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The Resistance Training Dose-Response:

Meta-Regressions Exploring the Effects of Weekly Volume and Frequency on Muscle Hypertrophy and Strength Gain

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ABSTRACT

Background: Weekly set volume and frequency are used to manipulate resistance training (RT) dosage. Previous research has identified higher weekly set volume as enhancing muscle hypertrophy and strength gains, but the nature of the dose-response relationship still needs to be investigated. Mixed evidence exists regarding the effects of higher weekly frequency.
Objective: Before meta-analyzing the volume and frequency research, all contributing RT sets were classified as direct or indirect, depending on their specificity to the hypertrophy/strength measurement. Then, weekly set volume/frequency for indirect sets was quantified as 1 for 'total,' 0.5 for 'fractional,' and 0 for 'direct.' A series of multi-level meta-regressions were performed for muscle hypertrophy and strength, utilizing 67 total studies of 2,058 participants. All models were adjusted for the duration of the intervention and training status.
Results: The relative evidence for the 'fractional' quantification method was strongest; therefore, this quantification method was used for the primary meta-regression models. The posterior probability of the marginal slope exceeding zero for the effect of volume on both hypertrophy and strength was 100%, indicating that gains in muscle size and strength increase as volume increases. However, both best fit models suggest diminishing returns, with the diminishing returns for strength being considerably more pronounced. The posterior probability of the marginal slope exceeding zero for frequency's effect on hypertrophy was less than 100%, indicating compatibility with negligible effects. In contrast, the posterior probability for strength was 100%, suggesting strength gains increase with increasing frequency, albeit with diminishing returns.
Conclusions: Distinguishing between direct and indirect sets appears essential for predicting adaptations to a given RT protocol, such as using the 'fractional' quantification method. This method's dose-response models revealed that volume and frequency have unique dose-response relationships with each hypertrophy and strength gain. The dose-response relationship between volume and hypertrophy appears to differ from that with strength, with the latter exhibiting more pronounced diminishing returns. The dose-response relationship between frequency and hypertrophy appears to differ from that with strength, as only the latter exhibits consistently identifiable effects.

1 INTRODUCTION

Resistance training (RT) outcomes depend on many factors, including the configuration of programming variables. Two variables, volume and frequency, are important for manipulating the RT dosage. Understanding the dose-response relationships between these variables and muscle hypertrophy and muscle strength gains is essential for making well-informed programming decisions.

Weekly RT set volume has been deemed a primary program design variable and therefore received considerable attention (1–4). Indeed, multiple meta-analyses have reported that the number of RT sets per muscle group per week has a positive dose-response relationship with muscle hypertrophy (1,5,6) and strength gains (7). However, many of these analyses explore a specific range of volumes and have limited conclusions due to a paucity of data at the time of analysis. For example, in 2017, Ralston et al. (7) meta-analyzed the effects of set volume, reporting greater strength gains with > 5 weekly sets compared to ≤ 5 weekly sets (SMD: 0.18 [95% CI: 0.06, 0.30]; p = 0.003). Therefore, this analysis does not address the higher end of the dose-response relationship. Similarly in 2017, for muscle hypertrophy, Schoenfeld et al. (1) reported greater improvements, albeit non-significantly (p = 0.076), in RT groups performing ≥ 9 sets per muscle group per week (ES: 0.46 [95% CI: 0.21, 0.71]) compared to groups performing < 9 sets per muscle group per week (ES: 0.32 [95% CI: 0.19, 0.46]). However, the authors noted conclusions could not be made regarding the dose-response relationship for greater than 9 weekly sets due to a paucity of data.

In 2020, with more data available, Baz-Valle et al. (5) explored the effects of 12-20 vs. 20+ weekly sets on hypertrophy, reporting that 20+ sets resulted in significantly more hypertrophy in the triceps brachii (SMD: -0.50 [95% CI: -0.88, -0.11]; p = 0.01) but not in the biceps brachii (SMD: -0.10 [95% CI: -0.46, 0.26]; p = 0.59) or quadriceps femoris (SMD: -0.20 [95% CI: -0.49, 0.10]; p = 0.19). Currently, readers looking to gain specific insight into the dose-response relationship between weekly RT set volume and hypertrophy may triangulate the results from Schoenfeld et al. (1) and Baz-Valle et al. (5), perhaps concluding that there are substantial diminishing returns beyond ~12-20 sets per muscle group per week. However, there are limitations to this interpretation, particularly given the categorical nature of these analyses. For example, comparing 10-20 weekly sets to 21-30 weekly sets wouldn't capture meaningful differences within the same arbitrary range (e.g., 21 vs. 30 weekly sets). Further, it has been suggested that the dose-response relationship may follow an inverted-U-shaped curve, in which additional volume eventually results in a

plateau and ultimately a detrimental impact on muscular adaptations (4). To rectify these limitations, we propose that volume be treated as a continuous variable (8,9) to gain insight into the magnitude and functional form of the dose-response relationship.

Furthermore, previous meta-analyses have quantified all sets for a given muscle group as equal whether it is the primary force generating muscle (e.g., pectoralis major in the bench press) or a synergist muscle (e.g., triceps brachii in the bench press). However, some data suggest synergists may experience less hypertrophy than the primary force generator (10,11). Nonetheless, the evidence remains unclear regarding how to quantify synergist muscle set volume accurately (12,13). Regarding muscle strength, no meta-analysis has explored the contribution of non-specific exercises training the muscles involved in the strength assessment (e.g., leg press training for squat one repetition maximum [1RM]). Therefore, the dose-response relationship with different quantification methods, such as counting sets for synergist muscles/non-specific exercises as half of a set, still needs to be explored (12).

Similar limitations in the volume research apply to research examining the effects of frequency (i.e., the number of times per week a muscle or exercise is trained) on muscle hypertrophy and strength gains. Meta-analyses on the effects of frequency have produced mixed results but generally suggest no independent effect of higher frequencies (14–19). Moreover, meta-regressions of volume-equated studies have yielded non-significant results for hypertrophy (14) and strength (17); however, to our knowledge, only linear meta-regressions have been performed. Thus, other functional forms should be considered to elucidate potential nonlinear effects.

Therefore, the purpose of this meta-analysis was to explore the nature of the continuous dose-response relationships between weekly set volume and muscle hypertrophy, weekly set volume and muscle strength gains, weekly frequency and muscle hypertrophy, and weekly frequency and muscle strength gains using various quantification methods.

2 METHODS

This meta-analysis was conducted according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines (20). Pre-registration on the Open Science Framework (https://osf.io/r958n) using the International Prospective Register of Systematic Reviews template was used, though some of the methods have changed since the original pre-registration.

2.1 Inclusion Criteria

Inclusion criteria included studies, pre-prints, theses, or abstracts (author correspondence permitting) 1) published or pre-printed before June 2024; 2) available in English; 3) employed a dynamic RT intervention with eccentric and concentric training utilizing a randomized experimental design (either within- or between-group) lasting a minimum of 4 weeks in healthy participants; 4) did not involve participants > 70 years old; 5) compared at least two groups featuring differences in set volume and/or frequency while controlling for the load (±5% of 1RM or ±2RM) and proximity to failure (failure, non-failure, or mixed); 6) included pre-intervention and post-intervention measurements of muscle hypertrophy with a direct, site-specific measurement (ultrasound, computed tomography, magnetic resonance imaging, muscle biopsies) or included pre-intervention and post-intervention measurements of dynamic (up to a 10RM), isometric, or isokinetic maximal strength; 7) not retracted or called into question by Vigotsky et al. (21).

2.2 Search Strategy

PubMed/Medline and Google Scholar databases were searched for studies until April 2023. The following search terms were used for PubMed/Medline: ("resistance training" OR "resistance exercise" OR "strength training") AND ("musc*" OR "hypertrophy" OR "muscle mass" OR "muscle thickness" OR "growth" OR "cross sectional area" OR "fat free mass" OR "lean body mass" OR "limb circumference" OR "muscle strength" OR "strength") AND ("volume" OR "dose" OR "dose response" OR "frequency" OR "multiple sets" OR "single sets" OR "sessions per week" OR "sessions"). The following search terms were used for Google Scholar: allintitle: ("resistance training" OR "resistance exercise" OR "strength training") AND ("musc *" OR hypertrophy OR "muscle mass" OR "muscle thickness" OR growth OR "cross sectional area" OR "fat free mass" OR "lean body mass" OR "limb circumference"). Screening was performed using abstrackr (http://abstrackr.cebm.brown.edu). Titles, abstracts, and full texts were examined for inclusion; data was extracted from full texts that met the inclusion criteria. JP and JR performed this process. Following screening and exclusion of studies deemed not to meet the inclusion criteria, the reference lists of included studies and publications that cited the included studies were also screened for inclusion. Finally, studies published between April 2023 and June 2024 authors became aware of were included.

2.3 Quality Assessment

The quality of the included studies was assessed using the TESTEX scale (22), designed specifically for exercise training studies. In addition to the pre-registered primary meta-regressions modeling the effect of a given set volume/frequency, three analyses were added to aid in interpretation of the effects: 1) funnel plots and effective sample size approximated bias-adjusted estimates (23) for assessing heterogeneity and small study bias (24), 2) contrast-based meta-analyses to assess the consistency of effects between higher vs. lower volume/frequency, 3) additional meta-regressions with strict inclusion criteria, described in section 3.

2.3 Data Extraction

Data was extracted/coded and included variables regarding study design, measurements, participant descriptives, RT protocol descriptives, and outcomes. Where data were not available in the full text, attempts were made to contact authors to request missing data. If there was no response, data was obtained using WebPlotDigitizer (v5.0, Ankit Rohatgi) where possible. RT protocol descriptive data were extracted as separate variables for 'total,' 'fractional,' and 'direct' volume and frequency classifications.

2.4 Volume and Frequency Classifications ('Total'/'Fractional'/'Direct')

All RT sets were classified as direct or indirect, allowing for three classifications of RT variables ('total'/'fractional'/'direct'). 'Total' was the sum of direct and indirect sets, 'Fractional' counted indirect sets as half a set (indirect × 0.5 + direct), and 'direct' did not account for indirect sets.

For hypertrophy, direct sets were those in which the measured muscle(s) was likely to be the primary force generator in the exercise. Indirect sets were those in which the measured muscle(s) was likely to be meaningfully trained but not the primary force generator of the exercise (i.e., synergist). For example, a study measuring biceps brachii hypertrophy consisting of 5 sets of biceps curls in one session and 5 sets of rows in another session would result in a weekly volume quantified as 'total,' 'fractional,' and 'direct' of 10, 7.5, and 5, respectively. This example would result in frequency quantified as 'total,' 'fractional,' and 'direct' of 2, 1.5, and 1, respectively.

For strength, direct sets were those that trained the exact exercise used for the strength assessment. Indirect sets were any that were likely to meaningfully train the muscle(s) involved in the strength assessment. This includes the primary force generator and synergists for the strength assessment. For example, a study measuring back squat 1RM strength consisting of 5 sets of back squats in one session, 5 sets of back squats in a second session, and 5 sets of leg presses in a third session would result in a weekly volume quantified as 'total,' 'fractional,' and 'direct' of 15, 12.5, and 10, respectively. This example would result in frequency quantified as 'total,' 'fractional,' and 'direct' of 3, 2.5, and 2, respectively.

This process was not wholly objective; therefore, table 1 reports the decisions made throughout the included studies to clarify the methods used and aid in interpretation. In addition to volume and frequency, RT protocol descriptives (i.e., repetition range, interset rest, etc.) were weighted in accordance with 'total,' 'fractional,' and 'direct' classifications using a custom calculator.

2.5 Control Group Estimates and Smallest Detectable Effect Size

Rather than omitting non-training control groups from our analysis, potentially discarding valuable information, their effects were included to improve power/precision and more realistically anchor the magnitude of model estimates. However, non-training control group data was only included from studies using untrained participants as the effects from studies using previously trained participants represent de-training protocols.

Further, to contextualize the results within sources of error present in RT studies, our intention was to utilize the extracted data from untrained, non-training control groups in the included studies to inform a smallest detectable effect size (SDES). However, only 13 included studies (25–37) featured untrained, non-training control groups, and this was particularly problematic given only two of these studies included hypertrophy measures (25,26). Therefore, we utilized untrained, non-training control group effect estimates from 124 strength studies (368 effects) and 69 hypertrophy studies (223 effects) from data made available by Steele et al. (38) to approximate errors associated with longitudinal RT studies. Specifically, the square root of the sum of the estimated variance components from a multi-level mata-analytic model was used as the SDES. This value is 2.05% and 3.96% for hypertrophy and strength, respectively (https://osf.io/3e67h).

Table 1A: Exercises Counted as Direct and Indirect Weekly Set Volume for Hypertrophy

Muscle(s) Assessed	Measurement(s)	Direct Exercise(s)	Indirect Exercise(s)
Quadriceps, Knee Extensors, Lateral Thigh, Anterior/Middle Thigh, Vastus Lateralis, Vastus Medialis, or Vastus Intermedius	MT, Sum of MT, CSA, Fiber Area, Muscle Volume	Back Squat, Leg Press, Dumbbell Lunge, Leg Extension, Hack Squat, Smith Machine Squat, Barbell Split Squat, Dumbbell Split Squat, Bulgarian Split Squat	N/A
Rectus Femoris	MT, CSA, Ultrasound-Derived Circumference	Leg Extension	Smith Machine Squat, Leg Press, Squat
Hamstrings or Posterior Thigh	MT, CSA, Muscle Volume	Leg Curl	N/A
Pectoralis Major	MT	Bench Press, Flat Dumbbell Fly	N/A
Anterior Deltoid	MT	Barbell Shoulder Press, Barbell Shoulder Front Raise	Bench Press, Chest Press, Barbell Close Grip Press On Bench
Trapezius	CSA	N/A	Lat Pulldown, Seated Row
Triceps Brachii or Elbow Extensors	MT, Muscle Volume	Tricep Push-Down, Triceps Extension, Tricep Kickback, Skullcrusher, Lying Triceps Press, Lying Tricep Extension, Cable Overhead Extension, Overhead Dumbbell Extensions, Close Grip Bench	Flat Bench Press, Incline Bench Press, Decline Bench Press, Shoulder Press, Dumbbell Shoulder Press, Incline Dumbbell Press, Incline Machine Press, Machine Press
Biceps Brachii or Elbow Flexors	MT, CSA, Muscle Volume	Bicep Curl, Dumbbell Bicep Curl, Hammer Curl, Dumbbell Incline Curl, Barbell Preacher Curl, Dumbbell Preacher Curl, Machine Curl	Lat Pulldown, Neutral Grip Lat Pulldown, Supine Grip Pulldown, Machine Lat Pulldown, Seated Row, Close-Grip Machine Row, Wide-Grip Machine Row, Bent-Over Barbell Row, Supine Grip Bent-Over Row

Effort was made to use similar verbiage as manuscripts to best represent the classification decisions. MT = muscle thickness; CSA = cross-sectional area.

Table 1B: Exercises Counted as Indirect Weekly Set Volume for Strength

Strength Assessment	Measurement(s)	Indirect Exercise(s)
Back Squat	1RM, 10RM	Leg Extension, Barbell Split Squat, Dumbbell Split Squat, Bulgarian Split Squat, Hack Squat, Dumbbell Lunge, Leg Press
Smith Machine Squat	1RM	Leg Press, Leg Extension
Leg Press	1RM, 5RM, 10RM, Estimated 1RM	Dumbbell Lunge, Leg Extension
Hack Squat	1RM	Back Squat
Leg Extension	1RM, Estimated 1RM	Squat, Leg Press
Leg Extension Isometric	Peak Torque	Leg Extension (Dynamic), Leg Press, Squat
Leg Extension Isokinetic	Peak Torque	Leg Extension (Dynamic), Squat, Leg Press, Barbell Lunge
Deadlift	1RM	Romanian Deadlift
Romanian Deadlift	Estimated 1RM	N/A

Leg Curl	1RM, 10RM	N/A
Leg Flexion Isometric	Peak Torque	Leg Curls (Dynamic)
Leg Flexion Isokinetic	Peak Torque	Leg Curls (Dynamic), Romanian Deadlift
Calf Raise	1RM	N/A
Torso Rotation Isometric	Peak Torque	Torso Rotation (Dynamic)
Back Extension Isometric	Peak Torque	Back Extension (Dynamic)
Bench Press	1RM, 5RM, Estimated 1RM	Close Grip Bench Press, Bench Press Machine, Chest Machine Press, Incline Bench Press, Incline Dumbbell Press, Incline Bench Press Machine, Incline Machine Press, Decline Bench Press, Shoulder/Overhead Press, Behind Neck Seated Shoulder Press, Machine Shoulder Press, Tricep Push-Down, Machine Triceps Extension, Tricep Kickback, Skullcrusher, Lying Triceps Press, Barbell Lying Arm Extension, Cable Overhead Extension, Triceps Extension, Dumbbell Tricep Extension, Tricep Pushdown, Dumbbell Overhead Extension, One Arm Triceps Extension, Flat Dumbbell Fly, Cross Cable Fly, Pec-Dec Fly, Pec Fly, Barbell Shoulder Front Raise, Front Dumbbell Raise
Smith Machine Bench Press or Chest Press Machine	1RM, 10RM	Shoulder Press, Bench Press, Arm Cross (Pec-Dec) Machine, Overhead Press Machine, Tricep Extension Machine
Bench Press Isometric	Peak Force	Bench Press (Dynamic), Shoulder Press
Shoulder Press	1RM, 5RM, 10RM	Chest Press, Bench Press, Tricep Extension, Incline Bench Press, Behind Neck Seated Shoulder Press, Lateral Raise, Upright Row
Dumbbell Overhead Press	Estimated 1RM	Bench Press
Overhead Press Machine	1RM	Chest Press, Lateral Raise Machine, Tricep Extension Machine
Upright Row	1RM	Lateral Raise, Posterior Lateral Raise
Lateral Raise	1RM	N/A
Bent Over Row	1RM	Bicep Curl, Lat Pulldowns
Seated Row	1RM, 10RM, Estimated 1RM	Wide-Grip Seated Row, Lat Pulldown, Neutral Grip Lat Pulldown, Dumbbell Hammer Curl, Machine Lat Pulldown, Dumbbell Incline Curl, Dumbbell Preacher Curl, Bicep Curl
Lat Pulldown	1RM, 5RM, 10RM, Estimated 1RM	Seated Row, Bicep Curls, Rowing, Supinated Bent-Over Row
Tricep Press	1RM	Bench Press
Lying Triceps Extension	1RM	N/A
Elbow Extension Isokinetic	Peak Torque	Barbell Bench Press, Seated Chest Press, Lying Barbell Triceps Extensions, Triceps Extension
Bicep Curl	1RM	Lat Pulldown, Seated Row, Supinated Lat Pulldown, Lat Rowing, Machine Bicep Curl, Supinated Bent-Over Row, Dumbbell Bicep Curl, Dumbbell Hammer Curl
Bicep Curl Machine	1RM	N/A
Elbow Flexion Isometric	Peak Torque	Bicep Curls (Dynamic), Supinated Bent-Over Row, Supinated Lat Pulldown
Elbow Flexion Isokinetic	Peak Torque	Lat Pulldown, Seated Row, Bicep Curl, Standing Barbell Bicep Curl, Scott Bench Bicep Curl

Effort was made to use similar verbiage as manuscripts to best represent the classification decisions. RM = repetition maximum.

3 STATISTICAL ANALYSIS

This meta-analysis was performed using the *brms* and *metafor* packages in the R language and environment for statistical computing (v 4.0.2; R Core Team, https://www.r-project.org). The extracted dataset, analysis scripts, estimates, plots, and supplementary materials are available on the Open Science Framework (https://osf.io/6z3xu). Given the goal of this analysis, we have opted to avoid dichotomizing our findings and therefore did not employ traditional null hypothesis significance testing (39). Rather, we took an estimation-based approach within a Bayesian framework in which effect estimates and their precision were interpreted continuously and probabilistically (40). As many of the included studies had multiple groups and reported effects within these groups for multiple outcomes, we opted to calculate effect sizes in a nested structure.

Therefore, for our primary analyses, multilevel arm-based meta-regression models (41,42) were performed with study, group, and observation included as nested random intercepts in the model (i.e., observations were nested within groups which were nested within studies). To account for potential heterogeneity in the fixed effects between studies, we planned to include random slopes on the study-level for the dose-related variables (i.e., volume/frequency). However, in nearly all cases there were unresolvable model warnings (e.g., divergent transitions); thus, random slopes were omitted in favor of model parsimony. Effects were weighted by inverse sampling variance to account for the observation-level, within-study, and between-study variance. Models were constructed with effect sizes, and variances thereof, calculated as response ratio using the *escalc* function (43,44). Specifically, response ratios were calculated as the sum of the natural logarithm of the ratio of post-test and pre-test means, which were later exponentiated (i.e., e^x) and thereby converted to percentage change scores to aid practical interpretation. Importantly, because typical standardized mean differences (i.e., hedges' g) and response ratios operate on different scales (i.e., additive vs. multiplicative) that may have implications on model selection (45), we also calculated effect sizes as a standardized mean change or the difference between post-test and pre-test means, divided by the pooled pre-test standard deviation with an adjustment (i.e., C) for small sample bias. Formulas for each effect size and their variances can be seen below:

$$SMC = C\left(\frac{Mean_{post} - Mean_{pre}}{SD_{pre}}\right) \;\; ; \; C = 1 - \left(\frac{3}{4(n-1)-1}\right)$$

$$var(SMC) = \frac{2(1-r)}{n} + \frac{(SMC)^2}{2 \cdot n}$$

$$RR = ln\left(\frac{Mean_{post}}{Mean_{pre}}\right)$$

$$var(RR) = \frac{(SD_{post})^2}{n \cdot (Mean_{post})^2} + \frac{(SD_{pre})^2}{n \cdot (Mean_{pre})^2} - \frac{2 \cdot r \cdot (SD_{post}) \cdot (SD_{pre})}{n \cdot (Mean_{post}) \cdot (Mean_{pre})}$$

$$RR_{exp} = \left(e^{lnRR} - 1\right) * 100$$

Few studies reported the pre-intervention to post-intervention correlations required to determine the variance for the effect sizes. Therefore, the available data were used to retroactively calculate pre-to-post correlations if possible (46). Then, we took the median of these approximated correlation coefficients and imputed this estimate for the studies where we were unable to obtain the required data. Similarly, if the standard deviations needed to calculate the effect sizes were missing, approximation methods were used via referencing a weighted coefficient of variation (47). Marginal and conditional R^2 were calculated to quantify the proportion of variance explained by only the fixed effects and the sum of the fixed and random effects, respectively (48).

To account for potential nonlinear dose–response relationships between volume/frequency and RT outcomes, the following functional forms for all model structures described above were preliminarily fit with the *metafor* package as random intercept models with both type of effect sizes and subsequently compared using the *performance* package (49), utilizing a Bayesian Information Criterion (BIC) approximated Bayes Factor to determine under which model the observed data are the most probable for each outcome (i.e., muscle hypertrophy and strength). Importantly, a Bayes Factor was calculated for each model relative to an intercept-only model and subsequently averaged between effect sizes. The model that performed the best after accounting for effect sizes on both additive and multiplicative scales was considered the “best fit”:

1. Linear
2. Restricted Cubic Spline (4 knots)
3. Linear-log
4. 2nd Order Polynomial
5. Square Root
6. Quadratic Term
7. Reciprocal

While both effect sizes were used for model selection, response ratio models are reported. All models included the following fixed effects: 1) weekly set volume or frequency ('total,' 'fractional,' or 'direct'), 2) a linear term of frequency in volume models or volume in frequency models, 3) duration (i.e., weeks) of the training intervention (continuous), and 4) training status of the participants (binary categorical).

Marginal effects (means) with 95% compatibility intervals (quartile-based credible and prediction intervals) were extracted for the main effect of weekly set volume or frequency (adjusted proportionally for all other predictors) using the *emmeans* package (50). To better approximate the absolute magnitude of all model predicted effect sizes, all presented estimates have been control adjusted in that the mean effect size predicted at a dose of 0 was contrasted with the mean effect size predicted at every other dose. Therefore, the models represent effect sizes and compatibility intervals of a given volume/frequency value relative to the control effect.

Following the determination of the best fit volume models for each outcome (i.e., muscle hypertrophy or strength), interaction moderator analyses were performed with the *metafor* package to investigate the influence of a variety of factors related to study design and participant characteristics primarily for future hypothesis generation. Specifically, separate models were fit for each moderator that maintained the same structure as the best fit model from the primary analysis, but also included a linear main effect and interaction term between weekly set volume and the moderator of interest (i.e., age, sex, proximity to failure, etc.). Given differences in the number of effects between levels of the moderator, non-training control groups and effects from frequency studies were not included to ensure undue weight was not provided to these effects.

To answer the research questions, our data set included studies that manipulated training volume and/or frequency. Therefore, the primary volume meta-regression models also included data from studies manipulating frequency. Similarly, the primary frequency meta-regression models also included data from studies manipulating volume. The inclusion of these indirect effects improves statistical power/precision and thus the ability to detect small but potentially practically relevant effects (51). Although between-study heterogeneity such as these design characteristics are explicitly accounted for in the multilevel structure and fixed effects of the primary meta-regression models, efforts were made to also acknowledge strict inclusion criteria approaches (i.e., only direct comparisons). Specifically, traditional multilevel contrast-based meta-analytic models were fit utilizing between condition effect sizes. First, we examined an intercept only model which compared "higher" vs. "lower" volumes/frequencies. Additionally, two-stage

fixed-effect meta-regression models were performed. In the first stage, independent sample size weighted linear models were fit for each outcome within each study, extracting the intercept and slope for each and then pooled per study. These estimates were then again weighted by sample size and pooled for each study in a multivariate model allowing for the residual correlations between the intercepts and slopes to be accounted for. In the second stage, the intercepts and slopes were meta-analyzed across studies again using a multivariate model to account for the residual correlation between estimates. The posterior distributions of the pooled intercept and slope were utilized to create dose-response predictions. A linear form was used for both stages due to limitations of the number of observations included per regression model in stage one. We view the purpose of these additional meta-analytic approaches that only utilize direct comparisons as verification that the primary meta-regression models are not unduly biased in some way by confirming their directionality and magnitude do not differ substantially from the models that only contain direct comparisons. This verification is with the understanding that these models contain far fewer observations and thus will have less precision in their effect estimates, on average, and potentially lose the beneficial aspects of effect regularization from partial pooling and shrinkage featured in the primary models. There was not an irreconcilable contradiction in the results of any of the best fit models; however, these models potentially aid in interpretation.

Finally, to assess the relative evidence for each volume/frequency quantification method ('total'/'fractional'/'direct'), Bayes Factors for each pairwise comparison between primary meta-regression models were calculated. The resulting Bayes Factor provided a measure of the relative evidence of which model (i.e., method of quantifying volume/frequency) was the most probable given the available data. The strength of evidence was interpreted based on the Kass and Raferty scale (52).

4 RESULTS

4.1 Search Results

Figure 1 details the search process (53). The search strings identified 6,677 publications for potential inclusion. Citation searching yielded 16 additional studies for screening, and this included studies the authors became aware of upon publication after April 2023. Once duplicates were removed, 6,515 studies remained. After title and abstract screening, 135 publications remained. Finally, full texts were assessed for eligibility, and 67 studies were included. In cases where the manuscript provided insufficient information for data

extraction, attempts were made to contact the authors to gain further information and include the publication.

4.2 Quality Assessment

The mode TESTEX score was 12/15 (range = 8-14/15; https://osf.io/z6rtb). The mode study quality score was 3/5 (range = 1-5/5). The mode study reporting score was 8/10 (range = 4-10/10). Qualitative assessment of funnel plots and effective sample size approximated bias-adjusted estimates did not indicate small-study bias. Contrast-based meta-analyses and two-stage meta-regressions returned no consistent indication of larger-than-expected heterogeneity in results. These analyses can be found in the supplementary materials (https://osf.io/6z3xu).

4.3 Study Characteristics

A breakdown of the 67 studies (25–37,54–107) consisting of 2,058 participants included in this analysis can be found in the supplementary files (https://osf.io/86g9r). Training interventions lasted 10.42 ± 4.48 weeks and the age of the participants was 25.16 ± 5.22 years. Twenty eight studies included untrained participants and 39 studies included trained participants. A visual summary of the training interventions from the included studies can be seen in Figure 2. The median values of the primary RT variables in training groups (i.e., excluding control effects) for muscle hypertrophy effects, using the 'fractional' quantification method, were as follows: volume–10.5 sets per week; frequency–2 sessions per week; interset rest–1.75 minutes; average repetitions per set–10. The average values for these metrics were 13.00 ± 8.87 sets per week, 2.33 ± 0.98 sessions per week, 1.80 ± 0.68 minutes, and 10.63 ± 3.53 repetitions per set. Regarding training groups for muscle strength effects, the median values were 6 sets per week, 2 sessions per week, 2 minutes, and 10 repetitions per set. The average values for these metrics were 8.14 ± 6.23 sets per week, 1.97 ± 0.92 sessions per week, 2.04 ± 0.79 minutes, and 9.85 ± 3.19 repetitions per set. The majority of effects utilized protocols with some sort of failure definition (e.g., momentary/concentric/muscular/volitional failure, 0 repetitions in reserve, repetition maximum) definition; 78.47% of effects were categorized as failure training for hypertrophy and 78.12% for strength. When reported, the time between the final RT session and post-testing muscle size assessments was ≥ 48 hours for 96.07% of hypertrophy effects; however, 30.45% of effects did not report this information. A visualization of muscle size assessment timelines can be found in the supplementary materials (https://osf.io/gx2zn).

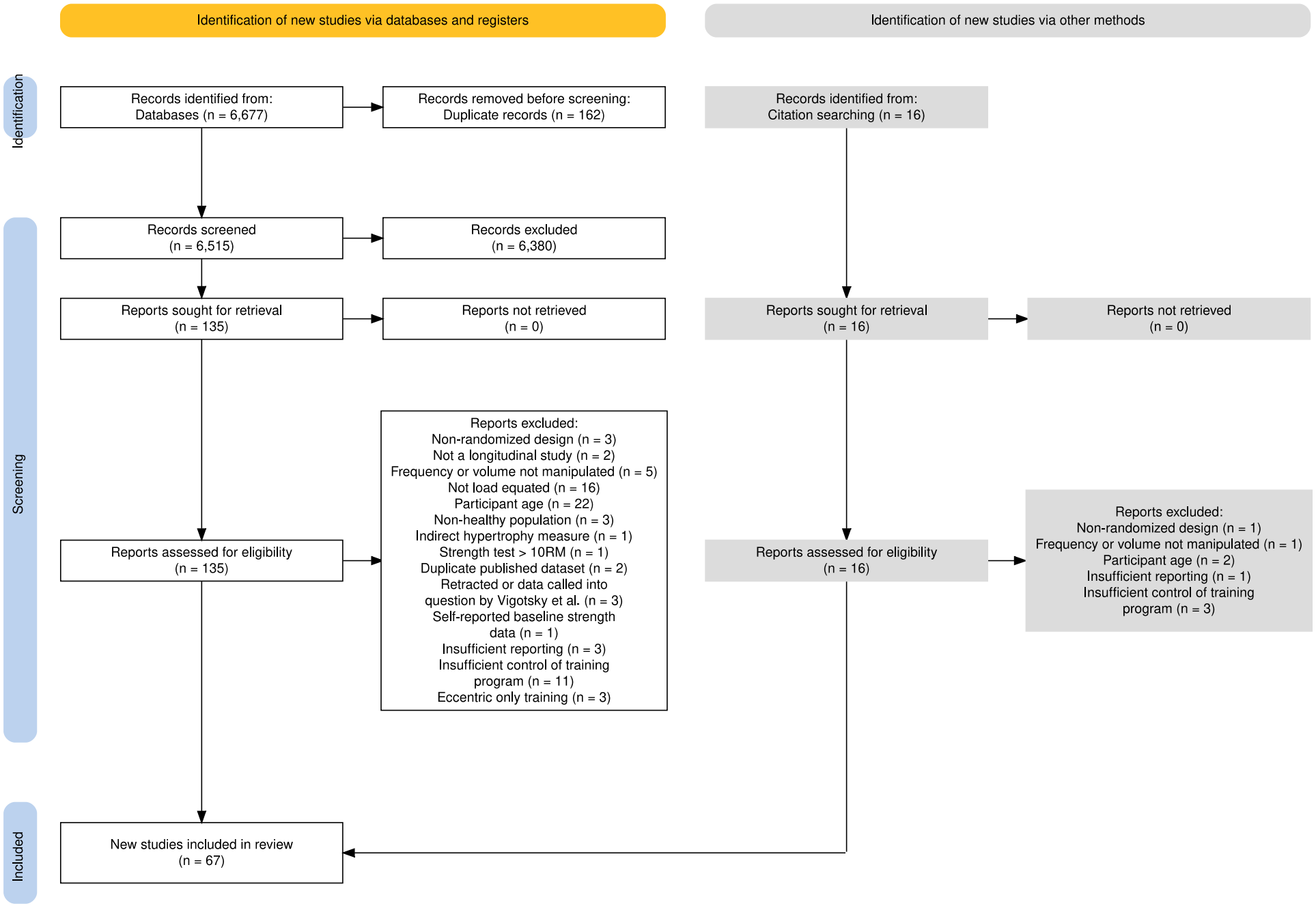

Figure 1: *PRISMA Flow Diagram*

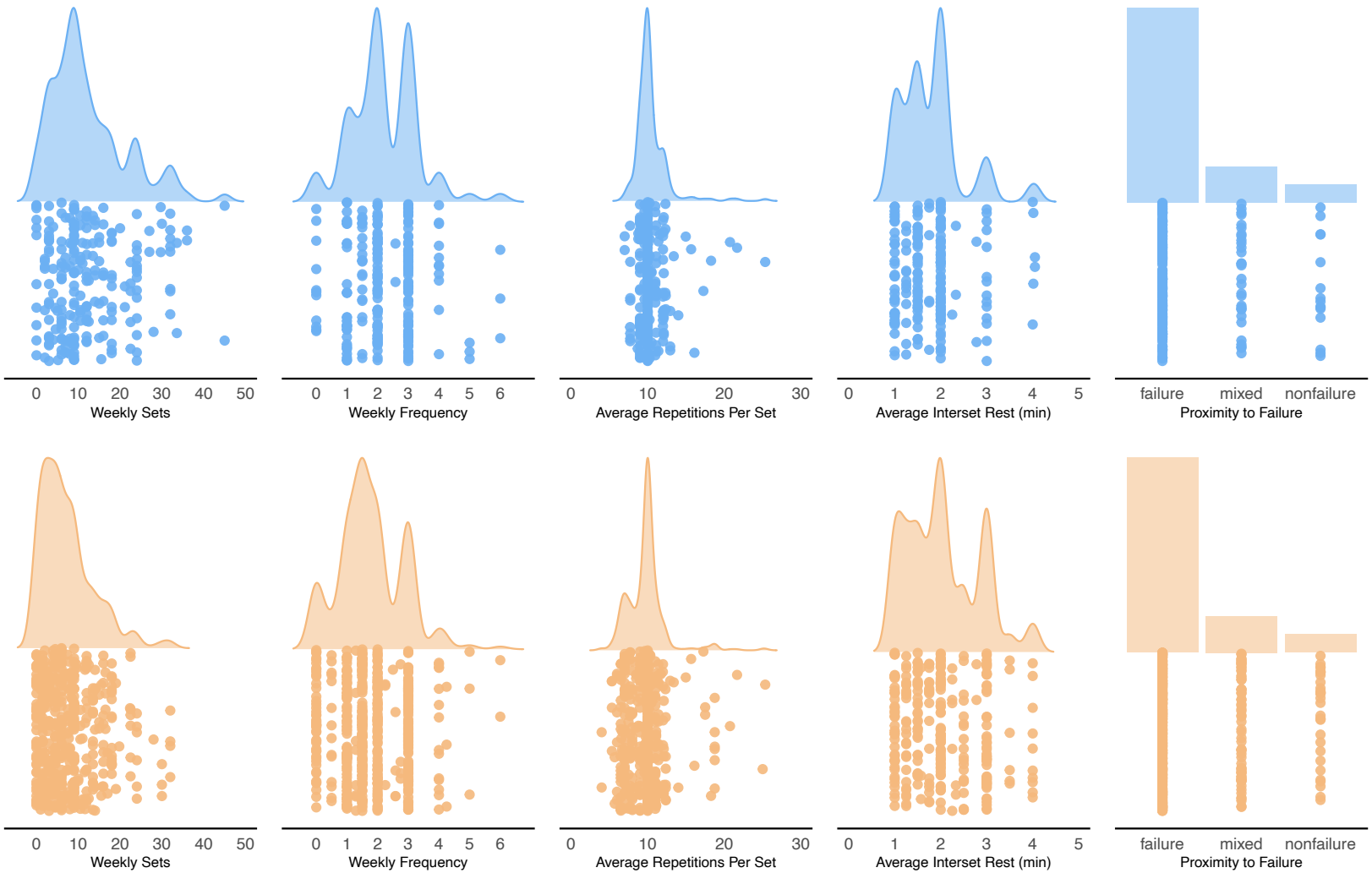

Figure 2: *Raincloud plots providing a visual summary of 220 hypertrophy (blue) and 490 strength (orange) effects included in the analysis. Each data point represents an effect. Values were weighted in accordance with the 'fractional' volume quantification method. Regarding repetitions per set, non-training control effects are not displayed and one data point at 51 repetitions for both hypertrophy and strength is not displayed for visual ease. Regarding interset rest, non-training control effects and single-set protocols are not displayed; additionally, 4 hypertrophy and 62 strength effects did not have a value (insufficient reporting). Regarding proximity to failure, non-training control effects are not displayed; additionally, 16 strength effects did not have a value (insufficient reporting).*

4.4 Volume/Frequency Quantification Method Comparison

Meta-regressions for each volume/frequency quantification method ('total'/'fractional'/'direct') were modeled for each strength and hypertrophy. The analysis of the relative evidence for each best fit model in terms of 2 x Log(Bayes Factor[BF]) values (52) is presented in Figure 3. Regarding frequency for muscle hypertrophy, there was strong evidence that 'fractional' outperforms 'total' (2 x Log(BF) = 9.96) and very strong evidence that 'fractional' outperforms 'direct' (2 x Log(BF) = 10.82). Regarding frequency for muscle strength, there was very strong evidence that 'fractional' outperforms 'total' (2 x Log(BF) = 31.27) and 'direct' (2 x Log(BF) = 54.84). Regarding weekly set volume for muscle hypertrophy, there was strong evidence that 'fractional' outperforms 'total' (2 x Log(BF) = 9.48) and very strong evidence that 'fractional' outperforms 'direct' (2 x Log(BF) = 10.29). Regarding weekly volume for muscle strength, there was very strong evidence that 'fractional' outperforms 'total' (2 x Log(BF) = 18.21) and 'direct' (2 x Log(BF) = 45.96). Given the evidence was strongest for the 'fractional' model, the following sections will focus on the results for this quantification method. Results for 'total' and 'direct' can be found in the supplementary materials (https://osf.io/6z3xu).

4.5 Frequency Analysis

The following sections will present the results of meta-regression models for the effects of 'fractional' frequency on hypertrophy and strength. Specifically, we will indicate the best fit of the candidate models; then, we will evaluate the overall quality of the model fit (i.e., R^2) and the marginal slope for the main effect of frequency (i.e., the slope at the mean of frequency after adjusting for volume, intervention duration, and training status). Full model summary tables with extracted estimates can be found in the supplementary materials (https://osf.io/6z3xu).

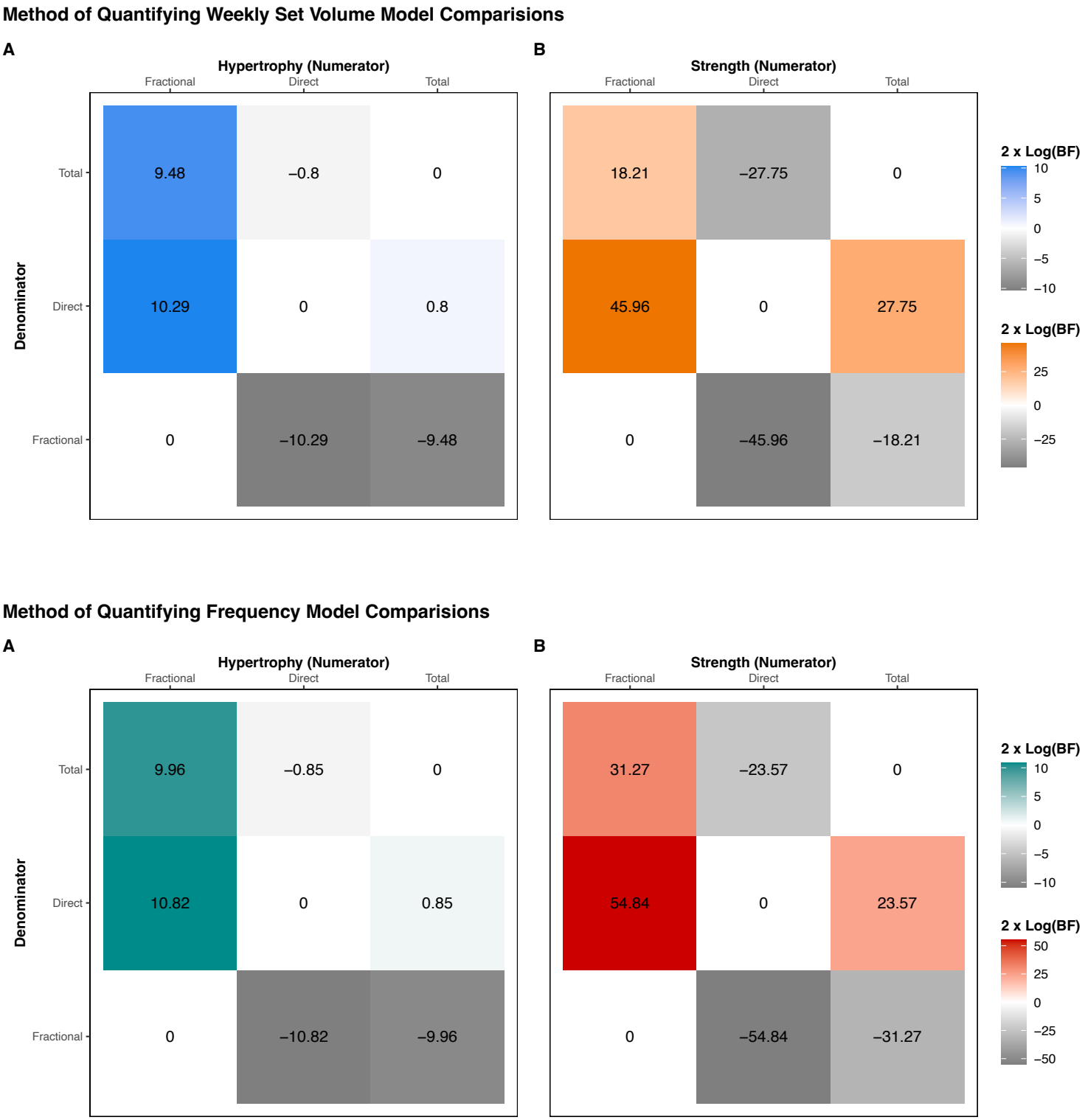

Figure 3: *Relative evidence for models using the Kass and Raftery scale: < 0 = negative evidence in favor of the numerator; 0 < 2 = weak evidence in favor of the numerator; 2 < 6 = positive evidence in favor of the numerator; 6 < 10 = strong evidence in favor of the numerator; ≥ 10 = very strong evidence in favor of the numerator.*

4.5.1 Frequency: Muscle Hypertrophy Outcomes

The multilevel meta-regression models for the effect of 'fractional' frequency on hypertrophy included 35 studies, 220 effects, and 1,032 participants. Model comparisons revealed the reciprocal model was the best fit (Figure 4). The fixed effects of the model explained less than a quarter of the total variance ($R^2_{marginal}$ = 21.9%; $R^2_{conditional}$ = 73.1%). The marginal slope was positive with a 91.3% probability the linear slope is greater than 0; thus, the credible interval contained the null point estimate (β = 0.32% [95% CrI: -0.14%, 0.82%]). The best fit model and slope indicates that hypertrophy may exhibit a positive dose-response relationship with increasing weekly frequency but the effect is inconsistent and compatible with negligible effects.

The additional models containing only direct effects — two-stage meta-regression and contrast-based meta-analysis — included 15 studies, 78 effects, and 370 participants. These models confirm the compatibility with negligible effects found in the primary meta-regression and can be found in the supplementary materials (https://osf.io/rakvh).

4.5.2 Frequency: Muscle Strength Outcomes

The multilevel meta-regression models for the effect of 'fractional' frequency on strength included 66 studies, 490 effects, and 2,020 participants. Model comparisons revealed the reciprocal model was the best fit (Figure 4). The fixed effects of the model explained about a quarter of the total variance ($R^2_{marginal}$ = 25.7%; $R^2_{conditional}$ = 75.1%). The marginal slope was positive with a 100% probability the linear slope is greater than 0; thus, the credible interval did not contain the null point estimate (β = 3.27% [95% CrI: 2.74%, 3.84%]). The best fit model and slope indicates that strength exhibits a dose-response relationship with increasing weekly frequency with diminishing returns.

The additional models containing only direct effects — two-stage meta-regression and contrast-based meta-analysis — included 27 studies, 148 effects, and 700 participants. These models qualitatively confirm the primary meta-regression results and can be found in the supplementary materials (https://osf.io/wt6y9).

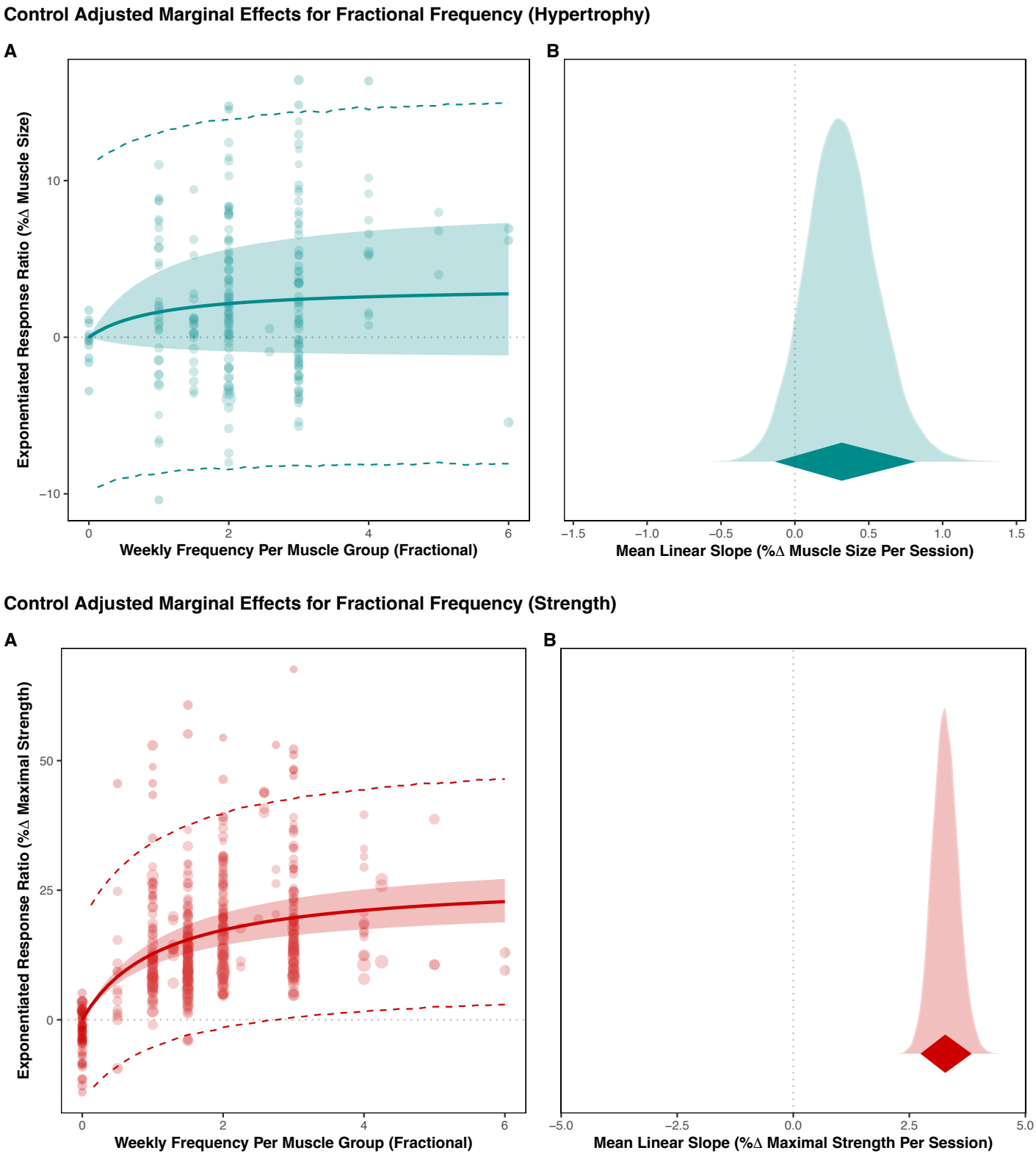

Figure 4: *Fractional weekly frequency best fit multilevel meta-regression for hypertrophy (reciprocal model) and strength (reciprocal model) analyzed as an exponentiated response ratio. Data are presented as estimated marginal means (solid line) with 95% quantile-based compatibility intervals (light band = credible, dotted band = prediction) after adjusting for volume, intervention duration, and training status. Colored circles represent the effect size of each observation included in the analysis, with the size of each circle representing its weight determined by inverse variance weighting. Panels labeled B represent the linear slope at the mean value of fractional frequency for all effects. In all panels, the main effect for fractional frequency is presented at the mean of the continuous fixed effects (i.e., fractional volume and intervention duration) and proportionally marginalized across the categorical fixed effect (i.e., training status).*

4.6 Volume Analysis

The following sections will present the results of meta-regression models for the effects of 'fractional' weekly set volume on hypertrophy and strength. Specifically, we will indicate the best fit of the candidate models; then, we will evaluate the overall quality of the model fit (i.e., R^2) and the marginal slope for the main effect of volume (i.e., the slope at the mean of volume after adjusting for frequency, intervention duration, and training status). Full model summary tables with all extracted estimates can be found in the supplementary materials (https://osf.io/6z3xu).

4.6.1 Volume: Muscle Hypertrophy Outcomes

The multi-level meta-regression models for the effect of 'fractional' weekly set volume on hypertrophy included 35 studies, 220 effects, and 1,032 participants. Model comparisons revealed the square root model was the best fit (Figure 5). The fixed effects of the model explained about a quarter of the variance ($R^2_{marginal}$ = 22.3%; $R^2_{conditional}$ = 73.3%). The marginal slope was positive with a 100% probability the linear slope is greater than 0; thus, the credible interval did not contain the null point estimate (β = 0.24% [95% CrI: 0.15%, 0.33%]). The best fit model and slope indicates that hypertrophy exhibits a dose-response relationship with increasing weekly volume with diminishing returns. The degree of diminishing returns relative to the SDES is displayed in Table 2A.

The additional models containing only direct effects — two-stage meta-regression and contrast-based meta-analysis — included 17 studies, 121 effects, and 544 participants. These models qualitatively confirm the primary meta-regression results and can be found in the supplementary materials (https://osf.io/47zgs).

4.6.2 Volume: Muscle Strength Outcomes

The multilevel meta-regression models for the effect of 'fractional' weekly set volume on strength included 66 studies, 490 effects, and 2,020 participants. Model comparisons revealed the reciprocal model was the best fit (Figure 5). The fixed effects of the model explained about a quarter of the variance ($R^2_{marginal}$ = 26.1%; $R^2_{conditional}$ = 74.8%). The marginal slope was positive with a 100% probability the linear slope is greater than 0; thus, the credible interval did not contain the null point estimate (β = 0.21% [95% CrI: 0.16%, 0.26%]). The best fit model and slope indicates that strength exhibits a dose-response relationship

with increasing weekly volume with strong diminishing returns and a functional plateau. The degree of diminishing returns relative to the SDES is displayed in Table 2B.

The additional models containing only direct effects — two-stage meta-regression and contrast-based meta-analysis — included 32 studies, 257 effects, and 972 participants. These models qualitatively confirm the primary meta-regression results and can be found in the supplementary materials (https://osf.io/sbqxy).

4.6.3 Volume: Interacting Moderators

Data visualization from all interaction moderator analyses for the effects of 'fractional' weekly set volume can be found in the supplementary materials (https://osf.io/6z3xu). These analyses should be interpreted with caution, as the number of observations that contribute to the effects are substantially reduced when compared to the main models, thereby reducing the precision of the estimates. Further, there were often no direct examinations of these interactions and we did not attempt to uniquely isolate the causal effect in the case of each moderator. Therefore, we view the role of these exploratory moderators primarily to generate future hypotheses.

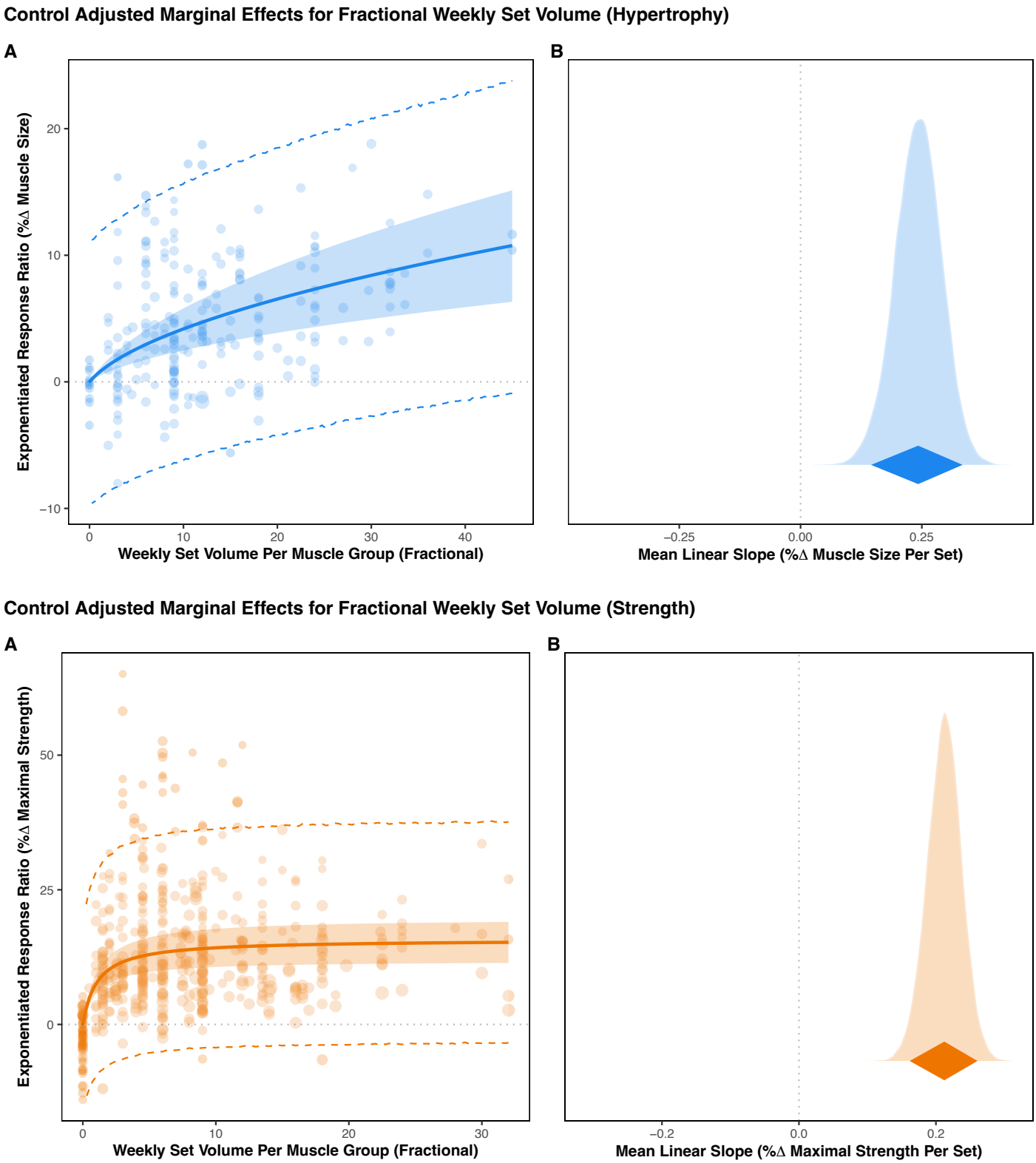

Figure 5: *Fractional weekly set volume best fit multilevel meta-regression for hypertrophy (square root model) and strength (reciprocal model) analyzed as an exponentiated response ratio. Data are presented as estimated marginal means (solid line) with 95% quantile-based compatibility intervals (light band = credible, dotted band = prediction) after adjusting for frequency, intervention duration, and training status. Colored circles represent the effect size of each observation included in the analysis, with the size of each circle representing its weight determined by inverse variance weighting. Panels labeled B represent the linear slope at the mean value of fractional volume for all effects. In all panels, the main effect for fractional volume is presented at the mean of the continuous fixed effects (i.e., fractional frequency and intervention duration) and proportionally marginalized across the categorical fixed effect (i.e., training status).*

Table 2A: Volume Efficiency Tiers for Hypertrophy

Tier	Fractional Weekly Sets	Description
Minimum Effective Dose	4	Sufficient to elicit detectable hypertrophy
Higher Efficiency	5 - 10	~6 additional weekly sets required for additional detectable hypertrophy
Intermediate Efficiency	11 - 18	~8.5 additional weekly sets required for additional detectable hypertrophy
Lower Efficiency	19 - 29	~10.75 additional weekly sets required for additional detectable hypertrophy
Lowest Efficiency	30 - 42	~12.5 additional weekly sets required for additional detectable hypertrophy
Unclear	43 +	Insufficient data to inform efficiency or potentially less hypertrophy

Table 2B: Volume Efficiency Tiers for Strength

Tier	Fractional Weekly Sets	Description
Minimum Effective Dose	1	Sufficient to elicit detectable strength gain
Higher Efficiency	2	~0.75 additional weekly set required for additional detectable strength gain
Intermediate Efficiency	3 - 4	~2.25 additional weekly sets required for additional detectable strength gain
Lower Efficiency	5 - ?	Additional weekly sets do not consistently enhance strength gains > SDES

The minimum effective dose was defined as the volume at which the estimated marginal mean exceeds the Smallest Detectable Effect Size (SDES). The SDES is 2.05% for hypertrophy and 3.96% for strength. Volume efficiency tiers were determined by the number of additional sets required for an incremental increase in the estimated marginal mean that exceeds the SDES.

5 DISCUSSION

The present meta-regressions explored the dose-response relationships of RT volume (weekly sets) and frequency (sessions per week) on the effects of muscle hypertrophy and strength gains. As volume increases, our results indicate that both muscle hypertrophy and strength gains tend to increase; however, the diminishing returns are stronger for strength gains. As frequency increases, our results indicate that there is a negligible effect for muscle hypertrophy but a meaningful effect with diminishing returns for strength gains. These relationships can inform future research and the conceptual understanding for practitioners in regard to how RT dosage influences muscle hypertrophy and strength gains.

5.1 Volume/Frequency Quantification Methods

Set volume and frequency have typically been quantified as the number of sets and sessions per muscle group/movement per week, respectively (1,3,6,7,14–18,108). Descriptions of these quantifications have been rather general, and given accurately exploring the RT dose-response requires accuracy of the independent variables, the present study explored multiple volume/frequency quantification methods. Each RT set was classified as direct or indirect based on its specificity to the hypertrophy or strength measurement. Then, weekly volume/frequency for indirect sets was quantified as 1 for 'total,' 0.5 for 'fractional,' and 0 for 'direct.' As a result, 'total' refers to the RT dosage with any meaningful involvement of the measured muscle for hypertrophy or the muscle(s) involved in the strength assessment. 'Direct' refers specifically to the primary force generator in the exercise for hypertrophy or the exact exercise assessed for strength. 'Fractional' represents a balance between 'total' and 'direct.'

All Bayes Factors, used to quantify the relative support for one model over another, favored the models for the 'fractional' quantification method. The support for the 'fractional' quantification method can be categorized as 'strong,' or 'very strong' per the Kass and Raftery scale (52). Indeed, it is unlikely that any involvement of a muscle group in an RT set should be quantified equally for muscle hypertrophy (10–13). For instance, direct sets are likely to expose the primary force-generating muscle to a closer proximity to failure, which may enhance the hypertrophic training stimulus (109). Regarding muscle strength, indirect sets generally contribute to the strength assessment but are unlikely to be as effective as the specific movement (10,11,110).

In addition to practical insight for volume/frequency quantification for researchers and practitioners, the present study provides indirect evidence into the effects of direct vs. indirect sets on muscle growth and strength gains. Specifically, it appears that on average, the hypertrophic and strength stimulus of an indirect set is close to half the effect of an indirect set. However, the 'fractional' quantification method suffers from the assumption that all indirect training should be quantified as half a set. Therefore, future research may wish to investigate factors influencing the stimulus from indirect sets.

5.2 Frequency & Hypertrophy Dose-Response

The primary meta-regression indicated an inconsistent dose-response relationship between weekly 'fractional' frequency and muscle hypertrophy, with a reciprocal model as

the best fit and a 91.3% posterior probability the linear slope is greater than zero. While this indicates a potential slight positive effect of frequency, it should be noted that: i) the credible interval of the marginal slope was compatible with negligible effects, and ii) the contrast-based meta-analysis and two-stage meta-regression of only direct effects did not indicate an effect of frequency. In aggregate, our results suggest that any independent effect of additional frequency is small and is not consistently identifiable across modeling methods.

These results align with previous meta-analyses (19,111) and are most comparable to a 2019 meta-analysis by Schoenfeld et al. (14) reporting no significant effect of frequency in volume-equated studies utilizing direct hypertrophy measures (ES = 0.07 [95% CI: -0.08, 0.21]). The present meta-analysis utilizes additional data and bolsters the lack of a consistently identifiable independent effect of frequency on muscle hypertrophy. However, the 91.3% likelihood the linear slope is greater than 0 for the primary meta-regression, along with the wide uncertainty interval of the linear slope, permits additional study into the potential programming configurations (e.g., muscle group trained, training status, proximity to failure) that may elicit greater muscle hypertrophy with higher frequencies.

Although more data is needed to conclusively establish the dose-response of frequency on hypertrophy, other data can be considered to generate hypotheses for future studies. Mechanistic data indicate that muscle protein synthesis (MPS) is meaningfully reduced 48 hours after an RT bout in untrained individuals (112) and may even return to baseline in trained individuals (113,114). When paired conceptually with the lack of a consistent, independent effect of frequency in the present meta-analysis, multiple potential explanations exist. These include: i) the MPS timelines reported in acute research do not necessarily represent hypertrophic effects, perhaps in part or entirely related to muscle damage repair confounding MPS elevations (115); ii) the collective training status of the included participants was not sufficiently advanced, resulting in an extended anabolism period post-training, which may have obscured the beneficial effects of higher frequency; iii) there is no plateau in hypertrophy with increasing per session volumes; iv) the average weekly ‘fractional’ set volume of 13.00 ± 8.87 in the included studies may have resulted in per session volumes that were either too high or too low, preventing beneficial effects of higher frequencies to be observed (116); v) an unidentified negative effect of higher frequency counteracts the theoretical positive effects. Please refer to our parallel project for additional insight on the effects of per session volume (117).

5.3 Frequency & Strength Dose-Response

The primary meta-regression indicated a positive dose-response relationship between weekly 'fractional' frequency and strength gains, with a reciprocal model as the best fit and a 100% posterior probability of the marginal slope exceeding zero. This, along with the contrast-based meta-analysis and two-stage meta-regression finding positive effects of frequency, indicates a dose-response relationship between frequency and strength gain. This finding is in contradiction to previous meta-analyses on the independent effects of frequency on strength gains (16–18) and adds additional insight to analyses reporting a significant effect (111). Across these previous meta-analyses, no consensus exists on the definition of frequency, and whether indirect training (i.e., exercises different from the strength assessment but training the involved muscles) counts towards weekly frequency has remained inconsistent.

The inclusion criteria and statistical analysis used in the present meta-regressions most closely align with a meta-regression by Grgic et al. (17), which reported no statistically significant relationship (p = 0.421) between frequency and 1RM strength gains in volume-equated studies. However, instead of necessarily different findings, the present meta-regressions build off of this analysis by exploring nonlinear models, a novel frequency quantification method, and additional data. Indeed, the effect size reported by Grgic et al. (17) increased notably from a frequency of 1 (ES = 0.53 [95% CI: 0.13, 0.93]) to a frequency of 2 (ES = 0.80 [95% CI: -0.25, 1.86]), which aligns with the increase seen in the control adjusted estimates for the reciprocal best fit model when increasing from a 'fractional' frequency of 1 (ES = 12.72% [95% CrI: 10.57%, 15.05%]) to 2 (ES = 17.32% [95% CrI: 14.34%, 20.56%]). Beyond this point, accelerating diminishing returns occur.

Higher frequencies allow for more frequent practice with the assessed exercise or a similar motor pattern. Indeed, simply practicing the test provides a robust stimulus for strength gains (118). The dose-response relationship found in the present meta-analysis indicates that additional exposures, and not simply additional sets, can enhance strength gains albeit with diminishing returns. Therefore, in addition to potential beneficial effects on muscular adaptations, it is possible that higher frequencies lead to higher *quality* practice, ultimately increasing training performance and therefore loads used (119). However, there is conceivably a point in which higher frequencies do not permit sufficient recovery and negatively impact training performance. Further research is necessary to investigate this hypothesis.

It should be noted that the dose-response relationship between frequency and strength gains is limited to the training protocols used in the included studies. The average weekly 'fractional' set volume of 8.14 ± 6.23 in the included studies is relatively low; therefore, further analysis is required to explore the dose-response of per session volume and strength gains. Please refer to our parallel project for additional insight on the effects of per session volume (117)**.**

5.4 Volume & Hypertrophy Dose-Response

The primary meta-regression indicated a positive dose-response relationship whereby higher weekly 'fractional' set volumes resulted in greater muscle hypertrophy, with a 100% posterior probability of the marginal slope exceeding zero. These findings align with previous meta-analytic work (1,5,6,19) and expands on them by including new data and exclusively site-specific, direct hypertrophy measures. Our analysis emphasizes within-study, between-group effects of different volumes in our multilevel meta-regression model structure and secondary analyses of only direct effects. These factors may explain why the present results report a stronger dose-response relationship compared to meta-analyses that explore the moderating effect of volume on hypertrophy in general RT studies with inclusion criteria allowing for indirect hypertrophy measurements (108,120).

Schoenfeld et al. (1), using only muscle-specific, direct hypertrophy measurements, analyzed weekly set volume as a continuous linear predictor, and reported a 0.38% increase in hypertrophy per additional set. This is comparable to the marginal linear slope in the present meta-analysis, which estimated a 0.24% increase in hypertrophy (95% CrI: 0.15%, 0.33%) per additional set at the average 'fractional' weekly volume of 12.25 sets. The present meta-analysis builds upon the analysis by Schoenfeld et al. (1) by exploring multiple functional forms, both linear and nonlinear, to inform the nature of the dose-response. Indeed, it has been suggested that as volume increases, diminishing marginal hypertrophy occurs, and potentially even an inverted-U in which additional volume will attenuate hypertrophy (1,4,5,84). Mechanistic data indicates greater-post exercise MPS and intracellular anabolic signaling for higher volume protocols in humans (102,121–125); however, a dose-response relationship has been explored using electrically stimulated isometric contractions in male rats, indicating a plateau in MPS but not in p70S6K phosphorylation with additional "sets" (126). The present meta-analysis quantifies this relationship using applied outcomes in humans and supports the notion of diminishing returns but not an inverted-U. The best fit model, as identified by Bayesian Information Criterion approximated Bayes Factors, was a square root model, and indicated diminishing

returns that accelerate with higher volumes. However, given the width of the credible intervals at higher volumes, the best fit model is still compatible with multiple functional forms (e.g., functional plateau, inverted-U).

To quantify the diminishing returns, we reported the dose-response using *efficiency tiers*, which contextualize the findings based on the number of 'fractional' sets required for the point estimate to exceed increments of the SDES. These tiers quantify the increasing incremental volume needed to achieve detectable additional hypertrophy. For instance, the volume required for the final increment of the SDES is more than three times that required for the first increment (i.e., the minimum effective dose). Although this approach indicated that the minimum effective dose occurs with low volume (4 'fractional' weekly sets), the tiers also indicate no clear plateau in the primary meta-regression. Instead, they suggest an increasing number of sets needed to elicit detectable additional hypertrophy. However, caution is warranted as few studies have explored ~25+ 'fractional' weekly sets. Therefore, future research may wish to explore these higher volumes to better inform the dose-response and potential plateau point.

Moderator analyses indicated that the marginal slope of the dose-response relationship between weekly 'fractional' sets and hypertrophy was not often influenced by other variables. However, extreme caution is warranted for all moderator analyses as by nature, these analyses are all indirect effects. Therefore, these moderator analyses should be viewed as hypothesis-generating; to properly explore potential moderators of the dose-response relationship, additional studies specifically designed to do so are required.

5.5 Volume & Strength Dose-Response

The primary meta-regression indicated a positive dose-response relationship between weekly 'fractional' set volume and strength gains, with a 100% posterior probability of the marginal slope exceeding zero. However, the best fit model was reciprocal and indicated strong diminishing returns and a functional plateau. These findings are generally consistent with those of previous meta-analyses (7,108,127,128). Ralston et al. (7) provides valuable insight on relatively low volumes (mean weekly direct set volume = 3.14 ± 2.63) and reported significantly greater strength gains in groups with > 5 compared to ≤ 5 weekly sets (ES = 0.18 [95% CI: 0.06, 0.30]). The present meta-analysis utilized a wider inclusion criteria, higher average volumes, accounted for indirect sets via the 'fractional' quantification method, and explored nonlinear dose-response relationships. As hypothesized by Ralston et al. (7), the present meta-regression provides support for a nonlinear relationship.

Similar to muscle hypertrophy, the best fit model is still compatible with other functional forms, including an inverted-U. Nonetheless, our findings indicate that the dose-response relationship is strongest with low weekly set volumes. Indeed, the estimated effect of one 'fractional' weekly set exceeded the SDES; therefore, one set was identified as the minimum effective dose. Additional increments in the SDES were observed up to approximately 4 'fractional' weekly sets, but not beyond this point. However, the SDES of 3.96% may be greater than what some deem practically relevant; additional sets beyond this point may produce additional strength gains, albeit less than the SDES, prior to the functional plateau. The tabulated data provides additional insight and can be found in the supplementary materials (https://osf.io/cf6p5).

While we did not venture to explore the mechanistic underpinnings of the dose-response relationship, it is interesting to consider the multi-faceted nature of adaptations contributing to muscle strength gains. Learning effects from additional direct sets, and to a lesser extent indirect sets, are likely to contribute to strength gains (118). Furthermore, while not unanimously agreed upon (129), greater hypertrophy from increased set volume may contribute to strength gains (130). Conversely, higher volumes may lead to increased fatigue, as evidenced by the beneficial effects of tapering (131). Notably, elevated fatigue may still be present at post-testing given most of the included studies did not include a taper.

The learning effect component may predominate in the present meta-analysis as many participants in the included studies were presumably performing a novel strength assessment. This may contribute to the large effect observed at one 'fractional' weekly set. Indeed, in well-trained powerlifters, 1-3 direct weekly sets was insufficient to result in meaningful strength gains, but 3-9 direct weekly sets was (132). Therefore, the minimum effective dose and dose-response relationship in novel vs. familiar strength assessments warrants further investigation. The moderator analysis in the present study may provide some insight, but given they rely on indirect effects, future studies directly examining this concept and other moderators are warranted.

5.6 Limitations & Considerations

Several limitations and considerations exist with this meta-analysis. While we have described and quantified the dose-response relationships, it should be emphasized that these relationships are limited to the contexts of the included studies (i.e., training variables, participant characteristics, etc.). For instance, proximity to failure appears to be

an important variable for maximizing muscle hypertrophy (109); however, although 78.47% of hypertrophy effects reported some form of a failure definition, only ~30% had a clear definition of momentary failure (133). Additionally, our moderator analyses on proximity to failure and other variables are extremely limited. Direct research is necessary to determine whether increased hypertrophic effectiveness per set influences the functional form of the dose-response relationships.

Additionally, we did not venture to describe potential indirect negative consequences of high RT dosage (e.g., sustainability, injury, psychological burnout). All analyzed participants must have tolerated the training intervention sufficiently well to receive a post-test value and inclusion in the respective study. These considerations are exacerbated when considering the relatively short average intervention duration of 10.42 ± 4.48 weeks. Further, our analysis focused on site-specific training volume and not overall RT volume. The RT protocols of many included studies were not necessarily balanced throughout the entire body and instead biased towards contributing to improvements in the measurement(s). It remains unclear if the site-specific dose-response relationships are impacted by the overall RT dosage.

Individual-level practical application of these findings depends on many factors. Various physiological factors may influence the hypertrophy or strength gains an individual experiences from a given dosage (102), which may have downstream implications on program requirements for maximum results. Future research may wish to explore individual response variation to different dosages with appropriate study design (134).

Potential inherent limitations exist regarding the independent variables of the present meta-analysis. While a primary aim was to explore the most probable model fits based on different quantification methods of the independent variables ('total'/'direct'/'fractional'), limitations still exist. For instance, volume and frequency were quantified on a weekly time scale, but any choice of time period for quantifying volume and frequency is arbitrary. Therefore, a parallel project by our group explores the dose-response relationships of set volume *per session* on muscle hypertrophy and strength gains (117).

Limitations also exist with the dependent variables used in the present meta-analysis. For instance, while only direct measures of muscle size were used, which are likely more sensitive to hypertrophy (1,135), other factors may influence muscle size measurements (136). For instance, edema sufficient to confound muscle size measurements in the days following training has been reported in novel, highly damaging eccentric training protocols

(137–139). While edema is unlikely to be a major confounder in trained individuals following an 8-set training session (140,141) or in previously untrained participants by the end of a typical training study (142), cautious interpretation of the present results is warranted. This is especially notable given the paucity of data exploring edema's effect on muscle size measurements following higher volume RT.

Although best fit models have been identified, it should be noted that each dose-response relationship remains compatible with multiple functional forms, especially upon the addition of new data at volume/frequency levels with limited data. In particular, additional hypertrophy studies including untrained, non-training control groups are warranted to better inform the initial dose-response.

6 CONCLUSIONS

The dose-response relationships describing the effects of weekly volume and frequency on muscle hypertrophy and strength gains are best represented with the 'fractional' quantification method, where indirect sets are counted as half a set. For muscle hypertrophy, there is a positive dose-response relationship between 'fractional' set volume and muscle hypertrophy, though with diminishing returns. No clear plateau in the dose-response relationship was identified; however, there is additional uncertainty at higher volumes. Increasing 'fractional' frequency, on a volume adjusted basis, appears to have a negligible effect on muscle hypertrophy. For muscle strength, there is a positive dose-response relationship between 'fractional' set volume and strength gains, but with strong diminishing returns and a functional plateau. 'Fractional' frequency also has a positive dose-response for strength gains, though with diminishing returns. The modest quality of overall model fits and the width of the uncertainty intervals suggest that multiple dose-response forms are compatible with the present analysis, particularly upon the addition of future data.

Data and Supplementary Material Accessibility

All materials, data, and code are available on the Open Science Framework project page (https://osf.io/6z3xu).

Author Contributions

JP conceptualized the project, extracted data, assisted with the statistical analysis, and wrote the manuscript. JR conceptualized the project, extracted data, and reviewed the manuscript. ZR conceptualized the project, performed the statistical analysis, and reviewed the manuscript. SH extracted data and reviewed the manuscript. MZ reviewed the manuscript.

Conflict of Interest

Joshua Pelland, Jacob Remmert, Zac Robinson, Seth Hinson, and Michael Zourdos are coaches and writers in the fitness industry.

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