Exploring the Dose-Response Relationship Between Estimated Resistance Training Proximity to Failure, Strength Gain, and Muscle Hypertrophy: A Series of Meta-Regressions

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ABSTRACT

Background: The proximity to failure in which sets are terminated has gained attention in the scientific literature as a potentially key resistance training variable. Multiple meta-analyses have directly (i.e., failure versus not to failure) or indirectly (e.g., velocity loss, alternative set structures) evaluated the effect of proximity to failure on strength and muscle hypertrophy outcomes categorically; however, the dose response effects of proximity to failure have not been analyzed collectively in a continuous manner. **Objective:** To meta-analyze the aforementioned areas of relevant research, proximity to failure was quantified as the number of repetitions in reserve (RIR). Importantly, the RIR associated with each effect in the analysis was estimated based on the available descriptions of the training interventions in each study. Data were extracted and a series of exploratory multi-level meta-regressions were performed for outcomes related to both strength and muscle hypertrophy. A range of sensitivity analyses were also performed. All models were adjusted for the effects of load, method of volume equating, duration of intervention, and training status. **Results:** The best fit models for both strength and muscle hypertrophy outcomes demonstrated modest quality of overall fit. In all of the best-fit models for strength, the confidence intervals of the marginal slopes for estimated RIR contained a null point estimate, indicating a negligible relationship with strength gains. However, in all of the best-fit models for muscle hypertrophy, the marginal slopes for estimated RIR were negative and their confidence intervals did not contain a null point estimate, indicating that changes in muscle size increased as sets were terminated closer to failure. **Conclusions:** The dose-response relationship between proximity to failure and strength gain appears to differ from the relationship with muscle hypertrophy, with only the latter being meaningfully influenced by RIR. Strength gains were similar across a wide range of RIR, while muscle hypertrophy improves as sets are terminated closer to failure. Considering the RIR estimation procedures used, however, the exact relationship between RIR and muscle hypertrophy and strength remains unclear. Researchers and practitioners should be aware that optimal proximity to failure may differ between strength and muscle hypertrophy outcomes, but caution is warranted when interpreting the present analysis due to its exploratory nature. Future studies deliberately designed to explore the continuous nature of the dose-response effects of proximity to failure in large samples should be considered.

1 INTRODUCTION

It is well established that the configuration of resistance training variables, such as set volume [1,2], load (percentage of one-repetition maximum (% of 1RM)) [3,4], and frequency [6] can impact resistance training outcomes. The impact of another variable, proximity to failure, operationally defined as the number of repetitions in reserve (RIR) prior to momentary failure (i.e., the inability to complete the concentric phase of a repetition despite maximal effort to do so) following set termination has gained recent attention in the scientific literature [7,8]. Despite the recent attention on this topic, the specific proximity to failure that maximizes various resistance training outcomes (i.e., muscular hypertrophy and strength gain) remains unclear. Indeed, recent meta-analyses from Grgic et al. [9] and Vieira et al. [10] reported no significant difference for muscle hypertrophy [SMD: 0.15 ($p = 0.237$); SMD: 0.59 ($p = 0.239$)], and strength gain [SMD: 0.01 ($p = 0.860$); SMD: 0.16 ($p = 0.566$)] when comparing volume-equated resistance training interventions in which sets were performed to or not to failure. Moreover, meta-analyses from Jukic et al. [11] and Davies et al. [12] show equivocal outcomes for muscle hypertrophy [SMD: -0.03 ($p = 0.708$); SMD: -0.05 ($p = 0.73$)] and strength gain [SMD: -0.06 ($p = 0.291$); SMD: -0.05 ($p = 0.56$)] when comparing the effects of traditional and alternative set structures; which alter proximity to failure via the manipulation of intra-set rest intervals [13].

Although the data from these meta-analyses [9–12] provide valuable insight into the influence of proximity to failure on resistance training outcomes, they investigate proximity to failure in a categorical (e.g., to failure versus not to failure; traditional versus alternative set structures) fashion despite its continuous nature. This is primarily due to the uncertainty of the proximity to failure achieved across relevant studies; for example, it is difficult to know the RIR upon set termination in non-failure groups due to a lack of reporting, individual differences, and set-to-set fatiuge. Additionally, there is ambiguity in the criteria for set termination [14] in failure groups, further limiting the applicability of these categorical comparisons. Fisher et al. [15] recently suggested investigating proximity to failure in a categorical fashion fails to inform the overall dose-response relationship between proximity to failure and resistance training outcomes. In other words, previous meta-analyses [9–12] have not attempted to ascertain the relationship between the number of RIR per set with muscle hypertrophy and strength gain, which limits the ability to make practical recommendations regarding proximity to failure. Specifically, if proximity to failure in resistance training is only examined in a categorical fashion, it cannot answer the question *"how far from failure should someone train to optimize muscle hypertrophy and strength gain?"*. To our knowledge, no meta-analysis to date has examined proximity to failure as a continuous variable on muscle hypertrophy and strength gain.

The most commonly used method that aims to rectify the limitations of categorically examining proximity to failure is intra-set velocity loss (VL). Intraset VL controls for proximity to failure by prescribing set termination once the concentric velocity of a repetition has declined by a predetermined percentage from a set's fastest (usually first) repetition (e.g., 70% of 1RM to 20%VL). In this way, higher VL thresholds terminate sets closer to failure, while lower VL thresholds terminate sets with a greater number of RIR. Recent meta-analyses [16–20], have indeed included meta-regressions examining the dose-response relationship between intra-set VL and various resistance training outcomes. However, while different VL thresholds lead to a different number of RIR, this method of set termination does not control for the number of repetitions performed in a set or the relative volume (repetitions x sets x % of 1RM) [21,22], which limits conclusions that can be made since training volume is related to muscle hypertrophy and strength gain [1,2]. For example, Pareja-Blanco et al. [23] compared the effects of training the Smith-machine squat to either a 20% or 40% VL threshold for eight weeks with the total number of sets and load equated. These intra-set VL thresholds resulted in the 20% and 40% groups training at an average mean propulsive velocity of 0.69 and 0.58 m·s-1, respectively, suggesting the groups trained at different proximities to failure. However, the 40% VL group performed an average of 40% more repetitions throughout the study (40% VL: 310.5 ± 42 vs. 20% VL: 185.9 ± 22.2 repetitions); thus, the relative volume load was not equated. Studies exist [24,25] that have compared different VL thresholds and controlled for relative volume load but have only been included in one meta-analysis to date [16].

Therefore, this exploratory meta-analysis aimed to investigate the effect of resistance training proximity to failure on muscle hypertrophy and maximal strength gain by combining all of the aforementioned areas of research. To best investigate the effect of proximity to failure continuously and explore potential dose-response relationships, RIR was estimated for the training intervention associated with each effect.

2 METHODS

This exploratory meta-analysis was performed without a systematic search and was not preregistered. First, all studies from the existing relevant meta-analyses [9–12,16–20] were collected. Then, any additional studies we were aware of, or were discovered during data extraction, that met the inclusion criteria were also collected. To be included in this meta-analysis, studies had to: (1) be published in English and either published in a peer-reviewed journal, on a pre-print repository, or as a MSc or PhD thesis; (2) ensure participants had no known medical conditions or injuries; (3) include either set and/or repetition volume-equated conditions; (4) include load-equated conditions (i.e., ± 5% of 1RM); (5) compare at least two different proximities to failure; (6) include measurement(s) of maximal strength (i.e., isometric, isotonic, or isokinetic) and/or direct measurements of muscle hypertrophy (i.e., ultrasound, magnetic resonance imaging [MRI], etc.). Studies that were initially gathered but did not meet these inclusion criteria were excluded. This process was performed by ZR.

Data describing the population studied, specifications of the training intervention, and the outcomes of interest (e.g., muscle hypertrophy and strength) were extracted from studies found to be eligible. In the case that any necessary data were not reported, ZR emailed the authors of the manuscripts requesting the raw or mean values. If the authors did not reply within three months, we resorted to calculating the desired data based on the figures and tables (data was digitized using WebPlotDigitizer; v4.3, Ankit Rohatgi; https://apps.automeris.io/wpd/).

RIR Estimation

To operationally define proximity to failure as a continuous variable, the primary predictor in this meta-analysis was the estimated RIR to which training was performed by each group. Because self-reported RIR was not reported in almost all studies, specific procedures were followed to estimate RIR for every group included in the analysis. A detailed breakdown of the estimation of each study included in the analysis and all estimation equations utilized can be found in supplementary file 1 (https://osf.io/dwbx3). All initial estimations were performed by ZR, and these estimations were subsequently verified by JP, MZ, MR, and IJ. All conflicting predictions were due to manual error and were resolved upon re-estimation. The estimation process categorized studies into one of the following five subgroups: 1) groups training to failure, 2) groups reporting velocity, 3) groups reporting RIR, 4) groups reporting load and repetitions performed, and 5) groups training with alternative set structures.

Groups Training to Failure

The first category of studies consisted of those that included a group training to failure [26–53]. Groups that trained to failure were estimated, by definition, to have trained to 0 RIR. However, due to the ambiguity of the terminology utilized to describe "failure" [7], studies that provided a clear definition (e.g., momentary failure, concentric failure, etc.) and did not indicate participants terminated sets upon their own volition (i.e., volitional failure) were separately coded with an RIR of "-1" for the linear-spline meta-regression model to potentially tease out differences associated with failure definition. All other groups with RIR estimates of 0, including volitional failure, were coded as "0."

In studies that included a group training to failure, if a group did not train to failure but performed sets at an equivalent load, subtraction of the repetitions performed per set was used to estimate RIR. For example, if the group training to failure (i.e., 0 RIR) performed 10 repetitions with 75% of 1RM and the group not training to failure performed 5 repetitions with 75% of 1RM, the number of RIR was estimated to be 5. This was also applied for groups training with a repetition maximum (e.g., 10RM). For example, if a group performed sets of 8 repetitions with a 10RM load, then the estimated RIR was 2.

Groups Reporting Velocity

The second category of studies reported velocity data that allowed for RIR estimations [23–25,54–66]. Utilizing the most representative citations available [67–70], equations were utilized or created to predict the maximum possible number of repetitions at a given load based on the repetitions performed and the intra-set VL. These equations were matched by exercise, loading range, training status, sex, and concentric intended velocity as closely as possible. After the maximum possible number of repetitions was estimated, subtraction could be performed from the repetitions per set provided.

For example, Pareja-Blanco and colleagues [23] reported a mean velocity loss of 41.9 ± 1.9% in the VL40 group. Using the reported average number of repetitions per set (6.5 ± 0.9) and load used (75% of 1RM), the maximum possible number of repetitions was predicted using the regression equations for the Smith-machine squat published by Rodriguez-Rosell et al. [67].

Specifically, at 70% of 1RM, the predicted maximum possible number of repetitions was 8.31. When subtracting the average number of repetitions performed per set reported by Pareja-Blanco et al. [23], the estimated RIR was 1.81. However, because the average load reported was 75% of 1RM, we averaged the estimated RIR created from the equations for 70% and 80% of 1RM from Rodriguez-Rosell [67], resulting in the final estimated RIR for the VL40 group of 1.67. The prediction equations that were used for each velocity loss study can be found in supplementary file 1 (https://osf.io/dwbx3).

Groups Reporting RIR

The third category of studies directly reported RIR, and these values were utilized verbatim for the RIR estimations [38,71–73]. For example, if a group reported the average RIR throughout the study was 2.3, the estimated RIR was also 2.3. If a study reported RIR but also fell into one of the two prior categories (i.e., training to failure or provided velocity data), the other method was used to predict RIR due to its objectivity.

Groups Reporting Load and Repetitions Performed

The next category of studies reported the load and repetitions performed from which RIR estimations were derived [29,30,74–80]. Once again, prediction equations were utilized from the most representative citations available [67–69,81–83] to establish the maximum possible number of repetitions at a given load, to which subtraction of the repetitions performed per set could estimate RIR. These equations were matched by exercise, loading range, training status, sex, and concentric intended velocity as closely as possible. For example, Carneiro et al. [78] had untrained women perform sets of 4 repetitions at 90% of 1RM on the bilateral knee extension. Using the prediction equation created from the data of Hoeger et al. [84], it was estimated that approximately 4.65 repetitions are possible at 90% of 1RM. Thus, subtracting 4 repetitions per set from that estimation led to an estimated RIR of 0.65.

Alternatively, some studies reported load as a percentage of a repetition maximum (RM) other than a 1RM. In this case, the load relative to a 1RM (i.e., % of 1RM), was first predicted. Next, utilizing the predicted percentage of 1RM, the same steps could be followed as previously outlined. For example, Drinkwater and colleagues [74] had trained men perform sets of bench press with percentages of 6RM loads. Therefore, using the prediction equation from Chapman et al. [69] the percentage of 1RM associated with 100% of 6RM was predicted, which equated to 89% of 1RM. Then, the percentages of this value used in Drinkwater et al. [74] were applied to calculate the load per set (e.g., 70% of 89% (6RM) = 62.3% of 1RM). The same steps outlined in the previous paragraph were then followed to predict the maximum possible repetitions at the given load. Finally, the number of repetitions performed per set was subtracted from the predicted maximum possible number of repetitions to estimate RIR.

Groups Training with Alternative Set Structures

For groups training with alternative set structures [27,29–32,34,36,39,41,42,51,65,66,74–80,85], a determination needed to be made as to what constitutes a “set” from which proximity to failure could be evaluated. We decided to treat each group of repetitions performed with any intra-set or inter-set rest between them as an individual set. For rest-pause groups, each of these sets was performed to failure, making the RIR estimation simple (i.e., 0 RIR) [77]. For cluster and rest redistribution groups, this RIR estimation method was chosen because of these set structures’ ability to maintain repetition performance, and thus RIR, compared to traditional set structures.

For example, Iglesias-Soler et al. [86] compared the total number of repetitions performed with a 4RM load on the Smith-machine squat between traditional and cluster set structures in a crossover design. The traditional set condition performed 3 sets to failure, whereas the cluster set condition performed as many repetitions as possible with an individualized inter-repetition rest period (i.e., single-repetition sets). The authors observed that participants were able to increase the total number of repetitions performed by approximately 5-fold with a cluster set structure (Cluster: 45.5 ± 32 repetitions; Traditional: 9.33 ± 1.87 repetitions), indicating RIR was likely maintained for many of the early repetitions. Due to this evidence, along with variability in the initial proximity to failure of each set, intra- and inter-set rest intervals, the load used, sex of the participants, and exercise selection, we determined this estimating RIR for cluster and rest redistribution groups in this manner to be the best course of action.

To illustrate, Farinas et al. [41] investigated the effects of set structure within a unilateral knee extension training program. Participants in the traditional group performed 4 sets of 8 repetitions with a 10RM load and 3-minute inter-set rest periods. Using an equivalent load (i.e., 10RM), the alternative set structure group instead performed 1 repetition every 17.4 seconds until 32 total repetitions were completed. The estimated RIR for each group was calculated by subtracting the number of repetitions performed in each single-repetition set from the maximum possible number of repetitions. Thus, the RIR estimation for the traditional group would be 2 and the alternative set structure group would be 9.

Special Cases

Throughout the estimation process, special case rules were applied to a few groups. Specifically, in these cases, even though a group fell into one of the aforementioned categories, the estimation approach led to subjectively implausible RIR values. These alternative approaches are outlined in supplementary file 1 (https://osf.io/dwbx3).

Additional Details

For each group in the analysis, the estimated RIR was used to represent the average proximity to failure at which sets were terminated. Specifically, averages were developed for both the “muscle” and the “exercise.” For the “muscle” RIR, if a study included multiple exercises, those that primarily trained the muscle site measured or were prime movers in the exercise or joint action tested counted towards the estimation. For example, if a lower body training program included the barbell back squat, knee extension machine, and knee flexion machine, only the RIR estimations of the barbell back squat and knee extension machine would be averaged for quadriceps specific outcomes (i.e., strength or muscle hypertrophy). Alternatively, for the “exercise” RIR, only sets performed on the same exercise that was tested were counted towards the estimation; thus, this is only relevant for dynamic strength outcomes. For example, in the same lower body training program that included the barbell back squat, knee extension machine, and knee flexion machine, only the RIR estimations of the barbell back squat would be used for the exercise RIR. When applicable, the RIR estimations of multiple sets performed by a single group were averaged for the final estimation. Finally, if a RIR estimate was negative, it was recorded as “0.”

3 STATISTICAL ANALYSIS

This exploratory meta-analysis was performed using the ‘*metafor*’ package [87] in R language and environment for statistical computing (v 4.0.2; R Core Team, https://www.r-project.org/). The extracted dataset, analysis scripts, models summaries, and supplementary materials are available on the Open Science Framework (https://osf.io/7knsj/). Given the goal of this analysis, we have opted to avoid dichotomizing our findings and therefore did not employ traditional null hypothesis significance testing [88]. Rather, we took an estimation-based approach in which effect estimates and their precision were interpreted cautiously and probabilistically [89]. As 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, multi-level mixed-effects models [90] with cluster-robust variance estimation [91] were performed with study, group, and observation included as explicitly nested random intercepts in the model (i.e., observations were nested within groups which were nested within studies). Moreover, a range of models were fit and compared including with (1) random intercepts only, (2) the addition of a single random slope for estimated RIR on the study level, (3) the addition of random slopes for estimated RIR on the study and group level to account for potential heterogeneity in the relationship of estimated RIR on these levels. 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 both standardized mean change and response ratio using the '*escalc*' function [92,93]. Specifically, standardized mean changes were calculated as the difference between post-test and pre-test means, divided by the pre-test standard deviation with an adjustment (i.e., C) for a small sample bias. In addition, response ratios were calculated as the sum of the natural logarithm of the ratio of post-test and pre-test means and an adjustment for small sample bias (i.e,. C), which were later exponentiated (i.e., e^x) and thereby converted to percentage change scores to aid practical interpretation. Formulas for each effect size and their variances can be seen below:

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

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

$$RR = C + ln\left(\frac{M_{post}}{M_{pre}}\right) \; ; C = \frac{1}{2}\left(\frac{\left(SD_{post}\right)^2}{n \cdot \left(M_{post}\right)^2} - \frac{\left(SD_{pre}\right)^2}{n \cdot \left(M_{pre}\right)^2}\right) \; ;$$

$$var(RR) = \frac{\left(SD_{post}\right)^2}{n \cdot M_{post}} + \frac{\left(SD_{pre}\right)^2}{n \cdot M_{pre}} + \frac{2r \cdot SD_{post} \cdot SD_{pre}}{M_{post} \cdot M_{pre} \cdot n}$$

$$RR_{exp} = (e^{RR} - 1) * 100$$

No studies reported the pre-intervention to post-intervention correlations required to determine the variance. Therefore, the available data were used to retroactively calculate pre-to-post correlations if possible [94]. Then, we meta-analyzed these approximated correlation coefficients (i.e., Fishers r-to-z transformed correlation coefficient) and imputed this estimate for the studies where we were unable to obtain the required data. Since all meta-analytic models included moderators, statistical heterogeneity was evaluated using I2, which represents the remaining variance that is not already accounted for by the moderators [95]. This heterogeneity was then partitioned across the three levels of the nested random effects (i.e., study, group, and observation). Additionally, 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 [96]. Both I^2 and R^2 were calculated using the '*orchaRd*' package for multi-level models [97]. To account for potential non-linear dose-response relationships between proximity to failure and resistance training outcomes the following functional forms for all model structures described above were fit and subsequently compared using the '*bayestestR*' package [98], utilizing BIC approximated Bayes factors to determine under which model the observed data are the most probable for each outcome (i.e., strength and muscle hypertrophy):

1) Linear
2) Linear Spline (knot at 0 RIR)
3) Linear-log
4) Quadratic
5) Cubic
6) Restricted Cubic Spline (4 knots at 5, 35, 65, and 95% quantiles)

All models included the following fixed effects: 1) Estimated RIR, 2) Load per set, 3) Method of volume equating (set, repetition, or both), 4) Duration (i.e., weeks) of the training intervention (continuous), and 5) Training status of the participants (binary categorical). Estimated marginal means (and their slopes) with 95% compatibility intervals (confidence and prediction) were extracted for the main effect of RIR (adjusted proportionally for all other predictors) using the '*emmeans*' package [99]. For RIR, estimates were extracted at 0 to 23 RIR to represent the range of values observed in the dataset.

Following the determination of the best fit models for each outcome (i.e., strength or muscle hypertrophy) and effect size (i.e., SMC or RR), interaction moderator analyses were performed to evaluate the influence of a variety of factors related to study design and participant characteristics (supplementary file 2: https://osf.io/3tcwx). Specifically, separate models were fit for each moderator that maintained the same structure as the best fit models from the main analysis, but also included main effects and an interaction term between estimated RIR and the moderator of interest. Finally, after inspecting the data, it appeared that some studies with very high RIR estimations may have been disproportionately influencing the models. Thus, a sensitivity analysis was performed where all models were refit only with effect sizes from groups that were estimated to train with less than or equal to 10 RIR.

4 RESULTS

Study Characteristics

A breakdown of all 55 studies included in this analysis can be found in supplementary file 0 (https://osf.io/wpx92). On average, training interventions lasted 8.28 ± 2.35 weeks and participants were 27.83 ± 12.84 years old. A visual summary of the training interventions from the included studies can be seen in Figure 1. Additionally, tables summarizing study characteristics can be seen in supplementary file 2 (https://osf.io/3tcwx). The most frequently occurring (i.e., mode) values of the primary training variables for effects included in the strength models were: volume- 6 sets per week; load- 75% of 1RM; and frequency- 2 sessions per week. The average values for these metrics were 9.58 ± 4.48 sets per week, 72.06 ± 13.27% of 1RM, and 2.23 ± 0.48 sessions per week. For the effects in the muscle hypertrophy models, the most frequently occurring values were 6 sets per week, 85% of 1RM, and 2 sessions per week. The average values for these metrics were 9.69 ± 4.61 sets per week, 72.27 ± 14.53% of 1RM, and 2.08 ±0.39 sessions per week.

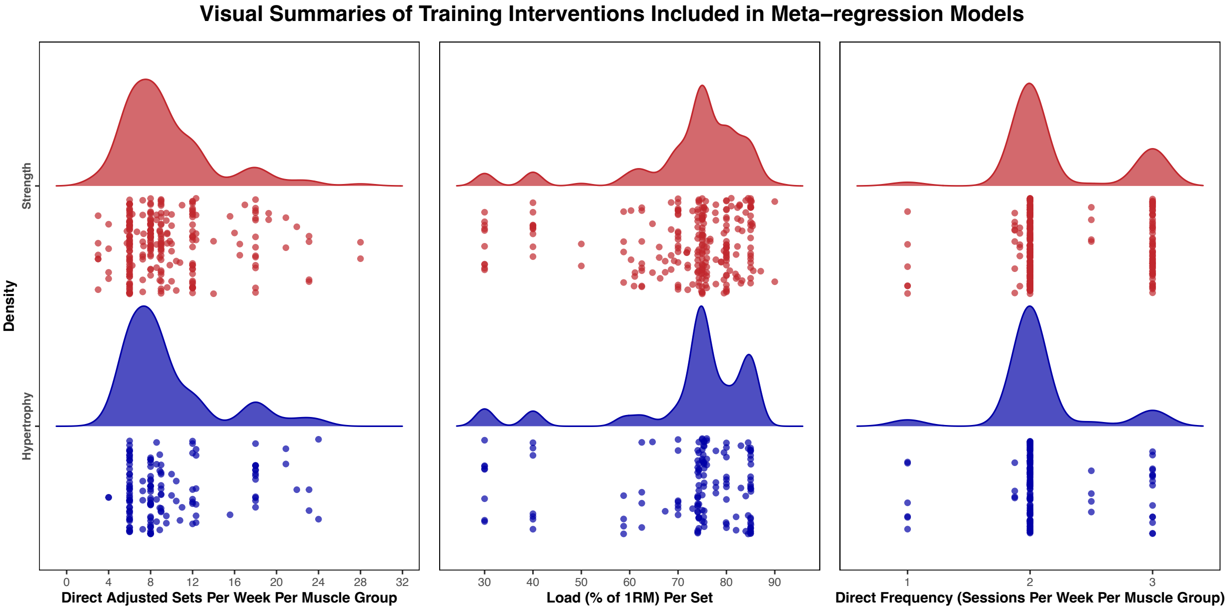

Figure 1: *Visual summary of training interventions included in the analysis. Data are presented as raincloud plots with each data point representing an effect. Direct adjusted sets per week per muscle group = Number of direct sets performed per week per muscle group while alternative set structure groups were adjusted to the same number of sets as the traditional set structure group in the same study.*

Primary Analysis

The following sections will present the results of all meta-regression models. Specifically, for each model, we will evaluate the overall quality of model fit (i.e., R^2 and I^2) and the marginal slope for the main effect of estimated RIR (i.e., the slope at the mean of RIR after adjusting for load, method of volume equating, intervention duration, and training status). Full model summary tables, comparisons thereof, and all extracted estimates are located at https://osf.io/7knsj/.

Strength Outcomes

The multi-level meta-regression models for strength included 243 total effects from 55 studies. Model comparisons revealed that the linear-log model was the best fit with effects as a standardized mean change (Figure 2). The fixed effects of the model explained less than a quarter of the total variance ($R^2_{marginal}$= 12.29%; $R^2_{conditional}$= 78.66%) with the primary source of remaining variance occurring at the study level (I^2_{study}= 52.37%; I^2_{group}= 13.44%; $I^2_{observation}$= 21.17%). The marginal slope of estimated RIR was positive but contained a null point estimate within the confidence interval (β= 0.003 [95% CI: -0.012, 0.018; 95% PI: -0.675, 0.682]). The slope indicates that strength gains improve negligibly as sets are terminated farther from failure.

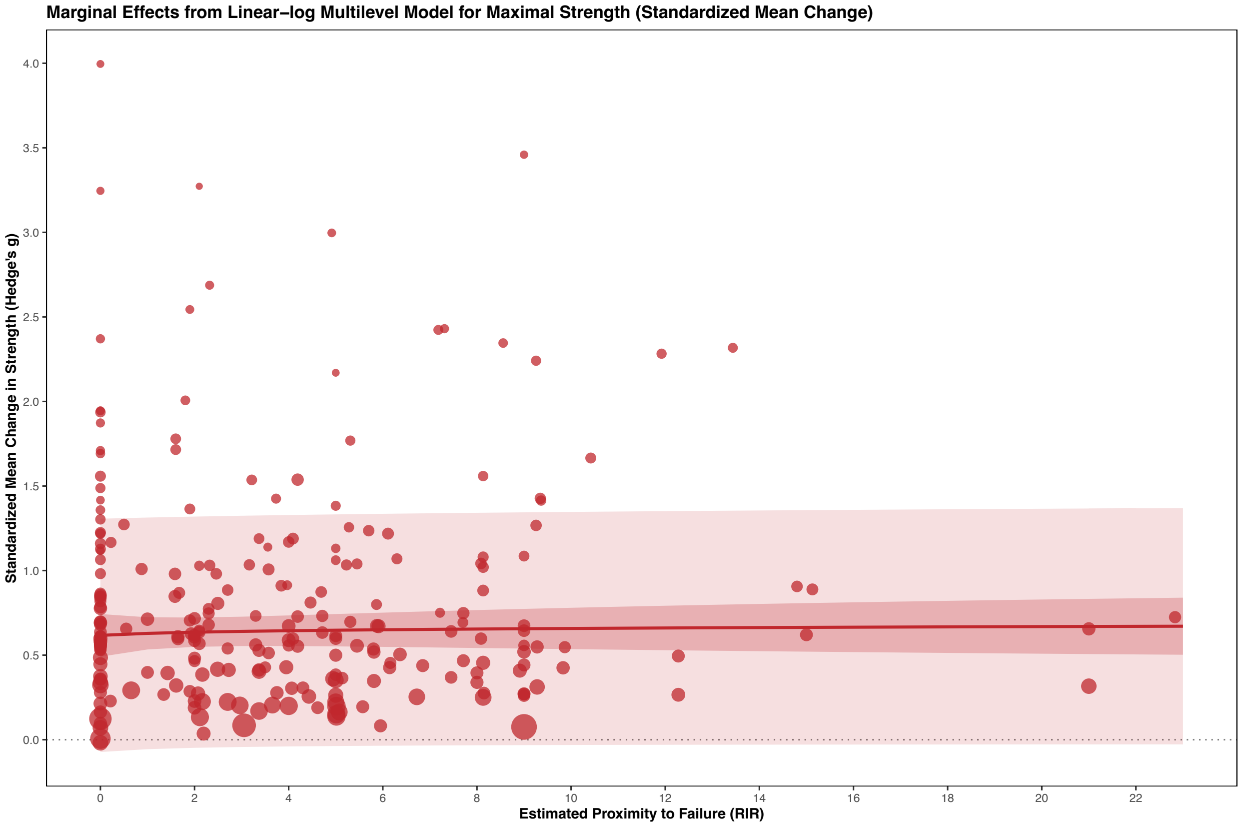

Figure 2: *Best fit (linear-log) multi-level meta-regression for maximal strength outcomes analyzed as a standardized mean change. Data are presented as estimated marginal means (solid line) with 95% compatibility intervals (dark band = confidence, light band = prediction) after adjusting for load, method of volume equating, intervention duration, and training status of the participants. 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. The main effect for estimated RIR is presented at the mean of continuous fixed effects (i.e., load and intervention duration) and proportionally marginalized across categorical fixed effects (i.e., method of volume equating and training status).*

Model comparisons revealed that the linear model was the best fit with effects as a response ratio (Figure 3). The fixed effects of the model explained less than a third of the total variance ($R^2_{marginal}$= 29.04%; $R^2_{conditional}$= 59.41%) with the primary source of remaining variance occurring at the observation level (I^2_{study}= 35.09%; I^2_{group}= 4.83%; $I^2_{observation}$= 53.35%). The marginal slope of estimated RIR was negative but contained a null point estimate within the confidence interval (β= -0.059 [95% CI: -0.304, 0.186; 95% PI: -12.944, 14.732]). The slope indicates that strength gains decrease negligibly as sets are terminated farther from failure.

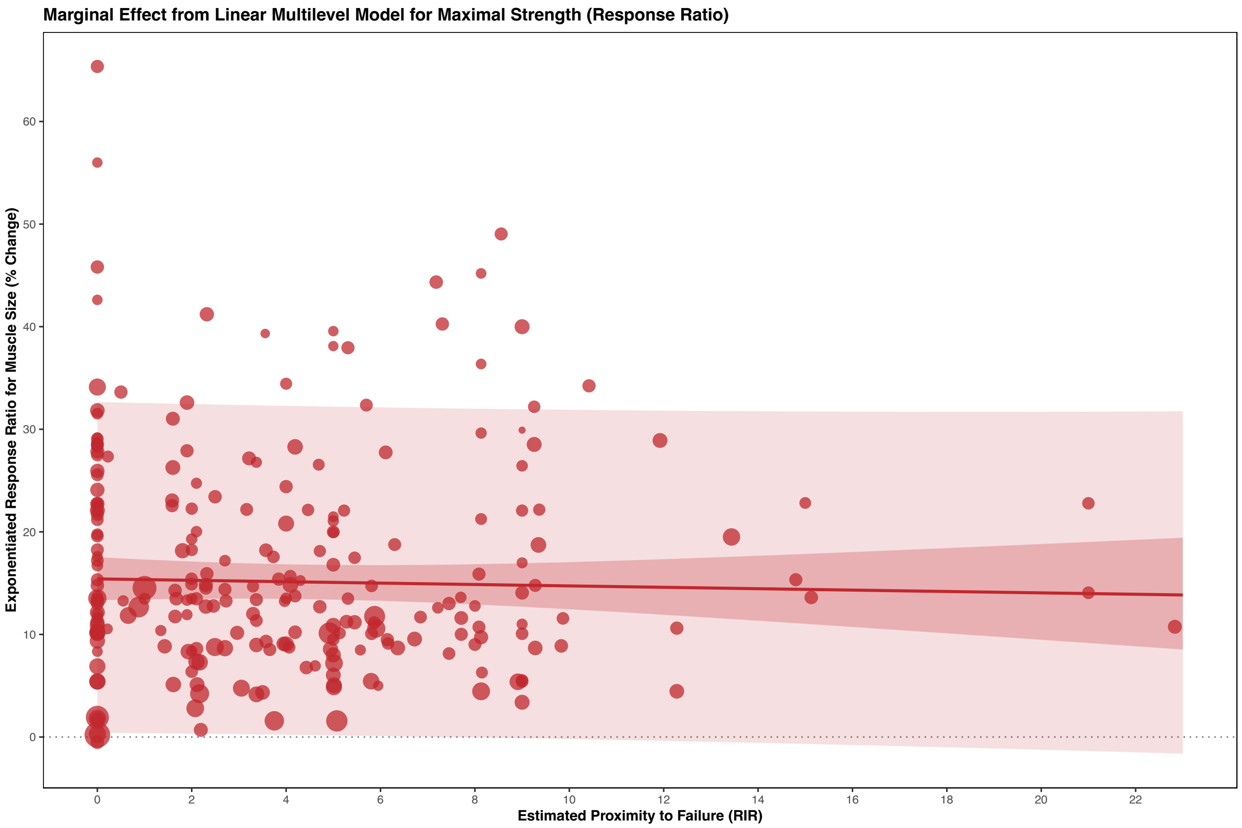

Figure 3: *Best fit (linear) multi-level meta-regression for maximal strength outcomes analyzed as an exponentiated response ratio. Data are presented as estimated marginal means (solid line) with 95% compatibility intervals (dark band = confidence, light band = prediction) after adjusting for load, method of volume equating, intervention duration, and training status of the participants. 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. The main effect for estimated RIR is presented at the mean of continuous fixed effects (i.e., load and intervention duration) and proportionally marginalized across categorical fixed effects (i.e., method of volume equating and training status).*

Muscle Hypertrophy Outcomes

The multi-level meta-regression models for muscle hypertrophy included 140 total effects from 26 studies. Model comparisons revealed that the linear model was the best fit with effects as a standardized mean change (Figure 4). The fixed effects of the model explained less than a quarter of the total variance ($R^2_{marginal}$= 19.2%; $R^2_{conditional}$= 72.09%) with the primary source of remaining variance occurring at the study level (I^2_{study}= 55.57%; I^2_{group}= 2.29%; $I^2_{observation}$= 30.53%). The marginal slope of estimated RIR was negative and did not contain a null point estimate within the confidence interval (β= -0.019 [95% CI: -0.035, -0.004; 95% PI: -0.551, 0.513]). The slope indicates that muscle hypertrophy improves as sets are terminated closer to failure.

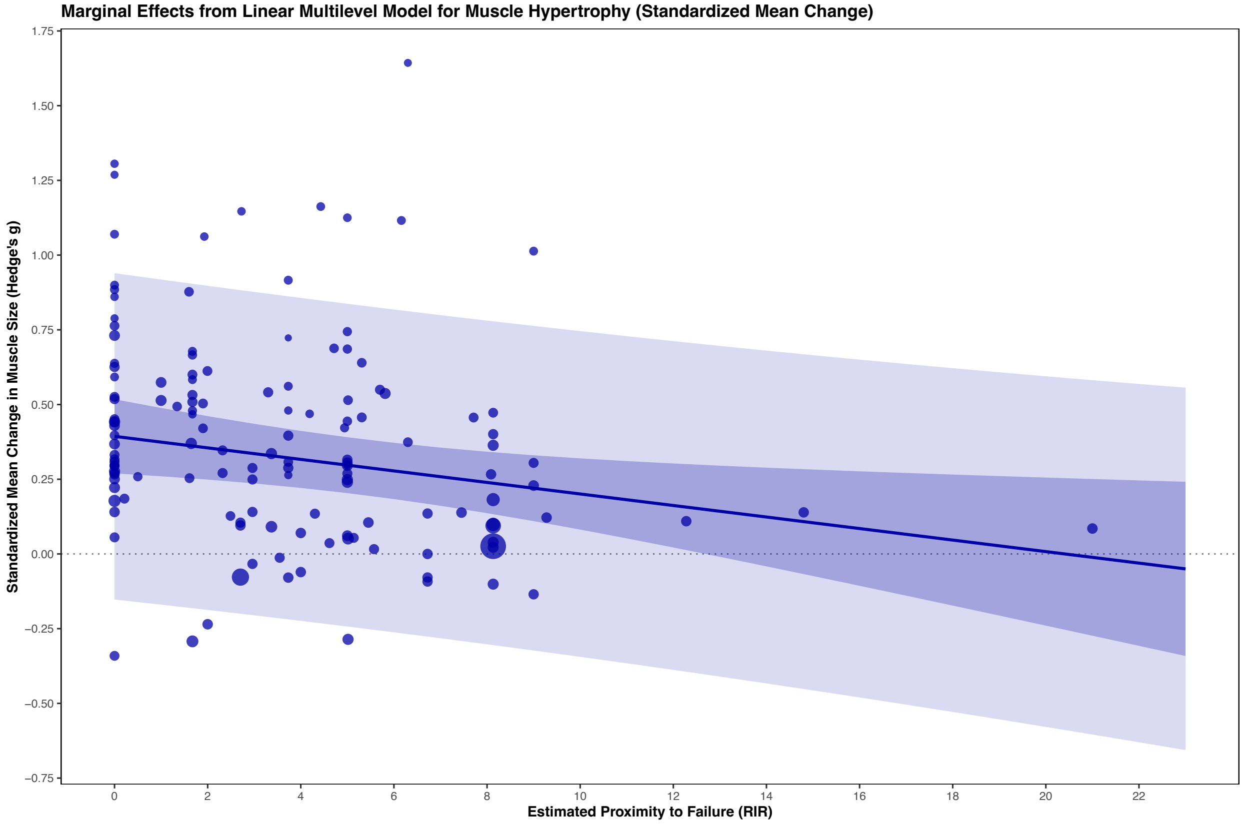

Figure 4: *Best fit (linear) multi-level meta-regression for muscle hypertrophy outcomes analyzed as a standardized mean change. Data are presented as estimated marginal means (solid line) with 95% compatibility intervals (dark band = confidence, light band = prediction) after adjusting for load, method of volume equating, intervention duration, and training status of the participants. 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. The main effect for estimated RIR is presented at the mean of continuous fixed effects (i.e., load and intervention duration) and proportionally marginalized across categorical fixed effects (i.e., method of volume equating and training status).*

Model comparisons revealed that the linear model was the best fit with effects as a response ratio (Figure 5). The fixed effects of the model explained less than a third of the total variance ($R^2_{marginal}$= 26.38%; $R^2_{conditional}$= 63.24%) with the primary source of remaining variance occurring at the observation level (I^2_{study}= 38.65%; I^2_{group}= 5.84%; $I^2_{observation}$= 44.35%). The marginal slope of estimated RIR was negative and did not contain a null point estimate within the confidence interval (β= -0.48 [95% CI: -0.78, -0.179; 95% PI: -9.811, 9.817]). The slope indicates that muscle hypertrophy improves as sets are terminated closer to failure.

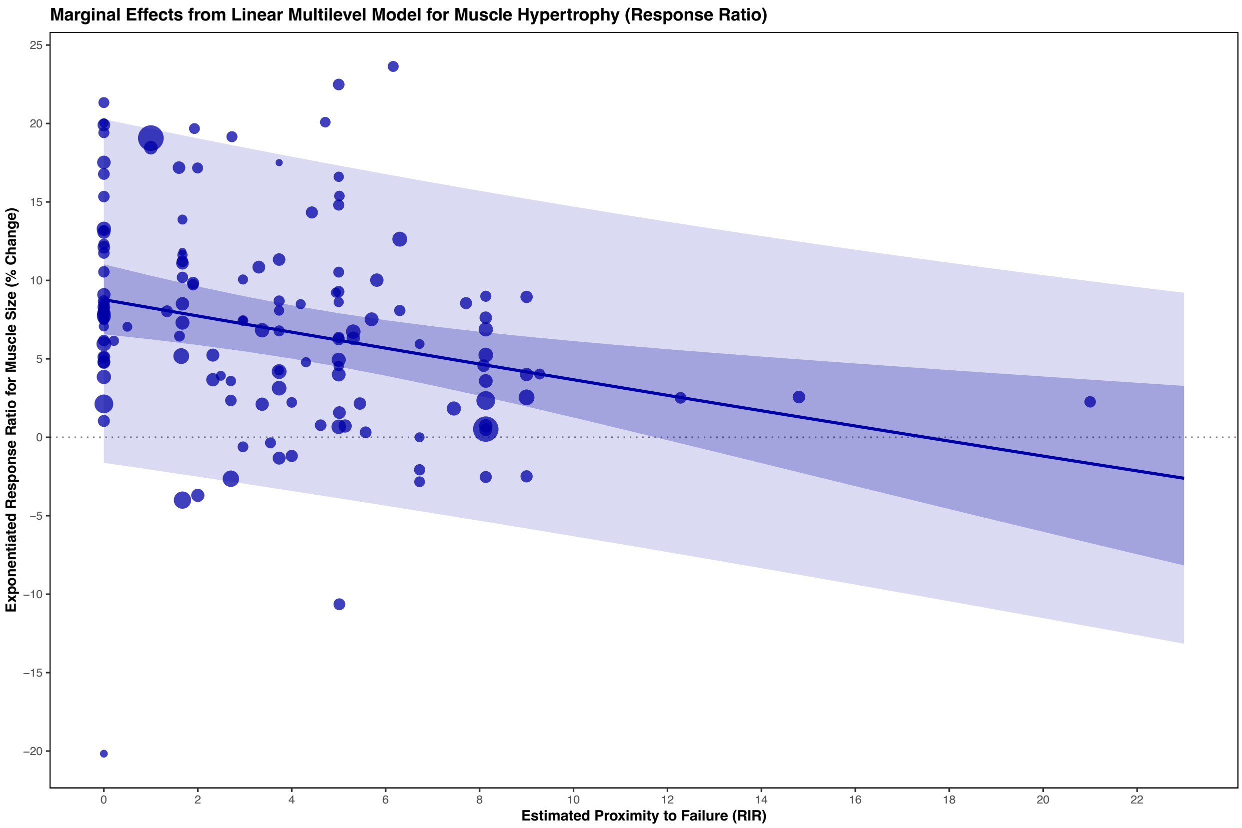

Figure 5: *Best fit (linear) multi-level meta-regression for muscle hypertrophy outcomes analyzed as an exponentiated response ratio. Data are presented as estimated marginal means (solid line) with 95% compatibility intervals (dark band = confidence, light band = prediction) after adjusting for load, method of volume equating, intervention duration, and training status of the participants. 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. The main effect for estimated RIR is presented at the mean of continuous fixed effects (i.e., load and intervention duration) and proportionally marginalized across categorical fixed effects (i.e., method of volume equating and training status).*

Sensitivity Analyses

Strength Outcomes

Upon refitting the multi-level meta-regression models for strength only with the effects with an RIR estimate of <10, they included 232 total effects from 54 studies. Model comparisons revealed that the linear-log model was the best fit with effects as a standardized mean change

(Figure 6). The fixed effects of the model explained less than a quarter of the total variance ($R^2_{marginal}$= 12.68%; $R^2_{conditional}$= 75.81%) with the primary source of remaining variance occurring at the study level (I^2_{study}= 51.63%; I^2_{group}= 11.03%; $I^2_{observation}$= 24.01%). The marginal slope of estimated RIR was positive but contained a null point estimate within the confidence interval (β= 0.004 [95% CI: -0.014, 0.022; 95% PI: -0.658, 0.666]). The slope indicates that strength gains improve negligibly as sets are terminated farther from failure.

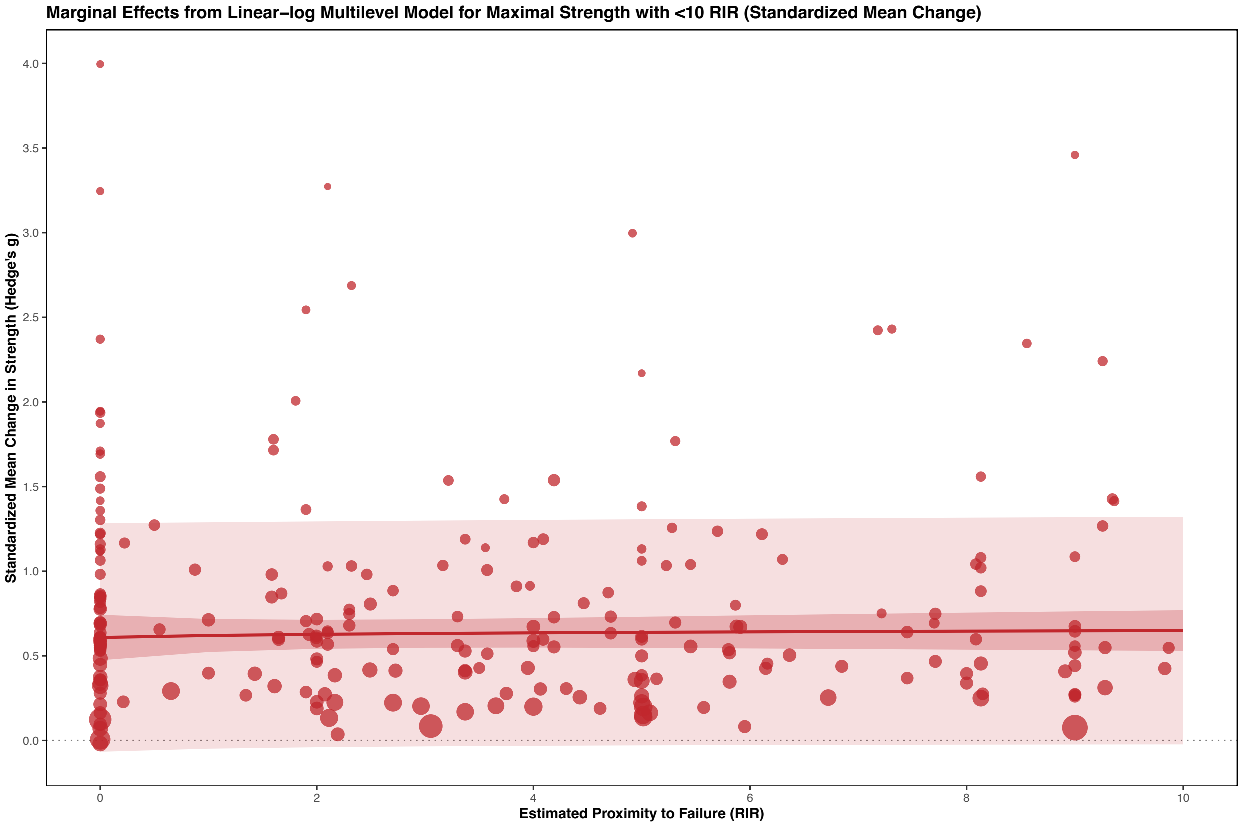

Figure 6: *Best fit (linear-log) multi-level meta-regression for maximal strength outcomes analyzed as a standardized mean change after effects with >10 estimated RIR were removed. Data are presented as estimated marginal means (solid line) with 95% compatibility intervals (dark band = confidence, light band = prediction) after adjusting for load, method of volume equating, intervention duration, and training status of the participants. 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. The main effect for estimated RIR is presented at the mean of continuous fixed effects (i.e., load and intervention duration) and proportionally marginalized across categorical fixed effects (i.e., method of volume equating and training status).*

Model comparisons revealed that the linear model was the best fit with effects as a response ratio (Figure 7). The fixed effects of the model explained less than a third of the total variance

($R^2_{marginal}$= 29.15%; $R^2_{conditional}$= 57.69%) with the primary source of remaining variance occurring at the observation level (I^2_{study}= 34.55%; I^2_{group}= 3.13%; $I^2_{observation}$= 55.87%). The marginal slope of estimated RIR was positive but contained a null point estimate within the confidence interval (β= -0.011 [95% CI: -0.411, 0.39; 95% PI: -13.085, 15.029]). The slope indicates that strength gains increase negligibly as sets are terminated farther from failure.

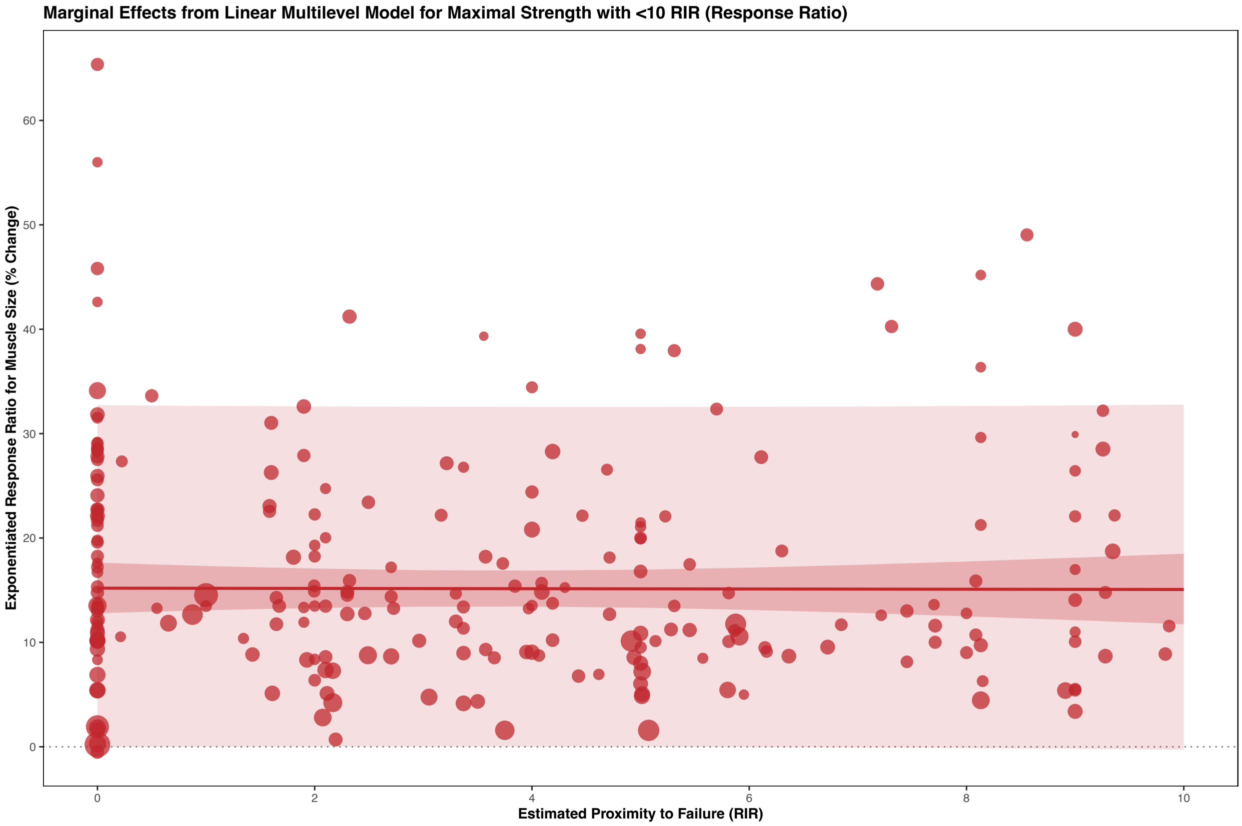

Figure 7: *Best fit (linear) multi-level meta-regression for maximal strength outcomes analyzed as an exponentiated response ratio after effects with >10 estimated RIR were removed. Data are presented as estimated marginal means (solid line) with 95% compatibility intervals (dark band = confidence, light band = prediction) after adjusting for load, method of volume equating, intervention duration, and training status of the participants. 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. The main effect for estimated RIR is presented at the mean of continuous fixed effects (i.e., load and intervention duration) and proportionally marginalized across categorical fixed effects (i.e., method of volume equating and training status).*

Finally, upon refitting all models with the RIR and load per set of the specific exercise evaluated as a dynamic strength outcome, a linear-log model was the best fit, regardless of effect size. All estimates were similar to the primary and secondary models.

Muscle Hypertrophy Outcomes

Upon refitting the multi-level meta-regression models for muscle hypertrophy only with the effects with an RIR estimate of <10, they included 137 total effects from 26 studies. Model comparisons revealed that the linear model was the best fit with effects as a standardized mean change (Figure 8). The fixed effects of the model explained less than a quarter of the total variance ($R^2_{marginal}$= 18.65%; $R^2_{conditional}$= 73.3%) with the primary source of remaining variance occurring at the study level (I^2_{study}= 57.55%; I^2_{group}= 2.31%; $I^2_{observation}$= 29.25%). The marginal slope of estimated RIR was negative and did not contain a null point estimate within the confidence interval (β= -0.023 [95% CI: -0.042, -0.004; 95% PI: -0.572, 0.526]). The slope indicates that muscle hypertrophy improves as sets are terminated closer to failure.

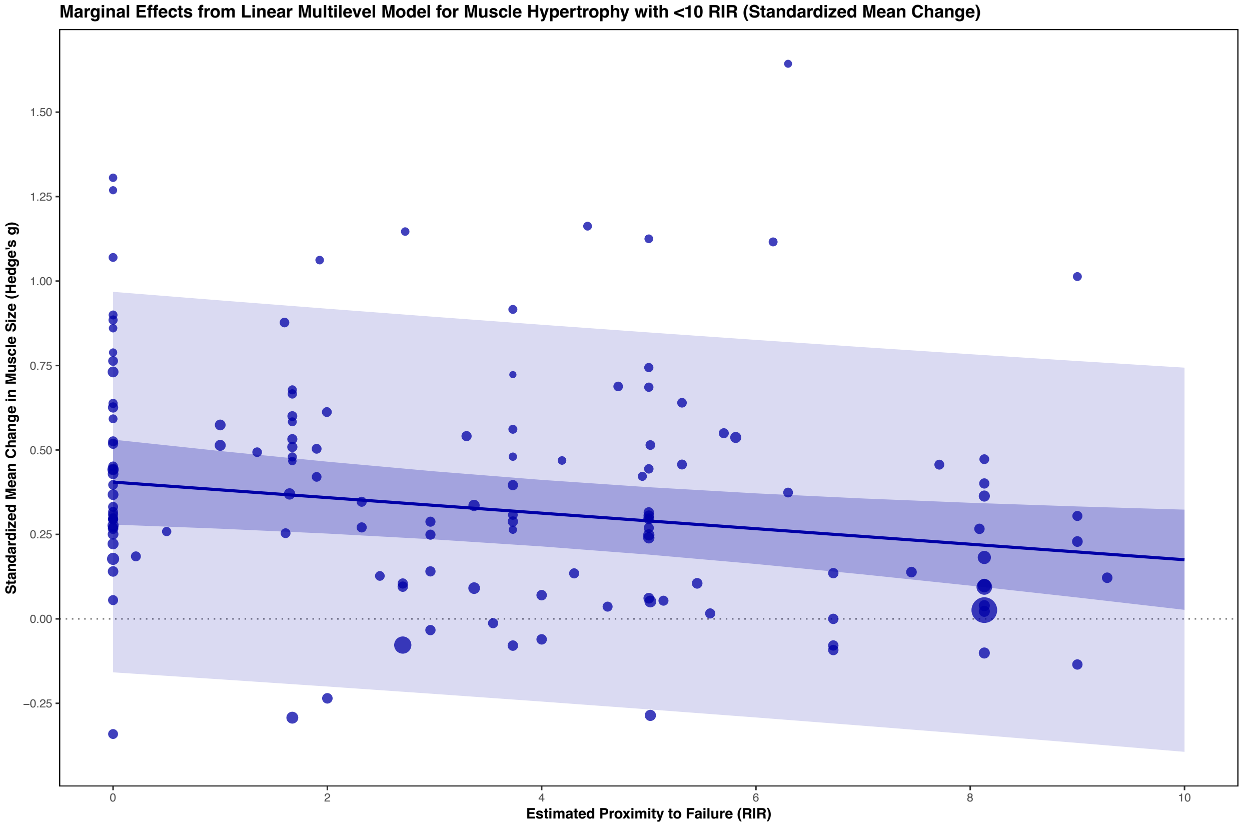

Figure 8: *Best fit (linear) multi-level meta-regression for muscle hypertrophy outcomes analyzed as a standardized mean change after effects with >10 estimated RIR were removed. Data are presented as estimated marginal means (solid line) with 95% compatibility intervals (dark band = confidence, light band = prediction) after adjusting for load, method of volume equating, intervention duration, and training status of the participants. 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. The main effect for estimated RIR is presented at the mean of continuous*

fixed effects (i.e., load and intervention duration) and proportionally marginalized across categorical fixed effects (i.e., method of volume equating and training status).

Model comparisons revealed that the linear model was the best fit with effects as a standardized mean change (Figure 9). The fixed effects of the model explained less than a third of the total variance ($R^2_{marginal}$= 25.52%; $R^2_{conditional}$= 64%) with the primary source of remaining variance occurring at the observation level (I^2_{study}= 39.71%; I^2_{group}= 6.48%; $I^2_{observation}$= 43.22%). The marginal slope of estimated RIR was negative and did not contain a null point estimate within the confidence interval (β= -0.544 [95% CI: -0.929, -0.158; 95% PI: -10.074, 9.996]). The slope indicates that muscle hypertrophy improves as sets are terminated closer to failure.

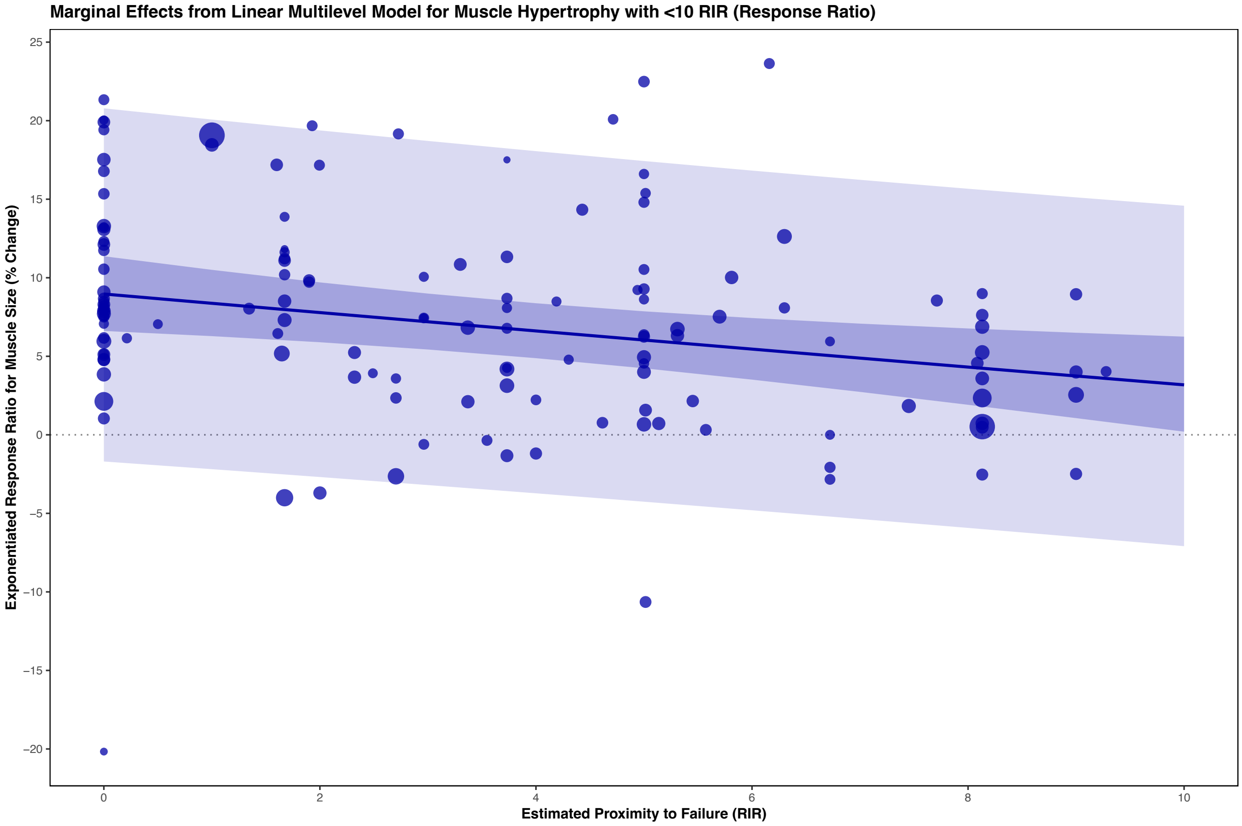

Figure 9: *Best fit (linear) multi-level meta-regression for muscle hypertrophy outcomes analyzed as an exponentiated response ratio after effects with >10 estimated RIR were removed. Data are presented as estimated marginal means (solid line) with 95% compatibility intervals (dark band = confidence, light band = prediction) after adjusting for load, method of volume equating, intervention duration, and training status of the participants. 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. The main effect for estimated RIR is presented at the mean of continuous*

fixed effects (i.e., load and intervention duration) and proportionally marginalized across categorical fixed effects (i.e., method of volume equating and training status).

Interacting Moderators

The following sections will present the results of the interaction moderator analyses. We evaluated the interaction contrasts of the two-way interactions between estimated RIR and the moderators of interest. Specifically, we will identify moderators that alter the qualitative inference of the relationship between estimated RIR and the outcome variable (i.e., directionality, magnitude, and uncertainty). These analyses should be cautiously interpreted, as the number of observations that contribute to the effects could be substantially reduced when compared to the main models, thereby reducing the precision of the estimates. Data visualization from all interaction moderator analyses are located at https://osf.io/7knsj/.

Strength Outcomes

For strength outcomes, interacting moderators were identified that altered the qualitative inference. When effects were analyzed as a standardized mean change in the primary analysis, upper body outcomes (n=104) demonstrated a more positive slope than lower body outcomes (n=139). Additionally, training programs that used multi-joint exercises (n=150) demonstrated a more positive slope than programs that included both multi- and single-joint exercises (n=27). In the sensitivity analysis of the effects with an RIR estimate of <10, training programs that used multi-joint exercises (n=150) demonstrated a more positive slope than programs that included both multi- and single-joint exercises (n=27).

When effects were analyzed as a response ratio in the primary analysis, training programs that used multi-joint exercises (n=150) demonstrated a more positive slope than programs that included both multi- and single-joint exercises (n=27). In the sensitivity analysis of the effects with an RIR estimate of <10, training programs that used multi-joint exercises (n=150) demonstrated a more positive slope than programs that included both multi- and single-joint exercises (n=27). Within-participant designs (n=32) also demonstrated a more positive slope than between-participant designs (n=211).

Muscle Hypertrophy Outcomes

For hypertrophy outcomes, interacting moderators were identified that altered the qualitative inference. When effects were analyzed as a standardized mean change in the primary analysis, training programs that did not employ progressive overload (n=5) exhibited a positive slope while those that included progressive overload (n=135) exhibited a negative slope. In the sensitivity analysis of the effects with an RIR estimate of <10, within-participant designs (n=18) demonstrated a positive slope, while between-participant designs (n=122) exhibited a negative slope.

When effects were analyzed as a response ratio in the primary analysis, training programs that did not employ progressive overload (n=5) exhibited a positive slope while those that included progressive overload (n=135) exhibited a negative slope. In the sensitivity analysis of the effects with an RIR estimate of <10, training programs that used heavier loads demonstrated a more positive slope than programs that used lighter loads. Within-participant designs (n=18) also demonstrated a more positive slope than between-participant designs (n=122). Finally, training programs that did not employ progressive overload (n=5) exhibited a positive slope while those that included progressive overload (n=135) exhibited a negative slope.

5 DISCUSSION

The present meta-analysis explored the dose-response relationship between proximity to failure (quantified as estimated RIR), strength gains, and muscle hypertrophy. Our results showed that strength gains are minimally influenced by proximity to failure, while muscle hypertrophy tends to increase as sets are terminated closer to failure. These relationships can inform future research and potentially improve the conceptual understanding of practitioners in regards to how proximity to failure influences muscular hypertrophy and strength outcomes, respectively.

Strength

In all of the best-fit models within the present analysis, the confidence intervals of the marginal slope for estimated RIR contained a null point estimate, suggesting a negligible relationship between proximity to failure and strength gains. There are multiple potential explanations for these findings. In the following sections, we will discuss the principle of specificity in regards to force production and opposing advantages of training far from and close to failure for strength gain to explain the observed relationship.

Force Production and The Principle of Specificity

The main estimates from the statistical models were extracted after adjusting for both load, the method in which volume was equated, intervention duration, and training status. Other meta-analytic data suggest that load, in particular, exhibits a positive dose-response relationship with strength gains [3,4]. These data, in concert with the present findings, suggest that load is a better predictor of strength outcomes than proximity to failure. Importantly, as load increases, the furthest obtainable proximity to failure decreases. For example, when training with a 10RM load (~75% of 1RM) a set could be terminated after a single repetition resulting in 9 RIR. However, a set terminated after a single repetition with a 2RM load (~95% of 1RM) will be much closer to failure (i.e., 1 RIR). This example illustrates the difference between a *load-mediated* and *intra-set-fatigue-mediated* change in proximity to failure. The present analysis would suggest that *intra-set-fatigue-mediated* changes in proximity to failure have a negligible influence on strength gains, while there is more research in support of *load-mediated* changes.

The contrast between load-mediated and intra-set-fatigue mediated changes in proximity to failure and their impact on strength outcomes could be potentially explained by the principle of specificity [100] in regards to force production. To align with the principle of specificity, one would expect that training with similar forces to the strength assessment of interest would result in favorable outcomes such as training with loads >85% of 1RM to maximize performance on a 1RM test. Importantly, however, force production declines as sets are taken closer to failure [101] but increases proportionally with load (i.e., % of 1RM) [102], thereby supporting the contrast between load-mediated and intra-set-fatigue mediated changes in proximity to failure and their impact on strength gains. Moreover, a recent meta-analysis by Zhang et al. [20] concluded that lower velocity loss thresholds resulted in higher strength gains per repetition than higher velocity loss thresholds. These results indicate that repetitions performed early in the set, which have the highest force production, lead to the greatest relative strength gain.

Advantages of Training Far From Failure for Strength

There are a number opposing advantages of training far from and close to failure for strength gains that may effectively counterbalance one another, leading to a negligible overall relationship. The first potential advantage of conditions training farther from failure is fatigue management. Multiple acute studies have demonstrated that training closer to failure results in greater indices of neuromuscular and perceptual fatigue compared to training farther from failure [33,103,104]. Since resistance training interventions often do not employ a formal tapering period in which training stress is reduced temporarily to allow for an improvement in acute performance [105], training farther from failure may allow participants to perform strength assessments in the absence of training-related fatigue compared to conditions training closer to failure.

Additionally, there may be proximity-to-failure-specific adaptations to rate of force development (RFD), which may contribute to the attenuation of maximal strength gains. While maximal strength (i.e., absolute force production measured in a specific context) is by definition a time-independent characteristic, the rate at which force is produced could influence an individual's ability to generate sufficient absolute force i) prior to the onset of fatigue, and ii) reaching the position in the range-of-motion with the greatest force requirements. Pareja-Blanco et al. [55] reported that training the Smith-machine squat to a 40% velocity loss threshold resulted in a reduction in the RFD measured from 0-50ms while lower velocity loss thresholds (i.e., 0, 10 and 20%) improved RFD, suggesting training closer to failure may harm RFD. However, differential adaptations seem to occur in the early (<200 ms) and the late (>200 ms) phases of RFD, with the latter being suggested as more predictive of maximal strength [106].

In an additional investigation, Pareja-Blanco et al. [56] reported that only groups training the Smith-machine bench press to higher velocity loss thresholds (i.e., 25 and 50%) saw improvements in RFD measured from 0-400ms, suggesting training closer to failure may harm early but not late phase RFD. However, as previously mentioned, these studies cannot delineate if the proximity to failure or relative volume load (i.e., % of 1RM × repetitions × sets) mediates effects on RFD, as both are manipulated via velocity loss thresholds. In studies that equate relative volume load and measure RFD, conditions training farther from failure usually result in superior changes in RFD, regardless of the phase examined [24,31,32,36,43]. Finally, a recent cross-sectional examination of strength-trained individuals demonstrate significant differences in earlier, but not later phases of RFD compared to untrained controls, potentially indicating that all phases of RFD may contribute to maximal strength [107]; however, this area lacks sufficient evidence to confidently describe the relationship between proximity to failure and phase-specific alterations to RFD.

Advantages of Training Close To Failure for Strength

In contrast to the potential advantages of training farther from failure, training closer to failure may offer exposure to motor patterns and psychological experiences more specific to a maximal strength assessment. It is well established that motor patterns change with increases in load, which require that single repetition sets are terminated closer to failure, in exercises with many degrees of freedom (e.g., barbell back squat) [108]. As maximal strength assessments occur at the threshold of failure - conditions training closer to failure may be more regularly exposed to similar motor demands, thereby aligning with the principle of specificity. Similarly, there seem to be psycho-physiological inputs to maximal strength (e.g., visualization) in which greater exposure to the subjective experience of performing resistance training near or to failure could be beneficial [109]. Practically, training closer to failure also allows for greater accuracy in subjectively reported RIR [110]. Given that loads are often selected via the perception of RIR (i.e., RIR-based RPE) [111], inaccuracy in this perception of RIR could also lead individuals to train with lower loads unnecessarily and potentially harm strength outcomes.

The second advantage of training closer to failure is greater increases in muscle size, as supported by the present meta-analysis. Although the contribution of changes in muscle size to changes in strength has been a topic of debate in the scientific literature [112,113], it is plausible that some relationship exists, though the degree of which is uncertain. Given this assumption, training closer to failure would benefit from greater muscle-size mediated strength gain than conditions training farther from failure.

Taken collectively, these opposing advantages of training far from and close to failure may explain the negligible dose-response relationship between estimated proximity to failure and strength gain in the present meta-analysis.

Hypertrophy

In contrast to results from the analysis of strength outcomes, the confidence interval of the marginal slope for estimated RIR did not contain a null point estimate in all best-fit models for muscle hypertrophy. In other words, the findings suggest a meaningful relationship between proximity to failure and changes in muscle size whereby muscle hypertrophy tends to increase as sets are performed closer to failure. In the following sections, we will discuss the mechanistic support for this relationship, potential explanations of the directionality of the observed effects, and other important considerations of the present findings.

Mechanistic Support of the Observed Relationship

The linear relationship observed in the present meta-analysis seems to support the proposed mechanistic models of resistance-training-induced muscle hypertrophy [114]. Specifically, Henneman's size principle suggests that motor units, and the muscle fibers they innervate, are recruited sequentially based on their size as force requirements rise [115]. As higher threshold motor units tend to innervate more type II fibers, which may have a greater potential for hypertrophy [116], the goal becomes to create the necessary and sufficient conditions to recruit these motor units allowing the muscle fibers they innervate to experience mechanical tension [117]. Critically, training to failure seems to allow for a stimulus to be delivered to these muscle fibers independent of load [118], while heavier loads may allow for greater motor unit recruitment farther from failure [119]. This rationale seems to be somewhat supported by our data as greater changes in muscle size were observed close to failure but this pattern was less pronounced as load increased (although only considered a "meaningful" interaction in the response ratio sensitivity analysis). Thus, the proximity to failure necessary to maximize muscle hypertrophy may be load-dependent, where that heavier loads may not require as low of RIR.

Explaining the Directionality of the Observed Effects

It is unclear why our findings suggest a linear increase in changes in muscle size while terminating sets closer to failure. While training to or close to failure is associated with increased acute fatigue [103,104] and performance decrements [120,121], there is a paucity of studies that examine fatigue longitudinally. It could be that the repeated bout effect strongly diminishes the fatigue associated with training to or close to failure as one habituates to the stimulus [122]. Alternatively, ambiguity in failure definitions could be playing a role. Halperin et al. [110] demonstrated that participants often under-predict the number of repetitions they are able to perform, thus, potentially training farther from failure than intended. If underprediction does occur, studies that state participants trained to “failure” without a clear definition of criteria for set termination would result in RIR estimations that were too low (i.e., estimated to be too close to failure) in the present meta-analysis. However, the failure definition interacting moderator analysis suggests that studies which provided a failure definition resulted in greater changes in muscle size than those that did not. Because both models suggest that gains in muscle size increase the closer to failure a set is terminated, ambiguity in failure definition does not seem to influence the shape of the dose-response relationship. Although, the magnitude of the expected effects may differ between studies providing explicit failure definitions and those that do not. Ultimately, it is difficult to explain the directionality of the observed relationship and future research should aim to explore its origins.

Other Findings

Another interesting finding of the present meta-analysis was that the marginal slopes for RIR were not meaningfully influenced by the method in which volume was equated (i.e., set or repetition volume-equated). In all of the recent velocity loss meta-analyses [16–18] the authors report positive linear dose-response relationships between the velocity loss threshold in which sets are terminated and changes in muscle size. However, as previously mentioned, velocity loss thresholds influence both proximity to failure and relative volume load, which makes it difficult to utilize the positive linear dose-response relationships to inform RIR prescriptions for muscle hypertrophy. With the present meta-analysis in mind, it seems that the method in which volume was equated (i.e., set or repetition volume-equated) does not meaningfully alter the dose-response relationship between estimated proximity to failure and changes in muscle size. Thus, a particular type of volume-equated study design (i.e., either set or repetition volume-equated) does not seem to be necessary to inform the relationship between proximity to failure and muscle hypertrophy.

Finally, it is important to mention that the present analysis predominantly focuses on the proximity to failure that optimizes the *average* muscle hypertrophy of the *prime movers* of a given exercise (e.g., a training intervention that features a leg press means that the quadriceps are the prime mover). There are considerably fewer studies that examine the effect of proximity to failure on synergistic muscle groups (e.g., triceps brachii in the bench press), thus the present findings should not be generalized blindly. Moreover, very few studies measure hypertrophy of multiple regions within a given muscle (e.g., proximal, middle, distal) which could exhibit differential relationships to the proximity to failure at which training is performed. To provide more context for these relationships, future research should aim to measure synergistic muscles and regional hypertrophy of all the sites of interest.

Limitations and Considerations

Several limitations exist with this meta-analysis. While considerable thought and collaboration were put into constructing the highest quality process of estimating RIR, the accuracy of these estimations is unknown. Previous research suggests that the number of repetitions performed at a given load is highly individual [123–126]. Thus, estimating RIR based on homogeneous RM values may be representative of the group-level RIR but likely only applies to some participants within a study. Additionally, multiple other factors that influence proximity to failure were not directly addressed. First, as participants perform multiple sets, set-to-set performance declines due to fatigue. Specifically, if the load is not adjusted from set to set and sets are performed to the same repetition target (e.g., 10 repetitions), there may be fewer RIR on later sets. Therefore, the estimated RIR values, on average, could be overestimated (i.e., the estimations are too far from failure) - although the exact extent to which this may occur is influenced by various factors (e.g., sex, exercise selection, load, rest period, and initially prescribed proximity to failure); thus, this could not be adequately accounted for.

Another factor that may influence RIR is strength gain. Specifically, if the load is not adequately adjusted as participants gain strength (i.e., progressive overload), and sets are performed to the same repetition target (e.g., 10 repetitions), there may be greater RIR in later sessions of the training program. Therefore, the estimated RIR values, on average, could be underestimated (i.e., the estimations are too close to failure) - although, again, the extent to which this may occur is influenced by various factors (e.g., exercise selection, load, weight increments available, and frequency of load progression); thus, this could not be adequately accounted for. Another limitation comes from the decision to average RIR values across all sets performed to describe each group. Therefore, this analysis does not take into account the variability in RIR throughout a training program. For example, at an average estimated RIR of 2, the group could have performed all sets at 2 RIR or an even proportion of 1 and 3 RIR sets.

From a practical perspective, the observed relationships between estimated RIR and strength or muscle hypertrophy outcomes may not hold on the individual level. For example, in the context of training volume, Damas et al. [127] demonstrated that some participants saw more favorable outcomes in a limb training with <10 sets per week compared to a limb training with >10 sets per week. Crucially, these findings contradict a well-cited meta-analysis by Schoenfeld et al. [1], which suggests that >10 sets per week are optimal for muscle hypertrophy outcomes, on average. This example demonstrates that training recommendations derived from meta-analytic estimates may be inappropriate for some individuals; however, in the absence of robust individual-level evidence (e.g., N of 1 trials) average effects may be the best estimate [128,129]. Moreover, applying these relationships outside the context of the volumes, loads, frequencies, and study designs included in this analysis should be done with caution (see Figure 1 and supplementary file 2: https://osf.io/3tcwx). For example, only volume-equated studies (i.e., either set or repetition equated) were included in the present analysis. While training closer to failure resulted in superior muscle hypertrophy outcomes, these results may change if participants could modify the number of sets performed to align with their recovery capacity. As training to failure results in greater acute fatigue [103,104], training with a greater number of RIR could allow for more weekly sets and could impact longitudinal strength and muscle hypertrophy outcomes. Finally, many studies did not provide the necessary data for the analysis, so much of it had to be estimated (e.g., pre- to post-test correlation coefficients).

Our goal with this analysis was to provide reasonably precise population average RIR estimates that, in the absence of better evidence, can describe the relationship between proximity to failure and resistance training outcomes. However, it is critical to mention that the quality of model fit is modest, suggesting that proximity to failure is only one piece to explain training outcomes. Further, the uncertainty intervals of all estimates are wide, indicating many dose-response shapes are compatible with the current analysis (particularly upon the addition of future high-quality data). While the limitations are notable, this analysis may be useful to explore the directionality of these relationships and identify potential RIR thresholds of interest for future research.

6 CONCLUSION

The dose-response relationships between estimated proximity to failure and strength gain appears to be different from that with muscle hypertrophy. Strength gains seem to be negligibly impacted by the proximity to failure in which sets are performed at a given load, while muscle hypertrophy improves as sets are terminated closer to failure. However, the quality of overall model fits was modest and the width of the uncertainty intervals of all estimates suggest many dose-response shapes are compatible with the current analysis, particularly upon the addition of future data. Considering these results and the RIR estimation procedures used, the exact relationship between RIR and muscle hypertrophy and strength remains unclear. Researchers and practitioners should be therefore be cautious interpreting the findings of the present analysis.

Data and Supplementary Material Accessibility

All materials, data, and code are available on the Open Science Framework project page.

Author Contributions

ZR extracted the data, performed the initial RIR estimations, performed the statistical analysis, and drafted the manuscript. JP, JR, and MZ provided the first peer-review of the RIR estimations and edited the manuscript. MR and IJ provided the second peer-review of the RIR estimations and edited the manuscript. JS assisted with the statistical analysis, and edited the manuscript.

Conflict of Interest

Zac Robinson, Joshua Pelland, Jacob Remmert, and Michael Zourdos are all coaches and writers in the fitness industry. Martin Refalo, Ivan Jukic, and James Steele declare that they have no conflicts of interest relevant to the content of this review.

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