *Geriatrics and Gerontology International*, *43*(1), 27–34.

Owens, D. J., Twist, C., Cobley, J. N., Howatson, G., & Close, G. L. (2018). Exercise-induced muscle damage: What is it, what causes it and what are the nutritional solutions? *European Journal of Sport Science*, *0*(0), 1–15.

Page, M. J., McKenzie, J. E., Bossuyt, P. M., Boutron, I., Hoffmann, T. C., Mulrow, C. D., Shamseer, L., Tetzlaff, J. M., Akl, E. A., Brennan, S. E., Chou, R., Glanville, J., Grimshaw, J. M., Hróbjartsson, A., Lalu, M. M., Li, T., Loder, E. W., Mayo-Wilson, E., McDonald, S., … Moher, D. (2021). The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. *International Journal of Surgery*, *88*. https://doi.org/10.1016/j.ijsu.2021.105906

Pietrangelo, T., Puglielli, C., Mancinelli, R., Beccafico, S., Fanò, G., & Fulle, S. (2009). Molecular basis of the myogenic profile of aged human skeletal muscle satellite cells during differentiation. *Experimental Gerontology*, *44*(8), 523–531. https://doi.org/10.1016/j.exger.2009.05.002

Ploutz-Snyder, L. L., Giamis, E. L., Formikell, M., & Rosenbaum, A. E. (2001). Resistance training reduces susceptibility to eccentric exercise-induced muscle dysfunction in older women. *Journal of Gerontology: BIOLOGICAL SCIENCES*, *56*(9), 384–390.

Reaburn, P. R., & Fernandes, J. F. T. (2023). Exercise stress and recovery in active ageing individuals and masters athletes. In *The Importance of Recovery for Physical and Mental Health* (pp. 242–265). Routledge. https://doi.org/10.4324/9781003250647-14

Romero-Parra, N., Maestre-Cascales, C., Marín-Jiménez, N., Rael, B., Alfaro-Magallanes, V. M., Cupeiro, R., & Peinado, A. B. (2021). Exercise-Induced Muscle Damage in Postmenopausal Well-Trained Women. *Sports Health*, *13*(6), 613–621. https://doi.org/10.1177/19417381211014134

Rothstein, Hannah., Sutton, A. J., & Borenstein, Michael. (2005). *Publication bias in meta-analysis : prevention, assessment and adjustments*. Wiley.

Sacheck, J. M., Milbury, P. E., Cannon, J. G., Roubenoff, R., & Blumberg, J. B. (2003). Effect of vitamin E and eccentric exercise on selected biomarkers of oxidative stress in young and elderly men. *Free Radical Biology and Medicine*, *34*(12), 1575–1588. https://doi.org/10.1016/S0891-5849(03)00187-4

Saka, T., Akova, B., Yazici, Z., Sekir, U., Gür, H., & Ozarda, Y. (2009). Difference in the magnitude of muscle damage between elbow flexors and Knee extensors eccentric exercises. *Journal of Sports Science and Medicine*, *8*(1), 107–115.

Schneider, C. A., Rasband, W. S., & Eliceiri, K. W. (2012). NIH Image to ImageJ: 25 years of image analysis. In *Nature Methods* (Vol. 9, Issue 7, pp. 671–675). https://doi.org/10.1038/nmeth.2089

Schutzer, K. A., & Graves, B. S. (2004). Barriers and motivations to exercise in older adults. In *Preventive Medicine* (Vol. 39, Issue 5, pp. 1056–1061). https://doi.org/10.1016/j.ypmed.2004.04.003

Sellami, M., Dhahbi, W., Hayes, L. D., Padulo, J., Rhibi, F., Djemail, H., & Chaouachi, A. (2017). Combined sprint and resistance training abrogates age differences in somatotropic hormones. *PLoS ONE*, *12*(8). https://doi.org/10.1371/journal.pone.0183184

Škarabot, J., Ansdell, X. P., Temesi, J., Howatson, G., Goodall, S., & Durbaba, R. (2019). Neurophysiological responses and adaptation following repeated bouts of maximal lengthening contractions in young and older adults. *J Appl Physiol*, *127*, 1224–1237. https://doi.org/10.1152/japplphysiol.00494.2019.-A

Sorensen, J. R., Skousen, C., Holland, A., Williams, K., & Hyldahl, R. D. (2018). Acute extracellular matrix, inflammatory and MAPK response to lengthening contractions in elderly human skeletal muscle. *Experimental Gerontology*, *106*, 28–38. https://doi.org/10.1016/j.exger.2018.02.013

Sorichter, S., Puschendorf, B., & Mair, J. (1999). Skeletal muscle injury induced by eccentric muscle action: Muscle proteins as markers of muscle fiber injury. *Exercise Immunology Review*, *5*, 5–21.

Sprung, V. S., Cuthbertson, D. J., Pugh, C. J. A., Aziz, N., Kemp, G. J., Daousi, C., Green, D. J., Cable, N. T., & Jones, H. (2013). Exercise training in polycystic ovarian syndrome enhances flow-mediated dilation in the absence of changes in fatness. *Medicine and Science in Sports and Exercise*, *45*(12), 2234–2242. https://doi.org/10.1249/MSS.0b013e31829ba9a1

Stenbäck, V., Mutt, S. J., Leppäluoto, J., Gagnon, D. D., Mäkelä, K. A., Jokelainen, J., Keinänen-Kiukaanniemi, S., & Herzig, K. H. (2019). Association of physical activity with telomere length among elderly adults - The Oulu cohort 1945. *Frontiers in Physiology*, *10*(APR). https://doi.org/10.3389/fphys.2019.00444

Steptoe, A., Deaton, A., & Stone, A. A. (2015). Subjective wellbeing, health, and ageing. In *The Lancet* (Vol. 385, Issue 9968, pp. 640–648). Lancet Publishing Group. https://doi.org/10.1016/S0140-6736(13)61489-0

Sultana, F., Abbiss, C. R., Louis, J., Bernard, T., Hausswirth, C., & Brisswalter, J. (2012). Age-related changes in cardio-respiratory responses and muscular performance following an Olympic triathlon in well-trained triathletes. *European Journal of Applied Physiology*, *112*(4), 1549–1556. https://doi.org/10.1007/s00421-011-2115-9

Tanaka, H., & Seals, D. R. (2008). Endurance exercise performance in Masters athletes: Age-associated changes and underlying physiological mechanisms. *Journal of Physiology*, *586*(1), 55–63.

Trivisonno, A. J., Laffan, M. R., Giuliani, H. K., Mota, J. A., Gerstner, G. R., Smith-Ryan, A. E., & Ryan, E. D. (2021). The influence of age on the recovery from worksite resistance exercise in career firefighters. *Experimental Gerontology*, *152*. https://doi.org/10.1016/j.exger.2021.111467

United Nations, D. of E. and S. A. (2017). *World population prospects: The 2017 revision*. https://doi.org/10.1017/CBO9781107415324.004

Urtamo, A., Jyväkorpi, S. K., & Strandberg, T. E. (2019). Definitions of successful ageing: A brief review of a multidimensional concept. In *Acta Biomedica* (Vol. 90, Issue 2, pp. 359–363). Mattioli 1885. https://doi.org/10.23750/abm.v90i2.8376

Valenzuela, P. L., Maffiuletti, N. A., Joyner, M. J., Lucia, A., & Lepers, R. (2020). Lifelong Endurance Exercise as a Countermeasure Against Age-Related V˙O2 max Decline: Physiological Overview and Insights from Masters Athletes. In *Sports Medicine* (Vol. 50, Issue 4, pp. 703–716). Springer. https://doi.org/10.1007/s40279-019-01252-0

Wilson, L. J., Cockburn, E., Paice, K., Sinclair, S., Faki, T., Hills, F. A., Gondek, M. B., Wood, A., & Dimitriou, L. (2018). Recovery following a marathon: a comparison of cold water immersion, whole body cryotherapy and a placebo control. *European Journal of Applied Physiology*, *118*(1), 153–163. https://doi.org/10.1007/s00421-017-3757-z

Wilson, L. J., Dimitriou, L., Hills, F. A., Gondek, M. B., & Cockburn, E. (2019). Whole body cryotherapy, cold water immersion, or a placebo following resistance exercise: a case of mind over matter? *European Journal of Applied Physiology*, *119*(1), 135–147. https://doi.org/10.1007/s00421-018-4008-7

Yasar, Z., Elliott, B. T., Kyriakidou, Y., Nwokoma, C. T., Postlethwaite, R. D., Gaffney, C. J., Dewhurst, S., & Hayes, L. D. (2021). Sprint interval training (SIT) reduces serum epidermal growth factor (EGF), but not other inflammatory cytokines in trained older men. *European Journal of Applied Physiology*, *121*(7), 1909–1919. https://doi.org/10.1007/s00421-021-04635-2

Yasar, Z., Ross, M. D., Gaffney, C. J., Postlethwaite, R. D., Wilson, R., & Hayes, L. D. (2023). Aerobically trained older adults show impaired resting, but preserved exercise-induced circulating progenitor cell count, which was not improved by sprint interval training. *Pflugers Archiv European Journal of Physiology*, *475*(4), 465–475. https://doi.org/10.1007/s00424-022-02785-6

Zouhal, H., Jayavel, A., Parasuraman, K., Hayes, L. D., Tourny, C., Rhibi, F., Laher, I., Abderrahman, A. Ben, & Hackney, A. C. (2022). Effects of Exercise Training on Anabolic and Catabolic Hormones with Advanced Age: A Systematic Review. In *Sports Medicine* (Vol. 52, Issue 6, pp. 1353–1368). Springer Science and Business Media Deutschland GmbH. https://doi.org/10.1007/s40279-021-01612-9

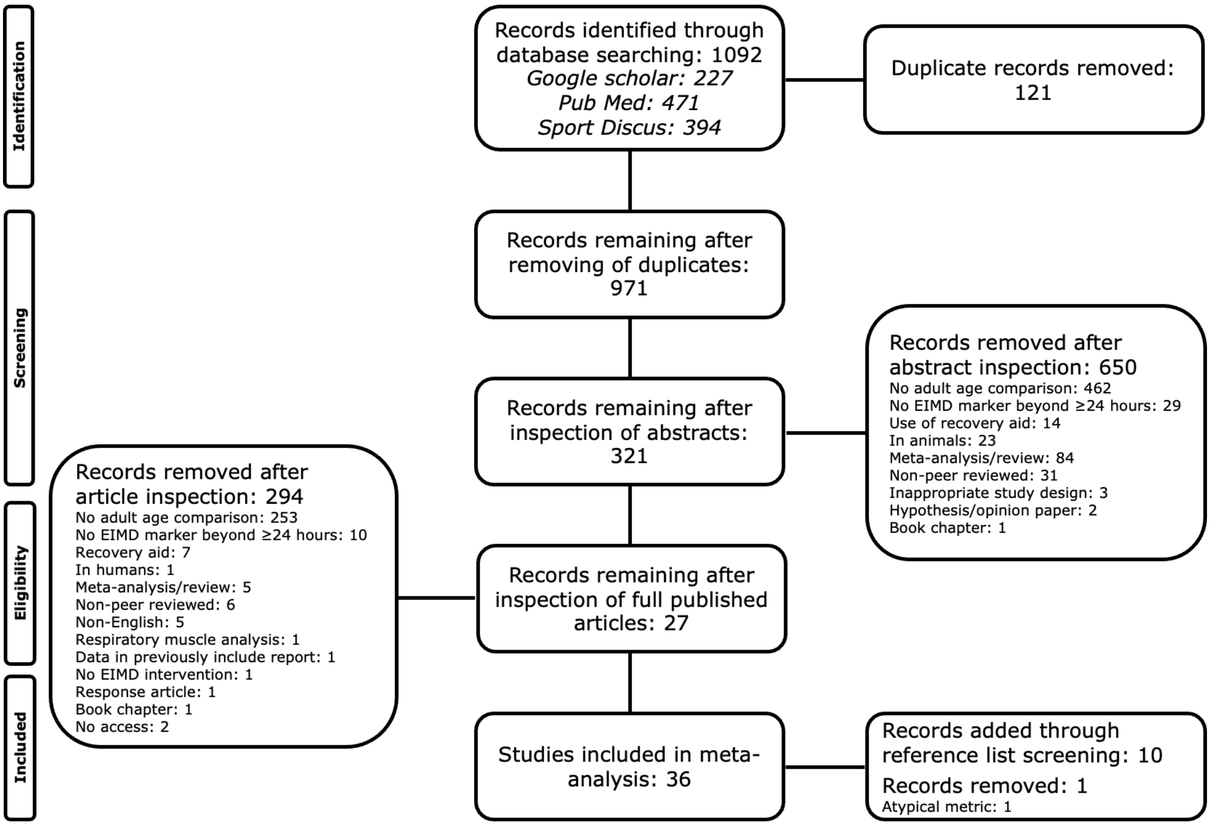

Figure 1. PRISMA Flow diagram displaying inclusion and exclusion of studies. EIMD = exercise-induced muscle damage.

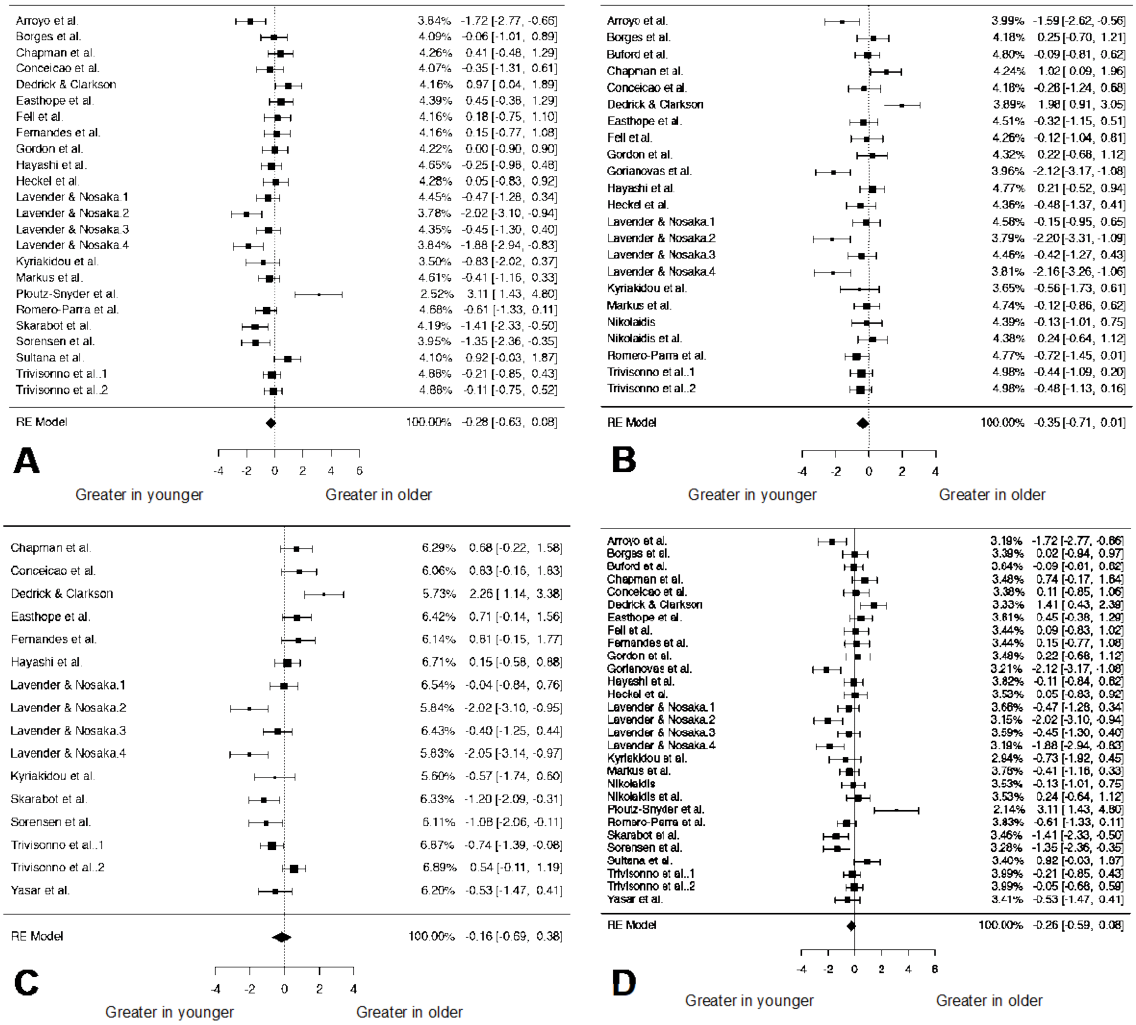

Figure 2. Forest plot of studies examining changes in muscle function at 24 (A), 48 (B) and 72 hours (C), and for peak changes (D) for older and young adults. Data are presented as the percentage weight each study contributes to the pooled standardised mean difference (SMD), and individual SMD [95% CIs]. Note that symbol size of individual studies is representative of the weighting towards the pooled SMD. The filled diamond indicates overall SMD. RE = random effects model. Lavender and Nosaka 1 and 2 are articles from (Lavender & Nosaka, 2008) and (Lavender & Nosaka, 2006), respectively. Lavender and Nosaka 3 and 4 are the young adult versus middle-aged and older adult comparisons (Lavender & Nosaka, 2007), respectively. Trivisonno et al. 1 and 2 are the upper- and lower-body comparisons, respectively (Trivisonno et al., 2021).

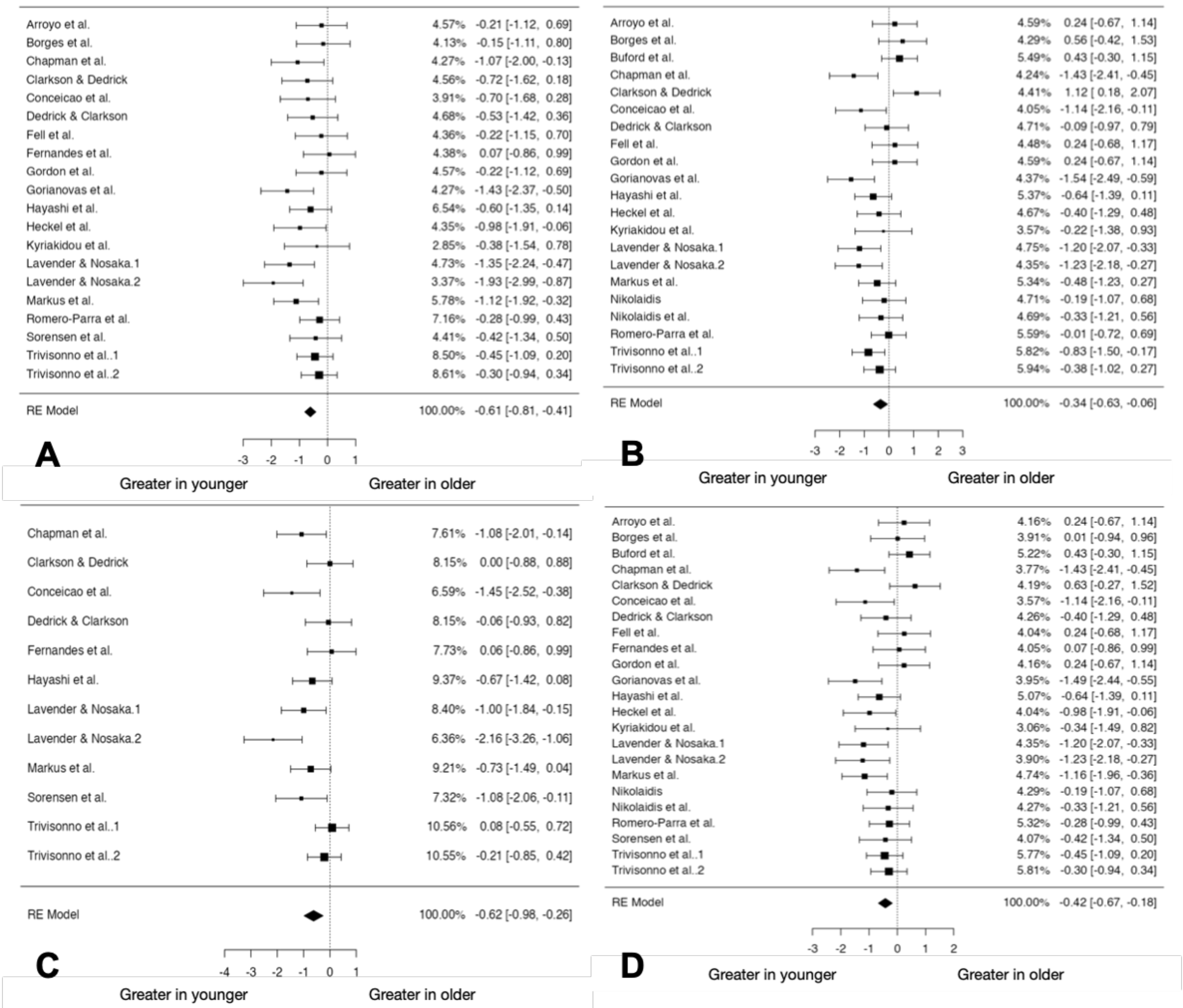

Figure 3. Forest plot of studies examining muscle soreness at 24 (A), 48 (B) and 72 hours (C), and for peak changes (D) for older and younger adults. Data are presented as the percentage weight each study contributes to the pooled SMD, individual SMD [95% CIs]. Note that symbol size of individual studies is representative of the weighting toward the pooled SMD. The filled diamond indicates overall SMD. RE = random effects model. Lavender and Nosaka 1 and 2 are articles from (Lavender & Nosaka, 2008) and (Lavender & Nosaka, 2006), respectively. Trivisonno et al 1 and 2 are the upper- and lower-body comparisons, respectively (Trivisonno et al., 2021).

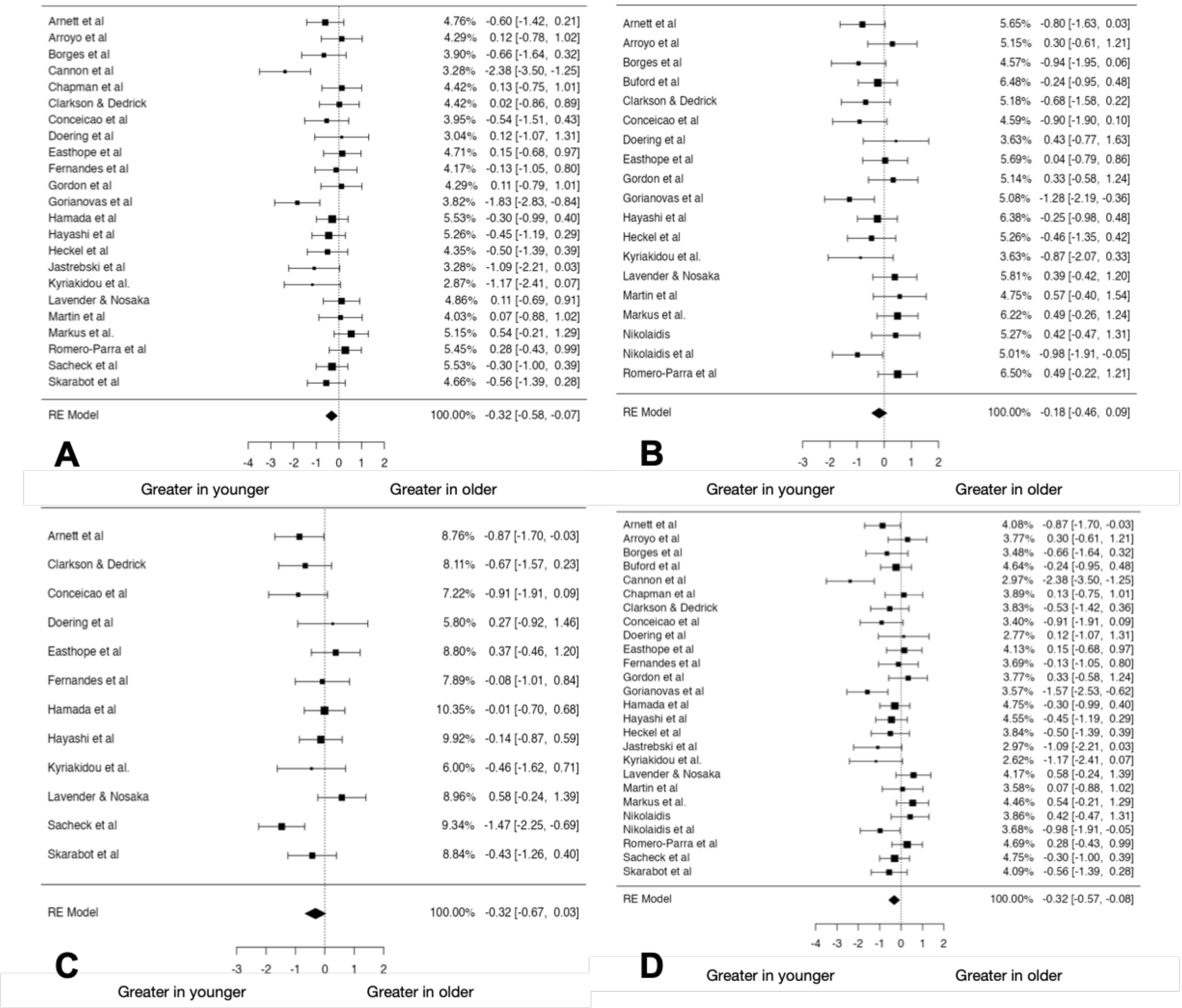

Figure 4. Forest plot of studies examining changes in CK at 24 (A), 48 (B) and 72 hours (C), and for peak changes (D) for older and younger adults. Data are presented as the percentage weight each study contributes to the pooled SMD, individual SMD [95% CIs]. Note that symbol size of individual studies is representative of the weighting towards the pooled SMD. The filled diamond indicates overall SMD. RE = random effects model.

Table 1. The National Institute of Health Quality Assessment Ratings

	Was the study question or objective clearly stated?	Were eligibility/selection criteria for the study population prespecified and clearly described?	Were the participants in the study representative of those who would be eligible for the test/service/intervention in the general or clinical population of interest?	Were all eligible participants that met the prespecified entry criteria enrolled?	Was the sample size sufficiently large to provide confidence in the findings?	Was the test/service/intervention clearly described and delivered consistently across the study population?	Were the outcome measures prespecified, clearly defined, valid, reliable, and assessed consistently across all study participants?	Were the people assessing the outcomes blinded to the participants' exposures/interventions?	Was the loss to follow-up after baseline 20% or less? Were those lost to follow-up accounted for in the analysis?	Did the statistical methods examine changes in outcome measures from before to after the intervention? Were statistical tests done that provided p values for the pre-to-post changes?	Were outcome measures of interest taken multiple times before the intervention and multiple times after the intervention?	If the intervention was conducted at a group level did the statistical analysis take into account the use of individual-level data to determine effects at the group level?	**Criterion fulfilled**
Arnett et al., (2000)	1	1	1	1	0	1	1	0	1	1	0	1	9 (64.3%)
Arroyo et al., (2017)	1	1	1	1	1	1	1	0	1	1	0	1	10 (71.4%)
Borges et al., (2015)	1	1	1	1	0	1	1	0	1	1	0	1	9 (64.3%)
Buford et al., (2014)	1	1	1	1	0	1	1	0	1	1	0	1	9 (64.3%)
Cannon et al., (1994)	1	1	1	1	1	1	1	0	1	1	0	1	10 (71.4%)
Chapman et al., (2008)	1	1	1	1	1	1	1	0	1	1	0	1	10 (71.4%)
Clarkson & Dedrick (1988)	1	1	1	1	0	1	1	0	1	1	0	1	9 (64.3%)
Conceição et al., (2012)	1	1	1	1	1	1	1	0	1	1	0	1	10 (71.4%)
Dedrick & Clarkson (1990)	1	1	1	1	0	1	1	0	1	1	0	1	9 (64.3%)
Doering et al., (2016)	1	1	1	1	0	1	1	0	1	1	0	1	9 (64.3%)
Easthope et al., (2010)	1	1	1	1	0	1	1	0	1	1	0	1	9 (64.3%)
Fell et al., (2006)	1	1	1	1	0	1	1	0	1	1	0	1	9 (64.3%)
Fell et al., (2008)	1	1	1	1	0	1	1	0	1	1	0	1	9 (64.3%)
Fernandes et al., (2019)	1	1	1	1	1	1	1	0	1	1	0	1	10 (71.4%)
Gordon III et al., (2017)	1	1	1	1	0	1	1	0	1	1	0	1	9 (64.3%)
Gorianovas et al., (2013)	1	1	1	1	1	1	1	0	1	1	0	1	10 (71.4%)
Hamada et al., (2005)	1	1	1	1	0	1	1	0	1	1	0	1	9 (64.3%)
Hayashi et al., (2019)	1	1	1	1	0	1	1	0	1	1	0	1	9 (64.3%)
Heckel et al., (2019)	1	1	1	1	0	1	1	0	1	1	0	1	9 (64.3%)
Jastrzębski et al., (2015)	1	1	1	1	0	1	1	0	1	1	0	1	9 (64.3%)
Kyriakidou et al., (2021)	1	1	1	1	0	1	1	0	1	1	0	1	9 (64.3%)
Lavender & Nosaka (2006)	1	1	1	1	0	1	1	0	1	1	0	1	9 (64.3%)
Lavender & Nosaka (2007)	1	1	1	1	0	1	1	0	1	1	0	1	9 (64.3%)
Lavender & Nosaka (2008)	1	1	1	1	1	1	1	0	1	1	0	1	10 (71.4%)
Markus et al., (2022)	1	1	1	1	1	1	1	0	1	1	0	1	10 (71.4%)
Martin et al., (2015)	1	1	1	1	1	1	1	0	1	1	0	1	10 (71.4%)
Nikolaidis et al., (2013)	0	1	1	1	1	1	1	0	1	1	0	1	9 (64.3%)
Nikolaidis (2017)	1	1	1	1	0	1	1	0	1	1	0	1	9 (64.3%)
Ploutz-Snyder et al., (2001)	1	1	1	1	0	1	1	0	1	1	0	1	9 (64.3%)
Romero-Parra et al., (2021)	1	1	1	1	0	1	1	0	1	1	0	1	9 (64.3%)
Sacheck et al., (2003)	1	1	1	1	0	1	1	0	1	1	0	1	9 (64.3%)
Škarabot et al., (2019)	1	1	1	1	1	1	1	0	1	1	0	1	10 (71.4%)
Sorensen et al., (2018)	1	1	1	1	0	1	1	0	1	1	0	1	9 (64.3%)
Sultana et al., (2012)	1	1	1	1	0	1	1	0	1	1	0	1	9 (64.3%)
Trivisonno et al., (2021)	1	1	1	1	0	1	1	0	1	1	0	1	9 (64.3%)
Yasar et al., (2021)	1	1	1	1	0	1	1	0	1	1	0	1	9 (64.3%)
Studies fulfilled	35 (97.2%)	36 (100%)	36 (100%)	36 (100%)	11 (30.6%)	36 (100%)	36 (100%)	0 (0%)	36 (100%)	36 (100%)	0 (0%)	36 (100%)	

Table 2. Characteristics of included studies

	Younger			Older						
	Age	n	Exercise type	Age	n	Sex	Activity level	Muscle	EIMD protocol	EIMD markers
Arnett et al., (2000)	23.4 ± 6.9	15	Resistance	59.4 ± 10.9	10	F	Untrained	KF	6 x 10 ECC at 110% CON 1RM	CK
Arroyo et al., (2017)	21.8 ± 2.2	9	Resistance	47.0 ± 4.4	10	M	Recreationally active	KE	8 x 10 CON-ECC at 60 deg°s^{-1}	Strength, soreness, CK
Borges et al., (2015)	25.9 ± 3.0	8	Aerobic Intermittent	55.6 ± 5.0	9	M	Well trained	LB	6 x 30 s intervals at 175% peak aerobic power	Strength, soreness, CK
Buford et al., (2014)	22.5 ± 3.7	15	Resistance	75.8 ± 5.0	15	M & F	Physically active	PF	150 unilateral eccentrics at 110% 1RM	Strength, soreness, CK
Cannon et al., (1994)	20 – 32	9	Aerobic	61 – 72	12	M & F	Sedentary	LB	45mins eccentric cycling at 78 ± 5 max HR and downhill running (-16% slope) for 45 min at 77 ± 2% max HR	CK
Chapman et al., (2008)	25.0 ± 5.69	10	Resistance	64.0 ± 3.79	10	M	No prior resistance training	EF	5 x 6 eccentric at 210 deg°s^{-1} from 60 to 180 deg° flexion	Strength, soreness, CK
Clarkson & Dedrick (1988)	23.6 ± 3.3	10	Resistance	67.4 ± 5.3	10	F	Mixed, all healthy	FF	24 unilateral eccentric contractions at 110% MIVC	Soreness, CK
Conceição et al., (2012)	23.9 ± 2.0	9	Resistance	51.1 ± 5.1	8	F	Healthy, no resistance training	EF	5 x 6 max eccentrics at 30 deg°s^{-1}	Strength, soreness, CK
Dedrick & Clarkson (1990)	23.6 ± 3.3	10	Resistance	67.4 ± 5.2	10	F	Healthy & active	FA	24 unilateral eccentric contractions at 115% MIVC	Strength, soreness
Doering et al., (2016)	27.0 ± 2.0	6	Aerobic	53.0 ± 2.0	5	M	Well trained	LB	30 min downhill running (-10% slope) at 70% $\dot{V}O_{2max}$	CK
Easthope et al., (2010)	30.5 ± 7.0	10	Aerobic	45.9 ± 5.9	13	NS	Long distance runners	LB	55 km trail run	Strength, CK
Fell et al., (2006)	24.0 ± 5.0	9	Concentric Aerobic	45.0 ± 6.0	9	M & F	Well trained	LB	3 x 30 min TT on consecutive days	Strength
Fell et al., (2008)	24.0 ± 5.0	9	Aerobic	45.0 ± 6.0	9	M	Well trained	LB	3 x 30 min TT on consecutive days	Strength, soreness
Fernandes et al., (2019)	22.3 ± .7	9	Resistance	39.9 ± 6.2	9	M	Resistance trained	LB	10 x 10 eccentric squats at 60% 1RM, 3 s eccentric	Strength, soreness, CK
Gordon III et al., (2017)	21.8 ± 2.2	9	Resistance	47.0 ± 4.4	10	M	Recreationally trained	KE	8 x 10 CON-ECC at 60 deg°s^{-1}	Strength, soreness, CK

Gorianovas et al., (2013)	20.8 ± 1.9	11	Plyometric	63.2 ± 3.6	11	M	Healthy, untrained	LB	100 intermittent drop jumps from 50cm box with 30 s rest between jumps	Strength, soreness, CK
Hamada et al., (2005)	26.3 ± 3.49	16	Eccentric aerobic	70.7 ± 3.87	16	M	Physically active	LB	3 x 15 min downhill running (-16% slope) at 75% $\dot{V}O_{2max}$	CK
Hayashi et al., (2019)	26.8 ± 6.97	15	Eccentric aerobic	57.5 ± 8.61	14	M & F	Aerobically trained	LB	3 x 15 min downhill running (-16% slope) at 65% $\dot{V}O_{2max}$	Strength, soreness, CK
Heckel et al., (2019)	25.1 ± 4.9	10	Resistance	64.5 ± 5.5	10	M	Physically active	KE	4 x 15 eccentric-concentric at 60 deg°s^{-1} between 20 and 80 deg° range	Strength, soreness, CK
Jastrzębski et al., (2015)	32.0 ± 5.3	7	Aerobic	50.6 ± 9.7	7	M	Experienced ultra-marathon runner	LB	100 km run	CK
Kyriakidou et al., (2021)	27.0 ± 1.5	7	Resistance	63.0 ± 1.0	5	M	Habitually physically active	KE	5 x 10 leg press at 120% 1RM, 2 x 10 at 100% 1RM. All with 3-5 s eccentric	Strength, soreness, CK
Lavender & Nosaka (2006)	19.4 ± 1.26	10	Resistance	70.5 ± 4.74	10	M	Physically active no resistance training	EF	6 x 5 max eccentric at 40% MIVC from 90 to 180 deg° flexion	Strength, soreness, CK
Lavender & Nosaka (2007)	20.4 ± 2.0	10	Resistance	48.0 ± 7.3 70.5 ± 4.1	12 10	M	Healthy, not resistance trained	EF	6 x 5 max eccentric at 40% MIVC from 90 to 180 deg° flexion	Strength
Lavender & Nosaka (2008)	19.4 ± 1.39	12	Resistance	48.0 ± 7.27	12	M	Habitually active no resistance training	EF	6 x 5 max eccentric at 40% MIVC from 90 to 180 deg° flexion	Strength, soreness, CK
Markus et al., (2022)	26.1 ± 2.9	14	Aerobic	43.6 ± 4.1	14	M	Competitive runners/triathletes	KE	60 min downhill running (-10% slope) at 60% heart rate max	Strength, soreness, CK
Martin et al., (2015)	31.9 ± 5.0	9	Aerobic	63.1 ± 4.6	8	M	Marathon runners	LB	Marathon run	CK
Nikolaidis et al., (2013)	20.6 ± 1.58	10	Resistance	64.6 ± 3.48	10	M	Healthy, moderately inactive	KE	5 x 8 eccentric MVC 0 to 90 deg° range at 60 deg°s^{-1} 2 min rest	Strength, soreness, CK
Nikolaidis (2017)	22.1 ± 3.9	10	Resistance	66.9 ± 5.4	10	M	Untrained, healthy	LB	5 x 15 eccentric biased squats with 2 min rest. 2 s eccentric phase	Strength, soreness, CK
Ploutz-Snyder et al., (2001)	23 ± 4	6	Resistance	66 ± 5	6	F	Sedentary	KE	10 x 10 eccentric knee extensions at 75% eccentric 1RM	Strength
Romero-Parra et al., (2021)	29.0 ± 6.0	19	Resistance	52.0 ± 4.0	13	F	Well trained	LB	10 x 10 eccentric squats at 60% 1RM, 4 s eccentric	Strength, soreness, CK
Sacheck et al., (2003)	26.4 ± 3.3	16	Aerobic	69.3 ± 3.5	16	M	Physically active	LB	3 x 15 min downhill running (-16% slope) at 75% $\dot{V}O_{2max}$	CK

Škarabot et al., (2019)	27.0 ± 5.0	12	Resistance	66.0 ± 4.0	11	M	Physically active	DF	10 x 6 eccentrics at 15 deg°s^{-1} from 10 to 40° range	Strength, CK
Sorensen et al., (2018)	22.7 ± 2.3	11	Resistance	70.9 ± 7.5	8	M & F	Physically active	KE	30 x 10 maximal lengthening contractions at 120 deg°s^{-1}	Strength, Soreness
Sultana et al., (2012)	28.4 ± 6.1	9	Aerobic	52.2 ± 10.0	10	M	Well trained	LB	Olympic distance triathlon	Strength
Trivisonno et al., (2021)	25.5 ± 3.4	19	Aerobic	50.3 ± 3.5	19	M	Resistance trained career firefighters	FB	8–10 and 4–6 repetitions with 1 min of rest between sets on 4 exercises.	Strength, Soreness
Yasar et al., (2021)	24 ± 3	9	Aerobic intermittent	70 ± 8	9	M & F	Physically active	LB	3 x 20 s maximal sprint efforts with 3 mins rest between	Strength

Note; NS = not stated; F = female; M = male; LB = lower body; KF = knee flexors; FF = forearm flexors; EF = elbow flexors; KE = knee extensors; EE = elbow extensors; DF = dorsiflexors; ECC = eccentric; CON = concentric; RM = repetition maximum; HR = heart rate; MIVC = maximal isometric voluntary contraction; CK = creatine kinase.

Table 3. Effect

		Younger (n)	Older (n)	Z	*P*	SMD (95% CIs)	I^2 (%)
Muscle function	***Involved limb***						
	Upper (k = 8)	90	91	-0.83	0.409	-0.33 (-1.11, 0.45)	84
	Lower (k = 21)	231	225	-1.27	0.203	-0.24 (-0.60, 0.13)	71
	Sex						
	Female (k = 4)	44	37	0.44	0.663	-0.44 (-0.89, 0.01)	88
	Male (k = 19)	191	192	-2.26	0.024	-0.45 (-0.85, -0.06)	73
	Exercise type						
	Resistance (k = 21)	212	202	-1.30	0.193	-0.28 (-0.70, 0.14)	79
	Aerobic (k = 7)	66	69	0.18	0.857	-0.03 (-0.32, 0.38)	14
Muscle soreness	***Involved limb***						
	Upper (k = 4)	41	40	0.45	0.657	-0.15 (-0.80, 0.50)	53
	Lower (k = 22)	246	238	-2.56	0.010	-0.36 (-0.63, -0.08)	53
	Sex						
	Female (k = 4)	53	46	-1.90	0.057	-0.44 (-0.89, 0.01)	34
	Male (k = 18)	185	183	-1.56	0.12	-0.22 (-0.51, -0.06)	44
	Exercise type						
	Resistance (k = 15)	166	153	-1.50	0.133	-0.21 (-0.49, 0.06)	33
	Aerobic (k = 10)	110	114	-1.62	0.106	-0.38 (-0.83, 0.08)	63
Creatine kinase	***Involved limb***						
	Upper (k = 4)	41	40	0.45	0.657	-0.15 (-0.80, 0.50)	53
	Lower (k = 20)	225	219	-2.72	0.007	-0.34 (-0.59, -0.09)	49
	Sex						
	Female (k = 4)	53	46	-1.90	0.057	-0.44 (-0.89, 0.01)	34
	Male (k = 16)	164	164	-2.29	0.022	-0.34 (-0.64, -0.05)	53
	Exercise type						
	Resistance (k = 24)	159	148	-1.22	0.223	-0.17 (-0.45, -0.10)	31
	Aerobic (k = 9)	96	100	-2.15	0.031	-0.48 (-0.92, -0.04)	54