Give it a Rest: A systematic review with Bayesian meta-analysis on the effect of inter-set rest interval duration on muscle hypertrophy

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ABSTRACT

We systematically searched the literature for studies with a randomized design that compared different inter-set rest interval durations for estimates of pre-/post-study changes in lean/muscle mass in healthy adults while controlling all other training variables. Meta-analyses on non-controlled effect sizes using hierarchical models of all 19 measurements (thigh: 10; arm: 6; whole body: 3) from 9 studies meeting inclusion criteria analyses showed substantial overlap of standardized mean differences across the different inter-set rest periods (binary: short: 0.48 [95%CrI: 0.19 to 0.81], longer: 0.56 [95%CrI: 0.24 to 0.86]; Four categories: short: 0.47 [95%CrI: 0.19 to 0.80], intermediate: 0.65 [95%CrI: 0.18 to 1.1], long: 0.55 [95%CrI: 0.15 to 0.90], very long: 0.50 [95%CrI: 0.14 to 0.89]), with substantial heterogeneity in results. Univariate and multivariate meta-analyses of controlled effect sizes showed similar results for the arm and thigh with central estimates favoring longer rest periods (arm: 0.13 [95%CrI: -0.27 to 0.51]; thigh: 0.17 [95%CrI: -0.13 to 0.43]). In contrast, central estimates closer to zero but favoring shorter rest periods were estimated for the whole body (whole body: -0.08 [95%CrI: -0.45 to 0.29]). Subanalysis of set end-point data indicated that training to failure or stopping short of failure did not meaningfully influence the interaction between rest interval duration and muscle hypertrophy. In conclusion, results suggest a small hypertrophic benefit to employing rest interval durations >60 seconds with unclear effects as to durations >90 seconds.

KEYWORDS: rest period; recovery interval; muscle growth; muscle development; muscle thickness; muscle cross-sectional area

INTRODUCTION

It has been proposed that the manipulation of resistance training (RT) program variables can help to optimize skeletal muscle hypertrophy (2). However, because of the onerous time commitment involved in conducting directly supervised longitudinal RT protocols, most research on the effects of manipulation of program variables have recruited relatively small sample sizes. Thus, meta-analytic techniques that pool and explore the results of all relevant studies on a given topic can provide additional insights on the topic by quantifying the magnitude of effects, which may help to guide prescription. To date, relatively recent meta-analyses have investigated the effect of manipulating a variety of RT program variables on muscle hypertrophy outcomes including load (23), volume (36), frequency (38), and proximity to failure (32), furthering our understanding of their practical implications.

The rest interval, operationally defined herein as the duration between sets during RT, is thought to be an important variable for promoting skeletal muscle hypertrophy. The National Strength and Conditioning Association recommends relatively short rest periods (30 to 90 seconds) to optimize muscle hypertrophy (15). This is largely based on acute research showing that short rest periods enhance the post-exercise hormonal response to RT, which has been theorized to promote muscular adaptations (20). However, emerging research suggests that transient post-exercise hormonal elevations may not play an important role in eliciting hypertrophy (27) (28), which calls into question the benefit of short rest intervals for optimizing muscle development. Indeed, McKendry et al. (24) reported that short rest intervals (1 min) blunted the myofibrillar protein synthetic response to RT compared to longer rest intervals (5 min) despite higher acute testosterone elevations in the short-rest condition.

Longitudinal research investigating the influence of rest intervals on muscle hypertrophy has been largely equivocal. A systematic review by Grgic et al. (14) concluded that both short and long inter-set rest periods are viable options for untrained individuals seeking to optimize hypertrophy, but that longer durations may be advantageous for those with previous RT experience. It should be noted that this review was published in 2017 and additional research has been conducted on the topic since that time. Moreover, no study to date has endeavored to quantify the magnitude of effect between different rest interval conditions to determine if differences may be practically meaningful for RT prescription. Therefore, the purpose of this study was to systematically review the literature and perform a Bayesian meta-analysis of the existing data on the effects of rest interval duration during resistance training on measures of muscle hypertrophy.

METHOD

We conducted this review in accordance with the guidelines of the "Preferred Reporting Items for Systematic Reviews and Meta-Analyses" (PRISMA) . The study was preregistered on the Open Science Framework (https://osf.io/ywevc).

Search strategy

To identify relevant studies for the topic, we conducted a comprehensive search of the PubMed/MEDLINE, Scopus, and Web of Science databases using the following Boolean search syntax: ("rest interval" OR "inter-set rest" OR "interset rest" OR "rest period*" OR "rest between sets" OR "resting interval" OR "resting period" OR "recovery interval") AND ("resistance training" OR "resistance exercise" OR "weight lifting" OR "weightlifting" OR "strength exercise" OR "strength training" OR "strengthening" OR "resistive exercise" OR "resistive training") AND ("muscle hypertrophy" OR "muscular hypertrophy" OR "muscle mass" OR "lean body mass" OR "fat-free mass" OR "fat free mass" OR "muscle fiber" OR "muscle size" OR "muscle fibre" OR "muscle thickness" OR "cross-sectional area" OR "computed tomography" OR "magnetic resonance imaging" OR "ultrasound" OR "DXA" OR "DEXA" OR "bioelectrical impedance analysis"). As previously described (30), we also screened the reference lists of articles retrieved and applicable review papers, as well as tapped into the authors' personal knowledge of the topic, to uncover any additional studies that might meet inclusion criteria (13). Moreover, we performed secondary “forward” and “backward” searches for citations of included studies in Google Scholar.

As previously described, the search process was conducted separately by 3 researchers (LG, AS and MR). Initially, we screened all titles and abstracts to uncover studies that might meet inclusion/exclusion criteria using online software (https://www.rayyan.ai/). If a paper was deemed potentially relevant, we scrutinized the full text to determine whether it warranted inclusion. Any disputes that could not be resolved by the search team were settled by a fourth researcher (BJS). The search was finalized in March 2024.

Inclusion criteria

We included studies that satisfied the following criteria: (a) had a randomized design (either within- or between-group design) and compared different inter-set rest interval durations for estimates of pre-/post-study changes in lean/muscle mass using a validated measure (dual-energy X-ray absorptiometry [DXA], bioelectrical impedance analysis, magnetic resonance imaging [MRI], computerized tomography [CT], ultrasound, muscle biopsy or limb circumference measurement) in healthy adults (≥18 years of age) of any RT experience while controlling all other training variables (in the case of volume, this represented either sets per muscle per session or volume load per session [i.e., sets x repetitions x load][1]; (b) involved at least 2 RT sessions per week for a duration of at least 4 weeks; (c) published in a peer-reviewed English language journal or on a preprint server. We excluded studies that (a) included participants with co-morbidities that might impair the hypertrophic response to RT (musculoskeletal disease/injury/cardiovascular impairments); (b) employed unequal dietary supplement provision (i.e., one group received a given supplement and the other received an alternative supplement/placebo).

Data extraction

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[1] In cases where studies equated sets between conditions, fewer repetitions may have been performed in the shorter rest conditions over multiple sets of a given exercise.

Three researchers (KD, EA and MW) independently extracted and coded the following data for each included study: Author name(s), title and year of publication, sample size, participant characteristics (i.e. sex, training status, age), description of the training intervention (duration, volume, frequency, modality), nutrition controlled (yes/no), method for lean/muscle mass assessment (i.e. DXA, MRI, CT, ultrasound, biopsy, circumference measurement), and mean pre- and post-study values for lean/muscle mass with corresponding standard deviations. In cases where rest periods fluctuated over time, we averaged values to report a mean. In cases where measures of changes in lean/muscle mass were not reported, we attempted to contact the corresponding author(s) to obtain the data as previously described (30). If unattainable, we extracted the data from graphs (when available) via online software (https://automeris.io/WebPlotDigitizer/). To account for the possibility of coder drift, a third researcher (AS) recoded 30% of the studies, which were randomly selected for assessment (5). Per case agreement was determined by dividing the number of variables coded the same by the total number of variables. Acceptance required a mean agreement of 0.90. Any discrepancies in the extracted data were resolved through discussion and mutual consensus of the coders.

Methodological quality

The methodological quality of the included studies was assessed using the "Standards Method for Assessment of Resistance Training in Longitudinal Designs" (SMART-LD) scale (30). The SMART-LD tool consists of 20 questions that address a combination of study bias and reporting quality as follows: general (items 1-2); participants (items 3–7), training program (items 8–11), outcomes (items 12–16), and statistical analyses (17–20). Each item in the checklist is given 1 point if the criterion is sufficiently displayed or 0 points if the criterion is insufficiently displayed. The values of all questions are summed, with the final total used to classify studies as follows: "good quality" (16–20 points); "fair quality" (12–15 points); or "poor quality" (≤ 11). Three reviewers (EE, AM and PAK) independently rated each study using the SMART-LD tool; any disputes were resolved by majority consensus.

Statistical analyses

All meta-analyses were conducted within a Bayesian framework enabling the results to be interpreted more intuitively compared to a standard frequentist approach through use of posterior probabilities (21). A Bayesian framework avoids dichotomous interpretations of meta-analytic results regarding the presence or absence of an effect (*e.g.*, with p values), and instead places greater emphasis on describing the most likely values for the average effect (21) while addressing practical questions such as which inter-set rest interval duration is likely to create the greatest muscle hypertrophy. To facilitate comparisons across the inter-set rest interval spectrum, durations were categorized using two sets of cut-points. The first was a binary categorization of shorter (duration ≤ 60 s) and longer (duration > 60 s), and the second comprised four categories (short: duration ≤ 60 s; intermediate: 60 s < duration < 120 s; long: 120 s ≤ duration < 180 s; and very long: duration ≥ 180 s). Due to the use of different measurement technologies, effect sizes were quantified by using standardized mean differences (SMDs). To account for the small sample sizes generally used in strength and conditioning, a bias correction was applied (25). The primary measure for this meta-analysis was controlled magnitude-based SMDs obtained by subtracting the baseline change of one inter-set rest interval category from another and dividing by the pre-intervention pooled standard deviation (25). To assess the overall effectiveness of the interventions included, initial analyses were conducted using non-controlled SMDs (26). Interpretation of the magnitude of effect sizes was facilitated by comparison to small, medium, and large thresholds developed for strength and conditioning outcomes (43).

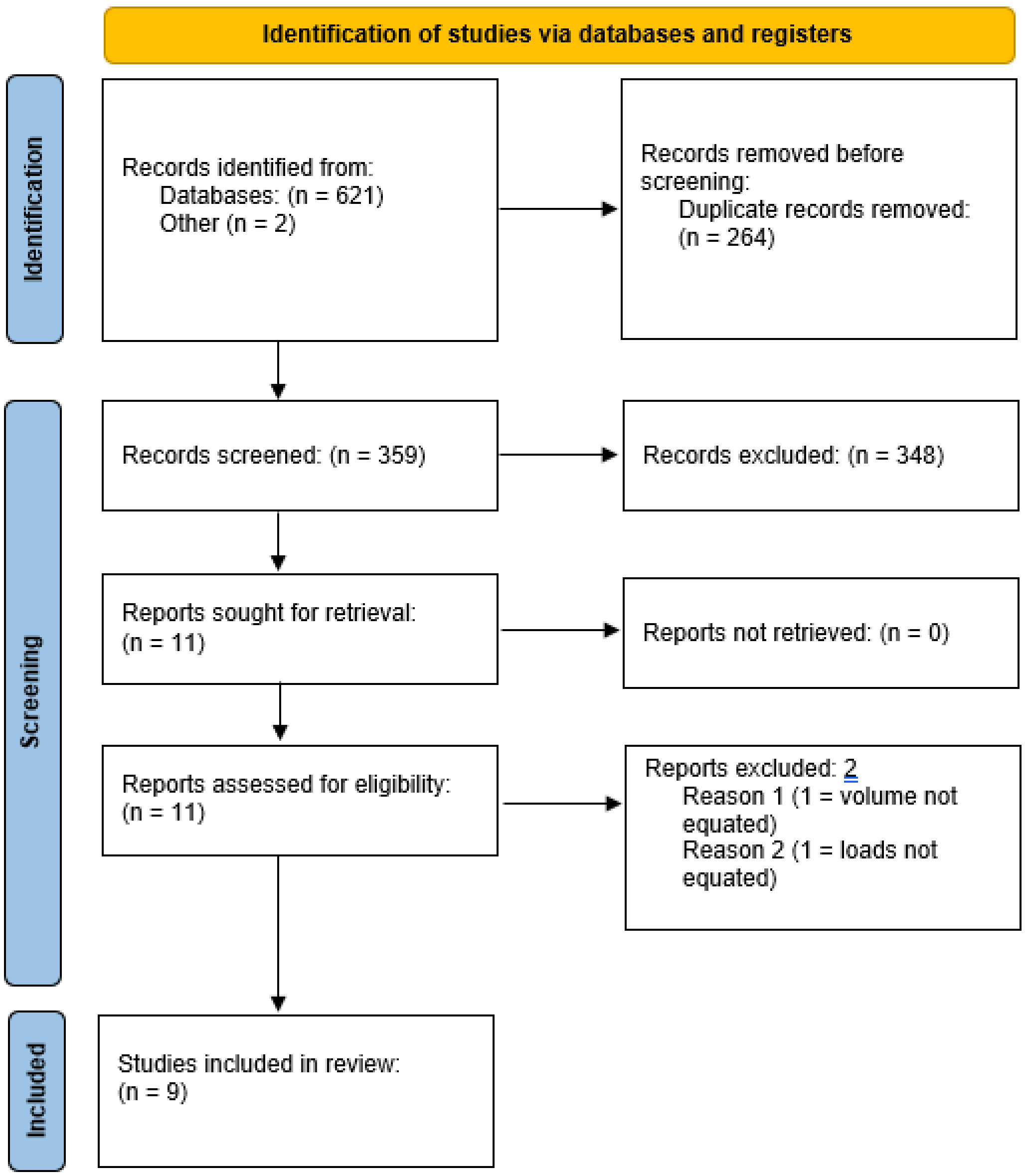
Three-level hierarchical models were used with inter-set rest interval included as a categorical variable to summarize the results using non-controlled SMDs. Pairwise (direct comparisons only) and network (direct and indirect comparisons) meta-analysis approaches were then used with controlled SMDs to compare across the binary and four category representations, respectively. Univariate analyses separated by measurement site (whole body, thigh, or arm) were also conducted. For the direct comparison, multivariate analysis was also conducted allowing for correlations between measurement sites. Network meta-analyses are becoming increasingly common in evidence synthesis and are most used to compare qualitatively different treatments where individual studies are unlikely to directly compare all levels (12). The technique calculates pairwise effect sizes from studies comparing two levels (direct evidence) and generates indirect evidence comparing other levels through a common comparator (12). To summarize potential differences in hypertrophy across all inter-set rest interval categories in a network, the Surface Under the Cumulative Ranking curve (SUCRA; (35) was used. For each category a SUCRA value expressed as a percentage was calculated representing the likelihood that muscle hypertrophy was highest or among the highest relative to other categories. Where applicable, we reported probabilities as *p*-values representing the proportion of the distribution that exceeded zero.

Informative priors were used for all models. For the hierarchical meta-regressions, the mean pre to post intervention change included an informative prior obtained from a large meta-analysis of strength and conditioning outcomes expressed in terms of SMDs (ref). For controlled effect sizes, similar research in strength and conditioning conducted with comparative effect sizes was used. For the between-studies standard deviation, informative priors were based on an analysis of the predictive distributions generated from a large number of previous meta-analyses (33). It is a common limitation in meta-analyses using SMDs from intervention change scores to use a fixed value for the pre- to post-study correlation (e.g. a value of 0.7) not based on any empirical data (6). To account for this limitation, the sampling error for each study was estimated using an informative uniform prior with lower bound based on the value calculated with a correlation of 0.9 and the upper bound based on the value calculated with a correlation of 0.5. All analyses were performed in R, using the R2OpenBUGS package (41) for Bayesian sampling.

Results

We initially screened 359 studies and identified 11 that potentially met inclusion criteria. After reviewing the full texts of these studies, 2 studies were excluded: one because neither set volume nor volume load was equated between conditions (1) and the other because the loading range was not equated in the initial set of the given exercise(s) (10). Figure 1 provides a flow chart of the search process.

Figure 1: PRISMA 2020 flow diagram for new systematic reviews which included searches of databases and registers only.



Study Characteristics

Eight studies employed young participants (18-35 years of age) (29) (3) (11) (22) (16) (8) (40) (37) and 1 employed older participants (>65 years of age) (45). Six studies employed untrained participants (29) (3) (11) (16) (22) (45) and 3 studies employed resistance-trained participants (8) (40) (37). Six studies employed male participants (29) (3) (8) (40) (37) (45), 1 study employed female participants (16), 1 study employed both male and female participants (22), and 1 study did not specify the sex of participants (11). Three studies assessed total body measures of hypertrophy (29) (3) (45), 5 studies assessed upper body measures of hypertrophy (biceps brachii and triceps brachii) (3) (11) (8) (40) (37), and 7 studies assessed lower body measures of hypertrophy (quadriceps femoris and total thigh) (3) (11) (22) (16) (8) (40) (37). The duration of the included studies ranged from 5 to 10 weeks. Table 1 provides a descriptive overview of each study's methodological design.

Table 1. Summary of the methods of included studies.

Study	Sample	Design	RT Protocol	Hypertrophy Measure	Duration
Buresh et al. (2009)	12 young, untrained men	Parallel group random assignment to 1 of 2 groups: (1) 60 sec RI; (2) 150 sec RI	TB protocol performed 2 d/wk consisting of 2–3 sets of 10 repetitions per exercise	- Hydrodensitometry: FFM - Skinfold and CIR: CSA of arm and thigh	10 wks
de Souza et al. (2010)	20 young, resistance-trained men	Parallel group random assignment to 1 of 2 groups: (1) 120 sec RI; (2) RI decreasing from 120 sec to 30 sec (mean RI = ~80 sec)	TB protocol performed 6 d/wk consisting of 3-4 sets of 8-12 repetitions per exercise	- MRI: CSA of arm and thigh	8 wks
Fink et al. (2016)	21 young, untrained individuals	Parallel group random assignment to 1 of 2 groups: (1) 30 sec RI; (2) 150 sec RI	4 sets of squats and bench performed 2 d/wk at 40% 1RM	- MRI: CSA of triceps brachii and thigh	8 wks
Hill-Haas et al. (2007)	18 young, untrained women	Parallel group random assignment to 1 of 2 groups: (1) 20 sec RI; (2) 80 sec RI	TB protocol performed 3 d/wk consisting of 2–5 sets of 15-20 repetitions per exercise	- CIR: thigh	5 wks
Longo et al. (2022)	28 young, untrained men and women	Within-participant random assignment of legs to 1 of 4 conditions: (1) 60 sec RI; (2) 180 sec RI; (3) 60	3 sets of leg press performed 2 d/wk at 80% 1RM	- MRI: CSA of quadriceps femoris	10 wks

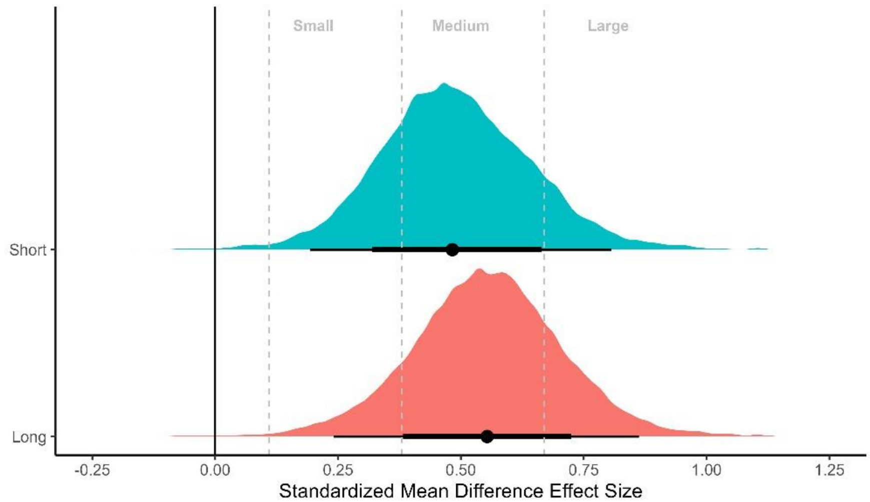
		sec RI with VL equated to long RI; (4) 180 sec RI with VL equated to short RI			
Piirainen et al. (2011)	21 young, untrained men	Parallel group random assignment to 1 of 2 groups: (1) 55 secs RI; (2) 120 sec RI	TB protocol performed 3 d/wk consisting of 3 sets of 10-20 repetitions per exercise	- BIA: FFM	7 wks
Schoenfeld et al. (2016)	21 young, resistance-trained men	Parallel group random assignment to 1 of 2 groups: (1) 60 secs RI; (2) 180 sec RI	TB protocol performed 3 d/wk consisting of 3 sets of 8-12 repetitions per exercise	- US: MT of biceps brachii, triceps brachii, quadriceps femoris	8 wks
Souza-Junior et al. (2011)	22 young, resistance-trained men	Parallel group random assignment to 1 of 2 groups: (1) 120 sec RI; (2) RI decreasing from 120 sec to 30 sec (mean RI = ~80 sec)	TB protocol performed 6 d/wk consisting of 3-4 sets of 8-12 repetitions per exercise	- MRI: CSA of upper arm and thigh	8 wks
Villanueva et al. (2014)	22 older, untrained men	Parallel group random assignment to 1 of 2 groups: (1) 60 secs RI; (2) 240 sec RI	TB protocol performed 3 d/wk consisting of 2-3 sets of 4-6 repetitions per exercise	- DXA: FFM	8 wks

RI = rest interval; TB = total body; VL = volume load; FFM = fat-free mass; MT = muscle thickness; CIR = circumference; US = ultrasound; VM = vastus medialis; DXA: dual-energy x-ray absorptiometry; MRI = magnetic resonance imaging; BIA = bioelectrical impedance analysis

Meta-analysis of non-controlled effect sizes

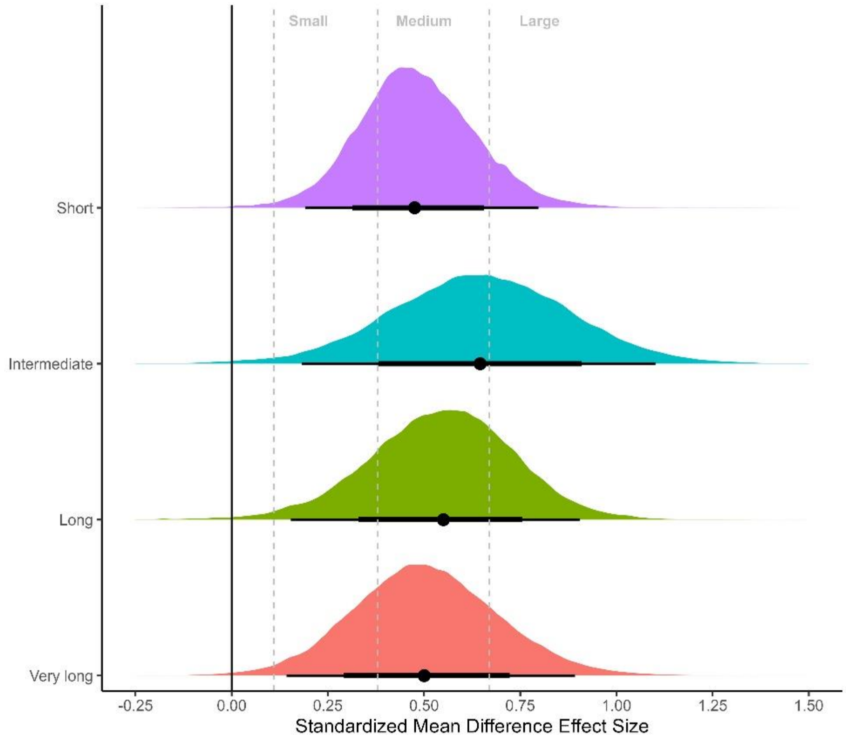
Meta-analyses on non-controlled effect sizes using hierarchical models of all 19 measurements (thigh: 10; arm: 6; whole body: 3) from nine studies are presented in figures 2 and 3. Both meta-analyses showed substantial overlap of SMDs across the different inter-set rest periods (Binary: short: 0.48 [95%CrI: 0.19 to 0.81], longer: 0.56 [95%CrI: 0.24 to 0.86]; Four categories: short: 0.47 [95%CrI: 0.19 to 0.80], intermediate: 0.65 [95%CrI: 0.18 to 1.1], long: 0.55 [95%CrI: 0.15 to 0.90], very long: 0.50 [95%CrI: 0.14 to 0.89]), with substantial heterogeneity in results. Central estimates suggested that improvements across the interventions were most likely to be between medium and large, highlighting that interventions included in this review were generally effective irrespective of rest interval duration.

Figure 2: Meta-analysis of non-controlled effect sizes separated by binary categorization of inter-set rest period.



Plots illustrate shrunken posterior distribution of effect sizes following application of meta-analytic model. Circle: Median, error bars represent 75 and 95% credible intervals. Small, medium, and large effect size thresholds are presented according to previous research in strength and conditioning (43).

Figure 3: Meta-analysis of non-controlled effect sizes separated by short to very long categorization of inter-set rest period.

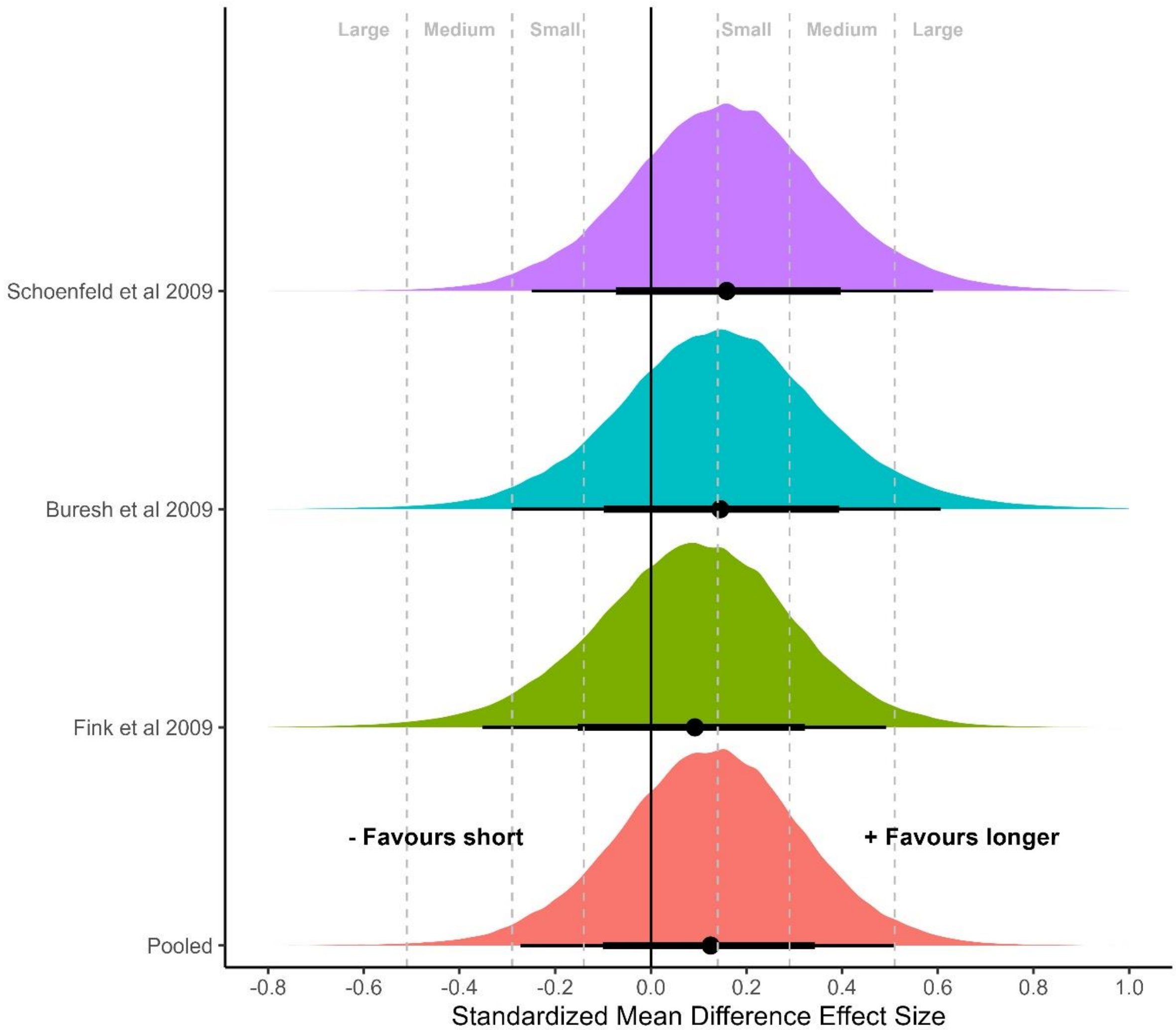


Plots illustrate shrunken posterior distribution of effect sizes following application of meta-analytic model. Circle: Median, error bars represent 75 and 95% credible intervals. Small, medium, and large effect size thresholds are presented according to previous research in strength and conditioning (43)..

Meta-analysis of controlled effect sizes

Univariate and multivariate meta-analyses of controlled effect sizes were conducted for outcomes separated by body region (arm, thigh, whole body; figures 4-6). Direct pairwise comparisons with binary categorization showed similar results for the arm and thigh with central estimates slightly favoring longer rest periods (arm: 0.13 [95%CrI: -0.27 to 0.51]; τ: 0.10 [95%CrI: 0.02 to 0.31], Figure 4; thigh: 0.17 [95%CrI: -0.13 to 0.43]; tau: 0.17 [95%CrI: 0.02 to 0.22], Figure 5). In contrast, central estimates closer to zero but slightly favoring shorter rest periods were estimated for the whole body (whole body: -0.08 [95%CrI: -0.45 to 0.29]; tau: 0.08 [95%CrI: 0.02 to 0.27], Figure 6). Application of the multivariate meta-analysis model resulted in slight reductions in uncertainty with smaller central estimates all modestly favoring longer rest periods (arm: 0.11 [95%CrI: -0.26 to 0.48]; thigh: 0.16 [95%CrI: -0.13 to 0.41]; whole body: 0.03 [95%CrI: -0.28 to 0.36]).

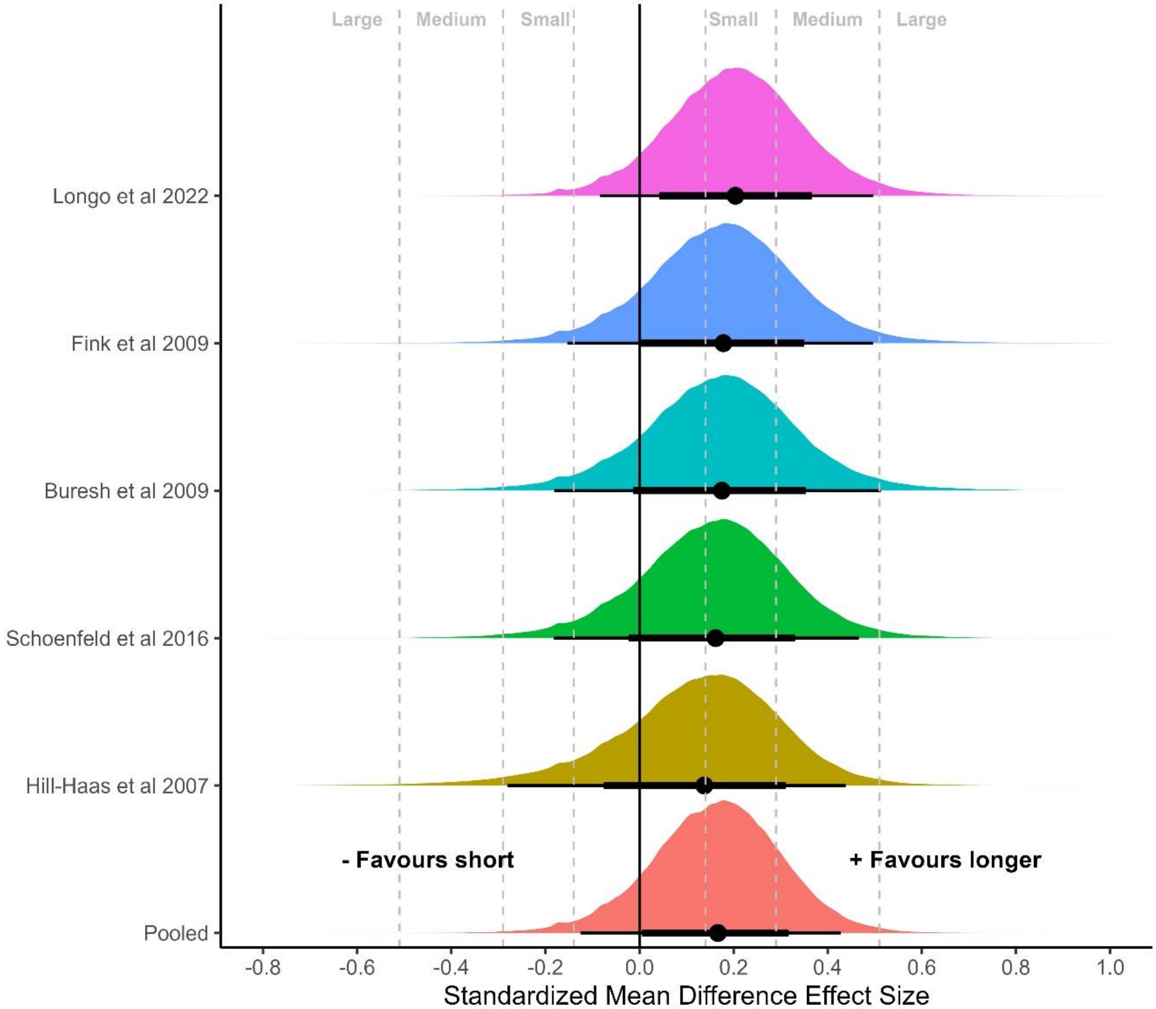
Figure 4: Meta-analysis of controlled effect sizes of muscular hypertrophy of the upper arm with direct comparisons of binary categorization of inter-set rest period.



Plots illustrate shrunken posterior distribution of effect sizes following application of meta-analytic model. Circle: Median, error bars represent 75 and 95% credible intervals. Small, medium, and large effect size thresholds are presented according to previous research in strength and conditioning (42). Probability of effect size greater than 0 favoring longer rest period = 0.74; Probability of effect size greater than small favoring longer rest period = 0.45;

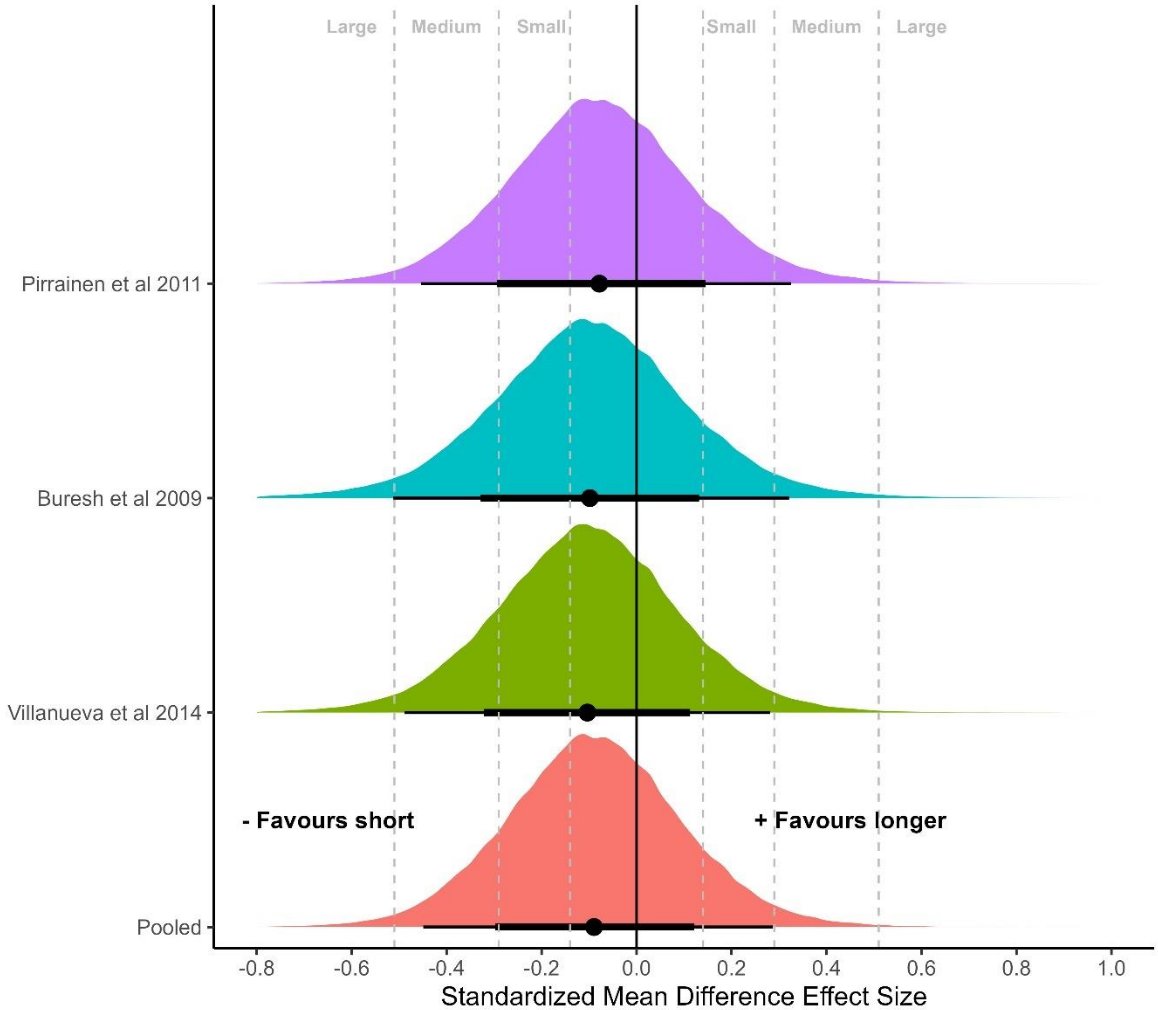
Probability of effect size greater than medium favoring longer rest period = 0.18; Probability of effect size greater than large favoring longer rest period = 0.03.

Figure 5: Meta-analysis of controlled effect sizes of muscular hypertrophy of the thigh with direct comparisons of binary categorization of inter-set rest period.



Plots illustrate shrunken posterior distribution of effect sizes following application of meta-analytic model. Circle: Median, error bars represent 75 and 95% credible intervals. Small, medium, and large effect size thresholds are presented according to previous research in strength and conditioning (42). Probability of effect size greater than 0 favoring longer rest period = 0.88; Probability of effect size greater than small favoring longer rest period = 0.54; Probability of effect size greater than medium favoring longer rest period = 0.15; Probability of effect size greater than large favoring longer rest period = 0.01.

Figure 6: Meta-analysis of controlled effect sizes of muscular hypertrophy of the whole body with direct comparisons of binary categorization of inter-set rest period.



Plots illustrate shrunken posterior distribution of effect sizes following application of meta-analytic model. Circle: Median, error bars represent 75 and 95% credible intervals. Small, medium, and large effect size thresholds are presented according to previous research in strength and conditioning (42). Probability of effect size greater than 0 favoring short rest period = 0.69; Probability of effect size greater than small favoring short rest period = 0.36; Probability of effect size greater than medium favoring short rest period = 0.12; Probability of effect size greater than large favoring short rest period = 0.01.

Controlled effect sizes for the four categories of inter-set rest period were analyzed with network meta-analyses. Sufficient data were available for univariate analysis of the arm and thigh. Network structures are presented in Supplemental Figure 1S, with effect size estimates combining direct and indirect estimates, and SUCRA values presented in Table 2. In general, effect size estimates and SUCRA values for both regions of the body indicated greater effectiveness for rest periods beyond the short categorization.

Table 2: Univariate network meta-analyses combining direct and indirect pairwise comparisons for hypertrophy at the thigh and arm for the four inter-set rest period categories.

Region	Category	Comparative effect size (95%CrI)	SUCRA
Arm	Short	-	0.40
	Intermediate	0.22 (-0.31 to 0.74)	0.49
	Long	-0.02 (-0.43 to 0.37)	0.52
	Very long	0.18 (-0.36 to 0.70)	0.60
Thigh	Short	-	0.18
	Intermediate	0.13 (-0.31 to 0.58)	0.54
	Long	0.01 (-0.39 to 0.41)	0.63
	Very long	0.32 (-0.10 to 0.68)	0.64

Comparative effect sizes are expressed relative to the short inter-set rest category. CrI: Credible interval. SUCRA: Surface Under the Cumulative Ranking curve

Subanalyses

Subanalyses were performed on direct comparisons separating studies based on set end-point (i.e., training to momentary muscular failure or non-failure) and training status (specific to designs that included untrained participants). A multivariate analysis comprised of data from three studies that incorporated training to momentary muscular failure was conducted for hypertrophy of the thigh (0.31 [95%CrI: -0.03 to 0.61]) and arm (0.04 [95%CrI: -0.37 to 0.44]). Similarly, a multivariate analysis comprised of data from three studies that incorporated non-failure RT was conducted for hypertrophy of the thigh (0.27 [95%CrI: -0.02 to 0.51]) arm (0.04 [95%CrI: -0.37 to 0.44]), and whole body (-0.06 [-0.40 to 0.27). Finally, sufficient data were available to perform a multivariate analysis comprised of data from six studies that included untrained participants and was conducted for hypertrophy of the thigh (0.17 [95%CrI:

-0.15 to 0.47]) arm (0.02 [95%CrI: -0.41 to 0.46]), and whole body (-0.05 [-0.43 to 0.26). Insufficient data were available to subanalyze results in trained individuals.

Methodological qualitative assessment

Qualitative assessment of included studies via the SMART-LD tool showed a mean score of 15 out of a possible 20 points (range: 12 to 17 points). Four studies were judged to be of good quality (8) (11) (40) (45), 4 studies were judged to be of fair quality (16) (22) (29) (37), and 1 study was judged to be of poor quality (3). See table S1 in the supplementary files.

Discussion

Our meta-analysis quantified data from studies that directly compared the effects of different rest interval lengths on measures of muscle hypertrophy. While the initial meta-regressions with non-controlled effect sizes highlighted substantial heterogeneity across studies (figures 2 and 3), they also demonstrated that most interventions were effective in eliciting hypertrophic adaptations regardless of rest interval duration, with SMDs that could be considered medium to large in magnitude. Binary categorization comparing shorter (≤60 secs) with longer (>60 s) rest intervals returned slightly greater central estimates favoring the longer rest condition (SMD = 0.56 vs 0.48, respectively; figure 2). When further stratifying data, results showed slight differences between short (SMD = 0.47), intermediate (SMD = 0.65), long (SMD = 0.55) and very long (SMD = 0.50) rest periods (figure 3). These results suggest no clear benefit to altering rest interval length for the purpose of promoting muscle hypertrophy. However, given substantial heterogeneity, meta-regressions with small numbers of studies provide limited ability to draw strong inferences as any differences observed can be the result of chance imbalances in the distribution of studies. Therefore, the primary inference from this study was focused on meta-analyses that comprised controlled effect sizes with either direct pairwise comparisons only (bivariate categorization), or both direct and indirect pairwise comparisons (four categories) through network models.

When subanalyzing the effects of rest interval length on hypertrophy of the limbs, the results suggest a small benefit for rest intervals >60 seconds. For the binary categorization, the pooled effect size for the arms slightly favored a hypertrophic benefit for longer vs shorter rest durations (SMD = 0.13). The probability of the effect being greater than zero was 0.74, with only a 0.45 probability that the difference in effect was greater than small. Similarly, the pooled effect size for quadriceps femoris modestly favored longer vs shorter durations (SMD = 0.17). There was a strong probability that this effect was greater than zero (p=0.88), but only a 0.54 probability that the difference in effect was greater than small. Both upper and lower limb analyses showed a very low probability that differences would be greater than a medium effect (SMD = 0.18 and 0.15, respectively). Conversely, measures of whole-body hypertrophy showed slightly greater effects favoring shorter vs longer rest durations (SMD = -0.08, p(>0)=0.69, p(>small)=0.36); however, with substantial uncertainty due to only three studies providing whole body data.

Potential discrepancies between findings of hypertrophy of the extremities vs the whole body may be related to the different methods of assessment. Whole-body measures of muscle growth were based on estimates of fat-free mass (FFM) via DXA, BIA and hydrodensitometry, which are often used as a proxy for muscle hypertrophy (4). However, FFM encompasses all bodily tissues other than fat mass; while alterations in skeletal muscle comprise the majority of FFM changes that occur during resistance training, other components such as water and mineral can influence results as well (31). Alternatively, the majority of assessments for the extremities employed direct measurements of changes in muscle mass via MRI and ultrasonography. Given that direct assessment methods have been shown to be more sensitive to detecting resistance training-induced hypertrophy than indirect assessments (9) (44), the results of our whole-body analysis should be interpreted with caution.

Potential beneficial effects of rest periods ≤ 60 s on muscle hypertrophy may be attributable to preservation of volume load during a training session. Research indicates that very short rest periods (≤ 60 seconds) appreciably reduce the number of repetitions performed across multiple sets compared to longer rest durations (19) (39) (34), which could have a detrimental effect on long-term muscular adaptations. This hypothesis is supported by Longo et al (22), who reported appreciably greater increases in quadriceps femoris cross-sectional area when training with 180 vs 60 inter-set rest periods over a 10-week intervention (13.1% vs 6.8%, respectively); of note, volume load was reduced to a significantly greater extent in the shorter vs longer rest condition. However, similar hypertrophy was observed with the performance of additional sets to equate volume load between conditions.

Alternatively, evidence suggests that differences in volume load tend to level off when comparing rest intervals of 120 vs 180 seconds (34) (19). When compared to very short rest intervals (≤ 60 s), our univariate network meta-analysis suggested that very long rest intervals (≥ 180 seconds) provided a modest advantage versus intermediate (61-119 seconds) and long (120-179 seconds) durations with respect to quadriceps femoris hypertrophy. However, these data showed a high degree of uncertainty and the U-shaped response between conditions casts further doubt on the veracity of the finding. Analyses of hypertrophy of the arms did not show an appreciable effect of rest interval durations beyond intermediate (>60 second) durations. Future research should explore this topic in greater detail to better determine whether graded increases in rest interval duration alter muscular adaptations as well as the extent to which volume load may play a role in the process.

Subanalysis of set end-point data indicated that training to failure or non-failure did not meaningfully influence the interaction between rest interval duration and muscle hypertrophy. Central estimates from both analyses suggested a hypertrophic benefit for longer rest periods in the quadriceps femoris, irrespective of the proximity-to-failure reached during RT. However, the magnitude of effect was relatively small (SMD = 0.27 and 0.31 for non-failure and failure conditions, respectively). Alternatively, negligible differences were observed for the influence of rest interval length in the arms (SMD = 0.04) regardless of set end-point. The findings are somewhat in contrast with data showing that shorter rest periods impair bench press performance to a greater extent than longer rest periods when training with closer proximities to failure (18). Further research is needed to better understand the potential discrepancies between acute and longitudinal outcomes.

Subanalysis of the potential influence of training status on rest interval length showed that untrained individuals displayed a slight hypertrophic benefit from longer rest periods when training the quadriceps femoris (SMD = 0.17). However, rest interval length appeared to have negligible effects on measures of hypertrophy for the arms and whole body in untrained individuals (SMD = 0.02 and -0.05, respectively). These data are relatively consistent with findings from a systematic review by Grgic et al. (14) that concluded both shorter and longer rest durations are equally viable options for promoting hypertrophy in novice trainees. The systematic review by Grgic et al. (14) also suggested that trained individuals might benefit from the use of longer rest intervals, conceivably by allowing for a greater volume load across multi-set protocols. Unfortunately, there was insufficient data to subanalyze results on experienced lifters, precluding our ability to either confirm or refute this claim. Further research is therefore needed to better understand how training status may influence the response to rest interval length.

Conclusion

Pooled analyses of the current body of literature suggest a small benefit to employing longer versus shorter inter-set rest intervals for muscle hypertrophy. The effect favoring longer inter-set rest intervals was relatively consistent between the arms and the legs musculature, and results were not meaningfully influenced by whether RT was performed to failure or non-failure. These findings are inconsistent with recommendations from the National Strength and Conditioning Association, which prescribe relatively short rest periods (30 to 90 seconds) for hypertrophy-related goals (15). Thus, current guidelines regarding rest interval prescription for achieving muscular hypertrophy warrant reconsideration. It should be noted that while the observed differences in effect are likely to be between zero and small, intervention durations were relatively short (between 5 to 10 weeks); thus, it is possible that accumulated differences in muscle mass accretion over longer terms may be more appreciable.

The current evidence remains equivocal as to whether resting more than 90 seconds between sets further enhances hypertrophic adaptations. Our analysis casts doubt as to any beneficial effects in this regard. However, given the uncertainty of evidence, additional studies are needed comparing measures of hypertrophy across a wide spectrum of rest periods to provide better insights on the topic.

From an applied standpoint, the benefit to employing longer rest periods may be practically significant for those seeking to optimize hypertrophic adaptations (i.e., bodybuilders, strength athletes). Although the magnitude of effect between conditions was marginal, even small alterations in muscular development can potentially make a difference in athletic outcomes. Alternatively, the results have questionable practical meaningfulness for individuals seeking to improve overall health and wellbeing. The tradeoff between greater time-efficiency vs attenuating hypertrophy to a small extent could make shorter rest periods an attractive option in this population, particularly given the fact that time is often reported as a significant barrier to exercise participation and adherence (17).

Finally, it is conceivable that autoregulation of rest intervals may be a viable method for individuals to determine rest interval duration. Preliminary evidence suggests that self-selecting the time taken between sets can result in similar number of repetitions performed across multiple sets with greater time-efficiency compared to a fixed 120 second rest interval (7). This hypothesis warrants further study using longitudinal designs that directly measure changes in muscle growth.

Conflict of interest

BJS serves on the scientific advisory board for Tonal Corporation, a manufacturer of fitness equipment. All other authors report no competing interests.

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Data and Supplementary Material Accessibility

Data and supplementary material are available on the Open Science Framework project page: https://osf.io/zp6vs/

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