



Biological Sex Differences in Absolute and Relative Changes in Muscle Size following Resistance Training in Healthy Adults: A Systematic Review with Meta-Analysis

Supplementary materials:

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For correspondence:

mrefalo@deakin.edu.au

Martin C. Refalo¹, Greg Nuckols², Andrew Galpin³, Iain Gallagher⁴, D. Lee Hamilton¹, Jackson Fyfe¹

¹Institute for Physical Activity and Nutrition (IPAN), School of Exercise and Nutrition Sciences, Deakin University, Geelong, Australia

²Stronger by Science LLC, Raleigh, NC 27605, USA.

³Department of Kinesiology, Center for Sport Performance, California State University, Fullerton, CA, United States.

⁴Centre for Biomedicine and Global Health, Edinburgh Napier University, Edinburgh, UK.

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Authors can be reached on X:
@MartinRefalo, @jacksonfyfe,
@dlhamilton82, @GregNuckols,
@DrAndyGalpin, @iainjgallagher

ABSTRACT

Muscle hypertrophy may be influenced by biological differences between males and females. This systematic review with meta-analysis investigated *absolute* and *relative* changes in muscle size following resistance training (RT) between males and females and whether key variables (i.e., assessment of muscle size, individual characteristics, and RT characteristics) moderate the results. Studies were included if male and female participants were apparently healthy (18-50 years old) adults of any RT experience that completed the same RT intervention, and a valid measure of pre- to post-intervention changes in muscle size was included. Out of 2199 retrieved studies, a total of 27 studies were included in the statistical analysis. Bayesian methods were used to estimate an effect size (ES) and probability of direction (*pd*) for each outcome. Superior increases in absolute muscle size were estimated in males versus females [ES = 0.35 (95% HDI: 0.20 to 0.49); *pd* = 100%], however, relative increases in muscle size were similar between sexes [ES = 0.05 (95% HDI: -0.07 to 0.16); *pd* = 80%]. Sub-group analyses found that the balance of probability favoured relative type I muscle fibre hypertrophy in males versus females [ES = 0.57 (95% HDI: -0.02 to 1.16) *pd* = 97%] and relative type II muscle fibre hypertrophy in females versus males [ES = -0.36 (95% HDI: -0.97 to 0.23) *pd* = 89%]. Other variables assessed (i.e., body region, measurement, RT experience, set volume, relative load) did not have a meaningful impact on sex differences in relative muscle hypertrophy.

1. INTRODUCTION

Resistance training (RT) promotes increases in muscle fibre and ultimately whole-muscle cross-sectional area, known as skeletal muscle hypertrophy [1]. The muscle hypertrophy experienced following resistance training may vary between individuals [2], and importantly, may be influenced by biological differences between males and females that arise after puberty [3]. For example, postpubescent males possess approximately tenfold higher endogenous testosterone levels compared to that of typical postpubescent females [4]. This difference in basal testosterone is believed to be the primary factor explaining greater average levels of muscle size in males versus females at adulthood. For example, in untrained and resistance-trained individuals, biceps brachii and quadriceps cross sectional area (CSA) of females is ~50-60% and ~70-80% of CSA in males, respectively [5]. The proportion of type II muscle fibres, which have greater hypertrophic potential than type I muscle fibres [6], is also greater in males than in females [7]. This difference in muscle fibre type distribution may contribute to females having ~50-60% and ~60-70% of male upper-body and lower-body strength, respectively (at the group level) [5]. Although general differences in absolute muscle size and strength between adult males and females exist [8], whether the anabolic response to RT and subsequent muscle (and muscle fibre type-specific) hypertrophy is also influenced by biological sex requires further investigation in young to middle-aged adults.

It has been postulated that males experience greater muscle hypertrophy following RT compared to females, potentially due to factors relating to gene expression [9] or the higher levels of testosterone in males versus females, on average [4]. A previous meta-analysis compared muscle hypertrophy outcomes between young to middle-aged males and females [10] and found no statistically significant differences in pre- to post-intervention changes in muscle size [ES = 0.07 (95% CI: -0.09, 0.23); $P = 0.31$]; however, this meta-analysis did not differentiate *absolute* (i.e., raw change in muscle size) and *relative* (i.e., percentage increase in muscle size from baseline) changes in muscle size. Considering the marked differences in baseline muscle size between males and females [5], exploring both absolute and relative changes in muscle size is important. For example, another meta-analysis [11] of studies in older adults (>50 years of age) revealed that absolute increases in muscle size following RT favour males versus females [ES = 0.45 (95% CI: 0.23, 0.67); $P < 0.001$] with no statistically significant difference in relative muscle hypertrophy found [ES = 0.10 (95% CI: -0.04, 0.23); $P = 0.16$]. Furthermore, other studies have revealed the possibility for muscle fibre type-specific hypertrophy to differ between males and females [12, 13], but previous meta-analyses [10, 11] have not investigated muscle fibre cross sectional area (fCSA) as an outcome. It is also unclear if the RT experience of participants, characteristics of the RT protocol completed (e.g., volume and

load), and the assessment of muscle size (e.g., body region assessed, type of measurement) employed, influence sex differences in muscle hypertrophy.

This systematic review with meta-analysis therefore extends previous meta-analytic findings by i) comprehensively analysing the relevant literature to investigate absolute and relative changes in muscle size following RT between young to middle-aged males and females, and ii) investigating whether key variables (i.e., method of muscle size assessment, individual characteristics, and RT characteristics) moderate the influence of biological sex on muscle hypertrophy. We employed a Bayesian approach for data analysis to improve the interpretation of the effect size (ES) estimate, directly model the uncertainty of the ES estimate, and enable the results to be presented with posterior probabilities that allow for meaningful and intuitive inferences [14]. The Bayesian hierarchical analysis we employed also i) incorporate a-priori scientific knowledge, and ii) allow for the “borrowing” of information across studies, ultimately leading to more precise ES estimates [14].

2. MATERIALS & METHODS

A systematic review and meta-analysis were performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [15]. The PRISMA checklist can be found in Supplementary File S6. The original protocol was registered with Open Science Framework on the 1st of June 2023 (<https://osf.io/trz3y/>).

2.1 Research Question(s)

The research question(s) were defined using the participants, interventions, comparisons, outcomes, and study design (PICOS) framework, as follows. The primary research question was: *“What is the estimated overall difference in muscle hypertrophy following RT between young to middle-aged males and females, in both absolute and relative (%) terms?”* To facilitate the interpretation of this research question, we also investigated whether the following variables had a moderating effect on the overall ES of muscle hypertrophy for each biological sex: i) assessment of muscle mass (i.e., body region assessed, type of measurement used, muscle fibre type), ii) participant resistance training experience, and iii) resistance training characteristics (i.e., set volume, relative load). Although not described in our pre-registration, we also conducted a secondary meta-analysis of studies that measured muscle fibre cross sectional area (fCSA) in both sexes to address the following question: *“Following resistance training, which muscle fibre type (i.e., type I or type II) experiences the most hypertrophy in young to middle-aged males and females?”*

2.2 Literature Search Strategy

The literature search followed the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines [15]. Literature searches of the PubMed, SCOPUS and SPORTDiscus databases were started in May 2023 and completed in June 2023 using the following search terms that were adapted for each individual database: “resistance training” OR “resistance exercise” OR “strength training” AND “gender” OR “women” OR “woman” OR “female” OR “sex” OR “sex difference” “muscle hypertrophy” OR “muscle size” OR “muscle growth” OR “muscle mass” OR “muscle thickness” OR “cross-sectional area”. Search terms were added using the NOT term to reduce the number of irrelevant studies according to exclusion criteria (e.g., older, elderly, sarcopenia, cancer). The reference list of previous meta-analyses [10, 11] and the retrieved articles were manually searched, and six additional studies [16-21] that met the inclusion criteria were identified and subject to the screening process, with full-text review confirming eligibility for inclusion (Figure 1). Only studies conducted in humans were included.

2.3 Study Selection

Covidence software (*Veritas Health Innovations, Melbourne, Australia*) was used to manage and conduct the systematic study selection process, including the removal of duplicates and the exclusion of ineligible studies at each stage of the screening process. An overview of the article identification process is shown in Figure 1. The article identification process was completed independently (to reduce any bias during this process) by two authors (MR and JF) with any disagreement resolved by discussion. Finally, the authors (MR and JF) reviewed the full text to determine eligibility for inclusion based on the inclusion criteria. If any studies were added through reference checking or manual searching, they were subjected to the same screening process as if they were found in the initial database search.

2.4 Inclusion Criteria

Studies were included if: 1) participants were apparently healthy young to middle-aged (18-50 years old) adults of any RT experience, 2) the experimental comparison involved male and female participants completing the same RT intervention (e.g., set volume, load, frequency, exercises, proximity-to-failure), and 3) one of the following measures of pre- to post-intervention changes in muscle size were included; a) muscle thickness, b) whole-limb or muscle CSA or volume, c) muscle fCSA, or d) lean body/fat free mass via dual x-ray absorptiometry (DXA) or bioelectrical impedance analysis (BIA). Only original research articles (English language) in peer reviewed journals were included. Articles that did not meet these criteria were excluded.

2.5 Data Extraction

Data extraction was carried out by the principal investigators (MR and JF) to capture key information in a table format (Table 1). The following participant characteristics were extracted: 1) RT status (i.e., untrained, or resistance-trained), 2) age, and 3) sex. The following article characteristics were also extracted: 1) first author, 2) sample size, 3) publication date, 4) intervention groups/protocol outlines and duration, and 5) key findings (i.e., percentage increase in muscle size from pre- to post-intervention and an indication of whether any muscle hypertrophy was statistically different between sexes). Raw data from pre- and post-intervention for muscle hypertrophy outcomes were extracted for meta-analysis [if figures were used instead of numerical data, those data were extracted using Web Plot Digitizer (Version 4.6, California, USA)]. Studies were classified as recruiting 'resistance-trained' participants if the participants had RT experience immediately prior to study commencement, whereas studies that involved a RT prohibitory period (e.g., "no RT 6-months prior to study commencement") were classified as recruiting untrained participants. Considering the absence of detail regarding training status in some studies further classification of training status (e.g., "beginner", "intermediate", "advanced",

“highly advanced”) with multiple criteria [22] is difficult. For studies that prescribed RT loads based on repetition-maximum, the relative loads (% of 1-RM) were calculated using an estimated repetitions at % of 1-RM chart [23]; for example, if a 10-RM was prescribed, it was estimated that a 75% of 1-RM load was lifted. When studies employed a combination of loading ranges (i.e., low = <50% of 1-RM, moderate = 50-77.5% of 1-RM, high = >77.5% of 1-RM) across the RT intervention, the median load was extracted for data analysis (e.g., if the load was altered from 60 to 80% of 1-RM, 70% of 1-RM was extracted as the median load). Similarly, if the sets performed for each exercise were altered across the RT intervention, the median number of sets completed was extracted for data analysis and multiplied with the number of exercises performed for the muscle group measured and the number of RT sessions completed per week (e.g., set volume = median number of sets completed x number of exercises completed for measured muscle group x number of sessions completed per week). Considering the ambiguity and variability in definitions of set failure throughout the RT literature [24], we derived the proximity-to-failure of the RT interventions by classifying studies as either prescribing ‘set failure’ or ‘non-failure’ based on the set termination methods reported.

2.6 Methodological Quality Assessment

Evaluation of methodological study quality (including risk of bias) was conducted (by MR) using the tool for the assessment of study quality and reporting in exercise (TESTEX) scale [25]. Any ambiguities in methodological quality assessment were resolved by discussion between MR and JF. The TESTEX scale is an exercise science-specific scale used to assess the quality and reporting of exercise training trials. The scale contains 12 criteria that can either be scored a ‘one’ or not scored at all; 1, eligibility; 2, randomisation; 3, allocation concealment; 4, groups similar at baseline; 5, assessor blinding; 6, outcome measures assessed in 85% of patients (3 possible points); 7, intention-to-treat; 8, between-group statistical comparisons (2 possible points); 9, point-estimates of all measures included; 10, activity monitoring in control groups; 11, relative exercise intensity remained constant; 12, exercise parameters recorded. The best possible total score is 15 points.

2.7 Statistical Analysis

2.7.1 Primary Investigation of Sex Differences in Muscle Hypertrophy

To provide a more flexible modelling approach and enable results to be interpreted intuitively through reporting of probabilities [14], we carried out a Bayesian meta-analysis using the “brms” (Bürkner, 2023) package in R (v 4.0.2; R Core Team, <https://www.r-project.org/>). A comprehensive and step-by-step overview of the statistical analysis can be found on the Open Science Framework (<https://osf.io/trz3y/>). Posterior draws were extracted using “tidybayes” (Kay,

2023) and ESs calculated using “emmeans” (Lenth, 2023). The absolute (mean and SD) and relative (percentage change and SD) changes in muscle size from pre- to post-intervention for both male and female participants were extracted from each study. If the relative change and associated SD were not reported, we estimated the respective values by dividing both absolute change and SD by the groups baseline mean. An ES for the difference in absolute and relative muscle hypertrophy between males and female was then estimated using the “escalc” function in the “metafor” (Viechtbauer, 2010) package. The ESs were calculated in such a manner that a positive ES indicated larger increases in muscle hypertrophy for male participants, whereas a negative ES indicated larger increases in muscle hypertrophy for female participants. Given that correlations between pre-test and post-test measures are rarely reported in original studies, we adopted a correlation coefficient value of $r = 0.87$ from a recent meta-analysis of differences in muscle hypertrophy between older males and females [11] and constrained it using prior distributions. However, sensitivity analyses were also performed using correlation coefficients ranging from $r = 0.7$ to 0.99 (Supplementary File S2). We used a hierarchical Bayesian model to account for the nested structure in the ESs from the included studies (i.e., some studies involve multiple effect sizes due to comprising various measures of muscle hypertrophy within each of the groups investigated). Weakly informative priors were used for the intercept parameter (based on previous research [10]) and a half-Cauchy prior was used for the sigma parameter (Supplementary File S1). Inferences from all the analyses were made from posterior distributions generated using the Hamiltonian Markov Chain Monte Carlo method and via the use of highest density intervals (HDI). Interpretations were based on the mean ES and associated HDI limits, along with the probability of direction (pd), which is a calculated percentage (ranging from 50% to 100%) that represents the posterior probability an ES goes in a particular direction [estimated with “bayestestR” (Makowski, 2019)]. We categorised ESs by qualitative thresholds (i.e., small, medium, and large) established from previous strength and conditioning interventions [26] that have been used in research investigating muscle hypertrophy [27]. Small-study effects (publication bias, etc.) were visually assessed using funnel plots. To enhance the accuracy, transparency, and replicability of our Bayesian analysis, we used the WAMBS-Checklist to audit the prior specification, estimation diagnosis, influence of priors, and interpretation of results [28].

2.7.1.1 Sub-Group and Meta-Regression Analyses

Sub-group and meta-regression analyses were also conducted to investigate the influence of specific variables on the outcome measure by employing similar methods as described in section 2.7.1 whilst categorising studies based on the criteria of interest. For example, additional sub-group analyses estimated an ES for the influence of i) body region (i.e., upper-body or lower-body), ii) assessment of muscle hypertrophy (i.e., muscle thickness, muscle CSA, fCSA, or LBM/FFM), and iii) resistance training experience (i.e., resistance-trained or untrained), iv) muscle

fibre type (i.e., type I or type II). Similarly, we used meta-regression to explore the influence of set volume completed (i.e., number of sets performed for a given muscle group per session) and relative-load lifted (i.e., percentage of 1-RM) on the overall ES.

2.7.2 Secondary Investigation of Type I and Type II Muscle Fibre Hypertrophy

Similar methods as described in section 2.7.1 were used to investigate differences in type I and type II muscle fibre hypertrophy across all studies measuring muscle fCSA as an outcome measure. Standardized ESs were calculated such that a positive ES value favours greater increases in type II muscle fibre hypertrophy, whereas a negative ES value favours increases in type I muscle fibre hypertrophy. To estimate an ES for the influence of biological sex on type I and type II muscle fibre hypertrophy, an additional sub-group analysis was conducted. Considering this was a secondary analysis aimed at providing context to our sub-group analysis of sex differences in muscle fibre type-specific hypertrophy, we did not perform sensitivity analyses, and as such, the findings should be interpreted with caution.

3. RESULTS

3.1 Search Results and Study Characteristics

A total of 28 studies met the inclusion criteria. A PRISMA diagram of the systematic literature search and study selection process is displayed in Figure 1. Data from one study [29] could not be retrieved; the remaining 27 studies were systematically reviewed and meta-analysed. Visual inspection of funnel plots (Supplementary File S3) identified no publication bias. Data from a total of 853 male participants and 1,082 female participants were included in the meta-analysis, with the mean age of males being 25.7 ± 3.9 (range: 20-42) and females 25.6 ± 3.7 (range: 19-41) years. Four [29-32] out of the 27 studies involved resistance-trained participants, with the remainder of the studies involving participants with either i) no RT experience ($n = 4$), or ii) no RT experience 5-years ($n=1$), 1-year ($n = 7$), 8-months ($n = 1$), 6-months ($n = 7$), and 3-months ($n = 2$) prior to study commencement. In total, 64 muscle hypertrophy outcomes were extracted, with some studies reporting numerous *direct* outcomes: i) muscle CSA using magnetic resonance imaging (MRI) [2, 29, 33, 34], ultrasound [18, 20, 31, 35], or computed tomography (CT) [32, 36, 37], ii) muscle fCSA using biopsy samples [12, 13, 19, 21, 35, 38], iii) muscle physiological CSA using ultrasound [39], iv) muscle volume using MRI [17, 33, 40], and v) muscle thickness using ultrasound [18, 30, 38, 41-44], and other studies using *indirect* outcomes: i) lean mass using DXA [16, 19, 41, 45], and ii) estimated skeletal muscle mass using bioelectrical impedance analysis (BIA) [46]. Most of the muscle hypertrophy outcomes were assessed in the lower body (70% of outcomes [12, 13, 17-21, 29-31, 33, 35, 36, 38, 39, 41-43, 45]; quadriceps and hamstrings) versus the upper-body (24% of outcomes [2, 18, 30, 32, 34, 36, 37, 40, 41, 44]; biceps, triceps, and chest), with 6% of outcomes [16, 19, 41, 46] assessing lean mass of the upper- and lower-body combined (i.e., total body lean mass).

The duration of the RT interventions ranged from six to 24 weeks, with a mean of 11 weeks. The most common number of times a muscle group was resistance trained per week was three (52%; 14 studies [12, 13, 16, 17, 19, 35-39, 41, 42, 44, 46]), with nine studies [2, 18, 20, 21, 31, 32, 34, 40, 43] involving two RT sessions per muscle group per week (33%), one study involving one RT session per muscle group per week [30], and three studies [29, 33, 45] involving two to three RT sessions per muscle group per week (11%). Many of the 27 meta-analysed studies employed a combination of loading ranges; one study [35] employed a median relative load of <50% of 1-RM (4%), 19 studies [2, 12, 13, 16, 18, 20, 21, 31-34, 37-42, 44, 46] employed 50 to 77.5% of 1-RM (70%), and seven studies [19, 29, 30, 35, 36, 43, 45] employed >77.5% of 1-RM (26%) with one of these studies [43] involving eccentric-only contractions of 120% of 1-RM. Another study [17] employed various loads of $\leq 85\%$ of 1-RM, but the median relative load is unclear. Although some studies altered the set volume completed throughout the RT intervention, the mean set

volume prescribed across all studies was 14 sets per muscle group per week, with nine studies [16, 18, 29, 31, 35, 36, 41, 43, 44] involving <10 sets (32%), 14 studies [2, 12, 17, 20, 21, 29, 30, 33, 34, 37, 38, 40, 45, 46] involving 10 to 20 sets (50%), and five studies [13, 19, 32, 39, 42] involving >20 sets (18%). However, a study by Hammarström et al. [29] comprised of two RT groups, one of which completed a set volume of <10 sets and the other involving 10 to 20 sets (this study is included in the previous qualitative assessment twice; percentage calculations are thus based on 28 total studies). Out of the 27 studies meta-analysed, nine studies [12, 13, 18, 35, 37, 38, 42, 44, 46] involved a set termination method that was clearly reported as set failure (33%), whereas the remainder of the studies (67%) did not either i) require participants to reach set failure, or ii) report a clear set termination method. Considering the large number of studies that did not clearly report a set termination method, we decided to omit proximity-to-failure as a variable of interest within our sub-group analysis to ensure that our results were not confounded by studies that may have involved participants performing RT to set failure but didn't explicitly report it. Finally, most of the studies involved traditional RT methods, however, one study involved blood flow restriction [35], one study involved eccentric-only contractions [43], and two studies utilised a flywheel device in at least one of the experimental groups [33, 45]. In some instances, studies were excluded from sub-group analyses because i) outcome measures were only employed in one study (e.g., pCSA [39] and skeletal muscle mass via BIA [46]), ii) relative load lifted was larger than 100% of 1-RM (for eccentric-only RT [43]), iii) relative load was unable to be estimated [17], and iii) measures of lean mass were not separated into upper- or lower-body [16, 19, 46].

For a comprehensive summary of included studies, see Table 1.

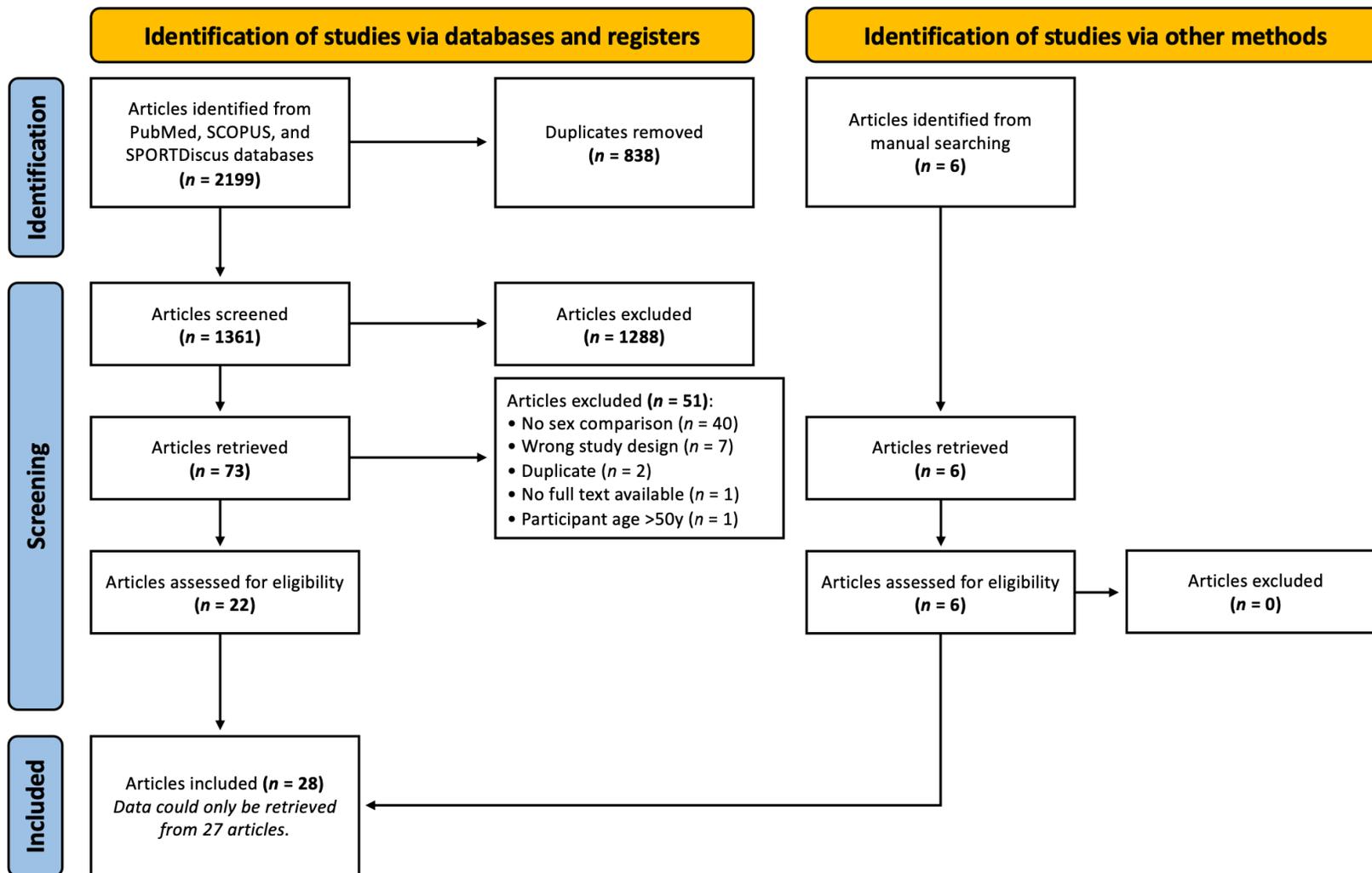


Figure 1. PRISMA flow chart. Summary of systematic literature search and article selection process.

Table 1. Summary of data extraction. Summary of studies included comparing changes in muscle size from pre-to post-intervention between males and females. Data presented as mean \pm SD.

Abbreviations: BB, barbell; BFR, blood flow restriction; BIA, bioelectrical impedance analysis; CSA, cross-sectional area; CT, computed tomography; EF, elbow flexor; fCSA, fibre cross-sectional area; MRI, magnetic resonance imaging; pCSA, physiological cross-sectional area; RF, rectus femoris; Reps, repetitions; RM, repetition maximum; RT, resistance training; sessions/week, sessions per muscle group per week; VeL, velocity loss; VL, vastus lateralis; \uparrow = increased; \downarrow = decreased; \leftrightarrow = no difference between sexes; * = results of statistical comparison between sexes not reported; \wedge = relative load estimated from repetitions at % of 1-RM chart; # = mean number of muscle fibres analysed for each participant across timepoints.

Study	Participants	Age (years)	RT protocol	(sessions /week)	Outcome measure (device; muscle)	Key findings
Abe et al. 2000 [41]	Males ($n = 17$) Females ($n = 20$) → Untrained: No RT 1 year prior	37.7 \pm 7.2 41 \pm 4.1	3 sets x 8-12 reps → 60-70% 1-RM Exercises: Leg extension, leg curl, chest press, horizontal row, biceps curl, triceps extension	12 weeks (3/week)	Lean mass (DXA; total body) Muscle thickness (ultrasound; biceps, triceps, chest, quadriceps, hamstrings)	\leftrightarrow Total body lean mass between males (+2.6%) and females (+1.7%) \leftrightarrow Muscle thickness between males (+10.3%) and females (+10.8%) for all muscle groups measured
Abou Sawan et al. 2021 [13]	Males ($n = 10$) Females ($n = 10$) → Untrained: No RT 3-months prior	23 \pm 4 23 \pm 5	4 sets x 10-12 reps → 75% 1-RM Exercises: Leg press, leg extension	8 weeks (3/week)	Muscle fCSA (biopsy + histochemistry; VL) # Type I = 84 # Type II = 92	\uparrow Type I VL fCSA observed in males (+21.1%) versus females (+5.6%) but \leftrightarrow Type II VL fCSA between males (+18%) and females (+27.5%)
Abou Sawan et al. 2022 [42]	Males ($n = 10$) Females ($n = 10$) → Untrained: No RT 3-months prior	23 \pm 4 23 \pm 5	4 sets x 10-12 reps → 75% 1-RM Exercises: Leg press, leg extension	8 weeks (3/week)	Muscle thickness (ultrasound; VL)	\leftrightarrow VL thickness between males (+10.7%) and females (+8.2%)
Alway et al. 1992 [32]	Males ($n = 5$) Females ($n = 5$) → Trained: ≥ 5 years of RT experience	32.8 \pm 4.5 34.8 \pm 2.7	3-5 sets x 6-14 reps → 60-85% 1-RM \wedge Exercises: Biceps curl (multiple variations)	24 weeks (2/week)	Muscle CSA [CT; biceps, flexor (brachialis + biceps)]	Biceps and flexor CSA \uparrow for both males (+5.6%) and females (+3.1%) *
Coratella et al. 2018 [43]	Males ($n = 13$) Females ($n = 13$)	21.2 \pm 2.6 20.8 \pm 3	4 sets x 10 reps → 120% 1-RM	8 weeks (2/week)	Muscle thickness (ultrasound; VL)	\leftrightarrow VL muscle thickness between males (+11.1%) and females (+13%)

	→ Untrained: No RT 6-months prior		Exercise: Leg extensions (eccentric only)			
Cureton et al. 1988 [36]	Males (<i>n</i> = 7) Females (<i>n</i> = 9) → Untrained: No RT 6-months prior	24.7 ± 2.1 25.5 ± 2.3	1-3 sets x <i>n</i> reps → 70-90% 1-RM Exercises: Multiple exercises targeting all primary muscle groups	16 weeks (3/week)	Muscle CSA (CT; biceps, quadriceps)	↔ Biceps and quadriceps CSA between males (+9.5%) and females (+13.1%) for both RT protocols
Fernandez-Gonzalo et al. 2014 [45]	Males (<i>n</i> = 16) Females (<i>n</i> = 16) → Untrained: No RT 6-months prior	23 ± 4.8 24 ± 4.9	4 sets x 7 reps → 83% 1-RM^ Exercise: Supine squat (flywheel)	6 weeks (2-3/week)	Lean mass (DXA; thigh)	↔ Thigh lean mass between males (+4.6%) and females (+5.4%)
Hakkinen et al. 1998 [20]	Males (<i>n</i> = 10) Females (<i>n</i> = 11) → Untrained: No RT experience	42 ± 2 39 ± 3	3-6 sets x 3-15 reps → 50-80% 1-RM Exercises: Leg press, leg extension	24 weeks (2/week)	Muscle CSA (ultrasound; quadriceps)	Quadriceps CSA ↑ for both males (+5.4%) and females (+9.3%) *
Hakkinen et al. 2001 [21]	Males (<i>n</i> = 10) Females (<i>n</i> = 11) → Untrained: No RT experience	42 ± 2 39 ± 3	3-6 sets x 3-15 reps → 50-80% 1-RM Exercises: Leg press, leg extension	24 weeks (2/week)	Muscle fCSA (biopsy + histochemistry; VL) # Type I = 41 # Type II = 37	VL fCSA ↑ for both males (Type I = +18.9%, Type II = +3.3%) and females (Type I = +22.5%, Type II = +39.2%) *
Hammarström et al. 2020 [29]	Males (<i>n</i> = 16) Females (<i>n</i> = 18) → Trained: Unknown years of RT experience	23.6 ± 4.1 22 ± 1.3	Group A: 1 set x 7-10 reps → 75-83% 1-RM^ Group B: 3 sets x 7-10 reps → 75-83% 1-RM^ Exercises: Leg press, leg extension, leg curl	12 weeks (2-3/week)	Muscle CSA (MRI; quadriceps)	Quadriceps CSA ↑ for both males (+4.4%) and females (+4.2%) *
Hubal et al. 2005 [2]	Males (<i>n</i> = 243) Females (<i>n</i> = 342) → Untrained: No RT 1 year prior	24.8 ± 6.2 23.9 ± 5.5	3 sets x 6-12 reps → 70-85% 1-RM^	12 weeks (2/week)	Muscle CSA (MRI; biceps)	↑ Biceps CSA observed in males (+19.7%) versus females (+17.6%)

			Exercises: Biceps curl (multiple variations)			
Hurlbut et al. 2002 [16]	Males (<i>n</i> = 10) Females (<i>n</i> = 9) → Untrained: No RT 6-months prior	25 ± 3.2 26 ± 3	1-3 sets x 12-15 reps → 60-70% 1-RM [^]	24 weeks (3/week)	Lean mass (DXA; total body)	↔ Total body lean mass between males (+2.9%) and females (+3.5%)
			Exercises: Multiple exercises targeting all primary muscle groups			
Ivey et al. 2000 [17]	Males (<i>n</i> = 11) Females (<i>n</i> = 11) → Untrained: No RT 6-months prior	25 ± 1 26 ± 1	5 sets x 5-20 reps → ≤85% 1-RM [^]	9 weeks (3/week)	Muscle volume (MRI; quadriceps)	↑ Quadriceps muscle volume observed in males (+12.1%) versus females (+6.3%)
			Exercise: Leg extension			
Kojic et al. 2021 [18]	Males (<i>n</i> = 9) Females (<i>n</i> = 9) → Untrained: No RT 8-months prior	24.7 ± 2.1 23.3 ± 0.5	3-4 sets x <i>n</i> reps → 60-70% 1-RM	7 weeks (2/week)	Muscle thickness (ultrasound; biceps)	↔ Biceps muscle thickness between males (+13.7%) and females (+21.2%)
			Exercises: Biceps curl, Back squat		Muscle CSA (ultrasound; RF, VI, VM, VL)	↔ Quadriceps CSA between males (+3.9%) and females (+5.9%)
Kosek et al. 2006 [19]	Males (<i>n</i> = 13) Females (<i>n</i> = 11) → Untrained: No RT 5 years prior	26.2 ± 5 27.9 ± 3.6	3 sets x 8-12 reps → 80% 1-RM	16 weeks (3/week)	Lean mass (DXA; total body)	Lean mass ↑ for both males (+1.7%) and females (+1.7%) *
			Exercises: Back squat, leg press, leg extension		Muscle fCSA (biopsy + histochemistry; VL) # Type I = 60 # Type II = 63	VL fCSA Both males (Type I = +25.6%, Type II = +31.5%) and females (Type I = +8.8%, Type II = +22.9%) ↑ VL fCSA *
Lundberg et al. 2019 [33]	Males (<i>n</i> = 8) Females (<i>n</i> = 8) → Untrained: Recreationally active	~26 ± 4	Group A: 4 sets x 8-12 reps → 70-80% 1-RM [^] Group B: 4 sets x 7 reps (flywheel)	8 weeks (2-3/week)	Muscle CSA (MRI; quadriceps)	Quadriceps CSA ↑ for both males (+6.9%) and females (+8.5%) for both RT protocols *
			Exercise: Leg extension		Muscle volume (MRI; Quadriceps)	Quadriceps (proximal and distal) muscle volume ↑ for both males (+7.7%) and females (+7.9%) for both RT protocols *
McMahon et al. 2018 [39]	Males (<i>n</i> = 8) Females (<i>n</i> = 8)	20 ± 2.8 19 ± 8.5	3-4 sets x 8-10 reps → 70% 1-RM	8 weeks (3/week)	Muscle pCSA (ultrasound; VL)	↔ VL pCSA between males (+22.5%) and females (+30%)

	→ Untrained: No RT 1 year prior		Exercises: Back squat, leg press, leg extension, lunge, split squat			
Moesgaard et al. 2022 [12]	Males (<i>n</i> = 12) Females (<i>n</i> = 12) → Untrained: No RT 1 year prior	28 ± 7 27 ± 7	3 sets x 8-12 reps → 70-80% 1-RM^ Exercises: Leg press, leg extension	8 weeks (3/week)	Muscle fCSA (biopsy + histochemistry; VL) # Type I = 191 # Type II = 166	↑ Type I VL fCSA observed in males (+22.7%) versus females (+6.3%) but ↔ Type II VL fCSA between males (+29%) and females (+25.8%)
Nunes et al. 2020 [44]	Males (<i>n</i> = 25) Females (<i>n</i> = 10) → Untrained: No RT 6-months prior	~23.7 ± 5.3	3 sets x 8-12 reps → 70-80% 1-RM^ Exercises: Biceps preacher curl	10 weeks (3/week)	Muscle thickness (ultrasound; biceps)	Biceps thickness ↑ for both males (+10.5%) and females (+8%) *
O'Hagan 1995 [37]	Males (<i>n</i> = 6) Females (<i>n</i> = 6) → Untrained: No RT experience	21.2 ± 1.2 20 ± 0.8	3-5 sets x 8-12 reps → 70-80% 1-RM^ Exercises: Biceps curl variations	20 weeks (3/week)	Muscle CSA [CT; flexor (brachialis + biceps)]	↔ Flexor CSA between males (+13.8%) and females (+26.9%)
Peterson et al. 2010 [40]	Males (<i>n</i> = 43) Females (<i>n</i> = 40) → Untrained: No RT 1 year prior	~25.1 ± 5.5	3 sets x 6-12 reps → 70-85% 1-RM^ Exercises: Biceps curl (multiple variations)	12 weeks (2/week)	Muscle volume (MRI; biceps)	↑ Biceps muscle volume observed in males (+15.2%) versus females (+12.1%)
Psilander et al. 2019 [38]	Males (<i>n</i> = 9) Females (<i>n</i> = 10) → Untrained: No RT experience	~25 ± 1	3 sets x 5-12 reps → 70-85% 1-RM Exercises: Leg press, leg extension	12 weeks (3/week)	Muscle thickness (ultrasound; VL) Muscle fCSA (biopsy + histochemistry; VL) # Type I = 198 # Type II = 374	VL thickness ↑ for both males (+9.8%) and females (+9.5%) * VL fCSA ↑ for both males (+15.1%) and females (+22.6%) *
Reece et al. 2023 [35]	Males (<i>n</i> = 14) Females (<i>n</i> = 16) → Untrained: No RT 1 year prior	21.5 ± 2.3 22.1 ± 3.6	Group A: 3 sets x 8-12 reps → 80% 1-RM Group B: 3 sets x <i>n</i> reps (BFR) → 30% 1-RM	6 weeks (3/week)	Muscle CSA (ultrasound; VL) Muscle fCSA (biopsy + histochemistry; VL)	VL CSA ↑ for both males (+5.3%) and females (+7.1%) for both RT protocols * VL fCSA ↑ for both males (Type I = +18.9%, Type II = +17.3%) and females (Type I = +11.3%, Type II = +21.3%) for both RT protocols *

			Exercise: Leg extension		# Type I = 38 # Type II = 55	
Ribeiro et al. 2014 [46]	Males (<i>n</i> = 30) Females (<i>n</i> = 34) → Untrained: No RT 6-months prior	22.7 ± 4.4 22.7 ± 4.1	3 sets x 8-12 reps → 70-80% 1-RM^ Exercises: Multiple exercises targeting all primary muscle groups	16 weeks (3/week)	Skeletal muscle mass (BIA; total body)	↔ Skeletal muscle mass between males (+4.2%) and females (+3.9%)
Rissanen et al. 2022 [31]	Males (<i>n</i> = 23) Females (<i>n</i> = 22) → Trained: ≥1 year of RT experience	26.4 ± 3.9 25.5 ± 3.8	Group A: 2-5 sets x 20% VeL → 65-75% 1-RM Group B: 2-5 sets x 40% VeL → 65-75% 1-RM Exercise: Back squat	8 weeks (2/week)	Muscle CSA (ultrasound; VL)	↔ VL CSA between males (+17.1%) and females (+21.5%) for both RT protocols
Schwanbeck et al. 2020 [30]	Males (<i>n</i> = 15) Females (<i>n</i> = 21) → Trained: >2 year of RT experience	~22.5 ± 3.5	Group A: 3-4 sets x 4-10 reps (free weights) → 75-90% 1-RM^ Group B: 3-4 sets x 4-10 reps (machines) → 75-90% 1-RM^ Exercises: Biceps curl variations, back squat, lunge	8 weeks (1/week)	Muscle thickness (ultrasound; biceps, quadriceps)	↔ Biceps and quadriceps muscle thickness between males (+5.4%) and females (+4.5%) for both RT protocols
Walsh et al. 2009 [34]	Males (<i>n</i> = 280) Females (<i>n</i> = 412) → Untrained: No RT 1 year prior	~24.8 ± 9 ~24 ± 6	3 sets x 6-12 reps → 65-90% 1-RM Exercises: Biceps curl (multiple variations)	12 weeks (2/week)	Muscle CSA (MRI; biceps)	Biceps CSA ↑ for both males (+19.7%) and females (+17.7%) *

3.2 Methodological Quality

A detailed overview of the methodological quality of included studies using the TESTEX scale [16] can be found in Supplementary Table S4. Study quality scores ranged from 9 to 12 (out of a possible 15), with mean and median scores of 10 (Supplementary Table S4). Although each study had some risk of bias, many studies lost points due to i) no activity monitoring, ii) no 'intention-to-treat' analysis of participants who had withdrawn, and iii) no reporting of adverse incidents or compliance rate of participants. Overall, a total of 17 out of 27 studies scored highly (>10) on the TESTEX scale and visual inspection of methodological quality results revealed no impact of study quality on the effect size estimates generated. Considering that all included studies involved a comparison between males and females, no randomisation procedures were required, allocation concealment was not possible, and muscle size differed at baseline, thus, criterion '2' (i.e., "randomisation specified"), criterion '3' (i.e., "allocation concealment"), and criterion '4' (i.e., "groups similar at baseline") were given one point for every study. Although randomisation of participants into groups was not necessary in the studies included in this systematic review with meta-analysis, studies that involved different RT groups for each sex, and/or a control group, did employ appropriate randomisation procedures [30, 31, 33, 35, 37-39, 41, 44].

3.3 Meta-Analysis Results

3.3.1 Primary Analysis: Sex Differences in Absolute Muscle Hypertrophy

The primary Bayesian meta-analysis model (including all 64 outcomes) generated to quantify absolute changes in muscle size from pre- to post-intervention (Figure 2) estimated a 100% probability of direction for superior absolute muscle hypertrophy in males versus females [ES = 0.35 (95% HDI: 0.20 to 0.49); *pd* = 100%]. The HDI covers ESs that suggest a small to medium effect (favouring males), with small between-study variance identified [τ = 0.16 (95% HDI: 0.01 to 0.33)].

Sub-group analyses investigating the moderating effect of multiple variables on absolute changes in muscle size between males and females are displayed in Figure 3. For the measure of muscle hypertrophy (62 outcomes; not including pCSA via ultrasound [39] and skeletal muscle mass via BIA [46]), we estimated medium ESs for muscle CSA [ES = 0.37 (95% HDI: 0.11 to 0.60); *pd* = 100%], muscle fCSA [ES = 0.36 (95% HDI: 0.03 to 0.70); *pd* = 98%], muscle thickness [ES = 0.36 (95% HDI: 0.05 to 0.65); *pd* = 99%], and muscle volume [ES = 0.35 (95% HDI: -0.10 to 0.80); *pd* = 94%]. Notably, the posterior probability for each of these effects substantially favours males and although some HDIs include zero, there is a substantive probability of direction that the ES favours males. However, a negligible ES with considerable uncertainty was estimated for lean mass [ES = 0.10 (95% HDI: -0.37 to 0.56); *pd* = 67%]. When analysing studies that only measured muscle fCSA (14 outcomes; Figure 3F),

we estimated a large ES with substantive posterior probability favouring males versus females for type I muscle fibres [ES = 0.60 (95% HDI: 0.0 to 1.18); $pd = 98\%$] albeit the range of the ES estimates is highly uncertain. We found a negligible ES for type II muscle fibres [ES = 0.00 (95% HDI: -0.60 to 0.58); $pd = 50\%$]. When categorising studies by the body region measured (60 outcomes; not including total body lean or skeletal muscle mass [16, 19, 41, 46]), we estimated a large ES favouring males versus females for upper-body muscles [ES = 0.58 (95% HDI: 0.36 to 0.78); $pd = 100\%$] and a small ES for lower-body muscles [ES = 0.25 (95% HDI: 0.09 to 0.42); $pd = 100\%$]. Further, a medium ES was estimated when participants were untrained [ES = 0.37 (95% HDI: 0.20 to 0.53); $pd = 100\%$] and when participants were resistance-trained albeit with more uncertainty [ES = 0.24 (95% HDI: -0.14 to 0.61); $pd = 89\%$].

Meta-regression was used to investigate the influence of relative load and set volume (as continuous variables) on absolute changes in muscle size between males and females (Figure 3A/B). Pooled ESs obtained across all outcomes were negligible for set volume [64 outcomes; $\beta = 0.01$ (95% HDI: -0.01 to 0.03); $pd = 90\%$] and relative load [62 outcomes; $\beta = 0.00$ (95% HDI: -0.01 to 0.02); $pd = 69\%$] on absolute changes in muscle size.

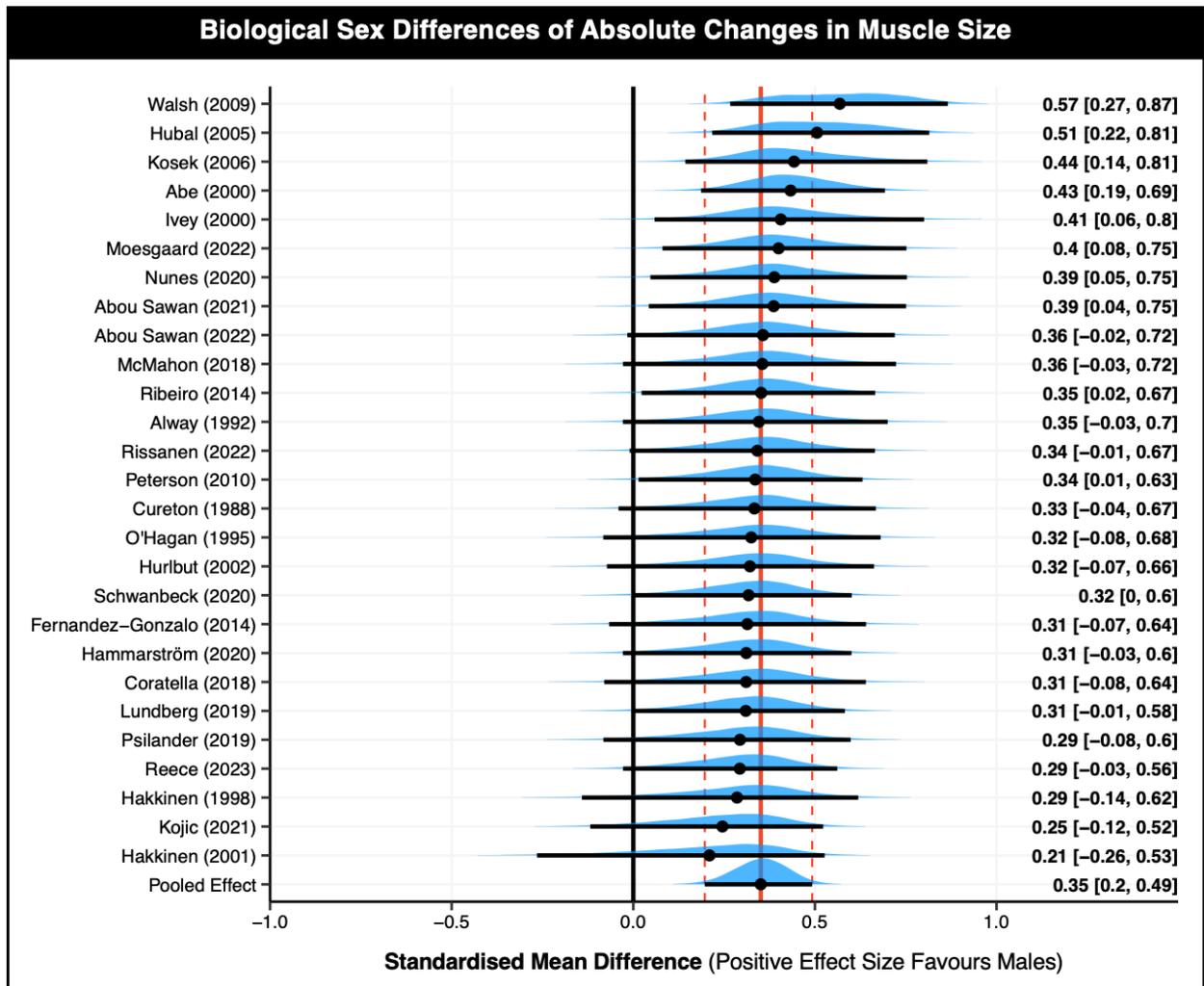


Figure 2. Bayesian meta-analysis results for absolute changes in muscle size from pre- to post-intervention between males and females. Positive effect size values favour greater absolute increases in muscle hypertrophy for male participants, whereas negative effect size values favour greater absolute increases in muscle hypertrophy for female participants. Point (mean) estimates and 95% high density credible intervals are shown by the point and interval line below each posterior distribution. Red vertical lines represent the point estimate (solid) and width of the highest density credible interval (dotted) for the pooled effect size.

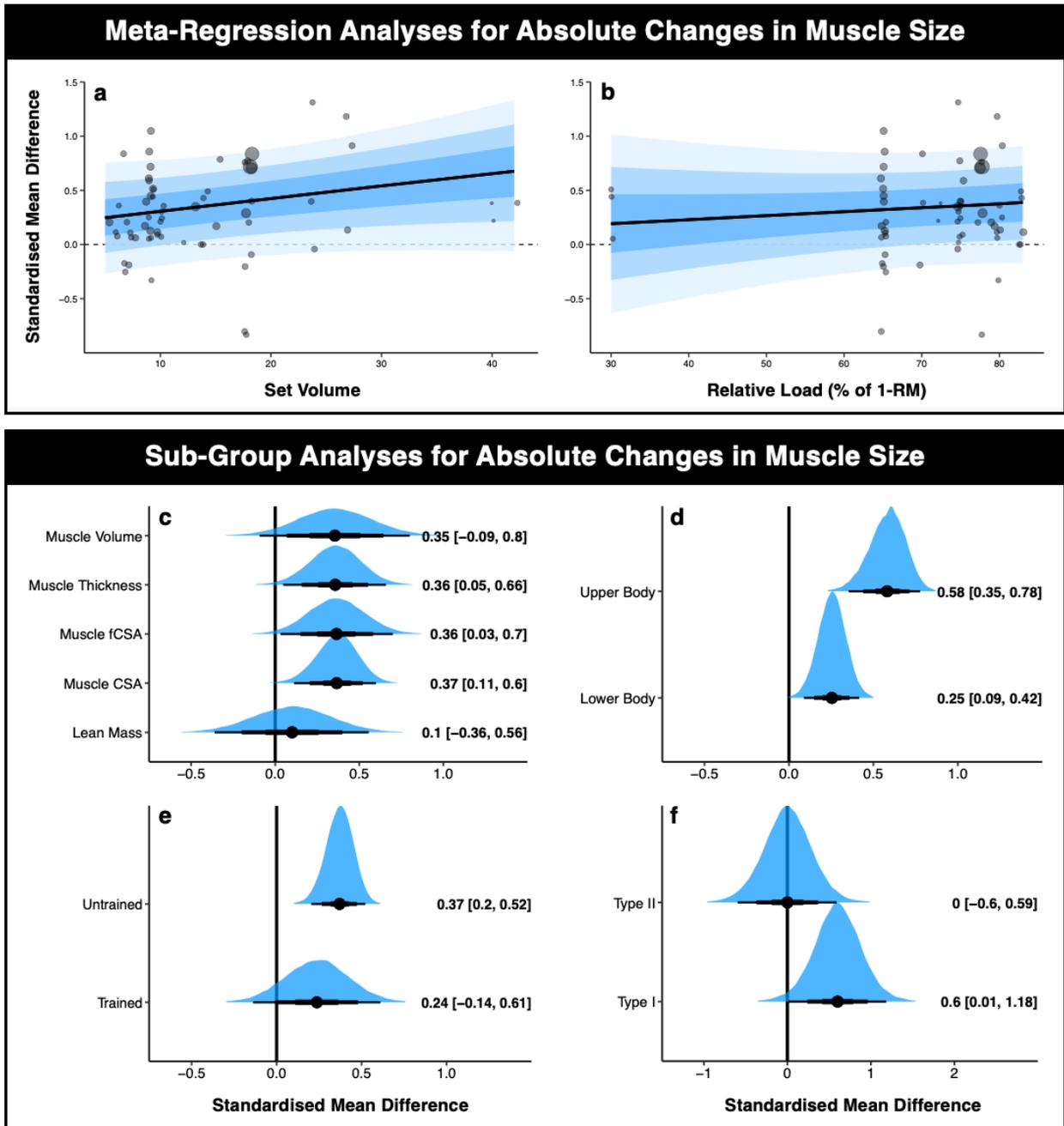


Figure 3. Sub-group and meta-regression results of absolute changes in muscle size for a) set volume, b) relative load, c) measurement of muscle size, d) body region assessed, e) resistance training experience, and f) muscle fibre type. Positive effect size values favour greater absolute increases in muscle hypertrophy for male participants, whereas negative effect size values favour greater absolute increases in muscle hypertrophy for female participants. Point (mean) estimates and 95% high density credible intervals are shown by the point and interval line below each posterior distribution. For meta-regression models, quantile intervals are categorised as 50% (darkest blue), 80%, and 95% (lightest blue) highest density intervals.

3.3.2 Primary Analysis: Sex Differences in Relative Muscle Hypertrophy

The primary Bayesian meta-analysis model (including all 64 outcomes) generated to quantify relative changes in muscle size from pre- to post-intervention (Figure 4) estimated similar relative muscle hypertrophy in males and females [ES = 0.05 (95% HDI: -0.07 to 0.16); *pd* = 80%]. The HDI covers ESs that suggest a negligible (favouring females) to small (favouring males) effect, with small between-study variance identified [τ = 0.08 (95% HDI: 0.00 to 0.22)].

Sub-group analyses investigating the moderating effect of multiple variables on relative changes in muscle size between males and females are displayed in Figure 5. For the measure of muscle hypertrophy (62 outcomes), we estimated small ESs for muscle volume [ES = 0.16 (95% HDI: -0.23 to 0.55); *pd* = 80%] and muscle fCSA [ES = 0.17 (95% HDI: -0.15 to 0.49); *pd* = 86%] both with considerable uncertainty but with posterior probability favouring males. We also estimated negligible and highly uncertain ESs for muscle thickness [ES = 0.02 (95% HDI: -0.25 to 0.28); *pd* = 58%], muscle CSA [ES = -0.01 (95% HDI: -0.22 to 0.18); *pd* = 51%], and lean mass [ES = 0 (95% HDI: -0.44 to 0.42); *pd* = 50%]. When analysing studies that only measured muscle fCSA (14 outcomes; Figure 5F), we estimated a large ES with substantive probability of direction favouring males for type I muscle fibres [ES = 0.57 (95% HDI: -0.02 to 1.16); *pd* = 97%] and a medium ES with considerable uncertainty but high probability of direction favouring females for type II muscle fibres [ES = -0.36 (95% HDI: -0.97 to 0.23); *pd* = 89%]. When categorising studies by the body region measured (60 outcomes), we estimated negligible and uncertain ESs for upper-body muscles [ES = 0.02 (95% HDI: -0.22 to 0.22); *pd* = 62%] and lower-body muscles [ES = 0.05 (95% HDI: -0.11 to 0.22); *pd* = 74%]. Further, negligible ESs with considerable uncertainty were estimated when participants were either untrained [ES = 0.06 (95% HDI: -0.08 to 0.18); *pd* = 82%] or resistance-trained [ES = -0.02 (95% HDI: -0.35 to 0.30); *pd* = 55%].

Meta-regressions were also generated to investigate the influence of relative load and set volume on relative changes in muscle size between males and females (Figure 5A/B).

Pooled ESs obtained across all outcomes were negligible for set volume [β = 0.01 (95% HDI: 0.00 to 0.03); *pd* = 93%] and relative load [β = 0.01 (95% HDI: -0.01 to 0.02); *pd* = 80%] on relative changes in muscle size.

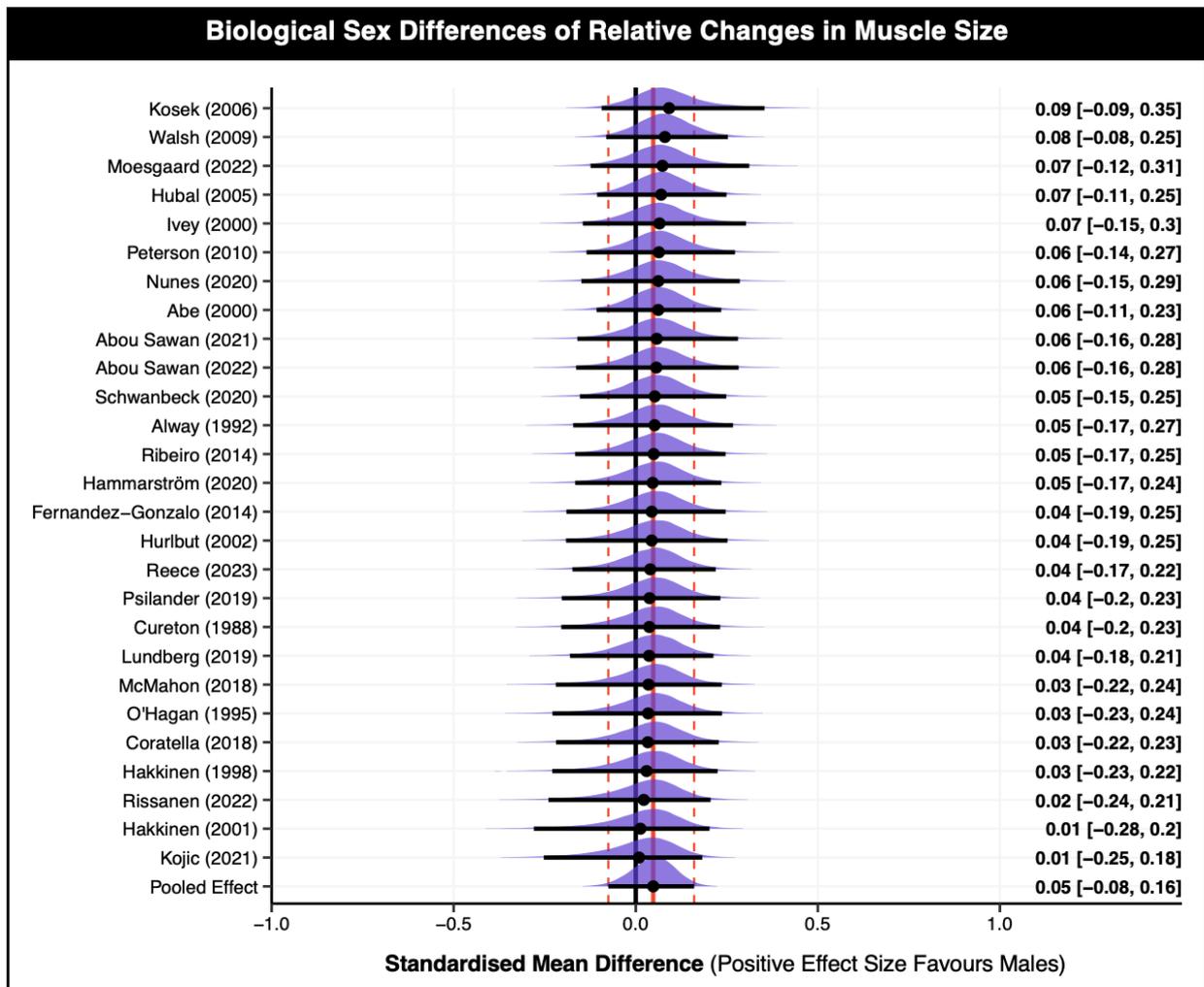


Figure 4. Bayesian meta-analysis results for relative changes in muscle size from pre- to post-intervention between males and females. Positive effect size values favour greater increases in relative muscle hypertrophy for male participants, whereas negative effect size values favour greater relative increases in muscle hypertrophy for female participants. Point (mean) estimates and 95% high density credible intervals are shown by the point and interval line below each posterior distribution. Red vertical lines represent the point estimate (solid) and width of the highest density credible interval (dotted) for the pooled effect size.

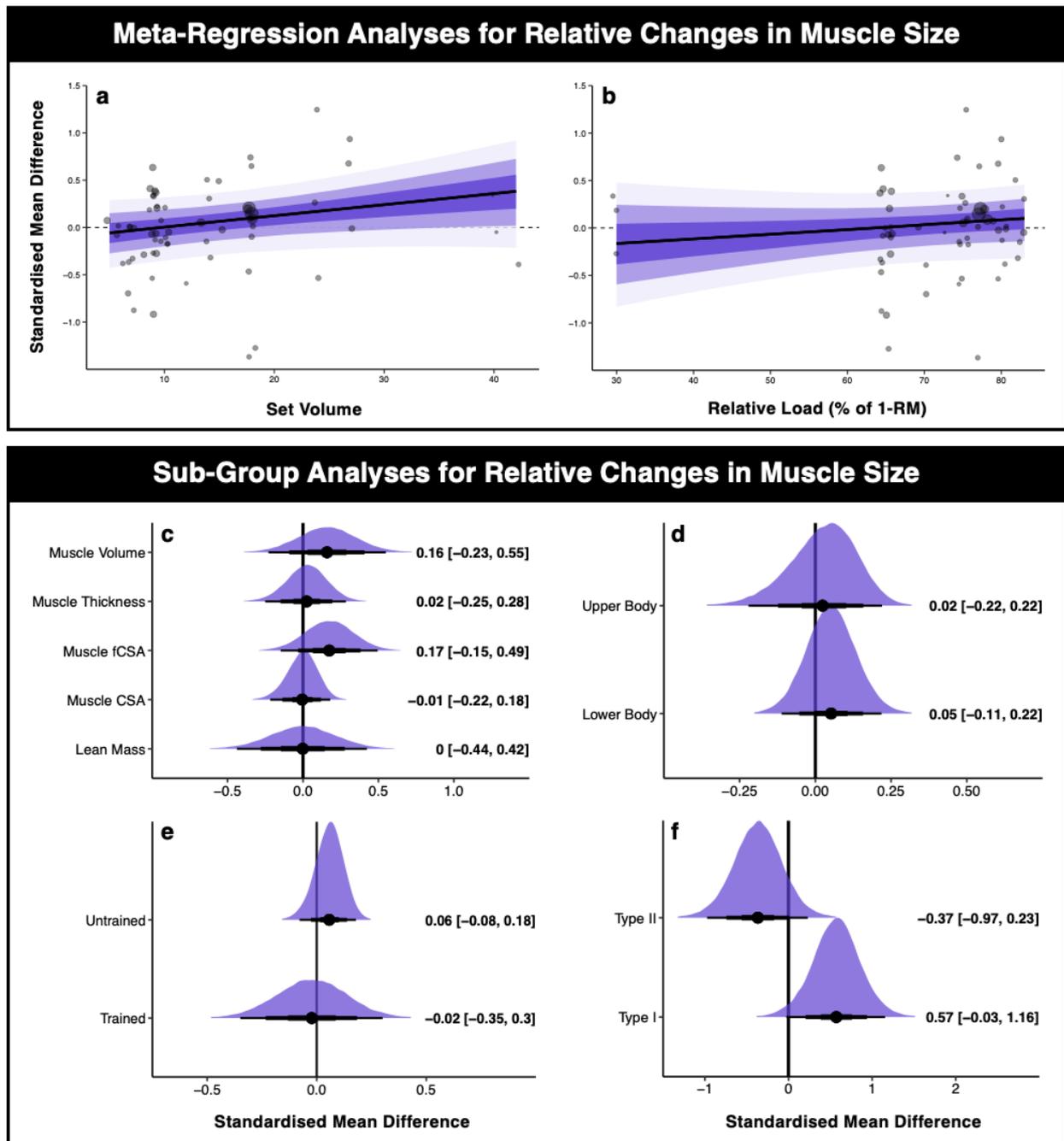


Figure 5. Sub-group and meta-regression results of relative changes in muscle size for a) set volume, b) relative load, c) measurement of muscle size, d) body region assessed, e) resistance training experience, and f) muscle fibre type. Positive effect size values favour greater relative increases in muscle hypertrophy for male participants, whereas negative effect size values favour greater relative increases in muscle hypertrophy for female participants. Point (mean) estimates and 95% high density credible intervals are shown by the point and interval line below each posterior distribution. For meta-regression models, quantile intervals are categorised as 50% (darkest purple), 80%, and 95% (lightest purple) highest density credible intervals.

3.3.3 Secondary Analysis: Absolute and Relative Differences in Type I and Type II Muscle Fibre Hypertrophy (No Sex Comparison)

The secondary Bayesian meta-analysis model (including all 14 outcomes) generated to quantify muscle fibre type-specific hypertrophy estimated greater absolute [ES = 0.38 (95% HDI: -0.12 to 0.89); $pd = 95\%$] and relative [ES = 0.38 (95% HDI: -0.18 to 0.94); $pd = 92\%$] hypertrophy of type II muscle fibres versus type I muscle fibres (Supplementary File S5) with a degree of uncertainty but high probability of direction in both estimates. A plausibly wide range of between-study variance was identified for both absolute [$\tau = 0.30$ (95% HDI: 0.01 to 1.0)] and relative [$\tau = 0.29$ (95% HDI: 0.01 to 1.01)] changes in muscle fibre type-specific hypertrophy. Further, our sub-group analyses (Supplementary File S5) estimated that type II and type I muscle fibre hypertrophy was similar in males [Absolute ES = 0.06 (95% HDI: -0.55 to 0.65); $pd = 59\%$, Relative ES = -0.1 (95% HDI: -0.66 to 0.46); $pd = 64\%$], but hypertrophy of type II muscle fibres was estimated to be greater than type I muscle fibres in females [Absolute ES = 0.71 (95% HDI: 0.12 to 1.31); $pd = 99\%$, Relative ES = 0.87 (95% HDI: 0.30 to 1.44); $pd = 100\%$].

3.4 Sensitivity Analysis

Sensitivity analyses were performed for primary Bayesian meta-analysis models with correlation coefficients ranging from $r = 0.70$ to 0.99 to assess whether the selected correlation coefficient ($r = 0.87$) influenced the meta-analytic outcomes (Supplementary File S2). For the meta-analysis estimating the absolute change in muscle size (section 3.3.1), ESs between 0.27 and 0.78 (meta-analysis result = 0.35) were observed. This analysis was conducted with an *a priori* assumption that the correlation coefficient between pre-test and post-test measures was $r = 0.87$; while this is a reasonable assumption that was obtained from previous literature [11], sensitivity analyses revealed ESs ranging from small to large (meta-analysis result = medium ES), but in all cases favouring superior muscle hypertrophy in males versus females. Conversely, for the meta-analysis that estimated the relative change in muscle size (section 3.3.2), ESs between 0.04 and 0.06 (meta-analysis result = 0.05) were observed, indicating little impact of different correlation coefficient values on the pooled ES for muscle hypertrophy. As such the estimated ES for the relative change in muscle size may be interpreted with increased confidence. Further sensitivity analyses were also conducted using uninformative ES and variance priors (instead of our weakly informative prior) along with a frequentist meta-analysis (Supplementary File S7). Our sensitivity analyses using non-informative priors generated identical ESs to the original results, however, when variance priors were used, slightly lower ESs were found for both absolute (ES = 0.33) and relative (ES = 0.02) muscle hypertrophy (Supplementary File S1).

4. DISCUSSION

The present systematic review with meta-analysis extends previous findings with a total of 27 included studies (versus 10 in a previous meta-analysis [10]), providing an up to date synthesis of the current literature investigating biological sex differences in both absolute and relative muscle hypertrophy in response to RT. The Bayesian methods we employed allow for improved ES interpretations to be made by i) directly modelling the uncertainty of the ES estimates, ii) presenting posterior probabilities that allow for intuitive interpretations (e.g. probability of direction) absent of *P* values, and iii) incorporating a-priori knowledge into the statistical analysis based on previous meta-analytic findings [10] and thus estimating ESs based on cumulative knowledge.

4.1 Absolute and Relative Changes in Muscle Size

We found that RT promotes larger absolute increases in muscle size in males versus females, however, the relative increase in muscle size (percentage increase from baseline) following RT is similar between sexes. Our meta-analysis indicated a medium ES of 0.35 favouring greater absolute increases in muscle size for males versus females ($pd = 100\%$) and a directly interpretable 95% probability that the ES ranges from 0.20 to 0.49. As such, not only are baseline levels of muscle size larger in males versus females before the commencement of RT (e.g., out of the 64 muscle hypertrophy outcomes meta-analysed, only two showed larger baseline muscle size in females), but males also experience greater absolute increases in muscle size following a RT intervention. Inherent differences in testosterone levels between sexes are known to be responsible for the greater baseline muscle size in males compared to females, on average [5]; however, physiological signals (e.g., mechanical tension mediated anabolic signalling, metabolic stress [47]) other than sex specific hormonal balance may also play a primary role in promoting muscle hypertrophy [47]. Indeed, our data suggest that the percentage increase in muscle size from baseline following a RT intervention is similar between sexes, indicated by a negligible ES of 0.05. It is therefore likely that the larger baseline musculature of males is subject to experiencing greater absolute hypertrophy than that of females, despite females having a similar potential to induce muscle hypertrophy as males when considering relative increases from baseline muscle size. Supportive of our findings is research highlighting i) the anabolic properties of estradiol that may contribute to muscle hypertrophy [48-50], ii) the positive association between androgen receptor content with muscle hypertrophy [51], and iii) similarities in post-exercise protein synthesis and molecular signalling between sexes that triggers muscle hypertrophy [52, 53]. Taken as a whole, our data suggest RT is likely to induce greater absolute increases in muscle size for males versus females, while similar percentage increases in muscle size from baseline suggest comparable muscle hypertrophic potential between males and females following RT.

4.2 Moderators of Absolute and Relative Changes in Muscle Size

The present meta-analysis also investigated whether the following variables had a moderating effect on the overall ES of muscle hypertrophy: *i)* assessment of muscle mass (i.e., body region assessed, type of measurement used, muscle fibre type), *ii)* participant resistance training experience, *and iii)* resistance training characteristics (i.e., set volume, relative load)

4.2.1 Assessment of Muscle Size

4.2.1.1 Measurement of Muscle Size and Body Region Assessed

Sex differences in relative muscle hypertrophy following RT were similar across all measurements of muscle size employed and body regions assessed. However, absolute differences in muscle hypertrophy between sexes were larger for the upper- or lower-body and for direct measures of muscle hypertrophy (i.e., muscle volume, muscle thickness, and muscle CSA and fCSA) versus indirect measures (i.e., lean mass). It has been noted that changes in muscle fCSA following RT are larger than changes in muscle size detected by other common measurements (e.g., muscle CSA, muscle thickness) [1], however, our sub-group analysis revealed similar ESs between muscle fCSA and other measurements of muscle size (Figure 3 and Figure 5). This suggests that the absolute and relative muscle hypertrophy observed between sexes was not dependent on the measurement of muscle size employed. We also categorised the body regions measured into either upper- or lower-body and estimated that relative changes in muscle size between sexes were similar independent of the body region assessed. However, when examining absolute changes in muscle size, a large ES was estimated for the upper-body favouring males, likely due to baseline differences in muscle size favouring males over females being larger in the upper- versus lower-body [5]. These data suggest that the difference in absolute muscle hypertrophy observed across males and females may be partially influenced by the body region assessed and its size (i.e., larger baseline muscle size leads to greater difference in absolute muscle hypertrophy favouring males versus females). Overall, the measurement of muscle size employed, and the body region assessed do not seem to impact sex differences in relative muscle hypertrophy. However, males experience greater absolute muscle hypertrophy versus females in body regions where baseline differences in muscle size are greater (i.e., in upper-body versus lower-body muscles).

4.2.1.2 Muscle Fibre Type

A total of six studies ($n = 138$) using histochemical analysis of skeletal muscle biopsies to determine fCSA [12, 13, 19, 21, 35, 38] suggest that sex differences in muscle hypertrophy may be muscle fibre type-specific. We estimated greater type I muscle fibre hypertrophy in untrained males versus females and greater type II muscle fibre hypertrophy in untrained females versus

males. Similar to findings from previous research [12, 13], we observed a >95% probability of direction for superior absolute (ES = 0.60) and relative (ES = 0.57) type I muscle fibre hypertrophy in males versus females, providing further support for the idea that males have a greater capacity to hypertrophy type I muscle fibres than females. However, the HDIs covered ESs ranging from negligible to large for both absolute (95% HDI: 0.0 to 1.18) and relative (95% HDI: -0.02 to 1.16) type I muscle fibre hypertrophy, suggesting considerable uncertainty of the ES estimate. Potentially influencing the wide HDIs we observed are i) variability in the mean number of muscle fibres analysed per participant (range = 37 to 374), and ii) studies reporting type II muscle fCSA based on the combination of type IIa and IIx values (which differ in size at baseline and in their physiological response to chronic exercise [35]), suggesting the need for a careful interpretation of our findings due to the intricate nature of measuring muscle fCSA in research. Conversely, we estimated an 89% probability of direction for greater relative hypertrophy of type II muscle fibres in females versus males [ES = 0.36 (95% HDI: -0.97 to 0.23)]. Moreover, no difference in absolute hypertrophy of type II muscle fibres was estimated between sexes despite the mean muscle fCSA across all studies included in our meta-analysis being larger for males ($5024 \pm 1791 \mu\text{m}^2$) versus females ($3376 \pm 1124 \mu\text{m}^2$) at baseline. Although all studies assessed muscle fCSA with histochemical analysis of skeletal muscle biopsies, variability in the number of muscle fibres chosen and subsequently analysed, and how type IIx and IIa muscle fibres were distinguished, may have influenced our findings. Therefore, evidence for muscle fibre type-specific hypertrophy differing between sexes should be interpreted tentatively and used to inform future research investigations. Possible physiological mechanisms explaining muscle fibre type-specific hypertrophy are subsequently discussed.

We also conducted a secondary meta-analysis (across all six studies [12, 13, 19, 21, 35, 38] that measured muscle fCSA as an outcome) to investigate which muscle fibre type experiences the most hypertrophy following RT, providing further context to our findings. As was expected based on previous research [6], we estimated a high probability of direction (>90%) for ESs favouring both absolute [ES = 0.38 (95% HDI: -0.12 to 0.89)] and relative [ES = 0.38 (95% HDI: -0.18 to 0.94)] type II over type I muscle fibre hypertrophy in our full sample including both males and females (with HDIs covering negligible to large ESs, suggesting potential variability in the outcomes). Moreover, we estimated that absolute and relative type II muscle fibre hypertrophy was greater than type I muscle fibre hypertrophy in females; however, similar absolute and relative hypertrophy between type I and type II muscle fibres was estimated in males (Supplementary File S5). Considering that i) type II muscle fibre hypertrophy was preferential in females (over type I) and was greater in females versus males, and ii) type I and II muscle fibre hypertrophy was similar in males, but type I muscle fibre hypertrophy was greater in males versus females, future research should further investigate the possible impact of biological sex on muscle fibre-

type specific hypertrophy. Nonetheless, these present data should be interpreted with caution as subsequent analysis of a larger body of literature could alter the findings.

The physiological mechanisms underpinning the possibility of muscle fibre type-specific hypertrophy observed following RT in untrained individuals are unclear but may be related to muscle fibre size and surface area to volume ratio. The surface area of smaller muscle fibres (i.e., where material exchange and anabolic signalling occur [54]) can facilitate the energy metabolism and protein synthesis requirements governed by its volume, however, as the volume of a muscle fibre increases so do its metabolic requirements. Indeed, when the volume of a muscle fibre increases (i.e., muscle fibre gets larger), the surface area of the muscle fibre will not increase at the same rate, eventually rendering the surface area to volume ratio of the muscle fibre insufficient to facilitate metabolic requirements necessary for subsequent hypertrophy. In line with this physiological rationale, we observed that the smallest muscle fibres at baseline (which have the highest surface area to volume ratio) experienced the greatest hypertrophy in both untrained males and females, whereas hypertrophy of the larger muscle fibres seemed to be reduced, potentially due to a decreased surface area to volume ratio that constrains the magnitude of hypertrophy induced. Although it is possible that the muscle fibre type-specific hypertrophy we observed is related to differences in the surface area to volume ratio of muscle fibres across untrained males and females, future investigations into the physiological mechanisms underpinning muscle fibre type-specific hypertrophy are required to elucidate this understanding further. Importantly, the surface area to volume ratio of individual muscle fibres and their subsequent potential for hypertrophy may not reflect the response of the whole muscle, whereby larger whole muscles, which potentially have more muscle fibres than smaller whole muscles, may be subject to greater absolute changes in whole muscle size due to having more individual fibres.

4.2.2 Resistance Training Experience of Participants

Our findings suggest that the RT experience of participants did not seem to influence absolute and relative muscle hypertrophy following RT. Nonetheless, analysis of absolute changes in muscle size estimated a medium effect size for untrained individuals [ES = 0.37 (95% HDI: 0.20 to 0.53); $pd = 100\%$] but a small effect size for resistance-trained individuals [ES = 0.24 (95% HDI: -0.14 to 0.61); $pd = 89\%$]. However, the difference between sub-samples was trivial (ES difference = 0.13), and the HDIs completely overlapped, indicating no meaningful impact of RT experience on absolute muscle hypertrophy. Moreover, analysis of relative muscle hypertrophy estimated negligible ESs for both untrained and resistance-trained individuals. Previous research has indicated that RT experience alters the physiological response to a given RT stimulus [55] and may also cause muscle fibre type transitions that could influence sex-specific muscle

hypertrophy [56]. For example, experimental research in highly competitive athletes (i.e., World/Olympic and National level) has concluded that years competing in a sport influence the proportion of type II muscle fibres more than biological sex *per se*, with females especially displaying a high abundance of type II muscle fibres compared to males [57]. Whether muscle fibre type transitions following years of RT experience influence the subsequent muscle hypertrophic response remains to be explored and given that only four out of 27 studies included in the meta-analysis involved resistance-trained participants, further research investigating sex differences in muscle hypertrophy within resistance-trained samples is encouraged.

4.2.3 Resistance Training Prescription Variables

4.2.3.1 Set Volume and Relative Load

Our data suggest a 93% probability of direction that *relative* muscle hypertrophy favours males over females as set volume rises. However, for every additional set completed, there is only a trivial increase in the ES (0.01), questioning whether these findings are practically meaningful. Considering that females may experience less neuromuscular fatigue than males under certain circumstances [58-61], theoretically enhancing their ability to recover from and adapt to high RT volumes, it is unclear why males would experience greater muscle hypertrophy with higher set volumes. These findings should be treated as exploratory and future research should investigate whether one's ability to recover from RT reflects their adaptive potential. Importantly, increases in the relative load lifted did not seem to impact the relative muscle hypertrophy observed across sexes, supporting the idea that an adequate set volume coupled with close proximities-to-failure, rather than the load lifted *per se*, are the key stimulators of muscle hypertrophy [62]. Taken as a whole, differences in relative muscle hypertrophy between sexes may be trivially influenced by set volume but not relative load.

4.3 Limitations

Considering the correlation coefficients (*r* value) between pre-test and post-test measures are rarely reported in research studies, we assumed $r = 0.87$ to conduct our meta-analyses (no attempt was made to contact the authors and obtain the exact *r* values). Although this *r* value was replicated from a previous meta-analysis related to this topic [11], sensitivity analysis suggests the results of our meta-analysis investigating absolute muscle hypertrophy should be interpreted with caution, as outcomes of 0.27 and 0.78 were observed with correlation coefficients between $r = 0.70$ to 0.99. Our sub-group analysis investigating hypertrophy of type I and type II fibres only involved six studies with a total of 138 participants and the wide HDIs observed highlight variability in outcomes. Although we believe that this total sample size ($n = 138$) is adequate to derive interpretations about muscle fibre type-specific hypertrophy, it is

possible that a larger pool of evidence may strengthen or weaken the findings. Similarly, our secondary meta-analysis of studies that only measured fCSA (section 3.3.3) should be interpreted with caution due to the i) small number of studies analysed and potential for additional research to alter the findings, and ii) absence of sensitivity analyses. Considering some studies employed various loads and set volumes across the RT intervention (Table 1), the median number was extracted and used for data analysis. As such, the results of our sub-group analyses for relative load and set volume should be treated as exploratory and used to inform future research investigations. Moreover, a description of the set termination method (e.g., set failure or non-failure) employed was absent in many studies and only four out of 27 studies were conducted in resistance-trained participants; future research should thus investigate sex differences in muscle hypertrophy amongst resistance-trained samples and explicitly report set termination methods. Although our methodological quality assessment identified that 63% of studies were of 'high' quality, it is possible that the lower quality studies influenced the findings; however, a brief overview of key findings in Table 1 suggests that is unlikely.

4.4 Practical Application of Key Findings

Our findings suggest that healthy adult males and females have a comparable muscle hypertrophic potential following RT, and thus, may experience similar benefits from RT-induced muscle hypertrophy. For example, i) low skeletal muscle mass index is associated with an increased risk of all-cause mortality [63], and ii) some physiological characteristics important for athletic performance (e.g., force production, rate of force development, fatigue resistance) may be influenced by muscle size [64, 65]. Considering we found minimal evidence of a moderating effect of RT variables and RT experience on sex differences in muscle hypertrophy, RT may be prescribed similarly between both untrained and resistance-trained males and females, with primary differences in RT prescription based on long-term goals (e.g., aesthetics or performance-based goals) and individual characteristics (e.g., enjoyment, perceptions of discomfort, preferences, stress tolerance etc.). However, differences in short-term responses to RT between sexes may exist, such that males may experience more neuromuscular fatigue and muscle damage consequent to RT versus females [58, 66, 67], and should be considered in RT prescription. However, individual fatigability should be the primary consideration in RT prescription (e.g., it is possible for some males to be more fatigable than some females [61]).

5. CONCLUSION

This Bayesian systematic review with meta-analysis investigated biological sex differences in muscle hypertrophy following RT in healthy adult males and females. The evidence suggests that males experience larger absolute increases in muscle size compared to females, however, relative changes in muscle size are similar. Sub-group analysis estimated the balance of probability to favour greater relative type I muscle fibre hypertrophy in males versus females and greater relative type II muscle fibre hypertrophy in females versus males, suggesting the possibility of muscle fibre type-specific hypertrophy between sexes. Larger absolute differences in muscle hypertrophy between sexes (favouring males) for the upper- versus lower-body and for direct measurements of muscle hypertrophy versus indirect were also estimated. Moreover, differences in relative muscle hypertrophy between sexes may be trivially influenced by set volume but not relative load and no impact of RT experience was identified. Our primary analyses strengthen the understanding that females have a similar potential to induce muscle hypertrophy as males when considering relative increases from baseline and findings of our secondary analyses may have implications for the practical application of RT and should therefore inform future research investigations.

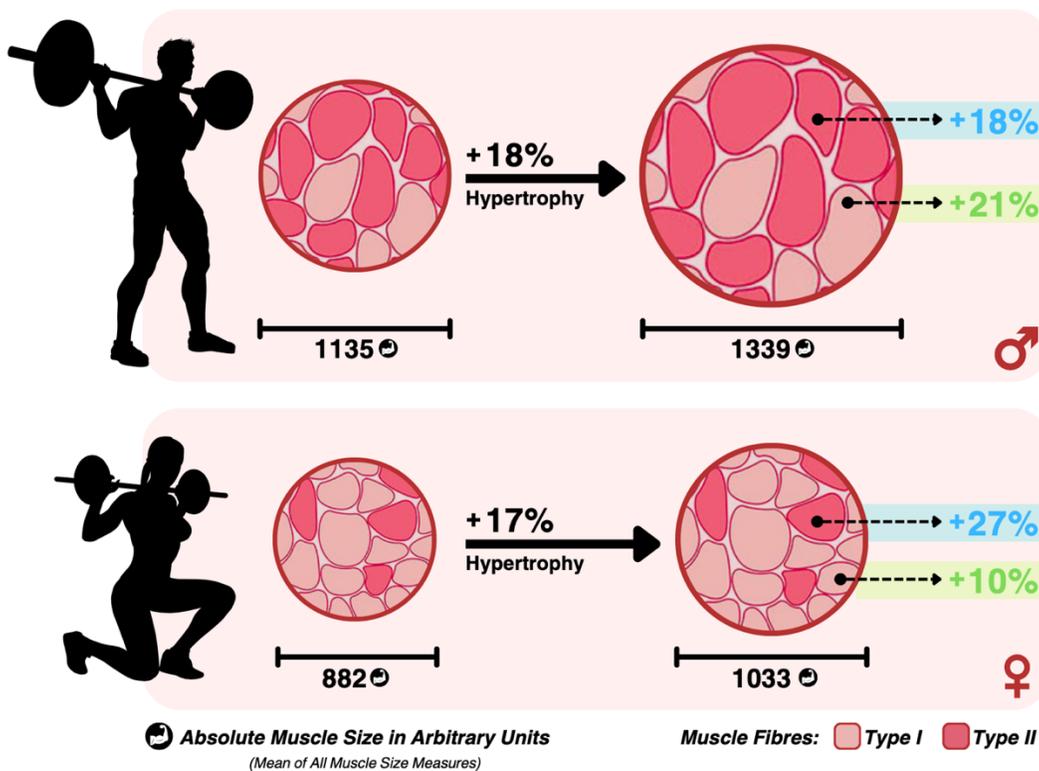


Figure 6. Graphical overview of absolute and relative changes in muscle size (including muscle fibre cross sectional area) following resistance training for males and females. To depict changes in absolute muscle size, the mean value of all muscle size outcomes (independent of the units of measurement) was calculated and described as “absolute muscle size in arbitrary units”.

6. STATEMENTS AND DECLARATIONS

Contributions

Article conceptualisation: MR, JF; literature search: MR and JF; data extraction: MR and JF; statistical analysis: MR and IG; drafted manuscript: MR and JF; critically revised manuscript: all authors.

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Data and Supplementary Material Accessibility

Data and code available on Open Science Framework (<https://osf.io/trz3y/>)

Competing interests

Lee Hamilton, Jackson Fyfe, and Iain Gallagher declare that they have no conflicts of interest or competing interests. Martin Refalo, Greg Nuckols, and Andrew Galpin are all coaches and writers in the fitness industry. No known companies will benefit from the results of the present study.

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