Influence of Resistance Training 'Proximity-to-Failure' on Muscle Hypertrophy.

by

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Doctor of Philosophy

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Acknowledgements

The past decade of my life has primarily consisted of full-time university commitments and face-to-face personal training. I haven't separated 'knowledge' from the 'gym floor' (i.e., theory from practice), but the consequence has been a heavy workload. I often get asked how I manage my workload, and to be honest, I'm not *exactly* sure. I know people who are much busier than I am, with much greater responsibilities, so I am always under the impression that 'more can be done'. In the early stages of my PhD, I heard Jordan Peterson mention that his PhD produced 15 publications – I immediately increased my goal of three publications to 10. I have worked hard to complete my PhD in three years, but it wouldn't be possible without my prolific supervisory team, led by Dr. Jackson Fyfe. Jackson's supervision over the past five years (including my Master's Degree) has been invaluable and has transformed me into the scientist I am today. My associate supervisor, Dr. Lee Hamilton, instils confidence within me and picks out holes in my thinking, of which I am grateful for. And lastly, my external supervisor, Dr. Eric Helms, who's 'Muscle & Strength Pyramids' were the first fitness related books I ever read, has helped me foster scientific traits that I will continue to portray inside and outside of academia. This 10-year academic journey wouldn't have been as successful without my family, who have been my side with every step. And my fiancé, Naly, who has seen the highs and lows, has been my rock; helping keep my head up when the stress was becoming too much to bear. Finally, I consider JPS Health & Fitness my second home and am thankful for the community and my colleagues, who keep me passionate about my job, sharp with my thinking, and are supportive of my endeavours. Summing up the mindset I have adopted over this 10-year journey is the following quote that I display as my computer wallpaper: *"Don't fear change. Don't fear failure. The only thing to fear is a loss of ambition. But if you have plenty of that, you have nothing to fear at all."* – Neil DeGrasse Tyson.

Publications and Conference Presentations

Related to this PhD

Published

- Refalo, M. C., Helms, E. R., Hamilton, D. L., & Fyfe, J. J. (2022). Towards an Improved Understanding of Proximity-to-Failure in Resistance Training and its Influence on Skeletal Muscle Hypertrophy, Neuromuscular Fatigue, Muscle Damage, and Perceived Discomfort: A Scoping Review. Journal of Sports Sciences, 40(12), 1369-1391. doi.org/ 10.1007/s40279-022-01784-y
  https://pubmed.ncbi.nlm.nih.gov/35658845/
- Refalo, M. C., Helms, E. R., Trexler, E. T., Hamilton, D. L., & Fyfe, J. J. (2022). Influence of Resistance Training Proximity-to-Failure on Skeletal Muscle Hypertrophy: A Systematic Review with Meta-Analysis. Sports Medicine, 53(3), 649-665. doi.org/ 10.1007/s40279-022-01784-y
  https://pubmed.ncbi.nlm.nih.gov/36334240/
- Refalo, M. C., Helms, E. R., Hamilton, D. L., & Fyfe, J. J. (2023). Influence of Resistance Training Proximity-to-Failure, Determined by Repetitions-in-Reserve, on Neuromuscular Fatigue in Resistance-Trained Males and Females. Sports Medicine - Open, 9(1), 10. doi.org/ 10.1186/s40798-023-00554-y
  https://pubmed.ncbi.nlm.nih.gov/36752989/
- Refalo, M. C., Remmert, J. F., Pelland, J. C., Robinson, Z. P., Zourdos, M. C., Hamilton, D. L., Fyfe, J. J., & Helms, E. R. (2023). Accuracy of Intra-Set Repetitions-in-Reserve Predictions During the Bench Press Exercise in Resistance Trained Males and Females. Journal of Strength and Conditioning Research, online ahead of print. doi.org/ 10.1519/jsc.0000000000004653
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- Refalo, M. C., Helms, E. R., Robinson, Z. P., Hamilton, D. L., & Fyfe, J. J. (2024). Similar Muscle Hypertrophy Following Eight Weeks of Resistance Training to Momentary Muscular Failure or with Repetitions-in-Reserve in Resistance-Trained Individuals. Journal of Sports Sciences, online ahead of print. doi.org/0.1080/02640414.2024.2321021 https://pubmed.ncbi.nlm.nih.gov/38393985/

In Preparation for Peer Review

- Refalo, M. C., Helms, E. R., Robinson, Z. P., Hamilton, D. L., & Fyfe, J. J. (2024). Sex Differences in Muscle Hypertrophy and The Influence of Proximity-to-Failure Following 8-Weeks of Resistance Training in Resistance-Trained Males and Females.
- Refalo, M. C., Helms, E. R., Robinson, Z. P., Hamilton, D. L., & Fyfe, J. J. (2024). The Relationship Between Proximity-to-Failure and Perceptual Responses Following Resistance Training to Momentary Muscular Failure or with Repetitions-in-Reserve in Resistance-Trained Individuals.

Conference presentations:

- ECSS 2022 Seville Congress (September 2022, in-person presentation)

Unrelated to this PhD

Published

- Refalo, M. C., Hamilton, D. L., Paval, D. R., Gallagher, I. J., Feros, S. A., & Fyfe, J. J. (2021). Influence of Resistance Training Load on Measures of Skeletal Muscle Hypertrophy and Improvements in Maximal Strength and Neuromuscular Task Performance: A Systematic Review and Meta-Analysis. Journal of Sports Sciences, 39(15), 1723-1745. doi.org/ 10.1007/s40279-022-01784-y
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In Peer Review:

- Amdi, C., Fyfe, J. J., Nuckols, G., Sanghoon, Y., Refalo, M. C. (2024). The Influence of Biological Sex on Neuromuscular Fatigue. Journal of Sports Sciences.
- Robinson, Z. P., Pelland, J. C., Remmer, J. F., Refalo, M. C., Jukic, I., Steele, J., Zourdos, M. C. (2023). Exploring the Dose-Response Relationship Between Estimated Resistance Training Proximity to Failure, Strength Gain, and Muscle Hypertrophy. Sports Medicine.
- Refalo, M. C., Nuckols, G., Galpin, A. J., Gallagher, I., Hamilton, D. L., Fyfe, J. J. (2024). Biological Sex Differences in Absolute and Relative Changes in Muscle Size

following Resistance Training in Healthy Adults: A Systematic Review with Meta-Analysis. Scandinavian Journal of Medicine and Science in Sports.

Table of Contents

Thesis Structure

Several thesis chapters are works previously peer-reviewed and accepted for publication. Specifically, Chapter Two and Chapters Four through Seven (Study One to Study Four) are published in peer-reviewed journals. These chapters are presented as the final version accepted by the journal, with the formatting adjusted to ensure consistency. To improve readability, abstracts are removed from each chapter and replaced with a preface, and the practical applications sections are also removed and integrated into Chapter Eight (General Discussion and Conclusions). The DOI of the full publications can be found at the beginning of each respective chapter. To summarise how Study Four fits within the broader context of the relevant literature, Chapter Eight includes an updated meta-analysis, like that presented in Study One, but incorporates the results of Study Four (Chapter Seven). Despite these modifications and due to the thesis-by-publication format, there remains unavoidable repetition of definitions and concepts related to proximity-to-failure mainly found in the introductions of each chapter. Nonetheless, each chapter, in addition to the broader thesis, offers useful insights into the influence of proximity-to-failure on muscle hypertrophy and other relevant outcomes.

Thesis Summary – Abstract

Introduction: Repetitions performed in a resistance training (RT) set lie on a continuum whereby the maximum termination point is 'momentary muscular failure'. Set termination can also occur a specified number of repetitions from momentary muscular failure, known as 'repetitions-in-reserve' (RIR). RIR is an important variable that not only influences physiological adaptations to RT, such as skeletal muscle hypertrophy, but also short-term responses (e.g., neuromuscular fatigue and perceived discomfort) that may negatively influence performance and adherence. The aim of this thesis was to address research limitations surrounding the application of proximity-to-failure during RT and further explore its influence on muscle hypertrophy, neuromuscular fatigue, and perceptual responses, allowing for improved practical recommendations.

Methods & Results: A scoping review was firstly conducted to summarise definitions for 'failure' in RT, discuss methods for controlling proximity-to-failure, identify current research limitations, and provide tentative conclusions about the influence of proximity-to-failure on muscle hypertrophy, neuromuscular fatigue, muscle damage and perceived discomfort. Studies retrieved from the scoping review that assessed muscle hypertrophy as an outcome measure were then meta-analysed (Study One). An original research study was also conducted to investigate the influence of proximity-to-failure on neuromuscular fatigue and perceptual responses (Study Two), along with the accuracy of intra-set RIR predictions (Study Three), in resistance-trained individuals. Finally, a second original research study was conducted to compare the effect of RT performed to momentary muscular failure versus with 1- to 2-RIR on muscle hypertrophy and neuromuscular fatigue (Study Four). The main findings were i) there is currently no strong evidence to support that RT performed to momentary muscular is superior to non-failure RT for muscle hypertrophy, ii) neuromuscular fatigue was greater and perceptual responses were less favourable when RT was performed with closer proximity-to-failure on the bench press exercise (FAIL > 1-RIR > 3-RIR), iii) resistance-trained individuals demonstrated high *absolute* RIR accuracy when predicting 1- and 3-RIR, and iv) quadriceps hypertrophy following eight weeks of RT was similar when sets were terminated with a perceived 1- to 2-RIR compared to reaching momentary muscular failure.

Conclusion: Performing RT closer to momentary muscular failure is effective, but not mandatory, for promoting muscle hypertrophy in resistance-trained individuals. Terminating sets at 1- to 2-RIR yields similar quadriceps hypertrophy as reaching momentary muscular failure. A linear relationship was observed between RT proximity-to-failure and acute neuromuscular fatigue, although the magnitude of acute neuromuscular fatigue depends on the exercise performed and the stage of the RT intervention. Perceived discomfort also had a linear relationship with RIR, increasing with closer proximities-to-failure. Further, controlling proximity-to-failure in resistance-trained individuals with RIR prescription seems effective as they may have high absolute RIR accuracy, ensuring sets are terminated sufficiently close to the RIR target to promote muscle hypertrophy. Overall, this thesis provides new insights into how proximity-to-failure influences both muscle hypertrophy and short-term responses to RT, informing practical applications and areas to be further explored in future research.

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List of Abbreviations

1-RM One repetition-maximum

AD Anterior deltoid

ASIS Anterior spina iliaca superior

AST Aspartate aminotransferase

BIA Bioelectrical impedance analysis

BP Flat barbell bench press

BW Bodyweight

CI Confidence interval

CK Creatine Kinase

CMJ Countermovement jump

CSA Cross-sectional area

CV Coefficient of variation

EF Elbow flexor

ES Effect size

g Grams

HDI Highest density credible intervals

ICC Intraclass correlation

kcal Kilocalories

kg Kilograms

LE Leg extension

LP 45-degree leg press

M Male

m·s-1 Metres per second

MMF Momentary muscular failure

MRI Magnetic resonance imaging

MV Mean velocity

MVC Maximum voluntary contraction

PCC Population, concept, and context

pd Probability of direction

pd > TE Probability of direction that exceeds typical error

PP Peak power

PM Pectorialis major

pQCT Peripheral quantitative computed tomography

p/w Per week

PR Prone barbell bench row

PRISMA Preferred reporting items for systematic reviews and meta-analyses

PRS Perceived recovery status

RDS Research data store

REML Restricted maximum likelihood estimation

Reps Repetitions

RF Rectus femoris

RIR Repetitions-in-reserve

RM Repetition-maximum

RPD Rating of perceived discomfort

RPE Rating of perceived exertion

RPE CR-10 Rating of perceived exertion category ratio 10

RT Resistance training

SD Standard deviation

SEM Standard error of mean

T Trained

TB Triceps brachii

TE Typical error

UT Untrained

VA Voluntary activation

VeL Velocity Loss

VI Vastus intermedius

VI Volitional interruption

VL Vastus lateralis

VM Vastus medialis

y Years

List of Appendices

Chapter One – General Introduction

1.1 Background

Resistance training (RT) is the most effective non-pharmacological intervention to promote neurological and morphological adaptations including increased force production (for maximal strength development) and skeletal muscle hypertrophy [1]. Less appreciated, however, are the benefits for various health outcomes, including a lower risk of all-cause mortality [2], reduced incidence of chronic diseases including type 2 diabetes [3], and improvements in glucose disposal [4], resting metabolic rate [5], sleep quality [6], and anxiety [7]. Some of these health improvements may be attributed to increased skeletal muscle mass following RT [8], highlighting the importance of employing RT to promote muscle hypertrophy in both males and females. Despite the potential health benefits, public health surveillance data suggests only 10-30% of adults meet the World Health Organisation's guideline of two or more 'muscle-strengthening exercise' sessions per week [9]. Further research is therefore needed to not only explore methods to promote muscle hypertrophy through effective RT prescription, but to increase participation and engagement, ultimately informing strategies employed by health and fitness practitioners to enhance population health.

During RT, one may perform as many repetitions as possible within a set to reach the maximum set end point [also known as 'failure' (Figure 1.1)] or terminate the set at a given 'proximity-to-failure'. The proximity-to-failure at which a set is terminated influences physiological adaptations (e.g., maximal strength development and muscle hypertrophy) [10-12], short-term responses (e.g., neuromuscular fatigue and muscle damage) [13], and also affective responses (e.g., enjoyment, pleasure, discomfort) [14, 15] potentially important for exercise adherence [16-18]. For clarity, this thesis will avoid using the term 'intensity' as its definition within exercise science is contentious [19] and will instead describe the external resistance lifted as absolute or relative [percentage of one-repetition maximum (1-RM)] load and will explore the term proximity-to-failure and its application in RT by quantitively describing it via a repetitions-in-reserve (RIR) scale indicating the number of repetitions remaining from failure.

Although proximity-to-failure is a RT variable that influences muscle hypertrophy [20], whether performing sets to failure is mandatory to maximise muscle hypertrophy is contentious. Importantly, the idea that RT must be 'hard' or be performed with 'maximal effort' to promote hypertrophy originated in the 1940's when Dr. Thomas L. DeLorme proposed his 'progressive resistance exercise' protocol [21] based on performing RM sets (i.e., as many repetitions as one believes they can perform with a given load). Since the development of DeLorme's protocol [21], performing sets until the maximum number of repetitions possible with a given load is reached has become known as 'training to failure' and has become a popular strategy to enhance muscle hypertrophy. Indeed, performing sets to failure ensures a sufficient RT stimulus is imposed on the target musculature, but whether the benefit of reaching failure in each set outweighs the possible downsides (e.g., high neuromuscular fatigue, muscle damage, and perceived discomfort [13]) over time is unclear. Conversely, non-failure RT using a predetermined repetition target with a given load may result in individuals reaching an insufficient proximity-to-failure to promote meaningful muscle hypertrophy. For example, on the popular *"Men's Health"* website (www.menshealth.com), a recent article titled *"Arnold Schwarzenegger's 5-Move Dumbbell Workout Delivers Speedy Gains"* offers a program consisting of a reverse lunge and row prescribed for two sets of 10 repetitions, a squat for two sets of 12 repetitions, and a dumbbell floor press prescribed for two sets of 15 repetitions [22]. Further, the website *"Muscle and Strength"* (www.muscleandstrength.com) hosts a *"3 Day Full Body Women's Dumbbell Workout"* [23] that only involves exercises prescribed for 15 repetitions. Importantly, proximity-to-failure is not mentioned in either example, potentially compromising muscle hypertrophy if the load selected to complete the repetition prescriptions is too low. For example, if an individual can perform 20 repetitions to failure with a given load but terminates each set at 15 repetitions, they would finish at 5-RIR. Although this proximity-to-failure may be sufficient to promote some degree of muscle hypertrophy, it is possible that closer proximities-to-failure may be more beneficial. Prescribing an RIR target may thus be a viable set termination strategy to ensure a sufficient RT stimulus to promote meaningful muscle hypertrophy is reached. However, whether closer proximities-to-failure always promote greater muscle hypertrophy or whether reaching failure on every set is required for maximising muscle hypertrophy is unclear and requires further investigation.

1.2 Overall Thesis Objectives

The aims of this thesis are to i) explore the efficacy of RIR prescription as a set termination strategy, and ii) investigate the influence of proximity-to-failure on muscle hypertrophy, neuromuscular fatigue, muscle damage, and perceptual responses, to improve practical recommendations. An overview of studies included in this thesis is provided in Figure 1.1. Firstly, a scoping review was conducted to summarise key definitions for ‘failure’ in RT, discuss methods for controlling proximity-to-failure, identify current research limitations, and provide tentative conclusions about the influence of proximity-to-failure on muscle hypertrophy, neuromuscular fatigue, muscle damage and perceived discomfort. In addition, studies retrieved from the scoping review that measure changes in muscle size from pre- to post-intervention were meta-analysed to investigate the influence of proximity-to-failure on muscle hypertrophy (Study One). An original research study was also conducted to investigate how proximity-to-failure impacts neuromuscular fatigue and perceptual responses to RT (Study Two), along with the accuracy of subjective RIR predictions (Study Three) in resistance-trained individuals. Finally, another original research study compared the effect of RT performed to momentary muscular failure versus with RIR on muscle hypertrophy and neuromuscular fatigue across an 8-week intervention (Study Four). This thesis by publication therefore includes our scoping review of the relevant literature (Chapter Two) and four published studies (Chapters Four to Seven).

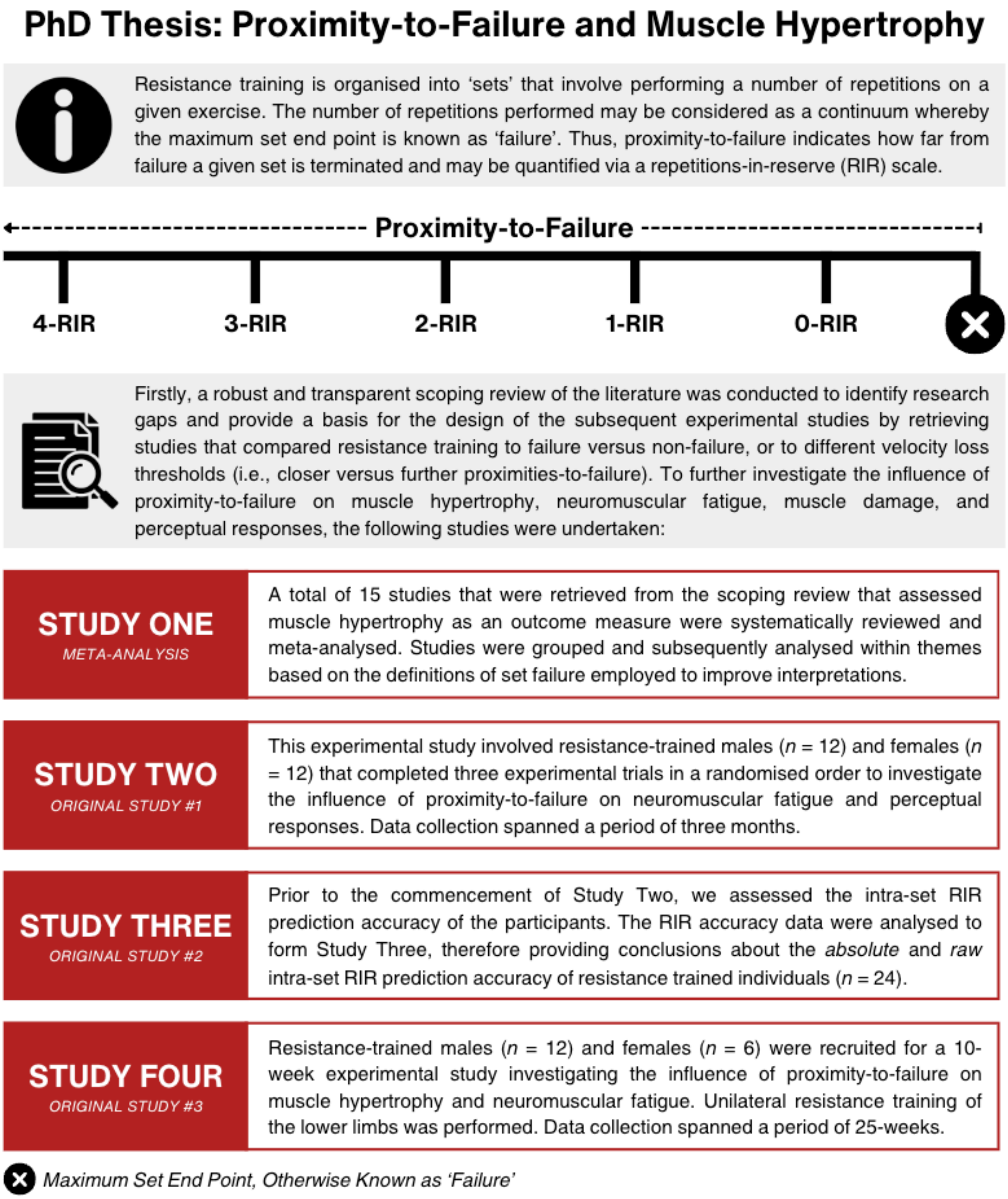

Figure 1.1. PhD thesis overview, including the key characteristics of each study conducted.

Chapter Two – Towards an Improved Understanding of Proximity-to-Failure in Resistance Training and its Influence on Skeletal Muscle Hypertrophy, Neuromuscular Fatigue, Muscle Damage and Perceived Discomfort: A Scoping Review

Please note, the following text in Chapter Two has been adapted from a peer-reviewed and published manuscript (DOI: 10.1080/02640414.2022.2080165).

2.1 Preface

To provide a framework for this thesis and inform the design of subsequent research studies, a comprehensive literature review on RT proximity-to-failure and its influence on relevant outcome measures (i.e., muscle hypertrophy, neuromuscular fatigue, muscle damage and perceived discomfort) was conducted. Considering the heterogeneity in the literature investigating proximity-to-failure; specifically, the variability in definitions of set failure employed and research questions posed, a scoping review was performed that grouped the relevant studies into 'themes' to allow for improved interpretations within each theme. Multiple research limitations were identified regarding the control and quantification of proximity-to-failure, with the intention to address these limitations in the subsequent experimental studies. The aims of this scoping review were to i) improve the understanding of RT proximity-to-failure and advance future research on the relationship between RIR and relevant outcomes, and ii) improve real-world RT practices with better informed RIR prescription.

2.2 Introduction

The repetitions performed in a resistance training (RT) set lie on a continuum whereby the maximum termination point is "momentary muscular failure", defined as when an individual is unable to complete the concentric portion of a given repetition with a full range-of-motion and without deviation from the prescribed form of the exercise [24]. Set termination may also occur a given number of repetitions from momentary muscular failure. This "proximity-to-failure" can be quantified as "repetitions-in-reserve" (RIR) upon set termination [25, 26], defined as the number of complete repetitions one believes they could perform before reaching momentary muscular failure (i.e., 1-RIR indicates the individual terminated the set when they believed they could still perform one additional repetition, while 0-RIR indicates the next repetition attempted would result in momentary muscular failure). Proximity-to-failure is considered an important variable influencing physiological adaptations to RT such as skeletal muscle hypertrophy [27]. As proximity-to-failure nears, there is a progressive increase in recruitment of higher-threshold motor units [28, 29] that exposes type II muscle fibres to mechanical tension, which is the key stimulus for myofibrillar protein synthesis [30] and subsequently muscle hypertrophy [31]. Proximity-to-failure during RT also influences short-term physiological responses including neuromuscular fatigue and muscle damage [32], which can impair contractile function during and subsequent to RT. For example, neuromuscular fatigue consequent to RT may arise from intramuscular perturbations in metabolite concentration or energy depletion that impair force production (known as peripheral fatigue), and/or due to the inability of the central nervous system to activate the musculature (known as central fatigue) [33, 34], ultimately preventing the development of the force required to complete a full range-of-motion repetition. In addition, proximity-to-failure also influences perceived discomfort [14], and along with neuromuscular fatigue and muscle damage, these short-term responses may impair one's ability to apply sufficient mechanical tension to promote muscle hypertrophy over time via their influence on post-RT recovery and subsequent RT performance, as well as potentially long-term adherence to RT.

A key barrier to further understanding of the influence of proximity-to-failure on RT adaptations is that no consensus definition for "failure" exists in the literature. As such, in this scoping review and the remainder of this thesis, "set failure" is used as an umbrella term to describe the set termination criteria for the definition of "failure" used in a given study. For example, participants in the set failure condition in some studies perform RT to volitional failure [35, 36] or to a repetition-maximum (RM) [37, 38], both of which can influence the proximity-to-failure achieved upon set termination as they are dependent on either one's subjective experience or a predetermined repetition prescription, respectively. In contrast, the most objective way to control set failure is by applying the definition of momentary muscular failure, which, by definition, involves an involuntary set termination [24]. Importantly, meta-analyses assessing the effect of "failure" on physiological adaptations have compared studies applying various definitions of set failure, potentially confounding the conclusions drawn [11-13]. Another limitation of current meta-analyses is the ambiguity and variability in the RIR achieved in the "non-failure" conditions in included studies, as proximity-to-failure is either not clearly quantified or differs substantially between studies. For these reasons, it is difficult to form practical recommendations regarding proximity-to-failure for maximising muscle hypertrophy whilst minimising other short-term responses, such as neuromuscular fatigue, muscle damage, and perceived discomfort, which may negatively influence long-term RT outcomes.

The objectives of this scoping review are therefore to: i) summarise key definitions for set failure in RT used throughout the literature, ii) discuss methods for controlling (or determining) proximity-to-failure in non-failure RT, and iii) review current evidence for the role of proximity-to-failure on physiological adaptations and responses to RT. The limitations of current research will also be summarised to inform recommendations for future studies on the influence of RT proximity-to-failure on physiological adaptations and responses to RT.

Table 2.1. Key terms and definitions. Key terms relevant to defining set failure and proximity-to-failure in resistance training used throughout this scoping review and the remainder of this thesis.

Key Term	Definition
Set	A continuum of repetitions of a resistance training exercise.
Set termination	The point during a resistance training set that an individual ceases performing repetitions and the set is terminated, either voluntarily or involuntarily.
Set failure	Umbrella term describing the set termination criteria for the definition of "failure" applied in a given study.
Momentary muscular failure	The point where, despite attempting to do so, an individual is unable to complete the concentric portion of their current repetition with a full range-of-motion without deviation from the prescribed form of the exercise.
Volitional failure	The point at which an individual perceives they have reached the set termination criteria.
Repetition-maximum	A predetermined repetition prescription with a given load, assuming that the final repetition performed is the last full repetition able to be completed prior to momentary muscular failure.
Proximity-to-failure	The number of repetitions remaining in a set prior to momentary muscular failure, quantified as the difference in the number of full repetitions between set termination and momentary muscular failure [known as repetitions-in-reserve (RIR)].

2.3 Methods

The protocol for this scoping review was registered with Open Science Framework on the 24th of September 2021 (https://osf.io/y4g8v/). Considering the heterogeneous nature of original research studies investigating the influence of proximity-to-failure during RT on relevant outcomes, a scoping review was chosen as a means of summarising the evidence within the available literature. A scoping review allows for the navigation of multiple nuanced themes where a systematic review is inappropriate, providing a robust and transparent overview of the literature whilst identifying research gaps [39, 40]. A population, concept, and context (PCC) framework [41] was therefore used to develop the following research question for this scoping review: “How does resistance training proximity-to-failure influence skeletal muscle hypertrophy, neuromuscular fatigue, muscle damage, and perceived discomfort (or affective responses), and what are the key methodological considerations for interpreting the findings of the literature and the gaps to be addressed in future research?”

The literature search followed the PRISMA-ScR (Preferred Reporting Items for Systematic Reviews and Meta-Analyses for Scoping Reviews) guidelines [42]. Literature searches of the PubMed, SCOPUS and SPORTDiscus databases were conducted in September 2021 using the following search terms for each individual database:

1. “resistance training” OR “resistance exercise” OR “strength training”
2. “failure” OR “muscular failure” OR “velocity loss”
3. “muscle hypertrophy” OR “muscle size” OR “muscle growth” OR “muscle mass” OR “muscle thickness” OR “cross-sectional area”
4. “fatigue” OR “neuromuscular fatigue” OR “peripheral fatigue” OR “muscle damage” OR “discomfort” OR “enjoyment” OR “affective” OR “affective response”

An overview of the article identification process for this scoping review is shown in Figure 2.1. The article identification process was completed independently by two authors (MR and JF) with any disagreement resolved by mutual discussion. Studies were included if: 1) participants were apparently healthy adults of any age and RT experience, 2) participants were randomized to experimental groups, 3) the experimental comparison involved a group performing RT to set failure (any definition of set failure) versus a non-failure group, or two groups terminating

RT sets at different proximities-to-failure [e.g., set termination informed by velocity loss thresholds or subjective ratings of perceived exertion (RPE)], 4) outcome measures included either a) muscle hypertrophy, b) mechanical or metabolic markers of neuromuscular fatigue, c) subjective or biochemical markers of muscle damage, or d) perceived discomfort or affective responses. Only original research articles in peer reviewed journals were included. Any additional articles that were identified through reference checking or manual searching were subjected to the same screening processes applied following the initial database search. Data charting was carried out by the principal investigator (MR) to capture key study information in a table format (Tables 2.2 - 2.4).

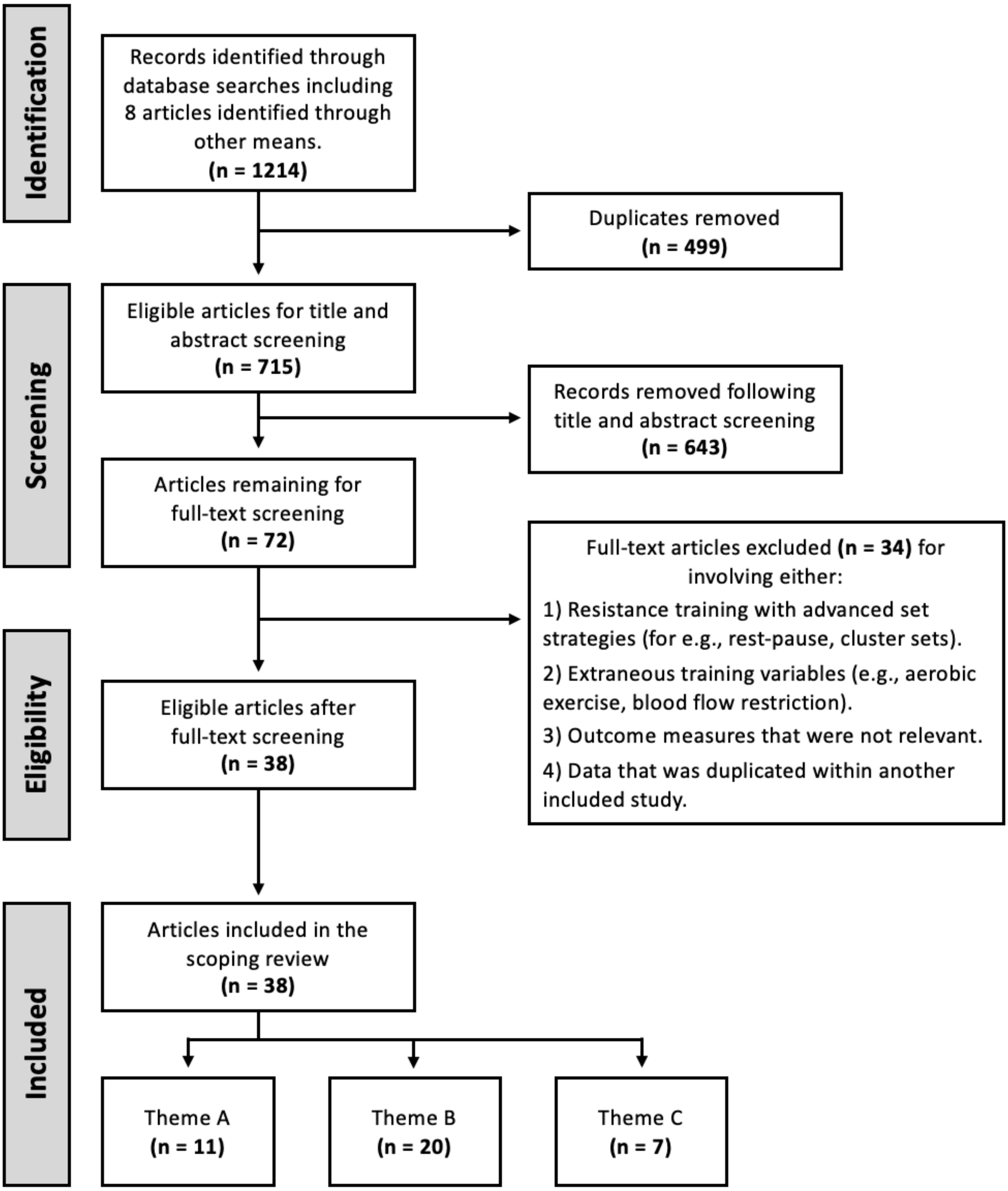

Figure 2.1. PRISMA flow chart. Summary of systematic literature search and article selection process.

2.4 Results

2.4.1 Selection of sources of evidence

The initial search yielded 1214 results and after duplicates were removed, 715 articles were entered for title and abstract review. Subsequently, 72 articles were selected for full-text review, with 34 full-text articles excluded for involving i) resistance training with advanced set strategies (for e.g., rest-pause, cluster sets), ii) extraneous training variables (e.g., aerobic exercise, blood flow restriction), iii) outcome measures that were not relevant, or iv) data that was duplicated within another included study. Thus, 38 articles were included in this scoping review (Figure 2.1).

Three broad study themes across the relevant literature were developed and agreed upon *a priori* by the research team. During data extraction, each included study was grouped into one of the three themes based on the following criteria:

1. Theme A: Studies comparing a group(s) performing RT to momentary muscular failure to a non-failure group(s) [14, 43-52].
2. Theme B: Studies comparing a group(s) performing RT to set failure (defined as anything other than the definition of momentary muscular failure) to a non-failure group(s) [32, 35-38, 53-67].
3. Theme C: Studies theoretically comparing different proximities-to-failure (i.e., applying different velocity-loss thresholds that modulate set termination and albeit indirectly, influence proximity-to-failure), with no inclusion of a group performing RT to momentary muscular failure *per se* [68-74].

For a comprehensive summary of included studies, see Tables 2.2 - 2.4.

Table 2.2. Summary of data extraction for Theme A. Summary of studies included within Theme A comparing a group(s) performing RT to momentary muscular failure to a non-failure group(s). *CK, creatine kinase; CMJ, countermovement jump; CSA, cross-sectional area; EF, elbow flexor; MRI, magnetic resonance imaging; MVC, maximum voluntary contraction; PP, peak power; RF, rectus femoris; Reps, repetitions; RM, repetition maximum; RPD, rating of perceived discomfort; VeL, velocity loss; VL, vastus lateralis; ↑ = increased; ↓ = decreased; ↔ = no change or difference; * = no statistical analysis reported to determine statistical within and/or between groups differences.*

Theme A studies assessing muscle hypertrophy

Study	Participants	Age (mean ± SD)	Intervention groups	Intervention duration (sessions/week)	Volume equated	Outcome measure (device; muscle)	Key findings
Lacerda et al. 2020 [43]	Young men (n=10) → Untrained: No RT 6-months prior	23.7 ± 4.9 y	Failure: 3-4 sets x *n* reps → 50-60% 1-RM Non-failure: 3-4 sets x mean of reps performed in Failure → 50-60% 1-RM	14 weeks (2-3/week)	Yes	Muscle CSA (ultrasound; VL, RF)	No between-group differences in VL and RF CSA.
Lasevicius et al. 2019 [46]	Young men (n=25) → Untrained: No RT 6-months prior	24 ± 4.9 y	Failure 1: 3 sets x *n* reps → 80% 1-RM Failure 2: 3 sets x *n* reps → 30% 1-RM Non-failure 1: ~5 sets x 60% of reps performed in Failure 1 → 80% 1-RM Non-failure 2: ~5 sets x 60% of reps performed in Failure 2 → 30% 1-RM	8 weeks (2/week)	Yes	Muscle CSA (MRI; quadriceps)	↑ Quadriceps CSA for both Failure groups and Non-failure 1, with no between-group differences and ↔ for Non-failure 2.
Martorelli et al. 2017 [44]	Young women (n=89) → Untrained: No RT 6-months prior	21.9 ± 3.3 y	Failure: 3 sets x *n* reps → 70% 1-RM Non-failure 1: 4 sets x 7 reps → 70% 1-RM	10 weeks (2/week)	Yes No	Muscle thickness (ultrasound; EF)	↑ EF thickness for Failure and Non-failure 1, with ↔ for Non-failure 2.*

			Non-failure 2: 3 sets x 7 reps → 70% 1-RM				
Nobrega et al. 2018 [45]	Young men (n=32) → Untrained: No RT 6-months prior	23 ± 3.6 y	Failure 1: 3 sets x *n* reps → 80% 1-RM Failure 2: 3 sets x *n* reps → 30% 1-RM Non-failure 1: 3 sets x *n* reps (volitional interruption) → 80% 1-RM Non-failure 2: 3 sets x *n* reps (volitional interruption) → 30% 1-RM,	12 weeks (2/week)	Yes	Muscle CSA (ultrasound; VL)	↑ VL CSA for all groups, with no between-group differences.
Santanielo et al. 2020 [47]	Young men (n=14) → Trained: ≥2 years of RT experience	23.1 ± 2.2 y	Failure: *n* sets x *n* reps → 75% 1-RM Non-failure: *n* sets x *n* reps (volitional interruption) → 75% 1-RM	10 weeks (2/week)	No	Muscle CSA (ultrasound; VL)	↑ VL CSA for both groups, with no between-group differences.

Theme A studies assessing neuromuscular fatigue, muscle damage, or perceived discomfort

Study	Participants	Age (mean ± SD)	Trials	Volume equated	Outcome measure (time point post-exercise; measure)	Key findings
Amdi et al. 2021 [51]	Young men and women (n=16) → Trained: ≥6 months of RT experience	27 ± 4.3 y	Failure: 5 sets x 4-6 reps → 4-6 RM Non-failure: 5 sets x 5 reps → 80% 1-RM	Yes	Neuromuscular fatigue: Lifting velocity at 80% 1-RM (+5-min, +24-hrs, +48-hrs, +72-hrs)	Greater ↓ lifting velocity at 80% 1-RM for men compared to women in Non-failure at all time points besides 72-hrs.

						↔ Lifting velocity at 80% 1-RM between men and women in Failure at all time points.
Fonseca et al. 2020 [48]	Young men (n=22) → Trained: 1-5 years of RT experience	21.4 ± 2.3 y	Failure: 4 sets x *n* reps → 12-RM Non-failure: 8 sets x 6 reps → 12-RM	Yes	Neuromuscular fatigue: CMJ, Lifting velocity at 70% 1-RM (+15-s, +10-min, +20-min, +30-min)	↓ CMJ performance at all time points for Failure and at 15-s for Non-failure, with greater ↓ observed at all time points for Failure compared to Non-failure. ↓ Lifting velocity at 70% 1-RM at 15-s, 10-min, and 20-min for Failure and at 15-s for Non-failure, with greater ↓ observed at 15-s, 10-min, and 20-min for Failure compared to Non-failure.
Gantois et al. 2021 [50]	Young men and women (n=29) → Trained: 1-5 years of RT experience	23.8 ± 3.8 y	Failure: 4 x *n* reps → 15-RM Non-failure: 5 x 12 reps → 15-RM	Yes	Neuromuscular fatigue: CMJ (+15-s, +30-min) Metabolic response: Blood lactate (+2-min)	↓ CMJ performance at all time points for both groups, with greater ↓ observed at 15-s for Failure compared to Non-failure. No between-group differences in blood lactate.*
Kassiano et al. 2021 [49]	Young men and women (n=28) → Trained: 6.8 years (mean) of RT experience	23.6 ± 3.7 y	Failure: 4 sets x *n* reps → 15-RM Non-failure: 5 sets x 12 reps → 15-RM	Yes	Neuromuscular fatigue: Isokinetic force (+30-min)	↓ Isokinetic force at all time points for both groups (except at 30-min for knee flexion at 120 degrees), with no between-group differences.
Mangine et al. 2022 [52]	Young men (n=14) → Trained: 7.6 years (mean) of RT experience	24.6 ± 3 y	Failure: 5 sets x *n* reps → 80% 1-RM Non-failure: 5 sets x *n* reps (3-RIR, last set to Failure) → 80% 1-RM	Yes	Neuromuscular fatigue: Lifting velocity at 80% 1-RM (+24-hrs, +48-hrs, +72-hrs) Muscle damage: Blood CK (+6-hrs,	No between-group differences in lifting velocity. ↑ Blood CK at 6-hrs and 48-hrs for both groups, with no between-group differences.

					+24-hrs, +48-hrs, +72-hrs)	
Santos et al. 2019 [14]	Young women (n=12) → Trained: 4.5 years (mean) of RT experience	24.9 ± 5 y	Failure: 4 sets x *n* reps → 10-RM Non-failure: 4 sets x *n* reps (performed to 20% VeL) → 10-RM	Yes	Neuromuscular fatigue: Mean lifting velocity from first to final set Perceived discomfort: RPD (post-set)	Greater ↓ lifting velocity for Failure compared to Non-failure. Greater ↑ perceived discomfort observed for Failure compared to Non-failure after all sets besides the final set.

Table 2.3. Summary of data extraction for Theme B. Summary of studies included within Theme B comparing a group(s) performing RT to set failure (defined as anything other than the definition of momentary muscular failure) to a non-failure group(s). *AD, anterior deltoid; AST, aspartate aminotransferase; CK, creatine kinase; CMJ, countermovement jump; CSA, cross-sectional area; EF, elbow flexor; MRI, magnetic resonance imaging; MVC, maximum voluntary contraction; PM, pectoralis major; Reps, repetitions; RM, repetition maximum; TB, triceps brachii; VA, voluntary activation; VeL, velocity loss; VM, vastus medialis; ↑ = increased; ↓ = decreased; ↔ = no change or difference; * = no statistical analysis reported to determine statistical within and/or between groups differences.*

Theme B studies assessing muscle hypertrophy

Study	Participants	Age (mean ± SD)	Intervention groups	Intervention duration (sessions/week)	Volume equated	Outcome measures	Key findings
Bergamasco et al. 2020 [55]	Older men and women (n=41) → Untrained: No RT 6-months prior	65.5 ± 4.5 y	Failure: 3 sets x *n* reps → 40% 1-RM Non-failure 1: 3 sets x *n* reps (volitional interruption) → 40% 1-RM Non-failure 2: 3 sets x 10 reps → 40% 1-RM	12 weeks (2/week)	No	Muscle CSA (ultrasound; VL)	↔ VL CSA for all groups.
Karsten et al. 2021 [53]	Young men (n=18) → Trained: 2-5 years of RT experience	23.5 ± 4.5 y	Failure: 4 sets x 10-RM → 75% 1-RM Non-failure: 8 sets x 5 reps → 75% 1-RM	6 weeks (2/week)	Yes	Muscle thickness (ultrasound; VM, EF, AD)	↑ VM and EF thickness for Failure and ↔ for Non-failure, with no between-group differences. ↑ AD thickness for both groups, with no between-group differences.
Sampson et al. 2016 [54]	Young men (n=28) → Untrained: No RT 6-months prior	23.8 ± 6.6 y	Failure: 4 sets x 6 reps → 85% 1-RM Non-failure 1 and 2: 4 sets x 4 reps → 85% 1-RM	12 weeks (3/week)	No	Muscle CSA (MRI; EF)	↑ EF CSA for all groups (pooled analysis), with no between-group differences.

Terada et al. 2021 [35]	Young men (n=27) → Untrained: No RT 12-months prior	20.03 ± 0.8 y	Failure: 3 sets x *n* reps (volitional failure) → 40% 1-RM Non-failure: 3 sets x *n* reps (performed to 20% VeL) → 40% 1-RM	8 weeks (2/week)	Yes	Muscle thickness (ultrasound; PM, TB)	↑ PM and TB thickness for both groups*, with no between-group differences.

Theme B studies assessing neuromuscular fatigue or muscle damage

Study	**Participants**	**Age (mean ± SD)**	**Trials**	**Volume equated**	**Outcome measure (time point post-exercise; measure)**	**Key findings**
Costa et al. 2021 [37]	Young men (n=11) → Trained: 1-5 years of RT experience	23.8 ± 2.3 y	Failure: 3 sets x 10-RM → 10-RM Non-failure: 6 sets x 5 reps → 10-RM	Yes	Neuromuscular fatigue: CMJ (+15-s, +30-min)	↔ CMJ performance at all time points for both groups.
Garcia-Ramos et al. 2020 [56]	Young men (n=10) → Trained: ≥3 years of RT experience	29.4 ± 3.5 y	Failure: 3 sets x 10-RM → 10-RM Non-failure: 6 sets x 5 reps → 10-RM	Yes	Neuromuscular fatigue: Mean lifting velocity from first to final set Metabolic response: Blood lactate (post-set)	Greater ↓ lifting velocity for Failure compared to Non-failure. Greater ↑ Blood lactate post-sets for Failure compared to Non-failure.
Gonzalez-Badillo et al. 2016 [38]	Young men (n=9) → Trained: 2-4 years of RT experience	23.3 ± 3.9 y	Failure: 3 sets x 8-RM → 80% 1-RM Non-failure: 3 sets x 4 reps → 80% 1-RM	No	Neuromuscular fatigue: CMJ, lifting velocity with V1-load (+0-min, +6-hrs, +24-hrs, +48-hrs) Muscle damage: Blood CK (+0-min, +48-hrs)	Greater ↓ CMJ performance at all time points for Failure compared to Non-failure. Greater ↓ lifting velocity at 0-min and 6-hrs for Failure compared to Non-failure. ↑ Blood CK at all time points for Failure and at 48-hrs for Non-

						failure, with no between-group differences.
Gonzalez-Hernande et al. 2021 [57]	Young men (n=12) → Trained: ≥1 year of RT experience	23.6 ± 1.5 y	Failure: 6 sets x 10-RM → 75% 1-RM Non-failure: 6 sets x 5 reps → 75% 1-RM	No	Neuromuscular fatigue: MVC, VA (+1-hr, +24-hrs, +48-hrs), mean lifting velocity from first to final set Peripheral fatigue: Potentiated doublet and single twitch (post-set, +1-hr, +24-hrs, +48-hrs) Muscle damage: Blood CK and AST (+1-hr, +24-hrs, +48-hrs)	↓ MVC at all time points except 48-hrs for both groups, no between-group differences. ↓ VA at all time points for both groups, with no between-group differences. ↓ Lifting velocity for Failure and ↔ for Non-failure. ↑ Peripheral fatigue markers from first set until 1-hr post-exercise for both groups, with greater ↑ observed from the third to the sixth sets for Failure compared to Non-failure. ↑ Blood CK and AST at all time points for Failure and at 1-hr for Non-failure, with no between-group difference.
Gorostiaga et al. 2012 [58]	Young men (n=6) → Trained athletes	34 ± 6 y	Failure: 5 sets x 10-RM → 83% 1-RM Non-failure: 10 sets x 5 reps → 83% 1-RM	No	Metabolic response: Blood uric acid (+16-min, +45-min), intramuscular ATP/PCr/lactate/IMP	↑ Blood uric acid at all time points for Failure and ↔ for Non-failure, with greater ↑ observed for Failure compared to Non-failure. Greater ↓ intramuscular ATP, PCr, IMP and ↑ intramuscular lactate for Failure compared to Non-failure.
Gorostiaga et al. 2014 [59]	Young men (n=13) → Trained athletes	34 ± 5 y	Failure: 5 sets x 10-RM → 83% 1-RM Non-failure: 10 sets x 5 reps → 83% 1-RM	No	Metabolic response: Blood lactate and ammonia (+0-min)	Greater ↑ blood lactate and ammonia for Failure compared to Non-failure.

Linnamo et al. 2005 [60]	Young men and women (n=16) → Untrained: No RT experience	25.2 ± 0.6 y	Failure: 5 sets x 10-RM → 10-RM Non-failure 1: 5 sets x 10 reps → 40% 10-RM Non-failure 2: 5 sets x 10 reps → 70% 10-RM	No	Neuromuscular fatigue: Isometric force (post-set, +1-hr, +2-hrs) Metabolic response: Blood lactate (+0-min)	Greater ↓ peak force at all time points for Failure compared to Non-failure 1 and 2.* ↑ Blood lactate for Failure and ↔ for Non-failure groups (except men in Non-failure 1).*
Martorelli et al. 2021 [66]	Young men (n=12) → Trained: ≥1 year of RT experience	24.2 ± 4.4 y	Failure 1: 5 sets x *n* reps → 75% 1-RM Failure 2: 5 sets x *n* reps → 90% 1-RM Non-failure: 5 sets x 6 reps → 50% 1-RM	No	Metabolic response: Blood lactate (+3-min) Muscle damage: Blood CK (+24-hrs)	↑ Blood lactate for all groups, with greater ↑ observed for Failure 1 compared to other trials. ↑ Blood CK for Failure 1 and 2, with no between-group differences and ↔ for Non-failure. Greater ↑ observed for Failure 1 compared to Non-failure.
Moran-Navarro et al. 2017 [61]	Young men (n=10) → Trained: 8.2 years (mean) of RT experience	21.5 ± 4 y	Failure: 3 sets x 10-RM → 75% 1-RM Non-failure 1: 3 sets x 5 reps → 75% 1-RM Non-failure 2: 6 sets x 5 reps → 75% 1-RM	 No Yes	Neuromuscular fatigue: CMJ, lifting velocity with V1-load (+0-min, +6-hr, +24-hrs, +48-hrs, +72-hrs) Metabolic response: Blood ammonia (+0-min, +6-hr, +24-hrs, +48-hrs, +72-hrs) Muscle damage: Blood CK (+0-min, +6-hr, +24-hrs, +48-hrs, +72-hrs)	Greater ↓ lifting velocity at 0-min, 24-hrs, and 48-hrs for Failure compared to Non-failure 1 and 2. Greater ↓ CMJ performance at 0-min for Failure compared to Non-failure 1 and 2. Greater ↑ blood ammonia at 0-min and 6-hrs for Failure compared to Non-failure 1 and 2. Greater ↑ blood CK at 6-hrs and 24-hrs for Failure compared to Non-failure 1 and 2.

Pareja-Blanco et al. 2017 [32]	Young men (n=10) → Trained: 2-4 years of RT experience	23.6 ± 3.7 y	Failure: 3 sets x 12-RM → 70% 1-RM Non-failure: 3 sets x 6 reps → 70% 1-RM	No	Neuromuscular fatigue: CMJ, lifting velocity with V1-load (+0-min, +6-hr, +24-hrs, +48-hrs) Muscle damage: Blood CK (+5-min, +48-hrs)	Greater ↓ lifting velocity at 6-hrs and 24-hrs for Failure compared to Non-failure. Greater ↓ CMJ performance at all time points for Failure compared to Non-failure. ↑ Blood CK at 48-hrs for both groups, with greater ↑ observed for Failure compared to Non-failure.
Pareja-Blanco et al. 2019 [62]	Young men (n=10) → Untrained: No RT experience	20.6 ± 2.7 y	Failure: 3 sets x 10-RM → 75% 1-RM Non-failure: 3 sets x 5 reps → 75% 1-RM	No	Neuromuscular fatigue: CMJ, lifting velocity at V1-load (+0-min, +6-hrs, +24-hrs, +48-hrs) Muscle damage: Blood CK (+0-min, +48-hrs)	Greater ↓ lifting velocity 0-min for Failure compared to Non-failure. ↓ CMJ performance at all time points for both groups besides 48-hrs for Failure, with no between-group differences. ↑ Blood CK at 48-hrs for both groups, with no between-group differences.
Pareja-Blanco et al. 2020 [63]	Young men (n=10) → Trained: 2-4 years of RT experience	22.1 ± 3.5 y	Failure: 3 sets x 4-, 6-, 8-, 10-, 12-RM → 70-90% 1-RM Non-failure: 3 sets x 50% of reps performed in Failure → 70-90% 1-RM	No	Neuromuscular fatigue: CMJ, lifting velocity at V1-load (+0-min, +6-hrs, +24-hrs, +48-hrs) Muscle damage: Blood CK (+5-min, +48-hrs)	Greater ↓ lifting velocity and CMJ performance at several timepoints for several of the Failure protocols compared to Non-failure protocols. ↑ Blood CK at 48-hrs for most Failure and Non-failure protocols, with greater ↑ observed in Failure protocols that completed the highest number of reps.*
Raastad et al. 2000 [64]	Young men (n=9) → Trained athletes	26.9 ± 4.2 y	Failure 1: 3 sets x 3-, 6-RM → 3-6-RM Non-failure: 3 x 3-6 reps → 70-76% 3-RM	No	Metabolic response: Blood lactate (during, +15-min,	↑ Blood lactate during exercise for Failure compared to Non-failure.

					+30-min, +45-min, +1-hr)	
Sanchez-Medina et al. 2011 [65]	Young men (n=18) → Trained: 3-5 years of RT experience	25.6 ± 3.4 y	Failure: 3 sets x 4-, 6-, 8-, 10-, 12-RM → 70-90% 1-RM Non-failure: 3 sets x *n* reps → 70-90% 1-RM	No	Neuromuscular fatigue: CMJ, lifting velocity with V1-load (+0-min), mean lifting velocity from first to final set Metabolic response: Blood lactate and ammonia (+1-min, +3-4-min, +5-7-min)	Greater ↓ lifting velocity from first to final set and lifting velocity with V1-load as performed repetitions approached the maximum predicted number of repetitions.* Greater ↑ blood lactate and ammonia as performed repetitions approached the maximum predicted number of repetitions.*
Shibata et al. 2019 [67]	Young men (n=10) → Trained: ≥6 months of RT experience	20.5 ± 1.1 y	Failure: 3 sets x *n* reps → 75% 1-RM Non-failure: 6 sets x *n* reps (same total number of repetitions as Failure) → 75% 1-RM	Yes	Neuromuscular fatigue: MVC (+0-min, +24-hrs) Metabolic response: Blood lactate (+5-min, +10-min, +15-min, +30min) Muscle damage: Perceived muscle soreness (+24-hrs)	↓ MVC strength for both groups at 0-min, with greater ↓ observed for Failure compared to Non-failure, and ↓ MVC strength only for Failure at 24-hrs. ↑ Blood lactate at all time points for both groups, with greater ↑ observed for Failure at all time points. ↑ Perceived muscle soreness for both groups, with no between-group differences.
Vasquez et al. 2013 [36]	Young men (n=12) → Trained: ≥2 year of RT experience	21.9 ± 1.3 y	Failure: 1 set x *n* reps (volitional failure) → 50-90% 1-RM Non-failure: 1 set x 3 reps → 50-90% 1-RM	No	Neuromuscular fatigue: Peak power from first to final set	↓ Peak power for all Failure protocols and ↔ for all Non-failure protocols.

Table 2.4. Summary of data extraction for Theme C. Summary of studies included within Theme C comparing different proximities-to-failure (e.g., by applying different velocity-loss thresholds), with no inclusion of a group performing RT to momentary muscular failure per se. *CMJ, countermovement jump; CSA, cross-sectional area; MRI, magnetic resonance imaging; PM, pectoralis major; RF, rectus femoris; Reps, repetitions; RM, repetition maximum; VeL, velocity loss; VI, vastus intermedius; VL, vastus lateralis; VM, vastus medialis; ↑ = increased; ↓ = decreased; ↔ = no change or difference; → = additional information. * = no statistical analysis reported to determine statistical within and/or between groups differences.*

Theme C studies assessing muscle hypertrophy

Study	Participants	Age (mean ± SD)	Intervention groups	Intervention duration (sessions/week)	Volume equated	Outcome measures	Key findings
Andersen et al. 2021 [74]	Young men and women (n=10) → Trained: ≥2 years of RT experience	23.0 ± 4.3 y	30% VeL: 2-3 sets x 75-80% 1-RM 15% VeL: 4-6 sets x 75-80% 1-RM	9 weeks (2/week)	Yes	Muscle thickness (ultrasound; VL, RF)	↑ VL and RF thickness for both groups (pooled analysis) with no between-group differences.
Pareja-Blanco et al. 2017 [71]	Young men (n=24) → Trained: 18 months to 4 years of RT experience	22.7 ± 1.9 y	40% VeL: 3 sets x 70-85% 1-RM 20% VeL: 3 sets x 70-85% 1-RM	8 weeks (2/week)	No	Muscle volume (MRI; VI, VL, VM, RF)	↑ VM and total quadriceps volume for both groups, with no between-group differences. ↑ VL + VI volume for 40% VeL, with ↔ observed in 20% VeL. ↔ RF volume for both groups.
Pareja-Blanco et al. 2020 [72]	Young men (n=64) → Trained: 18 months to 4 years of RT experience	24.1 ± 4.3 y	40% VeL: 3 sets x 70-85% 1-RM 20% VeL: 3 sets x 70-85% 1-RM 10% VeL: 3 sets x 70-85% 1-RM 0% VeL: 3 sets x 70-85% 1-RM	8 weeks (2/week)	No	Muscle CSA (ultrasound; VL)	↑ VL CSA for 40% and 20% VeL, with no between-group differences.

							↔ VL CSA for 10% and 0% VeL.
Pareja-Blanco et al. 2020 [73]	Young men (n=64) → Trained: ≥1.5 years of RT experience	24.1 ± 4.3 y	50% VeL: 3 sets x 70-85% 1-RM 25% VeL: 3 sets x 70-85% 1-RM 15% VeL: 3 sets x 70-85% 1-RM 0% VeL: 3 sets x 70-85% 1-RM	8 weeks (2/week)	No	Muscle CSA (ultrasound; PM)	↑ PM CSA for all groups, with greater ↑ observed in 50% compared to 0% VeL, and no other between-group differences.

Theme C studies assessing neuromuscular fatigue or muscle damage

Study	Participants	Age (mean ± SD)	Trials	Volume equated	Outcome measure (time point post-exercise; measure)	Key findings
Pareja-Blanco et al. 2019 [69]	Young men (n=17) → Trained: 2.8 years (mean) of RT experience	23.6 ± 3.6 y	40% VeL: 3 sets x 80% 1-RM 20% VeL: 3 sets x 80% 1-RM 40% VeL: 3 sets x 60% 1-RM 20% VeL: 3 sets x 60% 1-RM	No	Neuromuscular fatigue: CMJ, lifting velocity with V1-load (+0-min, +6-hrs, +24-hrs, +48-hrs)	↓ Lifting velocity at 0-min for all groups, with a greater ↓ observed for 40% VeL (60% 1-RM). ↓ Lifting velocity at 6-hrs for 20% VeL (60%1-RM) and at 24-hrs for 40% VeL (80% 1-RM). ↓ CMJ performance at IM for all groups, with a greater ↓ observed for 40% VeL (60% 1-RM). ↓ CMJ performance at 6-hrs and 24-hrs for 20% VeL (60%1-RM) and 40% VeL (60% 1-RM).
Rodriguez-Rosell et al. 2018 [70]	Young men (n=21) → Trained: 2-4 years of RT experience	23.5 ± 3.6 y	45% VeL: 3 sets x 50-80% 1-RM 30% VeL: 3 sets x 50-80% 1-RM 20% VeL: 3 sets x 50-80% 1-RM 10% VeL: 3 sets x 50-80% 1-RM	No	Neuromuscular fatigue: Lifting velocity with V1-load (+0-min)	↓ Lifting velocity for all protocols, with greater ↓ observed as VeL and the number of reps completed increased.*

					Metabolic response: Blood lactate (+0-min)	↑ Blood lactate for all protocols, with greater ↑ observed as velocity loss and the number of reps completed increased.*
Weakley et al. 2019 [68]	Young men (n=12) → Trained: ≥2 years of RT experience	23 ± 3 y	30% VeL: 5 sets x ~70% 1-RM 20% VeL: 5 sets x ~70% 1-RM 10% VeL: 5 sets x ~70% 1-RM	No	Neuromuscular fatigue: CMJ (+0-min) Metabolic response: Blood lactate (+0-min)	↓ CMJ performance as VeL increased (30% VeL < 20% VeL < 10% VeL).* ↑ Blood lactate as VeL increased (30% VeL < 20% VeL < 10% VeL).*

2.5 Discussion

2.5.1 The Definitions Applied to Set Failure in Resistance Training

There is no consensus definition for set failure in RT, with researchers commonly applying definitions consistent with either: a) momentary muscular failure, b) volitional failure, or c) a repetition maximum (RM). In many studies (allocated to Theme B), however, the definition of set failure applied is not explicitly stated and it is unclear how set termination was controlled, making it difficult to interpret study findings. This highlights the importance of clarifying key definitions related to proximity-to-failure in RT before making comparisons between studies and deriving practical recommendations from the literature.

2.5.1.1 Momentary Muscular Failure

Reaching momentary muscular failure during RT is, by definition, objective and involuntary, and can only be verified when an individual attempts, but cannot complete (i.e., fails), a final repetition (definition in Table 2.1). While some studies in Theme A use terms to describe set failure that are interchangeable with "momentary muscular failure", such as "concentric failure" or "muscle failure", the definitions of these terms are explicitly reported, and although minor variations exist, each make it clear that participants are unable to complete a final repetition with a full range-of-motion (Table 2.5). However, in other studies (allocated to Theme B), the definitions of set failure diverge, for example, Shibata et al. [67] defined "momentary failure" as occurring when "each participant failed to follow the given tempo or he was unable to lift the barbell after lowering it", highlighting the importance of establishing a consensus in the literature for terms related to proximity-to-failure. In some studies, the definition applied to momentary muscular failure also states that "proper form" must be maintained (Table 2.5) to uphold exercise safety, maintain repetition consistency, and ensure mechanical tension is directed to the target musculature. As such, we propose that future research uses the following definition adapted from Steele et al. [24]: the point where, despite attempting to do so, an individual is unable to complete the concentric portion of their current repetition with a full range-of-motion without deviation from the prescribed form of the exercise. When this definition is applied, the point of momentary muscular failure must be directly observed and not predicted, as highlighted by Steele and colleagues [24], "Without actually attempting a subsequent repetition upon completion of each previous repetition, it is impossible to be certain that a person has in fact reached momentary (muscular) failure, or indeed will do so on the subsequent repetition". For this reason, participants in a set failure condition should be instructed to simply perform RT repetitions with a given load until momentary muscular failure is reached, without a predetermined repetition target. Applying this definition of momentary muscular failure will likely improve the homogeneity of a RT stimulus within a set failure condition in research studies; however, doing so may not always be feasible or safe (e.g., the risks of technique breakdown and subsequent injury may be greater closer to momentary muscular failure, due to increased neuromuscular fatigue, particularly among less-trained individuals using complex exercises). Researchers and practitioners should therefore consider both exercise complexity and technical competency when applying momentary muscular failure to maintain safety during RT.

Table 2.5. Terms and definitions used to describe momentary muscular failure in the literature. The following terms and accompanying definitions are used in the studies allocated to Theme A, which applied a definition consistent with that of momentary muscular failure.

Study	Term used	Definition applied
Kassiano et al. 2021 [49]	Concentric muscle failure	"…inability to complete a repetition with a full range of motion and proper technique."
Lasevicius et al. 2019 [46]	Concentric failure	"…repetitions were performed until subjects were unable to perform a repetition with a full range of motion using proper form."

Martorelli et al. 2017 [44]	Concentric failure	"…the inability to complete a repetition in a full range of motion at a specific overload."
Lacerda et al. 2020 [43]	Muscle failure	"…performed until the subjects were unable to execute the concentric action of the pre-established range of motion."
Nobrega et al. 2018 [45]	Muscle failure	"…repetitions were performed to the point of inability to perform a repetition with full range of motion."
Santanielo et al. 2020 [47]	Muscle failure	"…the point of inability to complete a repetition with the full range of motion."
Fonseca et al. 2020 [48]	Muscular failure	"…the point of inability to complete a repetition with the full range of motion."
Gantois et al. 2021 [50]	Muscular failure	"…inability to complete concentric phase of movement."
Amdi et al. 2021 [51]	Muscular failure	"…the inability of the participant to complete the lift and required the assistance of the spotters."
Santos et al. 2019 [14]	Momentary failure	"…when the participant was not able to complete the concentric phase of a repetition despite a maximum effort."
Mangine et al. 2022 [52]	Momentary muscular failure	"…occurs when the trainee cannot correctly complete another concentric muscle action during a set without assistance."

2.5.1.2 Volitional Failure

In contrast to momentary muscular failure, volitional failure occurs when an individual perceives they have reached the prescribed set termination criteria. Because volitional failure is subjectively determined, this approach may result in between-individual variability in the proximity-to-failure achieved upon set termination. In one study [35] it was also unclear whether sets were terminated by the participants themselves or by the researchers, highlighting a potential misuse of the term "volitional". In another study by Vasquez et al. [36], the set termination criteria for volitional failure is not explicitly stated, and as such, it is unclear how participants terminated their sets. While only two studies [35, 36] included within this scoping review (Theme B) compared volitional failure to non-failure RT, considering no consensus definition exists for volitional failure, together with the subjective nature of this approach, caution should be applied when interpreting the findings of studies using volitional failure to control set termination.

2.5.1.3 Repetition-Maximum

Performing RT to a RM typically requires participants to first complete a RM test, which involves the determination of a load that results in a given number of repetitions (e.g., the load that results in 10 repetitions may be known as the 10-RM) performed to a predetermined definition of set failure. In some cases, participants may be required to end a RM test at volitional failure, whereas other times, momentary muscular failure may be reached on the subsequent repetition (e.g., on the 11^{th} repetition of a 10-RM set), in which case the RM indicates the maximum number of complete repetitions with the given load. Many studies determine a given RM load and prescribe a predetermined repetition target (e.g., 10 repetitions with a 10-RM load), but considering participants may experience neuromuscular adaptations or "learning effects" (i.e., increases in strength and/or performance due to improved motor control and familiarisation with a given protocol), whether the same proximity-to-failure will always be achieved with the specified repetition target is unclear. Some researchers also appear to assume a RM prescription implies momentary muscular failure is achieved upon set termination [12], while others use momentary muscular failure interchangeably with RM [52]. Importantly, a RM is not synonymous with momentary muscular failure as i) in some studies, how the RM test was conducted and whether momentary muscular failure was reached is unclear, and ii) it cannot be guaranteed that momentary muscular failure will always be reached on the final repetition of a RM set involving a predetermined repetition target. As evident in a study by Costa et al. [37], in which set failure was not explicitly defined, it remains unclear if participants achieved momentary muscular failure when performing RT with a 10-RM load.

Taken as a whole, set termination that is based on a RM prescription may not be synonymous with reaching momentary muscular failure unless otherwise stated by the researchers, and considering RM loads are commonly prescribed with a predetermined repetition target, it is plausible the true proximity-to-failure achieved varies between individuals when applying the same RM prescription. These observations highlight the importance of i) explicitly reporting the definitions applied to key terms such as RM, ii) establishing a consensus in the literature for the definition of key terms to avoid confusion and inaccuracies, and iii) ensuring that the methods used to implement a RM prescription are specific enough to allow for replication in future studies.

2.5.2 Control of Set Termination in Non-Failure Resistance Training

While the definitions of set failure applied in the literature are variable and often unclear, these same concerns often apply to non-failure RT, leading to difficulties in establishing and comparing the true proximity-to-failure between these conditions. Indeed, the set termination prescription used for a non-failure condition can influence the absolute difference in the proximity-to-failure between set failure and non-failure conditions in any given study, which likely influences conclusions on the influence of proximity-to-failure on outcome measures.

Current set termination prescriptions used in research are not able to accurately quantify the proximity-to-failure achieved during non-failure RT, and this is particularly true whereby RT is prescribed based on a predetermined number of repetitions performed with a given relative load (e.g., 3 sets of 5 repetitions with 75% 1-RM). It is well-established that both within- and between-individual variability exists in the maximum number of repetitions possible with the same relative load [75-77], due to multiple factors including day-to-day variations in performance as well as differences in absolute strength and RT experience between individuals.

For example, Cooke et al. [77] reported a range of 6-26 repetitions completed prior to reaching failure in a single set of back squats with 70% of 1-RM in a group of resistance-trained male participants. It is therefore likely that the proximity-to-failure reached by participants performing RT to a predetermined repetition target, as evident in numerous studies (see Tables 2.2 - 2.3), may vary considerably. Some studies also apply "volitional interruption" to non-failure conditions, allowing participants to terminate RT sets at their own volition. For example, Santanielo et al. [47] instructed participants to "interrupt repetitions voluntarily, according to each's own perception of fatigue…independently of how many repetitions short of failure they stopped at". This approach prevents insight into how differences in RT proximity-to-failure between conditions may affect study findings. To illustrate how set termination prescriptions in non-failure RT can influence study findings, Nobrega et al. [45] and Lasevicius et al. [46] both assessed muscle hypertrophy outcomes following RT performed to momentary muscular failure versus non-failure. Participants in the non-failure condition of the Nobrega et al. [45] study "voluntarily interrupted the exercise before muscle failure", while those in Lasevicius et al. [46] performed a predetermined number of repetitions in each set (60% of total repetitions perform in the set failure condition). As a result, the proximity-to-failure reached in the non-failure condition in Nobrega et al. [45] was likely closer to momentary muscular failure compared to Lasevicius et al. [46], which may influence conclusions regarding the relative efficacy of RT to momentary muscular failure versus non-failure for muscle hypertrophy. Recent studies have also controlled set termination by prescribing a percentage of the maximum possible repetitions in non-failure conditions (known as "level of effort"). Numerous studies [32, 38, 56, 57, 61, 65] have used this approach to assess short-term physiological responses to RT (Theme B), and it seems the term "failure" is used by these studies to describe the maximal number of full repetitions possible. For example, Gonzalez-Badillo et al. [38] compared a set failure condition performing "3 sets of 8 repetitions to failure", indicated as "3 x 8 (8)", with a non-failure condition performing "only half the maximum number of repetitions" possible, indicated as "3 x 4 (8)" and implying that participants would only be capable of performing four additional repetitions before reaching momentary muscular failure. This approach to non-failure RT, involving half the maximum number of repetitions possible, is applied in numerous studies (see Theme B), and while it improves the validity of comparisons between studies using similar approaches, it cannot inform how other proximities-to-failure influence outcomes of interest. Additionally, considering all participants use the same relative load and must perform the same number of repetitions, it is unclear whether the same proximity-to-failure is truly achieved by participants assumed to be performing sets to a given level of effort, which may ultimately influence study findings.

To address some of the issues associated with set termination prescriptions for non-failure RT, various studies [68-74] have employed a velocity-based approach whereby RT sets are performed until the lifting velocity (i.e., the absolute velocity of the concentric portion of the repetition) decreases by a specific percentage of the velocity achieved on the first (or fastest) repetition (e.g., performing repetitions with a given relative load until a 20% velocity loss occurs). While this approach theoretically results in differences in the proximity-to-failure achieved between different velocity loss conditions, the volume-load completed between conditions also differs, and participants in these studies are instructed to perform each repetition with maximal intended lifting velocity (unlike many other studies that don't use velocity loss thresholds), which can influence physiological adaptations independent of proximity-to-failure [78]. The proximity-to-failure achieved likely also varies between individuals performing RT to the same velocity loss, as evidenced by one study that found participants who performed the squat exercise until 40% velocity loss reached momentary muscular failure ~56% of the time [71]. As previously noted, there is also substantial variability between individuals in the number of repetitions that can be performed at the same relative load [75-77]. Two individuals performing RT to the same velocity loss may therefore achieve different proximities-to-failure at set termination. Further, in multiple-set protocols, neuromuscular fatigue does not accumulate homogenously among participants. These differences in fatigue accumulation influence the rate at which lifting velocity decreases, leading to between-individual differences in the proximity-to-failure achieved at set termination across multiple sets. Finally, the relative load prescribed influences the repetitions-in-reserve (RIR) achieved when using the same velocity loss percentage, as the lifting velocity of the first repetition performed is load-dependent, and therefore, the proximity-to-failure reached with a given velocity loss is also dependent on the relative load prescribed. For these reasons, among others summarised elsewhere [79], the magnitude of velocity loss during a set cannot be used to accurately inform proximity-to-failure during RT, particularly across successive sets and with different relative loads, but this approach may nonetheless inform relative differences in proximity to failure across different velocity loss conditions.

The within- and between-study variability in the proximity-to-failure reached in non-failure conditions makes it difficult to interpret the collective research findings on the influence of non-failure RT on muscle hypertrophy and short-term responses. Further, this heterogeneity presents a challenge when attempting to derive practical recommendations for manipulating proximity-to-failure in RT to achieve desired outcomes.

2.5.3 Quantifying Proximity-to-Failure in Non-Failure Resistance Training

Recently, both subjective and objective set termination approaches have emerged that may improve the ability to monitor and control proximity-to-failure during non-failure RT. For example, the subjective prediction of the number of full repetitions remaining prior to reaching momentary muscular failure (known as RIR prediction) has been proposed as a potential method to monitor proximity-to-failure during non-failure RT [25, 26]. The Borg's rating of perceived exertion (RPE) scale [80] has been adapted for the purposes of RIR prediction [26, 81], and although the use of an "RIR-based RPE" scale has been validated as a method for informing set termination and controlling proximity-to-failure during RT [25, 26, 82, 83], to our knowledge, few studies have used this approach to determine the influence of proximity-to-failure on physiological adaptations and responses to RT [15, 52, 84-86]. One of the major concerns with subjective RIR prediction, however, is the potential for inaccurate predictions given an individual's "predictive ability" is likely influenced by many factors. For example, predictive ability improves when RT sets are performed closer to momentary muscular failure [87] and particularly with higher versus lower loads [26], across subsequent sets when multiple sets are performed [82], and in resistance-trained versus untrained individuals [81, 88]. A recent meta-analysis [89] found individuals typically underpredict RIR by approximately one repetition, independent of RT experience. Participants in these meta-analysed studies were typically required to report an RIR value mid-set (e.g., calling out a 5-, 3-, or 1-RIR after completing a given repetition when they believed they had reached that proximity-to-failure), before continuing to perform repetitions until set failure was reached in aim of comparing predicted versus actual RIR. However, some studies included in the meta-analysis [89] did not apply the definition of momentary muscular failure, and it is therefore unclear what the true accuracy of the RIR predictions were. Individual tolerance to discomfort may also influence the accuracy of RIR prediction, as proximity-to-failure may be confused with perceptions of discomfort, leading to an underestimation of RIR [87] and highlighting the importance of familiarising individuals with, and distinguishing between, subjective assessments of discomfort and RIR. Despite the possibility for these inaccuracies, subjective RIR prediction is likely a practical and efficient method of monitoring RT proximity-to-failure given no equipment or data analysis is required; however, more research is required to elucidate how individual predictive ability can be improved.

Recently, lifting velocities associated with a specific number of RIR have been used as an objective and reliable measure of the RIR achieved during RT and to address some of the concerns with subjective RIR prediction. For example, Moran-Navarro et al. [90] had participants perform repetitions to "muscular failure" on the bench press, squat, prone row, and shoulder press with 65, 75, and 85% 1-RM on two separate occasions to assess the reliability of lifting velocity as an indicator of RIR. The lifting velocities associated with 2-, 4-, 6- and 8-RIR were highly reliable across multiple sets within all exercises and for all relative loads assessed. For example, mean (± SD) lifting velocities of 0.36 (± 0.04), 0.35 (± 0.04), and 0.35 (± 0.03) $m \cdot s^{-1}$ were associated with 4-RIR during bench press sets performed with loads of 65, 75, and 85% 1-RM, respectively. Although various studies have investigated the influence of different velocity loss thresholds (prescribed as a percentage loss in lifting velocity, not the lifting velocity at a specific RIR value) during RT on physiological adaptations [71-74], to our knowledge, no studies have used set termination velocities to control proximity-to-failure during RT and explore relevant outcome measures such as long-term changes in maximal strength and muscle hypertrophy. Thus, future research should aim to determine the efficacy of this approach for objectively quantifying the proximity-to-failure reached during non-failure RT.

Overall, set termination methods based on subjective and objective measures of RIR (e.g., RIR prediction and set termination velocities) may provide insights into proximity-to-failure during RT that are not possible with current methods in the literature. Considering the practicality of subjective RIR prediction, which can be easily prescribed and monitored, research that is able to implement valid methods of set termination based on RIR would improve our understanding of the influence of proximity-to-failure on muscle hypertrophy and short-term responses, and therefore, improve practical recommendations.

2.5.4 Current Evidence for the Role of Proximity-to-Failure on Muscle Hypertrophy & Short-Term Responses to Resistance Training

The systematic literature search conducted for this scoping review retrieved a total of 38 studies, with 13 studies investigating muscle hypertrophy as an outcome measure, and the remaining 25 studies investigating short-term responses (neuromuscular fatigue, muscle damage, and perceived discomfort) to RT as outcome measures (Table 2.6). Depending on the specific definition of set failure used (and therefore the research question being examined), each included study was grouped into one of the three themes to improve the validity of study comparisons and interpretations within each theme.

Table 2.6. Study allocation. Overview of the number of studies included in each theme based on the outcome measures assessed.

Theme	**Outcome Measure**	
	Muscle Hypertrophy	Neuromuscular Fatigue, Muscle Damage, or Perceived Discomfort
A	5	6
B	4	16
C	4	3
Total Studies	13	25

2.5.4.1 Influence of Resistance Training Proximity-to-Failure on Muscle Hypertrophy

The five studies [43-47] included in this scoping review that compared RT performed to momentary muscular failure versus non-failure (Theme A) found no statistically significant differences in muscle hypertrophy from pre- to post-intervention. This suggests reaching momentary muscular failure in RT is not mandatory to maximise muscle hypertrophy, particularly in untrained individuals, who were involved in four [43-46] of the five studies. Findings from Lasevicius et al. [46] highlight the loads used in RT may influence the importance of proximity-to-failure on muscle hypertrophy in untrained men, with an advantage of momentary muscular failure versus non-failure found on muscle hypertrophy when RT was performed with a low-load (30% 1-RM) versus a high-load (80% 1-RM). In contrast, another study in Theme A [45] found no statistically significant differences in muscle hypertrophy between RT performed to momentary muscular failure versus non-failure with both high- and low-load loads, but between-study differences in the proximity-to-failure achieved in the non-failure conditions may explain these divergent findings.

Four studies [35, 53-55] that investigated the effects of RT performed to set failure versus non-failure on muscle hypertrophy applied various definitions of set failure (not including momentary muscular failure) had relatively consistent findings (Theme B), with three [35, 53, 54] out of the four studies finding no statistically significant difference in muscle hypertrophy between conditions and one study [55] in older adults finding no statistically significant pre- to post-intervention changes in muscle size for either condition. Importantly, one of the studies included in Theme B did not explicitly state the definition of set failure used [54] and considering a traditional prescription (sets x repetitions x relative load) was applied to both set failure (4 sets x 6 repetitions) and non-failure (4 sets x 4 repetitions) conditions, it is unclear whether momentary muscular failure was reached, highlighting the importance for future research to state definitions of key terms and clearly explain how set termination was controlled.

The influence of different proximities-to-failure (but not momentary muscular failure per se) on muscle hypertrophy (Theme C) was investigated in four studies [71-74] that used velocity loss thresholds to inform set termination in resistance-trained participants. Each of these studies provide evidence that the velocity loss achieved during RT sets is a key variable influencing muscle hypertrophy in resistance-trained individuals, with lower velocity losses (0-15%) shown to induce minimal-to-no muscle hypertrophy, while higher velocity losses (20-50%) are associated with greater muscle hypertrophy in a non-linear manner. However, considering different velocity loss thresholds are also accompanied by differences in volume-load, it is difficult to discern conclusions regarding the influence of proximity-to-failure on muscle hypertrophy from these studies. Importantly, a recent meta-analysis found velocity losses of >25% (40% or 50% in all the analysed studies) were superior to velocity losses of ≤25% for muscle hypertrophy [79]; however, sub-analyses indicated this effect was largely driven by comparisons of higher velocity losses (40% and 50%) with those ≤20% (small to moderate differences), versus comparisons between >25% and 20-25% velocity losses (trivial differences), highlighting that the hypertrophic response to RT seems to plateau as velocity loss increases. For example, one study [72] compared changes in muscle hypertrophy between 0, 10, 20, and 40% velocity loss conditions, with participants theoretically performing RT to a different proximity-to-failure in each condition. The 20 and 40% velocity loss conditions experienced significantly greater muscle hypertrophy than the 0 and 10% velocity loss conditions, however despite the 40% velocity loss condition performing over 100 repetitions more than the 20% velocity loss condition, no statistically significant differences in muscle hypertrophy were observed between the 40% and 20% velocity loss conditions. Similar results were found in an additional two studies [71, 73], highlighting that when RT is performed using sufficiently high velocity loss thresholds (e.g., >20%), differences in volume-load have little additional impact on outcome measures in resistance-trained samples. To minimise the influence of differences in volume-load on outcome measures, a study by Anderson et al. [74], which was not included in the aforementioned meta-analysis [79], equated volume-load between velocity loss conditions by adjusting the number of sets total sets performed during two unilateral RT protocols performed to ~20 and ~36% velocity loss, and in support of previous findings [71-73], found no statistically significant between-group differences in muscle hypertrophy.

Although current literature suggests RT performed to momentary muscular failure is not superior to non-failure RT for muscle hypertrophy, and that achieving a closer proximity-to-failure does not always promote greater muscle hypertrophy, it is unclear how far from momentary muscular failure RT sets should be terminated to theoretically maximise muscle hypertrophy. Uncertainty surrounding the "optimal" proximity-to-failure for set termination is likely due to the variability and ambiguity in the RIR achieved amongst non-failure conditions throughout the literature, the inability to translate the magnitude of velocity loss during RT to specific RIR values, and the difficulty in interpreting research that uses velocity loss thresholds due to between-group differences in volume-load. The importance of controlling and/or quantifying the proximity-to-failure (via RIR) during non-failure RT should not be dismissed, as non-failure RT may involve a multitude of proximities-to-failure that may influence study findings. To improve the ability to derive practical recommendations, future research should use an RIR-based approach to set termination that highlights how far from momentary muscular failure sets were terminated. Although RIR-based methods of set termination (e.g., RIR prediction or set termination velocities) may not always provide a completely accurate representation of the actual RIR achieved, appropriate familiarisation and experience with these methods may improve their validity and their application is likely an improvement on current methods that are unable to infer proximity-to-failure. Considering there is some evidence that RT load may modulate muscle hypertrophy outcomes in response to training to different proximities-to-failure [46], it is likely that other RT variables (e.g., volume-load, number of sets, exercise selection) may also play a role. Thus, researchers should investigate the interaction between RT variables and proximity-to-failure in future studies on muscle hypertrophy. Further, considering the variability in definitions applied to set failure in current meta-analyses on this topic, and the potential for the inconsistencies between studies to confound results, future meta-analyses should perform sub-analyses based on the specific definition of set failure used to increase the validity of their findings and interpretations.

2.5.4.2 Influence of Proximity-to-failure on Short-Term Responses to Resistance Training

The collective findings of six studies [14, 48-52] involving resistance-trained participants suggest mechanical and metabolic measures of neuromuscular fatigue and muscle damage are greater when RT is performed to momentary muscular failure versus non-failure (Theme A). Four [14, 48-50] out of the six studies equated volume-load between RT conditions and found that neuromuscular fatigue (indicated by decreases in jump height, lifting velocity, and isokinetic force) was greater for up to 30-min post-RT when RT was performed to momentary muscular failure, suggesting that RT performed to momentary muscular failure promotes additional impairments in neuromuscular function beyond the influence of the volume-load completed. One study [52], which found no difference in neuromuscular fatigue between-conditions, used subjective RIR prediction to inform set termination in the non-failure condition, requiring participants to terminate sets when they “perceived that no more than 3 repetitions were possible”. Although the researchers stated the non-failure condition involved 3-RIR, considering the instructions provided, it is possible that participants could have terminated their sets anywhere between 0–3-RIR, demonstrating how the proximity to failure achieved by participants may be influenced by the quality of instruction provided, independent of individual predictive ability. Only one study [11] investigated the influence of proximity-to-failure on perceived discomfort and demonstrated that when RT was performed to momentary muscular failure, ratings of perceived discomfort were greater than for non-failure RT (20% velocity loss), even though volume-load was similar between-conditions [11]. Lastly, Amdi et al. [51] investigated the influence of proximity-to-failure on neuromuscular fatigue (via changes in lifting velocity) in men and women (as there may be sex differences in neuromuscular performance and fatiguability [91]), reporting that during non-failure RT (i.e., five repetitions performed with 80% 1-RM for both sexes), men experienced significantly more neuromuscular fatigue than women, however, this effect was not observed when RT was performed to momentary muscular failure. Nonetheless, individual fatiguability (which may be influenced by sex) is an important consideration when prescribing proximity-to-failure, and future research should aim to explore the potential sex-based difference in fatiguability during RT.

A number of studies (as part of Theme B) investigated neuromuscular fatigue and muscle damage in response to RT performed to set failure versus non-failure [32, 36-38, 56-67], with most studies demonstrating these short-term responses are exacerbated when RT is performed to set failure. For example, when RT was performed to set failure versus non-failure, greater delayed neuromuscular fatigue (assessed >30-min post-RT via jump height, lifting velocity, isometric force, or maximum voluntary contraction) was observed in six studies [32, 38, 60, 61, 63, 67] and greater acute neuromuscular fatigue (assessed ≤30-min post-RT via lifting velocity, peak power, or peak force) was observed in four studies [36, 56, 60, 65]. Indeed, numerous studies [32, 38, 61, 63, 67] suggest the time-course for recovery of neuromuscular function was between 24- and 48-hours when RT was performed to set failure, supporting the notion that muscle groups should be trained less frequently if RT is performed to set failure, although the time course of recovery may also be influenced by the exercises performed (e.g., longer recovery periods may be required for multi-joint exercises [92]) and the volume-load completed. Of the eight studies [32, 38, 57, 61-63, 66, 67] that measured indirect muscle damage using biochemical (e.g., creatine kinase) or subjective methods (e.g., muscle soreness), most studies found greater mean increases in these markers when RT was performed to set failure versus non-failure, particularly at 48-hours post-RT. However, this evidence is mixed as four studies [38, 57, 63, 67] found no statistically significant difference between-conditions and four studies [32, 61, 62, 66] did. Greater muscle damage was also observed as the number of repetitions performed within a given set increased [63, 66], possibly mediated by peripheral mechanisms that activate chemical degradation pathways leading to muscle damage [93]. Indeed, blood lactate concentration, which is an indicator of metabolite accumulation and increased anaerobic glycolysis, and a biomarker of peripheral fatigue [94], is consistently greater when RT is performed to set failure versus non-failure [56-59, 61, 64-66].

Three studies [68-70] investigated the influence of different proximities-to-failure (using velocity loss) on neuromuscular fatigue, providing insight into the physiological response of RT performed close to, but not to, momentary muscular failure (Theme C). Collectively these studies highlight that higher velocity loss thresholds for set termination result in greater neuromuscular fatigue than lower velocity loss thresholds. As previously mentioned, however, the results observed in these studies may be due to between-group differences in not only proximity-to-failure, but also volume-load (due to differences in the number of repetitions performed per set). Nonetheless, two studies [69, 70] found significantly greater decreases in mechanical measures of neuromuscular fatigue (lifting velocity and jump height) after RT was performed to a high velocity loss (30-40%) versus a low velocity loss (10-20%), lasting up to 24-hours, with neuromuscular fatigue and blood lactate concentration observed to be higher as relative load decreased and the total number of repetitions completed in a set increased (i.e., set duration increased). Also investigating the influence of proximity-to-failure on neuromuscular fatigue was a study by Weakley et al. [68], who observed decreases in jump height and increases in blood lactate concentration with every 10% increase in velocity loss (between 10% to 30%). This study also measured changes in jump height and blood lactate from set-to-set and concluded that neuromuscular fatigue may not substantially accumulate across multiple sets, but these results are likely due to the fact that participants did not perform RT to momentary muscular failure. Overall, these findings have practical implications for RT prescription and highlight that RT performance may be sustained across multiple sets if momentary muscular failure is not achieved.

In summary, proximity-to-failure in RT is a primary driver of alterations in neuromuscular function, with acute and delayed neuromuscular fatigue observed to a) increase as proximity-to-failure nears, and b) is greatest when momentary muscular failure is reached. However, only one of the studies comparing the effect of RT to set failure versus non-failure on neuromuscular fatigue involved a longer-term intervention (10 weeks) [62], whereas other studies involved acute trials, and as such, the influence of proximity-to-failure on long-term neuromuscular fatigue accumulation is unclear. The possibility remains that neuromuscular fatigue accumulates in the long-term, exacerbating the impact on post-RT recovery and subsequent RT performance, whilst potentially hindering physiological adaptations to RT. In contrast, it is also possible that the effect of proximity-to-failure on muscle damage is attenuated with repeated bouts of RT, a phenomenon known as the "repeated-bout effect" [95]. This protective mechanism seems to be partially explained by a modification in the central nervous system [96], and as such, repeated exposure to RT may also be protective of central fatigue that may arise after damaging exercise. At present, the long-term effects of cumulative neuromuscular fatigue on physiological adaptations, and the degree to which these potential effects are ameliorated by the repeated-bout effect, is unknown. Considering the non-failure conditions in numerous studies required set termination to occur once 50% of the maximal possible repetitions was complete [32, 37, 38, 56-59, 61-63], it is also unclear how performing RT closer to set failure would influence study findings. Future research should thus investigate the effect of different proximities-to-failure on neuromuscular fatigue with an RIR-based approach following thorough familiarisation to improve the validity of study findings. Although the role of biological sex in modulating the influence of RT proximity-to-failure on neuromuscular fatigue is contentious, the known sex differences in fatigability [91] highlight the need for future research to inform sex-specific practical recommendations. Further, considering the potential link between affective responses to exercise and long-term adherence [17], and higher perceived discomfort reported after RT to momentary muscular failure versus non-failure [14], future research should focus on methods of RT prescription that may reduce perceived discomfort whilst inducing desired outcomes (e.g., muscle hypertrophy), and whether that may positively influence long-term adherence.

2.6 Conclusion

This scoping review compiled key definitions for set failure in the literature, discussed the control of proximity-to-failure in RT, and summarised current evidence on the influence of proximity-to-failure on muscle hypertrophy and short-term responses (neuromuscular fatigue, muscle damage, and perceived discomfort) to RT. A major limitation of the current literature is not only that there is not a consensus definition of set failure, but many studies fail to explicitly state the definition of set failure applied. As a result, each study including in this scoping review was grouped into one of the three themes to improve the validity of study comparisons and interpretations within each theme. Further, in many of the studies reviewed, the proximity-to-failure achieved by participants in non-failure conditions was unclear and likely subject to within- and between-study variability, influencing the absolute difference in proximities-to-failure being compared and thus affecting study findings. These shortcomings highlight the potential utility of an RIR-based approach to set termination that allows for the quantification of proximity-to-failure in non-failure conditions, which would potentially improve future practical recommendations for proximity-to-failure in RT. Nonetheless, current research suggests that for both untrained and resistance-trained individuals, performing RT to set failure is likely not superior to non-failure RT to promote muscle hypertrophy, but the optimal proximity to failure for muscle hypertrophy remains unclear, and may be moderated by other RT variables (e.g., load, volume-load, number of sets, exercise selection). Performing RT to set failure also induces greater neuromuscular fatigue and muscle damage (lasting up to 48-hours post-RT), and greater post-set perceived discomfort, than non-failure RT. Increasing the time-course for recovery of neuromuscular function post-RT could limit the volume and/or frequency of subsequent RT, and higher ratings of perceived discomfort may negatively influence long-term adherence to RT, both of which may negatively impact long-term muscle hypertrophy responses.

Chapter Three – Thesis Rationale

3.1 Study One

Objectives: Considering the methodological limitations identified by the scoping review (e.g., variability in definitions of set failure applied across studies), relevant studies are systematically reviewed and meta-analysed as a whole and within the 'themes' established in the scoping review. The primary objectives of this systematic review with meta-analysis are to investigate i) differences between RT performed to set failure versus non-failure on muscle hypertrophy, and ii) whether the definitions applied to set failure (based on 'theme'), or the volume-load and relative load, influenced the results. Secondary objectives are to examine whether the magnitude of velocity loss achieved during RT influences muscle hypertrophy and what magnitude of muscle hypertrophy is achieved when RT is performed to momentary muscular failure, to set failure, or to a high velocity loss.

Significance: This is the first meta-analysis to group relevant studies into themes based on the definition of set failure applied and the research question asked. Considering the definition of set failure may influence the proximity-to-failure reached, and thus impact the comparisons made with non-failure groups, interpretations should be made within each theme.

3.2 Study Two

Objectives: The primary objective of this study is to examine the influence of RT proximity-to-failure on markers of acute neuromuscular fatigue in resistance trained males and females, by comparing RT performed to momentary muscular failure with 1-RIR and 3-RIR. Neuromuscular fatigue is assessed via changes in lifting velocity with a fixed load [65] between pre-exercise to immediately (4-min) post-exercise and the associated time-course of recovery (at 24 and 48 hours post-exercise). Within-session changes in lifting velocities (from the first to final set) are also assessed as markers of neuromuscular fatigue. Secondary objectives are to examine biological sex differences in changes in lifting velocity, and to assess other perceptual responses to RT, including subjective ratings of perceived discomfort, recovery, exertion, muscle soreness, and general feelings.

Significance: This is the first study to investigate neuromuscular fatigue and compare the effect of RT sets terminated when participants believed they reached a prescribed RIR target, to all sets performed to momentary muscular failure. The findings allow for specific RIR prescription recommendations that limit negative short-term responses to RT.

3.3 Study Three

Objectives: The utility of RIR-based set prescription (e.g., 3 sets of 10-15 repetitions with 2-RIR) is contingent upon the accuracy of the individual's RIR prediction. As such, the objective of this study is to assess the accuracy of intra-set RIR predictions (1- and 3-RIR) on the barbell bench press exercise (75% of 1-RM load) over two sessions in resistance-trained males and females who terminated each set at momentary muscular failure. Secondary objectives are to explore the relationship between RIR accuracy and i) years of RT experience, ii) biological sex, and iii) relative bench press strength.

Significance: Most of the previous research investigating intra-set RIR prediction accuracy was conducted in untrained or recreationally trained individuals who may not have sufficient RT experience to predict RIR accurately. Allowing better generalisability to resistance-trained populations, this study included one of the most highly-trained samples in the existing literature

[89] (average of 8.3 and 7.2 years of RT experience for males and females, respectively), with 96% of participants having experience with RIR prediction.

3.4 Study Four

Objectives: Although previous research examined the influence of different RT proximities-to-failure (e.g., set failure versus non-failure, or different velocity loss thresholds [97]) on muscle hypertrophy, to our knowledge, no studies compared the effect of momentary muscular failure to non-failure (using RIR) on muscle hypertrophy and longitudinal markers of neuromuscular fatigue. As such, the primary objective of this study is to examine the influence of eight weeks of RT performed to either momentary muscular failure or with 1- to 2-RIR on quadriceps hypertrophy in resistance-trained individuals. Secondary objectives are to explore changes in lifting velocity and repetitions performed, and volume accumulation, to quantify acute neuromuscular fatigue.

Significance: This study is conducted on a highly-trained sample of participants with the longest duration of RT experience (7.8 and 7.5 years for males and females, respectively) reported in previous similar studies [47, 53, 71-74, 98, 99], 50% of whom had experience in competitive strength and/or physique sports. This allows results to be generalised to multiple demographics that regularly partake in RT (i.e., general population, sports athletes, bodybuilders). Further, the statistical analysis involves a Bayesian approach to directly model uncertainty and intuitively present the results through posterior probabilities to allow meaningful inferences to be made regarding the influence of proximity-to-failure on muscle hypertrophy [100].

3.5 Thesis Overview and Study Integration

This thesis comprises eight chapters. Chapter One establishes the importance of RT interventions designed to promote muscle hypertrophy and elicit both aesthetic improvements and health benefits, the history of proximity-to-failure and its importance in RT prescriptions, how RT prescriptions may influence exercise adherence, and the rationale for the remainder of the thesis. Chapter Two involves a comprehensive scoping review that i) summarises the available literature investigating proximity-to-failure and its influence on muscle hypertrophy, neuromuscular fatigue, muscle damage, and perceived discomfort, ii) groups studies into themes specific to the definition of set failure applied and the research question asked, and iii) identifies key research limitations. The following studies, which span Chapters Four to Seven (studies are described in Chapter Three, along with a summary of their significance in exercise science research and practice), are purposefully designed to inform one another, such that findings from earlier studies informed that of later studies, and together form a comprehensive body of research (as represented in Figure 1.1). Study One (Chapter Four) meta-analyses all studies retrieved from the scoping review that assessed muscle hypertrophy to provide more robust conclusions on the influence of RT proximity-to-failure on muscle hypertrophy within each theme. With the key limitations identified and discussed in the scoping review, the following three original research studies further explore proximity-to-failure and extend previous research findings. The findings from Study Two (Chapter Five) provide novel insights on the influence of RIR on neuromuscular fatigue and perceptual responses by comparing RT performed to momentary muscular failure (defined as per the scoping review) versus with 1- and 3-RIR, improving practical recommendations to limit negative short-term responses to RT. Based on the limited understanding of the efficacy of intra-set RIR predictions as identified in the scoping review, intra-set RIR prediction accuracy is also assessed in Study Two, with the data presented and analysed in Study Three (Chapter Six). The final study, Study Four (Chapter

Seven), incorporates findings from each of the previous studies and compares muscle hypertrophy and neuromuscular fatigue following eight weeks of RT performed to momentary muscle failure versus with 1- to 2-RIR. Chapter Eight integrates all the studies, synthesising their findings, their significance, and practical applications, and includes an updated meta-analysis incorporating the results from Studies One and Four. Chapter Eight concludes by summarising the thesis findings and their contribution to the broader literature, including how they inform practical applications for athletes and the general population, and avenues to be explored in future RT research investigating proximity-to-failure.

Chapter Four – Influence of Resistance Training Proximity-to-Failure on Skeletal Muscle Hypertrophy: A Systematic Review with Meta-Analysis.

Please note, the following text in Chapter Four has been adapted from a peer-reviewed and published manuscript (DOI: 10.1007/s40279-022-01784-y).

4.1 Preface

Previous meta-analyses investigating the influence of RT proximity-to-failure on muscle hypertrophy have not addressed the inconsistent definitions of set failure used across the literature [11, 12], possibly confounding their results. Our scoping review [97] identified three 'themes' of studies based on the definition of set failure, of which were subsequently meta-analysed to investigate the influence of proximity-to-failure on muscle hypertrophy within each theme. Momentary muscular failure is the most objective definition of set failure within the literature, making it more likely that the per-set stimulus is similar across a group of participants performing RT to 'failure' (Theme A). However, other definitions of set failure likely led to more variability in the actual proximity-to-failure achieved across participants, and therefore the imposed stimulus (Theme B). Our meta-analysis also involved studies that used velocity loss thresholds to determine set termination (Theme C), allowing further comparison of closer versus further proximities-to-failure on muscle hypertrophy. This comprehensive analysis of the literature within themes not only allows practitioners to improve RT prescription but also encourages researchers to use clearer, more consistent methods and terminology when investigating the relationship between proximity-to-failure and muscle hypertrophy. For the interested reader, Fonseca et al. [101] wrote a letter to the editor with questions regarding our statistical analysis and interpretation, which we subsequently responded to [102], explaining our rationale in greater detail.

4.2 Introduction

Resistance training (RT) promotes skeletal muscle hypertrophy, a physiological adaptation involving the structural remodelling of muscle tissue that leads to an increase in muscle fibre, and ultimately, whole-muscle cross-sectional area [103]. Although multiple RT variables (e.g., volume, load, frequency, lifting velocity) influence muscle hypertrophy, 'proximity-to-failure' specifically influences the exposure of muscle fibres to *mechanical tension*, the key stimulus for muscle hypertrophy [31]. Proximity-to-failure is defined as the number of repetitions remaining in a set prior to *momentary muscular failure* (i.e., when an individual cannot complete the concentric portion of a given repetition with a full range-of-motion without deviation from the prescribed form of the exercise) [97]. As proximity-to-failure nears within a given set, more repetitions are completed [thus increasing volume-load (sets x repetitions x load)] and muscle fibre activation progressively increases [28, 29], ultimately exposing type II muscle fibres (capable of greater hypertrophy than type I muscle fibres [104]) to greater mechanical tension. However, whether the increased mechanical tension and volume-load within a given set are worth the additional neuromuscular fatigue from reaching momentary muscular failure over multiple sets is contentious, as cumulative neuromuscular fatigue could impede the total volume-load completed within an entire session or from session-to-session, and therefore decrease the total exposure to mechanical tension over time [97]. Nonetheless, inconsistencies in the literature limit understanding of the influence of RT proximity-to-failure on muscle hypertrophy and pose a challenge for deriving practical recommendations for manipulating proximity-to-failure during RT to achieve desired outcomes.

To our knowledge, three meta-analyses [11, 12, 79] investigated the influence of RT proximity-to-failure on muscle hypertrophy by comparing either RT performed to *set failure* (i.e., umbrella term describing the set termination criteria for the definition of 'failure' applied in a given study) versus non-failure [11, 12], or RT performed to different velocity loss thresholds that indirectly influence proximity-to-failure [79]. Results showed that RT performed to set failure does not elicit superior muscle hypertrophy compared with non-failure RT when volume-load is equated [11, 12]. Further, RT performed to a higher velocity loss (>25%) was found to be superior to a lower velocity loss (≤25%) [79]. Although, trivial differences in muscle hypertrophy were found between 20-25% and >25% velocity loss conditions (across a small number of studies that were sub-analysed) [79]. Collectively, these data suggest that the relationship between proximity-to-failure and muscle hypertrophy is likely non-linear [105] or that it is moderated by other RT variables such as volume-load [12]. One of the major limitations of these data, however, is that no consensus definition for 'failure' exists in the literature. As such, these meta-analyses compare studies applying various definitions of set failure that alter the RT stimulus achieved. These differences in the RT stimulus achieved could potentially confound the conclusions drawn as the true proximity-to-failure compared between set failure conditions across studies is likely inconsistent.

To summarise the available evidence regarding the influence of RT proximity-to-failure on muscle hypertrophy while addressing critical research limitations, we identified three broad themes of studies in our recent scoping review [97], based on the definition of set failure applied and the research question asked (Table 4.1). We tentatively concluded that RT to set failure is likely not superior to non-failure RT for promoting muscle hypertrophy [97], but it is uncertain if meta-analysing these data within the themes we identified would alter this conclusion. Therefore, due to the methodological limitations identified in the current literature, the influence of proximity-to-failure on muscle hypertrophy is unclear and requires further investigation. Since the publication of previous meta-analyses [11, 12, 79] on the influence of proximity-to-failure on muscle hypertrophy, six additional studies were published [35, 47, 55, 74, 98, 99] on this topic. Thus, this systematic review with meta-analysis extends previous findings by including new evidence and grouping studies into broad themes exclusive to the definition of set failure applied and the research question asked (Table 4.1). Specifically, we estimated: i) the overall effect of resistance training performed to set failure versus non-failure on muscle hypertrophy and the individual effect of A) definitions applied to set failure (based on 'theme'), B) volume-load, and C) relative load on muscle hypertrophy, ii) whether the magnitude of velocity loss achieved during resistance training influences muscle hypertrophy, and iii) the magnitude of muscle hypertrophy achieved when resistance training is performed to momentary muscular failure, to set failure, and to a high velocity loss.

Table 4.1. 'Themes' of studies investigating proximity-to-failure in resistance training. Description of specific criteria used to allocate studies to each theme, based on the definition of set failure applied and the research questions asked.

Theme	Criteria
A	Studies comparing a group(s) performing RT to momentary muscular failure to a non-failure group(s). [43-47]
B	Studies comparing a group(s) performing RT to set failure (defined as anything other than the definition of momentary muscular failure) to a non-failure group(s). [35, 53-55]
C	Studies theoretically comparing different proximities-to-failure (i.e., applying different velocity-loss thresholds that modulate set termination and albeit indirectly, influence proximity-to-failure), with no inclusion of a group performing RT to momentary muscular failure *per se*. [71-74, 98, 99]

4.3 Methods

A systematic review with meta-analysis were performed in accordance with the Preferred

Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [106]. The original protocol was registered with Open Science Framework on the 27th of April 2022 (https://osf.io/rzn63/) but since was slightly adjusted to improve the suitability of the analysis with the data and research questions (we did not perform the pre-registered meta-regression analysis). Due to the heterogeneity of studies investigating the influence of proximity-to-failure, a scoping review was previously conducted as a means of summarising the available evidence [97]. The systematic search used in the scoping review was adopted for this systematic review with meta-analysis, to provide a consistent and objective understanding of the data. To reduce bias during the process, two authors (MR and JF) were involved in each step of the study identification process (including the literature search and study screening/selection), subsequent data extraction, and methodological quality assessment for this systematic review with meta-analysis, with any disagreement resolved by mutual discussion.

4.3.1 Research Questions

The research questions were defined using the participants, interventions, comparisons, outcomes, and study design (PICOS) framework, as follows. In apparently healthy adults of any age and training status:

1. What is the overall effect of resistance training performed to set failure versus non-failure on muscle hypertrophy? And what is the individual effect of the definitions applied to set failure (based on 'theme'), volume-load, and relative load on muscle hypertrophy?
2. Does the magnitude of velocity loss achieved (and theoretically, the proximity-to-failure reached) during resistance training influence muscle hypertrophy?

3. What magnitudes of muscle hypertrophy are achieved when resistance training is performed to momentary muscular failure, to set failure, and to a high velocity loss?

4.3.2 Literature Search Strategy

As described in our previous scoping review [97], the literature search followed the PRISMA-ScR (Preferred Reporting Items for Systematic Reviews and Meta- Analyses for Scoping Reviews) guidelines [42]. Literature searches of the PubMed, SCOPUS and SPORTDiscus databases were conducted in September 2021, and the following PubMed search string was used and adapted for each individual database: (("resistance training" OR "resistance exercise" OR "strength training") AND ("failure" OR "muscular failure" OR "velocity loss") AND (("muscle hypertrophy" OR "muscle size" OR "muscle growth" OR "muscle mass" OR "muscle thickness" OR "cross-sectional area") OR ("fatigue" OR "neuromuscular fatigue" OR "peripheral fatigue" OR "muscle damage" OR "discomfort" OR “enjoyment” OR "affective" OR "affective response"))). Since the initial search, however, two recently published studies [98, 99] in 2022 have been manually added to this systematic review with meta-analysis and subject to the same screening process as studies retrieved in the initial database search.

4.3.3 Study Selection

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

4.3.4 Inclusion Criteria

Studies were included if: 1) participants were apparently healthy adults of any age and RT experience, 2) participants were randomized to experimental groups, 3) the experimental comparison involved a group performing RT to set failure (any definition of set failure) versus a non-failure group, or two groups terminating RT sets at different proximities-to-failure [e.g., set termination informed by velocity loss thresholds or subjective ratings of perceived exertion (RPE)], 4) one of the following measures of muscle hypertrophy were included; a) muscle thickness, b) whole-limb or muscle cross-sectional area (CSA) or volume, c) muscle fibre CSA (fCSA), or d) lean body/fat free mass via dual x-ray absorptiometry (DXA) or bioelectrical impedance analysis (BIA). Only original research studies in peer reviewed journals were included, and studies were excluded if they involved i) advanced set strategies (e.g., rest-pause, cluster sets), ii) extraneous training variables (e.g., aerobic exercise, blood flow restriction), iii) outcome measures that were not relevant, and iv) data that was duplicated within another included study.

4.3.5 Data Extraction

Data charting was carried out by two authors (MR and JF) to capture key information in a table format (Table 4.2). The following participant characteristics were extracted: 1) RT status (i.e., untrained, or resistance-trained), 2) age, and 3) sex. The following study characteristics were also extracted: 1) first author, 2) sample size, 3) publication date, and 4) intervention groups/protocol outlines and duration. Raw data (mean and standard deviation) from pre- and post-intervention for muscle hypertrophy outcomes was also extracted from each individual study for generation of standardised mean differences, confidence intervals and subsequent meta-analysis. If figures were used instead of numerical data, those data were extracted from the figures using Web Plot Digitizer, and if the mean and standard deviation data was not reported, we contacted the authors of the respective study directly to obtain the relevant data. Our previous scoping review [97] identified three broad study themes across the relevant literature, and as such, each included study was grouped into one of the themes based on the criteria outlined in Table 4.1.

4.3.6 Methodological Quality Assessment

Evaluation of methodological study quality (including risk of bias) was conducted by two authors (MR and JF) using the tool for the assessment of study quality and reporting in exercise (TESTEX) scale [107] shown in Appendix A. The TESTEX scale is an exercise science-specific scale used to assess the quality and reporting of exercise training trials. The scale contains 12 criteria that can either be scored a 'one' or not scored at all; 1, eligibility; 2, randomisation; 3, allocation concealment; 4, groups similar at baseline; 5, assessor blinding; 6, outcome measures assessed in 85% of patients (3 possible points); 7, intention-to-treat; 8, between-group statistical comparisons (2 possible points); 9, point-estimates of all measures included; 10, activity monitoring in control groups; 11, relative exercise intensity remained constant; 12, exercise parameters recorded. The best possible total score is 15 points.

4.3.7 Statistical Analysis

All statistical analyses were conducted with the 'metafor' [108] package in R (v 4.0.2; R Core Team, https://www.r-project.org/) and all the code utilized is openly available. Standardized effect sizes and standard errors were calculated using the 'escalc' function in 'metafor'. The magnitude of standardized effect sizes was interpreted with reference to Cohen's *d* (1988) thresholds: trivial (<0.2), small (0.2 to <0.5), moderate (0.5 to <0.8), and large (>0.8). Point estimates and their 95% confidence intervals (CIs) were produced. Restricted maximal likelihood estimation was used in all models. Given that correlations between pre-test and post-test measures are rarely reported in original studies, a correlation coefficient of $r = 0.75$, which was replicated from Grgic et al. [11], was used to calculate the variance (or standard error) for all studies and sensitivity analyses were performed using correlation coefficients ranging from $r = 0.6$ - 0.9 (Appendix A). Funnel plots were generated (Appendix A) and Egger's test was applied to assess the risk of bias from small-study effects. The I^2 heterogeneity statistic was also produced and reported to indicate the proportion of the observed variance (for all effect sizes generated) that is not due to sampling error [109]. To complement traditional null hypothesis significance testing, we also considered the practical implications of all results by qualitatively assessing the effect size estimate and associated confidence interval width.

Quantitative synthesis of studies in Theme A and B (combined), and Theme C, were performed using multi-level mixed effects meta-analysis, as there is a nested structure to the effect sizes that were calculated from the studies included (i.e., multiple effect sizes from various measures of muscle hypertrophy nested within groups and nested within studies). Standardised effect sizes were calculated such that a positive effect size favours the set failure conditions (or high velocity loss conditions), whereas a negative effect size favours non-failure conditions (or moderate velocity loss conditions). A multi-level model for studies in Theme A and B was produced including all standardised effect sizes to provide a general estimate of the effect and answer review question one. Studies from Theme A and B were also categorised by: i) theme (A or B), ii) the difference in volume-load between set failure and non-failure conditions (volume equated or not volume-equated), and iii) the relative load lifted [high-load (>50% 1-

RM) or low-load (≤50% 1-RM)], and sub-group analyses were employed to estimate an effect size for the influence of these individual variables (i.e., theme, volume-load, relative load) on the outcome measure and compare and contrast the estimates. Another multi-level model was produced for studies in Theme C comparing high velocity loss conditions (>25%) versus moderate velocity loss conditions (20-25%), to provide a general estimate of the effect and help answer review question two. Three [72, 73, 99] out of the six studies [71-74, 98, 99] in Theme C also involved groups performing RT to low velocity loss thresholds (<20%); however, considering only six effect sizes could be retrieved (versus 11 effect sizes for both moderate and high velocity loss thresholds) and the low practical importance of performing RT with <20% velocity loss, we excluded low velocity loss conditions from this comparative model and therefore did not perform the pre-registered meta-regression analysis (https://osf.io/rzn63/). However, an individual standardized effect size was calculated for the low velocity loss conditions, along with all other RT conditions analysed [i.e., momentary muscular failure, set failure, non-failure, and moderate (20-25%) and high (>25%) velocity loss thresholds] across all studies in each theme to provide a general estimate of the effect and help answer review questions two and three.

4.4 Results

4.4.1 Search Results and Systematic Review of Included Studies

The original literature search results were described previously [97], and an updated flowchart of the systematic literature search and study selection process is displayed in Figure 4.1. For this systematic review with meta-analysis, two additional studies [98, 99] were found through manual checking and subject to the same screening process as studies retrieved in the initial database search. Further, all studies retrieved from the original search that did not measure muscle hypertrophy outcomes were excluded from this systematic review with meta-analysis, leaving a total of 15 studies eligible for analysis. Subsequently, studies were grouped into one of the three themes identified based on the criteria outlined in Table 4.1 to improve the validity of study comparisons and interpretations within each theme. Results from Egger's test found no publication bias (P = <0.05) for studies in Theme A and B, and studies in Theme C. For a summary of included studies, see Table 4.2.

A total of nine studies [35, 43-47, 53-55] compared RT performed to set failure (including all definitions of set failure) versus non-failure and measured muscle hypertrophy in one or more of the following muscle groups: quadriceps (vastus lateralis, vastus medialis, rectus femoris), elbow flexor, triceps bacchii, pectoralis major, or anterior deltoid. Five [43-47] out of the nine [35, 43-47, 53-55] studies applied the definition of momentary muscular failure and were thus allocated to Theme A, and the remaining four studies [35, 53-55] applied various definitions of set failure other than momentary muscular failure and were thus allocated to Theme B. Importantly, five [35, 43, 45, 46, 53] out of the nine studies [35, 43-47, 53-55] equated volume-load between conditions, whereas three studies [47, 54, 55] did not equate volume-load. The final study [44] involved two non-failure conditions, of which one was volume-equated (compared to the set failure condition), while the other was not. Further, five [43, 44, 47, 53, 54] out of the nine studies [35, 43-47, 53-55] used a high-load (>50% 1-RM), and two studies [35, 55] used a low-load (≤50% 1-RM). The remaining two studies [45, 46] used both high- and low-loads allocated across two set failure and two non-failure conditions. Of the five studies in Theme A, four studies [43, 45-47] found no statistically significant differences between conditions in muscle hypertrophy from pre- to post-intervention, while one study [44] did not perform a between-group statistical analysis. Similarly, three [35, 53, 54] of the four studies [35, 53-55] in Theme B found no statistically significant differences in muscle hypertrophy between conditions, and one study [55] found no statistically significant pre- to post-intervention changes in muscle size for either condition. A total of seven studies [35, 43-46, 54, 55] from both Theme A and B involved untrained participants, whereas only two studies involved resistance-trained participants [47, 53].

Additionally, a total of six studies [71-74, 98, 99] in resistance-trained participants compared high velocity loss conditions (>25%) with moderate velocity loss conditions (20-25%) and measured muscle hypertrophy (Theme C) in one or more of the following muscle groups: quadriceps (vastus lateralis, vastus intermedius, vastus medialis, rectus femoris) or pectoralis major. Five [71-74, 98] out of the six [71-74, 98, 99] studies in Theme C observed increases in muscle hypertrophy when RT was performed to both high and moderate velocity loss; however, no statistically significant differences between conditions were found in each of the studies. The remaining study [99] only found increases in muscle hypertrophy for the high velocity loss condition. All studies [71-74, 98, 99] in Theme C involved a high-load and were conducted on resistance-trained participants.

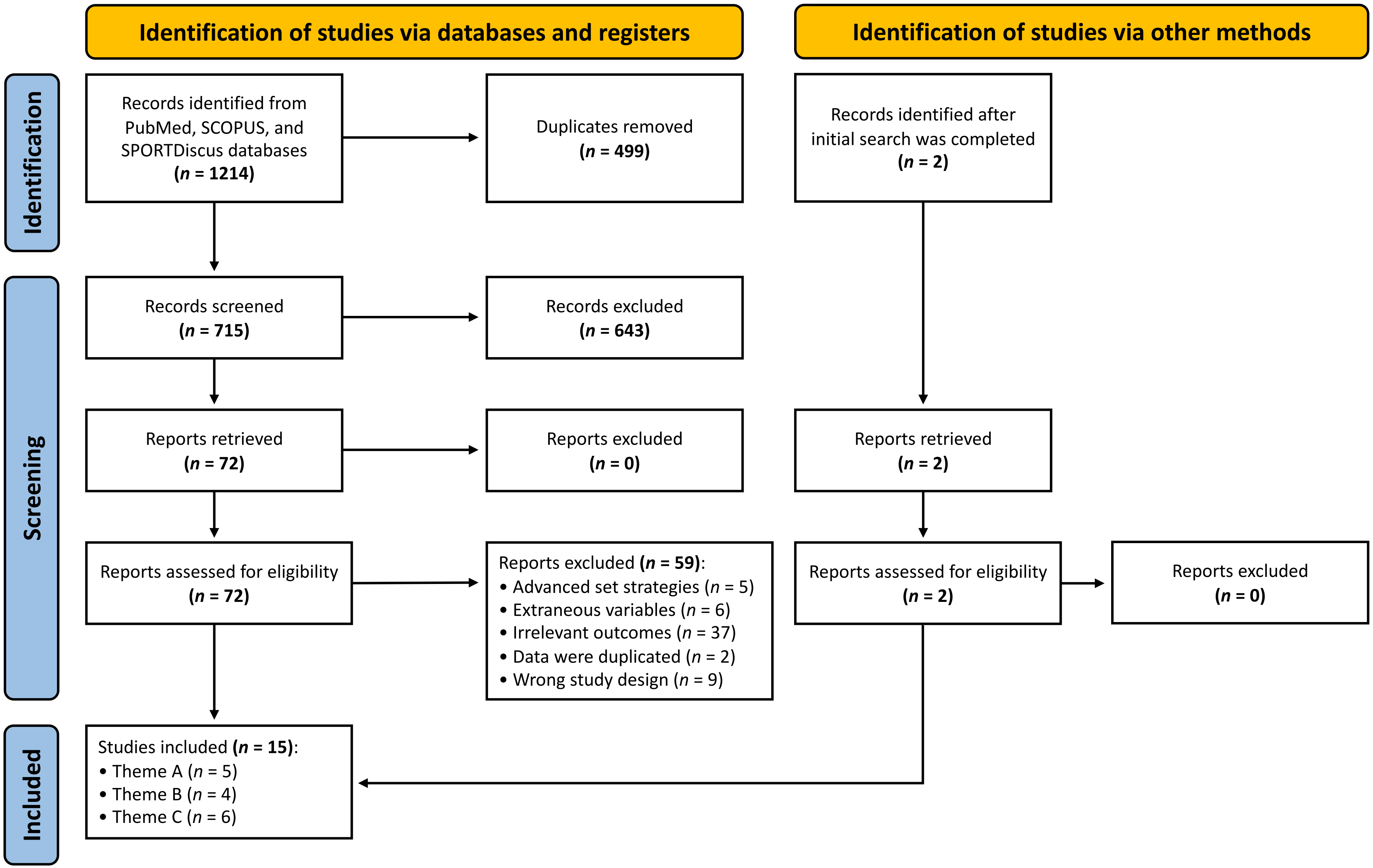

Figure 4.1. PRISMA flow chart. Summary of systematic literature search and study selection process.

Table 4.2. Summary of data extraction. Brief summary of all studies including in this systematic review with meta-analysis. *F, female; M, male; RM, repetition maximum; T, trained; UT, untrained; VeL, velocity loss; VF, volitional failure; VI, volitional interruption; y, years.*

Study	Theme	*Sample Size (n)*	Sex	Age (y)	Intervention Groups / Duration (sessions/week)	Volume Equated	Training Status
Lacerda et al. 2020 [43]	A	10	M	23.7 ± 4.9	**Failure:** 3-4 sets x *n* reps (50-60% 1-RM) **Non-failure:** 3-4 sets x *n* reps (50-60% 1-RM) → 14 weeks (2-3/week)	Yes	UT
Lasevicius et al. 2019 [46]	A	25	M	24 ± 4.9	**Failure 1:** 3 sets x *n* reps (80% 1-RM) **Failure 2:** 3 sets x *n* reps (30% 1-RM) **Non-failure 1:** ~5 sets x *n* reps (80% 1-RM) **Non-failure 2:** ~5 sets x *n* reps (30% 1-RM) → 8 weeks (2/week)	Yes	UT
Martorelli et al. 2017 [44]	A	89	F	21.9 ± 3.3	**Failure:** 3 sets x *n* reps (70% 1-RM) **Non-failure 1:** 4 sets x 7 reps (70% 1-RM) **Non-failure 2:** 3 sets x 7 reps (70% 1-RM) → 10 weeks (2/week)	Yes No	UT
Nobrega et al. 2018 [45]	A	32	M	23 ± 3.6	**Failure 1:** 3 sets x *n* reps (80% 1-RM) **Failure 2:** 3 sets x *n* reps (30% 1-RM) **Non-failure 1:** 3 sets x *n* reps to VI (80% 1-RM) **Non-failure 2:** 3 sets x *n* reps to VI (30% 1-RM) → 12 weeks (2/week)	Yes	UT
Santanielo et al. 2020 [47]	A	14	M	23.1 ± 2.2	**Failure:** *n* sets x *n* reps (75% 1-RM) **Non-failure:** *n* sets x *n* reps to VI (75% 1-RM)	No	T
Bergamasco et al. 2020 [55]	B	41	M/F	65.5 ± 4.5	**Failure:** 3 sets x *n* reps (40% 1-RM) **Non-failure 1:** 3 sets x *n* reps to VI (40% 1-RM) **Non-failure 2:** 3 sets x 10 reps (40% 1-RM)	No	UT

					→ 12 weeks (2/week)		
Karsten et al. 2021 [53]	B	18	M	23.5 ± 4.5	**Failure:** 4 sets x 10-RM (75% 1-RM) **Non-failure:** 8 sets x 5 reps (75% 1-RM) → 6 weeks (2/week)	Yes	T
Sampson et al. 2016 [54]	B	28	M	23.8 ± 6.6	**Failure:** 4 sets x 6 reps (85% 1-RM) **Non-failure 1**: 4 sets x 4 reps (85% 1-RM) **Non-failure 2**: 4 sets x 4 reps (85% 1-RM) → 12 weeks (3/week)	No	UT
Terada et al. 2021 [35]	B	27	M	20.03 ± 0.8	**Failure:** 3 sets x *n* reps to VF (40% 1-RM) **Non-failure:** 3 sets x 20% VeL (40% 1-RM) → 8 weeks (2/week)	Yes	UT
Andersen et al. 2021 [74]	C	10	M/F	23.0 ± 4.3	**High VeL:** 2-3 sets x 30% VeL (75-80% 1-RM) **Low VeL:** 4-6 sets x 15% VeL (75-80% 1-RM) → 9 weeks (2/week)	Yes	T
Pareja-Blanco et al. 2017 [71]	C	24	M	22.7 ± 1.9	**High VeL:** 3 sets x 40% VeL (70-85% 1-RM) **Mod VeL:** 3 sets x 20% VeL (70-85% 1-RM) → 8 weeks (2/week)	No	T
Pareja-Blanco et al. 2020 [72]	C	64	M	24.1 ± 4.3	**High VeL:** 3 sets x 40% VeL (70-85% 1-RM) **Mod VeL:** 3 sets x 20% VeL (70-85% 1-RM) **Low VeL:** 3 sets x 10% VeL (70-85% 1-RM) **Low VeL:** 3 sets x 0% VeL (70-85% 1-RM) → 8 weeks (2/week)	No	T

Pareja-Blanco et al. 2020 [73]	C	64	M	24.1 ± 4.3	**High VeL:** 3 sets x 50% VeL (70-85% 1-RM) **Mod VeL:** 3 sets x 25% VeL (70-85% 1-RM) **Low VeL:** 3 sets x 15% VeL (70-85% 1-RM) **Low VeL:** 3 sets x 0% VeL (70-85% 1-RM) → 8 weeks (2/week)	No	T
Rissanen et al. 2022 [98]	C	45	M/F	25.95 ± 3.85	**High VeL:** 2-5 sets x 40% VeL (65-75% 1-RM) **Mod VeL:** 2-5 sets x 20% VeL (65-75% 1-RM) → 8 weeks (2/week)	No	T
Rodiles-Guerrero et al. 2022 [99]	C	50	M	23.3 ± 3.3	**High VeL:** 3 sets x 50% VeL (55-70% 1-RM) **Mod VeL:** 3 sets x 25% VeL (55-70% 1-RM) **Low VeL:** 3 sets x 15% VeL (55-70% 1-RM) **Low VeL:** 3 sets x 0% VeL (55-70% 1-RM) → 8 weeks (2/week)	No	T

Studies were grouped into broad themes that involved RT performed to either Theme A) momentary muscular failure versus non-failure, Theme B) set failure (defined as anything other than momentary muscular failure) versus non-failure, or Theme C) different velocity loss thresholds.

4.4.2 Methodological Quality

A detailed overview of the methodological quality of included studies using the TESTEX scale [16] can be found in Appendix A. Study quality scores ranged from 7 to 12 (out of a possible 15), with mean and median scores of 9.9 and 10, respectively (Appendix A). Although each study had some risk of bias, all studies lost two points due to i) no allocation concealment, and ii) no activity monitoring, and only one study clearly stated if an 'intention-to-treat' analysis was performed on outcomes of interest. Overall, a total of 11 out of 15 studies scored highly (>10) on the TESTEX scale and visual inspection of methodological quality results revealed no impact of study quality on the effect size estimates generated.

4.4.3 Meta-Analysis Results

4.4.3.1 What is the overall effect of resistance training performed to set failure (irrespective of the definition applied) versus non-failure on muscle hypertrophy?

Meta-analytic outcomes for the overall effect of RT performed to set failure (irrespective of the definition applied) versus non-failure on muscle hypertrophy from all studies in Theme A and B are shown in Figure 4.2. There was a statistically significant advantage for RT performed to set failure versus non-failure on muscle hypertrophy, which was trivial in magnitude [ES = 0.19 (95% CI: 0.00, 0.37), P = 0.045] with a very low heterogeneity (Q = 6.65, P = 0.988, I^2 = 0%).

4.4.3.1.1 Influence of volume-load, relative load, and the definition of set failure on muscle hypertrophy following resistance training performed to set failure versus non-failure

Outcomes for sub-group analyses of studies categorised into either Theme A or Theme B are shown in Figure 4.2. Sub-group analysis of studies applying the definition of momentary muscular failure (Theme A) found no statistically significant difference between RT performed to momentary muscular failure and non-failure on muscle hypertrophy, with a trivial standardised effect involving [ES = 0.12 (95% CI: –0.13, 0.37), $P = 0.343$] a low heterogeneity (Q = 4.58, $P = 0.801$, $I^2 = 7.38\%$). Similar results were found when analysing studies that applied definitions of set failure other than momentary muscular failure (Theme B), with no statistically significant difference between RT performed to set failure (not including momentary muscular failure) and non-failure on muscle hypertrophy, with a trivial standardised effect involving [ES = 0.27 (95% CI: –0.03, 0.57), $P = 0.077$] a very low heterogeneity (Q = 1.60, $P = 0.991$, $I^2 = 0\%$). Individual effect sizes were calculated for subgroups categorized by volume-load standardisation (equated versus not equated) and relative load lifted (higher-load versus lower-load); these pooled effect sizes are presented in Table 4.3. Moderator analyses revealed that neither volume-load standardisation ($P = 0.884$) nor relative load lifted ($P = 0.525$) had statistically significant impacts on the overall effect size for muscle hypertrophy.

Table 4.3. Influence of volume-load and relative load on muscle hypertrophy outcomes in response to resistance training (RT) performed to set-failure versus non-failure. Data shown are presented as a standardised effect size estimate (signifying the standardised mean difference between set failure and non-failure conditions) with 95% confidence interval (CI) and associated *P*-value. Positive effect size values favour RT performed to set failure versus non-failure.

Sub-group analysis	Classification	ES (95% CI)	*P*-value
Volume-load	Volume-equated	0.20 (–0.03, 0.43)	0.09
	Not volume-equated	0.17 (–0.13, 0.47)	0.27
Relative load	Higher-load (>50% 1-RM)	0.15 (–0.07, 0.37)	0.18
	Lower-load (≤50% 1-RM)	0.28 (–0.06, 0.62)	0.11

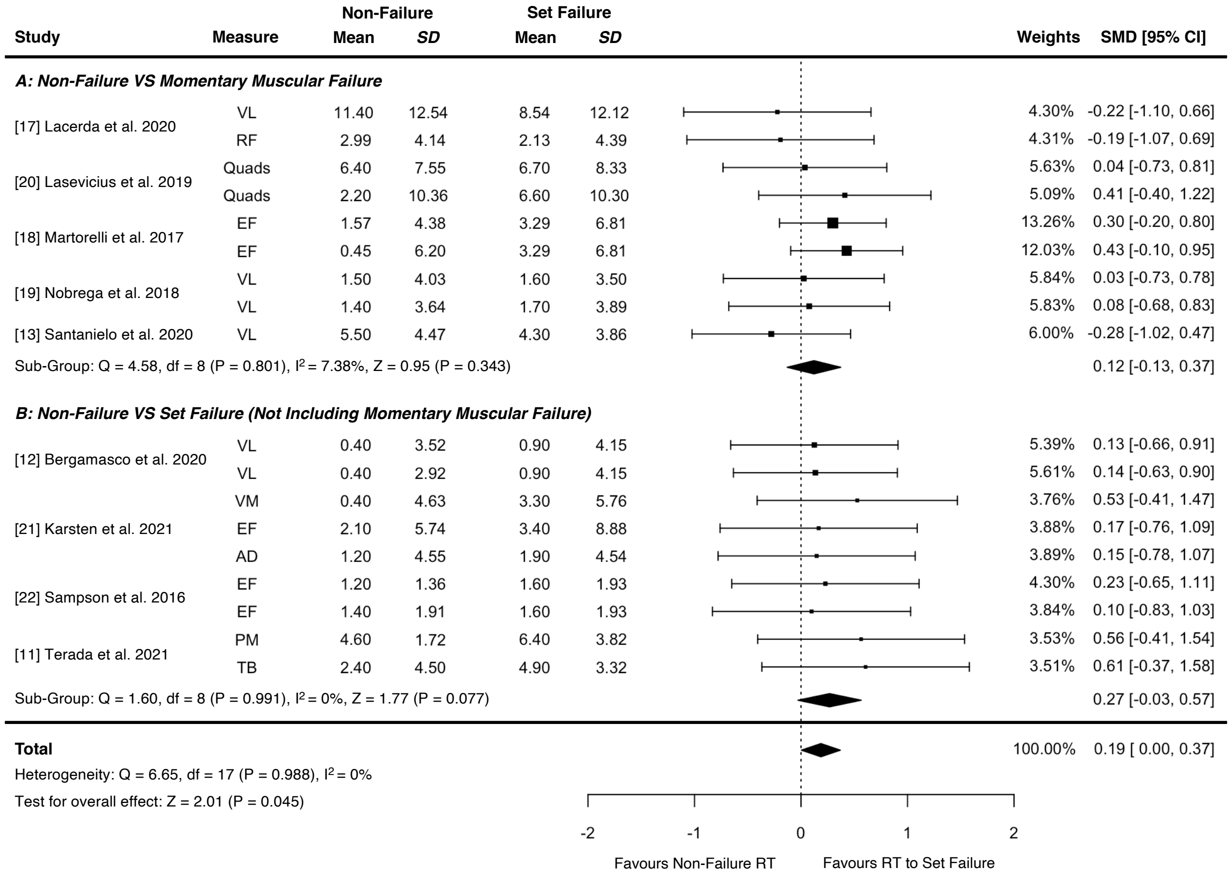

Figure 4.2. Influence of resistance training (RT) performed to set failure vs. non-failure on muscle hypertrophy with subgroup analyses based on study 'theme' (A or B). Studies presented were grouped into broad themes that involved RT performed to either Theme A) momentary muscular failure versus non-failure, or Theme B) set failure (defined as anything other than momentary muscular failure) versus non-failure. Point estimates and error bars signify the standardised mean difference between set failure and non-failure conditions and 95% confidence interval (CI) values, respectively. *AD, anterior deltoid; EF, elbow flexors; PM, pectoralis major; Quads, quadriceps; RF, rectus femoris; TB, triceps brachii; VL, vastus lateralis; VM, vastus medialis.*

4.4.3.2 Does the magnitude of velocity loss achieved (and theoretically, the proximity-to-failure reached) during resistance training influence muscle hypertrophy?

Meta-analytic outcomes for the influence of high (>25%) and moderate (20-25%) velocity loss thresholds on muscle hypertrophy are shown in Figure 4.3. Results of the multi-level meta-analysis model indicated no statistically significant difference between high velocity loss and moderate velocity loss conditions on muscle hypertrophy, revealing a trivial standardised effect [ES = 0.08 (95% CI: –0.16, 0.32), P = 0.529] with a very low heterogeneity (Q = 4.08, P = 0.944, I^2 = 0%). Individual standardized effect sizes for velocity loss conditions in each study from Theme C are displayed in Figure 4.4. Velocity loss conditions were also categorised as either low (<20%), moderate (20-25%), or high (>25%), and the mean values and confidence intervals for each velocity loss condition are also shown in Table 4.4.

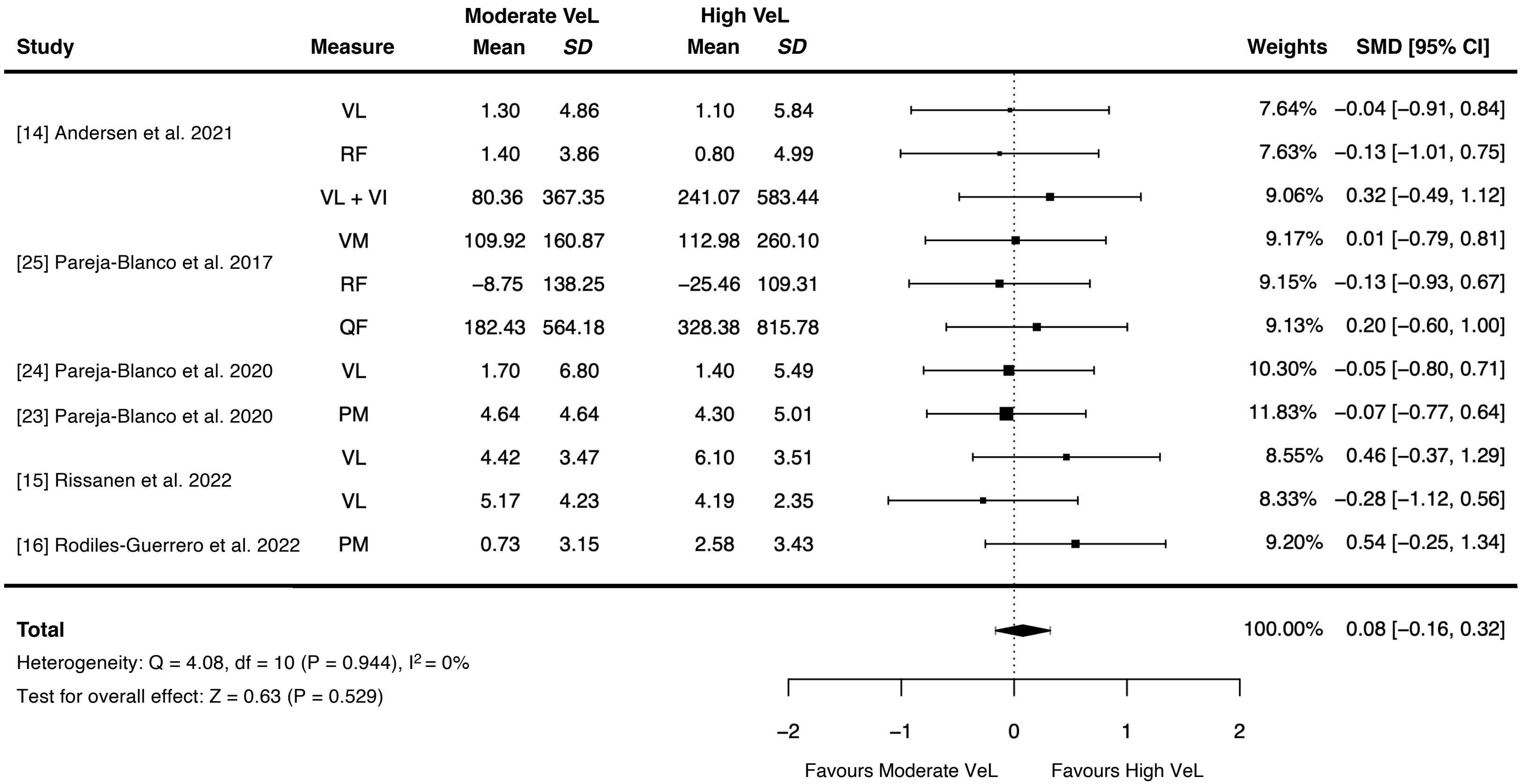

Figure 4.3. Influence of resistance training (RT) performed to high (>25%) and moderate (20-25%) velocity loss on muscle hypertrophy based on studies in Theme C. Studies presented were grouped into Theme C that involved RT performed to different velocity loss thresholds. Point estimates and error bars signify the standardised mean difference between high and moderate velocity loss conditions and 95% confidence interval (CI) values, respectively. *PM, pectoralis major; QF, quadriceps femoris; RF, rectus femoris; VI, vastus intermedius; VL, vastus lateralis; VM, vastus medialis.*

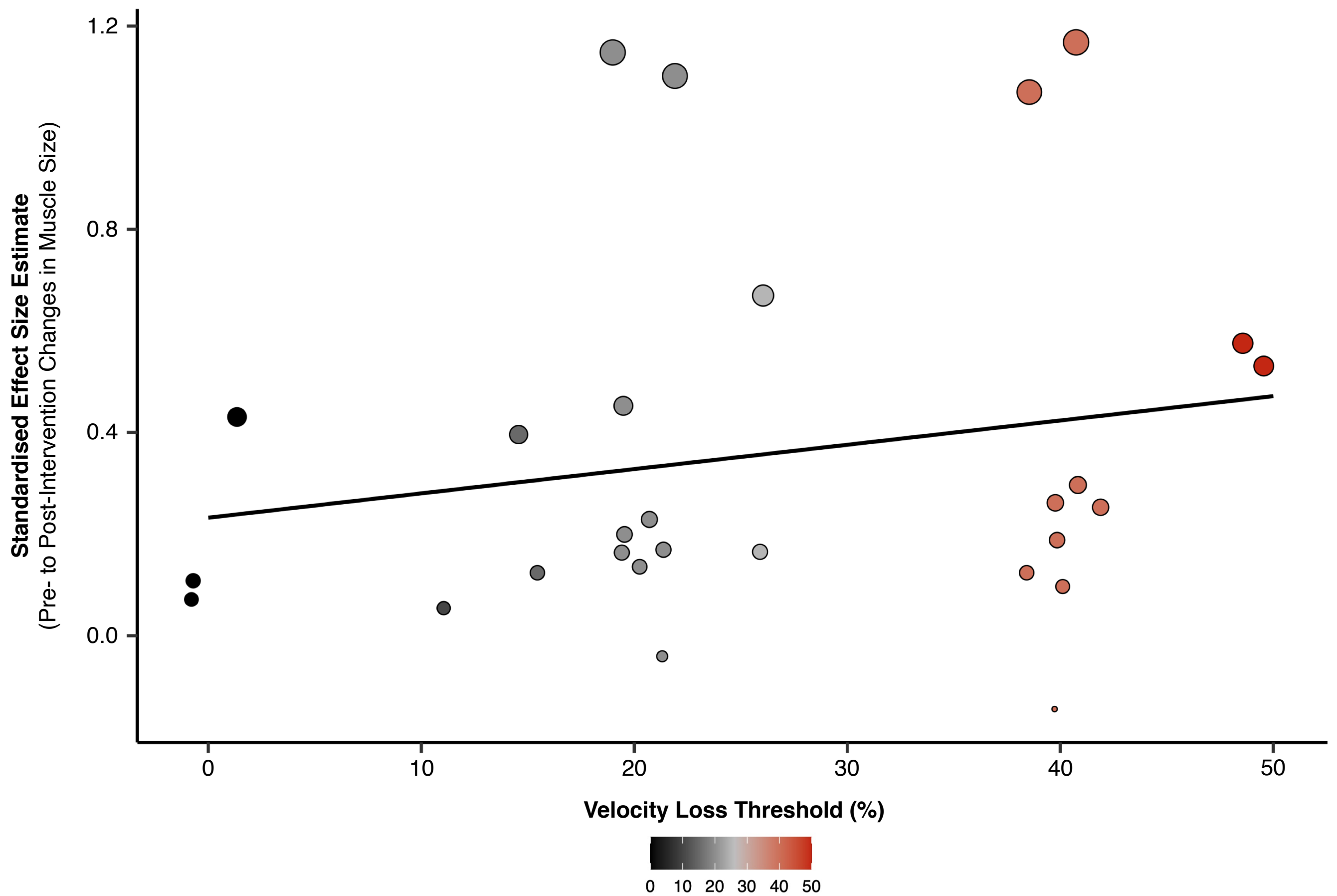

Figure 4.4. Individual standardised effect sizes (pre- to post-intervention changes in muscle size) for all velocity loss conditions [low (<20%), moderate (20-25%), high (>25%)] in each study from Theme C. Data presented were extracted from studies grouped into Theme C that involved RT performed to different velocity loss thresholds. Size of dot point is based on standardised effect size and a horizontal 'jitter' was applied to limit overlap of dot points (as such, dot point position on the x-axis is not a true representation of the velocity loss achieved and is rather limited to 0, 10, 15, 20, 25, 40 and 50% velocity losses). Positive effect size values indicate increases in muscle size from pre- to post-intervention for each velocity loss condition.

4.4.3.3 What magnitudes of muscle hypertrophy are achieved when resistance training is performed to momentary muscular failure (Theme A), to set failure (Theme B), and to a high velocity loss (Theme C; 40 or 50% velocity loss)?

Individual standardised effect sizes for pre- to post-intervention changes in muscle size for each RT condition (i.e., momentary muscular failure, set failure, non-failure, and low, moderate, and high velocity loss thresholds) across all studies in each 'theme' (A, B, and C) are shown in Table 4.4.

Table 4.4. Individual standardised effect sizes for resistance training (RT) conditions across all studies in each 'theme' (A, B, and C). Data shown are presented as a standardised effect size estimate (signifying the standardised mean difference for pre- to post-intervention changes in muscle size for each RT condition) with 95% confidence interval (CI) and associated *P*-Value.

Theme	Condition	ES (95% CI)	*P*-Value
A	Momentary Muscular Failure	0.41 (0.27, 0.55)	<0.001
	Non-Failure	0.37 (0.15, 0.58)	0.001
B	Set failure	0.46 (0.12, 0.80)	0.077
	Non-Failure	0.32 (0.05, 0.60)	0.023
C	Low velocity loss (<20%)	0.20 (–0.02, 0.41)	0.072
	Moderate velocity loss (20-25%)	0.39 (0.09, 0.70)	0.010
	High velocity loss (>25%)	0.42 (0.12, 0.71)	0.005

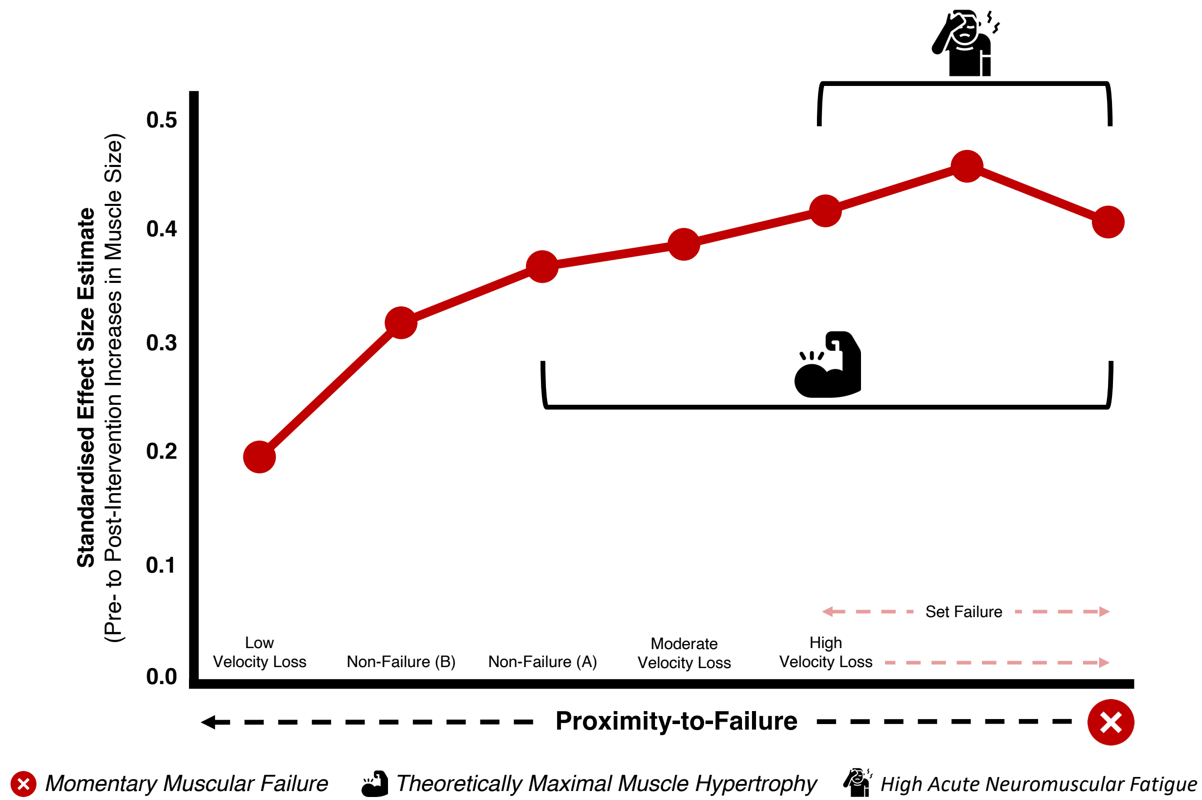

Figure 4.5. Conceptual non-linear relationship between proximity-to-failure and muscle hypertrophy. Our results suggest that closer proximities-to-failure are associated with muscle hypertrophy in a non-linear manner. Although the order of resistance training (RT) conditions displayed allows for visual inspection of a potential non-linear relationship between proximity-to-failure and muscle hypertrophy, the true proximities-to-failure achieved in each of these RT conditions are unclear and likely vary. The far-right dot point represents the 'momentary muscular failure' condition. It is also likely that participants in the 'set failure' and 'high velocity loss' conditions reached momentary muscular failure at times. Data shown are effect size estimates for pre- to post-intervention increases in muscle size for each RT condition.

4.4.4 Sensitivity-Analysis Results

Sensitivity analyses were performed for all multi-level meta-analysis models, with correlation coefficients ranging from *r* = 0.6-0.9 (per hundredth decimal), to assess whether the selected correlation coefficient (*r* = 0.75) influenced the meta-analytic outcomes (Appendix A). For the meta-analysis estimating the overall effect of RT performed to set failure versus non-failure on muscle hypertrophy, effect sizes between 0.15-0.25 and *P*-values between 0.016-0.104 were observed. Although our meta-analysis found a statistically significant effect (*P* = 0.045) of RT performed to set failure versus non-failure on muscle hypertrophy, this result should be interpreted with caution. In accordance with previous literature [11], this analysis was conducted with an *a priori* assumption that the correlation coefficient between pre-test and post-test measures was *r* = 0.75; while this is a defensible assumption, sensitivity analyses revealed outcomes that were not statistically significant with correlation coefficients below *r* = 0.73 (Appendix A). Conversely, the meta-analysis that compared studies in Theme C to determine whether the magnitude of velocity loss influenced muscle hypertrophy observed effect size and *P*-value ranges of 0.06-0.11 and 0.356-0.612, respectively. Our meta-analysis found no statistically significant difference between high velocity loss and moderate velocity loss conditions on muscle hypertrophy (*P* = 0.529) and considering that no statistically significant *P*-values were observed (*P* = <0.05) across the range of correlation coefficients analysed (Appendix A), the results of this meta-analysis may be interpreted with increased confidence.

4.5 Discussion

4.5.1 Influence of Resistance Training Performed to Set Failure (Including Momentary Muscular Failure and Other Definitions) Versus Non-Failure on Muscle Hypertrophy

A key barrier to further understanding the influence of proximity-to-failure on muscle hypertrophy is that no consensus definition for set failure exists in the literature. Previous meta-analyses [11, 12] compared studies that involved various definitions of set failure, and no statistically significant differences between RT performed to 'failure' versus non-failure on muscle hypertrophy were found. However, due to the heterogeneity in proximities-to-failure achieved, these results may not provide an accurate insight into the true effect of reaching momentary muscular failure during RT, which is the most objective way of defining set failure [97].

Similar to previous meta-analyses [11, 12], we first aimed to estimate the overall effect of RT performed to set failure (irrespective of the definition applied) versus non-failure on muscle hypertrophy. We also investigated whether the definition of set failure applied influenced the results. In our analysis of studies that applied any definition of set failure (Theme A and B), we found a trivial advantage for RT performed to set failure versus non-failure on muscle hypertrophy [Figure 4.2; ES = 0.19 (95% CI: 0.00, 0.37), $P = 0.045$]. These findings contrasted previous meta-analytic results [11, 12]; however, due to the aforementioned limitations of this approach the validity of these results is uncertain. Of greater importance is our sub-group analysis of studies that applied the definition of momentary muscular failure (Theme A), finding no evidence to support that RT performed to momentary muscular failure is superior to non-failure RT for muscle hypertrophy [Figure 4.2; ES = 0.12 (95% CI: –0.13, 0.37), $P = 0.343$]. Indeed, the definition of momentary muscular failure involves involuntary set termination and is the only way to standardise the RT stimulus both within- and between-studies when RT is performed to 'failure'. Thus, applying the definition of momentary muscular failure likely improves the validity of outcomes as demonstrated by a narrower confidence interval width (i.e., lower uncertainty) [Table 4.4; ES = 0.41 (95% CI: 0.27, 0.55)] compared to when RT is performed to set failure (definitions other than momentary muscular failure) and the true proximity-to-failure achieved likely varies [Table 4.4; ES = 0.46 (95% CI: 0.12, 0.80)]. Our sub-group analysis of studies that did not apply the definition of momentary muscular failure (Theme B) also demonstrated no statistically significant difference between conditions [Figure 4.2; ES = 0.27 (95% CI: –0.03, 0.57), $P = 0.077$] and it is likely that these studies simply compared different proximities-to-failure, therefore preventing inferences about the specific effect of reaching momentary muscular failure on muscle hypertrophy. Although differences in confidence interval width between our sub-group analyses (Theme A versus Theme B) may be due to the definition of set failure applied, considerable variability and ambiguity in the proximity-to-failure achieved in non-failure RT conditions also exists within the literature, which likely also contributes to differences in the effect size estimates observed for pre- to post-intervention changes in muscle size and their associated confidence intervals. To reiterate, despite finding a trivial advantage for RT performed to set failure versus non-failure on muscle hypertrophy when meta-analysing studies that applied any definition of set failure, our sub-group analyses that evaluated studies based on the definition of set failure applied and found i) no advantage of performing RT to momentary muscular failure versus non-failure on muscle hypertrophy, and ii) that closer proximities-to-failure do not always elicit greater muscle hypertrophy. Overall, this analysis demonstrated that skeletal muscle can be effectively stimulated to hypertrophy prior to reaching momentary muscular failure during RT, but due to methodological limitations, it is difficult to discern the proximity-to-failure that would theoretically maximise muscle hypertrophy.

4.5.1.1 Effect of Volume-Load on the Influence of Proximity-to-Failure on Muscle Hypertrophy

We also generated a sub-group analysis on all studies (irrespective of the definition of set failure applied) to assess whether volume-load moderated the influence of proximity-to-failure on muscle hypertrophy. We found similar effect size estimates (and confidence interval width) for muscle hypertrophy between set failure (irrespective of the definition applied) and non-failure conditions in studies that equated volume-load [Table 4.3; ES = 0.20 (95% CI: –0.03, 0.43)], and those that did not equate volume-load [Table 4.3; ES = 0.17 (95% CI: –0.13, 0.47)]. These findings support the idea that equating volume-load between conditions may be unnecessary when evaluating the effect of proximity-to-failure on muscle hypertrophy. Rather, it remains possible that set-volume (i.e., the number of sets performed to, or close to momentary muscular failure per muscle group per week [110]), which was equated between conditions in seven [35, 43-45, 47, 54, 55] out of the nine [35, 43-47, 53-55] studies, has a more potent effect on muscle hypertrophy than volume-load [110]. Although our analysis found no moderating effect of volume-load on the overall effect size for muscle hypertrophy ($P = 0.884$), the effect of volume-load as a moderator variable is limited by the set-volume prescribed in research interventions, which may be lower than set-volumes commonly achieved in practice [111]. Considering the similarities in set-volume completed across studies included in our meta-analysis, it is also unlikely that set-volume had a moderating effect on the overall effect size for muscle hypertrophy. As such, future research investigating the effect of proximity-to-failure on muscle hypertrophy should thus i) focus on equating set-volume between conditions, ii) investigate whether the number of sets performed for a given muscle group/exercises moderates the influence of proximity-to-failure on muscle hypertrophy, and iii) employ set-volumes that reflect current scientific guidelines for best practice [112] to improve the practical recommendations derived.

4.5.1.2 Effect of Relative Load on the Influence of Proximity-to-Failure on Muscle Hypertrophy

Our sub-group analysis on studies that employed any definition of set failure also assessed whether the relative load lifted moderated the influence of proximity-to-failure on muscle hypertrophy. We found a larger effect size estimate for muscle hypertrophy favouring set failure (irrespective of the definition applied) compared to non-failure conditions when lower loads were employed [≤50% 1-RM; ES = 0.28 (95% CI: –0.06, 0.62)] versus higher loads [>50% 1-RM; ES = 0.15 (95% CI: –0.07, 0.37)]. Differences in confidence interval width between loading conditions was likely due to the variability in proximity-to-failure achieved amongst both set failure and non-failure conditions; particularly during lower-load RT, as individuals are more likely to underestimate their proximity-to-failure when performing RT with lower-loads versus higher-loads [26], potentially due to the high levels of perceived discomfort that often accompany lower-load RT [113]. Nonetheless, it is hypothesised that RT should be performed with a closer proximity-to-failure when lower-loads are lifted versus higher-loads. This strategy would theoretically maximise muscle fibre activation and subsequent muscle hypertrophy [114], and although the effect size differences may provide support for this hypothesis, more research comparing lower-load and higher-load RT is required to elucidate the influence of relative load on muscle hypertrophy when RT is performed to different proximities-to-failure. Although we found no moderating effect of relative load on the overall effect size for muscle hypertrophy (P = 0.525), future research should continue exploring the interaction of RT variables (e.g., set volume, relative load, exercise selection etc.) with proximity-to-failure to foster insights that may improve RT prescription for muscle hypertrophy.

4.5.2 Influence of Different Velocity Loss Thresholds on Muscle Hypertrophy

A recent meta-analysis investigated the effect of different velocity loss thresholds on muscle hypertrophy and found that velocity losses of >25% (40% or 50% in all the analysed studies) were superior to velocity losses of ≤25% for muscle hypertrophy [79]; however, sub-analyses indicated that this result was largely driven by comparisons of higher velocity losses (40% and 50%) with those ≤20% as opposed to those between 20-25%. Considering the small number of studies employing velocity loss thresholds of <20%, which likely confounded the validity of these sub-analyses, we therefore decided to define three velocity loss thresholds (low = <20%, moderate = 20-25%, high = >25%) and generated individual effect sizes for pre- to post-intervention changes in muscle size for each velocity loss condition.

Similar to the results of previous research [79], we found that higher velocity losses (20-50%), and theoretically, closer proximities-to-failure, were associated with greater muscle hypertrophy in a *non-linear* manner (Figure 4.5). Smaller effect size estimates for pre- to post-intervention changes in muscle size were observed for the low velocity loss condition (ES = 0.20) versus the moderate (ES = 0.39) and high (ES = 0.42) velocity loss conditions, with meta-analytic results showing no advantage of performing RT to a high velocity loss (>25%) versus a moderate velocity loss (20-25%) on muscle hypertrophy [Figure 4.3 (ES = 0.08, 95% CI: –0.16 to 0.32*;* *P* = 0.529)]. While differences in velocity loss between conditions may provide indirect insights into the influence of proximity-to-failure on muscle hypertrophy, suggesting that closer proximities-to-failure during RT do not always elicit greater muscle hypertrophy, these findings should be interpreted with caution given the substantial variability in the proximity-to-failure achieved between individuals performing RT to the same velocity loss. For example, one study found that participants who performed the squat exercise until 40% velocity loss reached momentary muscular failure ~56% of the time [71], suggesting that the occurrence of momentary muscular failure likely varies between high velocity loss conditions across studies and contributes to the variability in muscle hypertrophy outcomes observed [highlighted by a relatively wide confidence interval width for the high velocity loss threshold (95% CI: 0.05, 0.76)]. Importantly, the results of our meta-analysis were found despite greater volume-load being accumulated when RT was performed to a high versus moderate velocity loss (for example: the 40% velocity loss condition in one study performed over 100 repetitions more than the 20% velocity loss condition [79]), and although it has been claimed that differences in muscle hypertrophy between velocity loss conditions are due to differences in volume-load [79], we propose that if velocity loss conditions of >20% are compared (with set-volume and relative load equated between conditions), differences in volume-load have little to no additional impact on muscle hypertrophy in resistance-trained populations. As such, factors other than volume-load (e.g., neuromuscular fatigue) may moderate the influence of proximity-to-failure on muscle hypertrophy when RT is performed to different velocity losses, or proximities-to-failure. Despite the limitations, relative differences in proximity-to-failure across different velocity loss thresholds remain and our findings provide evidence for a potential *non-linear relationship* between proximity-to-failure and muscle hypertrophy; however, future research that more accurately quantifies proximity-to-failure is required to better understand the relationship between proximity-to-failure and muscle hypertrophy.

4.5.3 Limitations

A total of 11 out of 15 studies scored highly (>10) on the TESTEX scale and visual inspection of methodological quality results revealed no impact of study quality on the effect size estimates generated. However, four studies didn't state the percentage of participants that completed the study (i.e., didn't withdraw), and five studies didn't state the number of exercise sessions completed by participants who did not withdraw from study. The procedure used to randomise participants into intervention groups was also not described in eight studies, and no studies stated whether group allocation was concealed. Although it is unlikely that these limitations had a confounding influence on the outcomes of this review, future research should ensure that this information is clearly presented. Considering the correlation coefficients (r value) between pre-test and post-test measures are rarely reported in research studies, we assumed $r = 0.75$ to conduct our meta-analyses. Although this r value was replicated from a previous meta-analysis related to this topic [11], sensitivity analysis suggests the results of our meta-analysis comparing set failure (irrespective of the definition applied) versus non-failure RT on muscle hypertrophy should be interpreted with caution, as outcomes of $P = >0.05$ were observed with correlation coefficients below $r = 0.73$. Furthermore, considering the relatively small body of available literature on the influence of RT proximity-to-failure on muscle hypertrophy, our meta-analytic results are likely confounded by statistical power limitations, particularly in our sub-group analyses. As such, although we found no supporting evidence that RT performed to momentary muscular failure is superior to non-failure RT for muscle hypertrophy, considering the low number of studies analysed, it is unclear if analysing a larger number of studies (and generating a greater statistical power) would alter this conclusion. Results of our analyses may also be influenced by the current set termination methods used during set failure (not including momentary muscular failure) and non-failure RT conditions, which limit insight into the true proximity-to-failure achieved. For example, the proximity-to-failure achieved in these conditions likely varied within- and between-studies, and particularly when velocity loss thresholds were used to control set termination, as highlighted by the relatively wide confidence interval width for our effect size estimates (Table 4.4). Overall, to improve the validity and practical applicability of results of future research investigating the influence of proximity-to-failure on muscle hypertrophy, researchers should i) embrace thorough data reporting and dedication to open science so that future meta-analyses may start to use actual, observed correlation coefficients (between pre-test and post-test measures), instead of estimating or assuming the *r* value, ii) not treat the prescription of RT dichotomously (i.e., set failure or non-failure), and ii) employ methods to control and report the proximity-to-failure reached during RT interventions.

4.6 Conclusion

Our main findings show that: i) RT performed to set failure is advantageous versus non-failure RT for muscle hypertrophy (trivial effect) when studies applying any definition of set failure are analysed; however, our sub-group analyses found no evidence to support that RT performed to momentary muscular failure [or to set failure (irrespective of the definition applied)] is superior to non-failure RT for muscle hypertrophy, and ii) higher velocity loss thresholds, and thus, theoretically closer proximities-to-failure, elicit greater muscle hypertrophy but in a non-linear manner. Although other RT variables may moderate the influence of proximity-to-failure on muscle hypertrophy, our findings revealed no effect of either volume-load or relative load on muscle hypertrophy when RT was performed to set failure (using any definition) versus non-failure; however, larger effect size estimates favouring RT to set failure were found for lower-load versus higher-load RT, providing some support for the idea that RT needs to be performed to closer proximities-to-failure when lower-loads are lifted versus higher-loads. Overall, these findings provide evidence for a potential non-linear relationship between proximity-to-failure and muscle hypertrophy. However, current methods used to control set termination during non-failure RT limit insight into the actual proximity-to-failure achieved, and as a result, the proximity-to-failure that would theoretically maximise muscle hypertrophy is unclear and requires further investigation.

Chapter Five – Influence of Resistance Training Proximity-to-Failure, Determined by Repetitions-in-Reserve, on Neuromuscular Fatigue in Resistance-Trained Males and Females.

Please note, the following text in Chapter Five has been adapted from a peer-reviewed and published manuscript (DOI: 10.1186/s40798-023-00554-y).

5.1 Preface

While our previous systematic review with meta-analysis identified little evidence for the superiority of performing RT to momentary muscular failure for muscle hypertrophy [115], proximity-to-failure may influence neuromuscular fatigue and perceived discomfort, exertion, recovery, and muscle soreness that may subsequently impact muscle hypertrophy. Previous research has compared RT performed to set failure and non-failure, and different velocity loss thresholds, on neuromuscular fatigue, but the effect of RIR on neuromuscular fatigue is under studied [97]. Likewise, despite the importance of affective responses to RT in promoting long-term adherence, few studies were included in our scoping review that investigated the influence of proximity-to-failure on perceived discomfort and exertion [97]. This experimental study therefore employs intra-set RIR predictions to control set termination and evaluate the influence of RIR on surrogate measures of neuromuscular fatigue, perceived discomfort, exertion, recovery, and muscle soreness. This study provides insight into the relationship between RIR and relevant outcome measures that may not only improve future study designs, but also allow practitioners to better understand the impact of RIR prescription on short-term responses to RT (e.g., neuromuscular fatigue and perceived discomfort, exertion, muscle soreness, and general feelings) that may influence performance and potentially long-term exercise adherence.

5.2 Introduction

Proximity-to-failure is defined as the number of repetitions remaining in a resistance training (RT) set prior to momentary muscular failure (i.e., when the concentric portion of a given repetition cannot be completed with a full range-of-motion without deviation from the prescribed exercise form) [97]. As proximity-to-failure nears in a given set, type II skeletal muscle fibres are required to produce higher forces [28, 29], ultimately exposing the active musculature to greater mechanical tension and influencing the subsequent physiological adaptation(s) induced. Neuromuscular fatigue consequent to RT also increases as proximity-to-failure nears [32], potentially impairing contractile function during and subsequent to RT and ultimately hampering maximal strength development or muscle hypertrophy by reducing the absolute load lifted or the exposure of muscle fibres to mechanical tension [116], respectively. This understanding highlights the importance of investigating the specific effect of different proximities-to-failure on neuromuscular fatigue, along with the associated time-courses of recovery, which are practically important for RT prescription to maximise long-term physiological adaptations.

A key barrier to understanding the influence of proximity-to-failure on neuromuscular fatigue and other short-term responses (e.g., muscle damage, perceived discomfort and exertion, general feelings, perceived recovery etc.) that may negatively influence physiological adaptations to RT is the current set termination prescriptions used in research investigating proximity-to-failure [97]. Firstly, no consensus definition of ‘failure’ exists in the literature, and as such, studies employ various definitions of *set failure* (i.e., umbrella term describing the set termination criteria applied to ‘failure’ in a given study) that alter the RT stimulus achieved and do not provide an accurate insight into the true effect of reaching momentary muscular failure during RT. Although momentary muscular failure is the most objective definition of set failure, our recent scoping review [97] only identified six studies (out of 25) that assessed the influence of proximity-to-failure on short-term responses to RT and explicitly stated that the definition of momentary muscular failure was employed. Further, a recent meta-analysis found greater increases in neuromuscular fatigue and muscle damage after RT performed to set failure versus non-failure [13]; however, these findings are limited to males and considering the potential for biological sex differences in neuromuscular fatigability [91], how proximity-to-failure influences short-term responses to RT in females requires future investigation. It is also likely that the proximity-to-failure reached by participants in non-failure conditions varies considerably within- and between-studies due to commonly employed predetermined repetition prescriptions and individual variability in the maximum number of repetitions possible with a given load [75-77]. Some studies have attempted to address this research limitation by employing 'velocity loss' thresholds to control and standardise set termination; however, even the magnitude of velocity loss achieved during a given set cannot accurately inform proximity-to-failure during RT [97] as evidenced by one study that found participants who performed the squat exercise until 40% velocity loss reached momentary muscular failure ~56% of the time [71]. As such, although mechanical and metabolic indicators of neuromuscular fatigue increase with the magnitude of velocity loss achieved [68-70], the proximity-to-failure reached across velocity loss conditions is unknown and likely varies. Taken as a whole, neuromuscular fatigue is greater when RT is performed to set failure versus non-failure and increases as the magnitude of velocity loss rises (and theoretically, as proximity-to-failure nears), but inconsistencies in the literature regarding the proximity-to-failure achieved during RT limit understanding of the influence of proximity-to-failure on neuromuscular fatigue and other short-term responses to RT.

Quantifying the proximity-to-failure reached during RT with the number of repetitions-in-reserve (RIR) is emerging as a popular strategy that requires set termination to occur once the individual performing RT believes they can only perform a certain number of full repetitions before reaching momentary muscular failure. This 'subjective RIR prediction' was recently tested in a study comparing the effect of RT performed to 3-RIR versus momentary muscular failure on neuromuscular fatigue. While neuromuscular fatigue was similar between conditions [52], limitations with the nature of instruction provided to participants meant set termination may have varied between 0–3-RIR in the 3-RIR condition, limiting insight into the specific effect of proximity-to-failure on neuromuscular fatigue. Few studies have investigated the effect of subjective RIR prediction on RT outcomes [52, 84-86], likely due to the many factors that may influence the accuracy of subjective RIR predictions (e.g., accuracy is improved when RIR prediction is performed closer to momentary muscular failure [87], as the relative load lifted and number of successive sets performed increases [26, 82], and in resistance trained versus untrained individuals [81, 88]). Nonetheless, subjective RIR prediction is likely the most practical method of controlling proximity-to-failure during RT as it can be easily implemented in a RT prescription (e.g., 3 sets of 10-15 repetitions with 2-RIR), particularly in resistance-trained individuals, and its rigorous application in research may address current methodological limitations and help better translate findings to practical recommendations.

5.2.1 Objectives

The primary objective of this study was to examine the influence of RT proximity-to-failure on the level of neuromuscular fatigue incurred in resistance trained males and females. Therefore, we assessed changes in lifting velocity (i.e., mean velocity of the concentric portion of a repetition), a valid indicator of neuromuscular fatigue [65], with a fixed load from i) pre-exercise to post-exercise in aim of quantifying acute neuromuscular fatigue (4-min post-exercise) and the associated time-course of recovery of neuromuscular function (24- and 48-hrs post-exercise), and ii) from the first to the final set performed. We also assessed biological sex differences in acute neuromuscular fatigue. Perceptual responses to RT were also assessed, including perceptions of discomfort, recovery, exertion, muscle soreness, and general feelings. We hypothesised that reaching closer proximities-to-failure during RT would induce greater neuromuscular fatigue at all post-exercise time points and greater subjective perceptions of discomfort, exertion, muscle soreness, and reduced recovery. Further, we expected neuromuscular fatigue to be lower in females compared to males.

5.3 Methods

5.3.1 Experimental Approach

This was a randomised cross-over trial (conducted at JPS Health & Fitness, Melbourne) whereby participants attended two pre-visit sessions and three experimental trials, each trial involving one resistance training session followed by two testing sessions (24- and 48-hrs post-exercise) (Figure 5.1). In pre-visit one, the 1-RM load was determined for the flat barbell bench press (BP) and used to inform load selection during each experimental RT protocol (75% 1-RM). A repetitions-to-failure assessment was also conducted for the BP in pre-visit one and two. After the pre-visits, participants completed three experimental trials that involved RT protocols performed to either momentary muscular failure (defined as: the point where despite attempting to do so, the individual was unable to complete the concentric portion of their current repetition with a full range-of-motion without deviation from the prescribed form of the exercise) or to a subjectively predicted 1-RIR or 3-RIR. To provide surrogate measures of neuromuscular fatigue consequent to RT, changes in lifting velocity were assessed from the first to the final set, and from pre-exercise to post-exercise (4-min, 24-hrs, and 48-hrs post-exercise). Perceived muscle soreness and recovery were also assessed 24- and 48-hrs post-exercise. To assess perceptual responses to RT, participants rated their perceived discomfort after the completion of each set, and their general feelings and perceived exertion upon completion of each RT protocol.

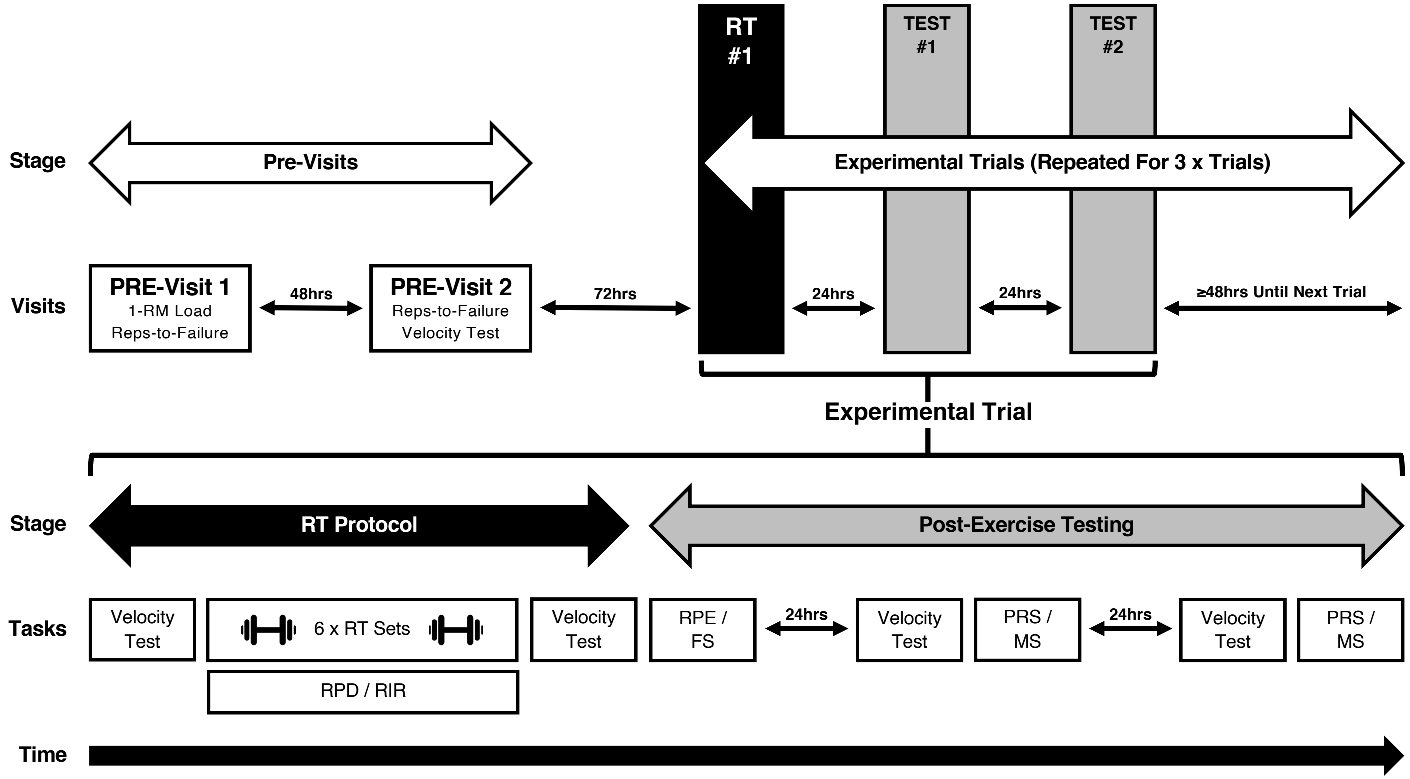

Figure 5.1. Schematic overview of study design and experimental trials. Participants completed two pre-visit sessions and three experimental trials. Each trial consisted of a resistance training protocol (FAIL, 1-RIR, or 3-RIR) involving six sets performed on the barbell bench press exercise (75% 1-RM load), whereby changes in lifting velocity were assessed from the first to the final set and from pre-exercise to 4-min post-exercise. RPD was assessed after the completion of each set, and RPE and FS were assessed after the completion of the RT protocol. Following the RT protocol, two testing sessions 24- and 48-hrs thereafter were also completed to assess the recovery time-course of lifting velocity, MS, and PRS. *FS, feeling scale; MS, muscle soreness; PRS, perceived recovery status; RIR, repetitions-in-reserve; RPD, rating of perceived discomfort; RPE, rating of perceived exertion; RT, resistance training.*

5.3.2 Subjects

Pre-exercise participant characteristics are presented in Table 5.1. A total of 12 males and 12 females were recruited. All participants: i) were between 18-40 years old, ii) had no existing musculoskeletal injuries or neuromuscular disorders, iii) confirmed they had not used anabolic steroids or any illegal agents known to increase muscle size for the previous year, and iv) had a minimum of three years RT experience involving a minimum of three or more RT sessions completed per week. The mean 1-RM for the bench press exercise was also greater than 120% and 80% of bodyweight for males and females, respectively, indicating an advanced sample of participants as specified by Santos Junior et al. [117]. All participants reported experience working with a private fitness coach in a face-to-face setting, 12 participants declared they had previously competed in strength or physique sports (e.g., powerlifting or bodybuilding), and 23 participants reported experience with subjective RIR prediction.

5.3.2.1 Sample Size Justification

The target sample size of 24 participants was based on the following pragmatic considerations: i) recruiting more than 24 participants was not feasible given resource constraints including the time and costs associated with data collection and subsequent analyses, and ii) the chosen sample size is greater than most published studies investigating the influence of RT proximity-to-failure on neuromuscular fatigue using similar research designs [32, 58, 61, 63, 69]. An α-priori sample size calculation was therefore not performed for this study. Instead, a sensitivity power analysis was performed in G*Power software (Version 3.1.9.7) using an ANOVA: repeated-measures, within-between interaction to determine the minimum (critical) effect size (Cohen's d = 0.27) for between-protocol differences in loss of lifting velocity (from the first to final set for a given exercise) that could be statistically rejected based on a pre-specified sample size ($n = 24$) and both type I (0.05) and type II (0.20) error rates. Given previous research [65] reported an effect size of d = 2.5 for the difference in velocity loss between RT performed to set failure versus non-failure (i.e., a 12-RM versus 10 repetitions with the 12-RM load), we considered a critical effect size of d = 0.27 sufficient to detect/reject likely effect sizes for between-protocol differences in this study.

Table 5.1. Baseline participant characteristics. An overview of the relevant characteristics for each participant. Relative strength calculated as: barbell bench press 1-RM (kg) divided by bodyweight (kg). *1-RM, one repetition maximum; BP, bench press; kg, kilograms; p/w, per week; RT, resistance training; y, years.*

	Men (*n* = 12)		**Females (*n* = 12)**	
Variable	**Mean ± SD**	**Range**	**Mean ± SD**	**Range**
Age (y)	28.50 ± 5.3	19 - 39	31.58 ± 5.70	23 - 40
Bodyweight (kg)	85.1 ± 8.3	74 - 99	62.3 ± 11.0	52 - 90
RT experience (y)	8.3 ± 3.7	3 - 15	7.2 ± 2.3	4 - 13
RT frequency (per wk)	4.4 ± 0.7	3 - 5	4.4 ± 0.7	4 - 6
1-RM BP (kg)	116.0 ± 20.8	92.5 - 157.5	54.9 ± 13.0	35 - 77.5
Relative strength	1.37 ± 0.26	1.14 - 1.93	0.88 ± 0.17	0.56 - 1.08

5.3.3 Procedures

5.3.3.1 Exercise and Nutrition Control

Participants were asked to not perform any RT or high-intensity aerobic exercise in the 24-h period before each study visit to minimise any potential confounding influences on outcome measures. To ensure recovery and performance were not influenced by sub-optimal nutritional status, participants consumed sufficient protein (2 g/kg body mass) and energy based on their body weight and estimated energy expenditure (at minimum, energy intake was matched with total daily energy expenditure) consistent with published guidelines [118]. Considering the number of study visits required, it was not feasible for participants to replicate their nutritional intake before each study visit. As such, participants were asked to track their nutritional intake on a food tracking application and measure their bodyweight each week to ensure that no weight loss occurred.

5.3.3.2 Menstrual Cycle Considerations

Upon recruitment, female participants started using a menstruation diary to ensure accurate information regarding the menstrual cycle was retrieved and recorded for future use. When possible (based on scheduling and practical constraints), females commenced their experiential trials in the early follicular phase of their menstrual cycle where the ratio between estrogen and progesterone is small [119]. For this reason, oral contraceptive use was not controlled for, as endogenous estrogen and progesterone levels are similar in the early follicular phase for females that are eumenorrheic and using oral contraceptives [120]. Participants that were amenorrheic ($n = 2$) were permitted to start their experimental trials at any time. If participants experienced menstrual symptoms during the study period that were perceived to affect training performance, study visits were rescheduled as necessary. Notably, recent meta-analyses indicate that both i) current menstrual cycle phase [121] and ii) modern oral contraceptive use [122], have at most trivial effects on exercise performance at the *group* level.

5.3.3.3 Pre-Visit Sessions

Approximately one month before the commencement of the study period (depending on participant availability and time constraints), participants underwent a pre-study familiarisation to establish appropriate exercise technique with maximal intended lifting velocity. Participants performed two sets of five repetitions with the minimum load on the BP exercise to ensure appropriate technique as follows: the advanced participants employed and replicated their own lifting grip based on their previous experience with the BP exercise (at minimum, the barbell had to be grasped slightly outside shoulder width) and lowered the barbell until it contacted their chest (below the nipple line) and then lifted it back to the starting position without excessive bouncing off the chest, or raising of the shoulders, trunk, or glutes off the bench. Participants were instructed to perform the concentric (lifting) phase of each repetition with maximal lifting velocity (i.e., as fast as possible), followed by a controlled eccentric (lowering) phase (~2 seconds). The amount of time in-between repetitions (maximum of one breath) was kept consistent throughout the whole set. Similar to previous research [57], the mean velocity (i.e., described herein as the 'lifting velocity') for each repetition was measured using a linear position transducer (GymAware, Kinetic Performance Technology, Canberra, Australia) attached to one side of the barbell (just inside the collar). If fluctuations in the lifting velocity were identified across successive repetitions, the participant was required to attempt another set of five repetitions until a similar lifting velocity was achieved on each repetition (i.e., a range of ≤0.02m/s across repetitions). Once the lifting velocity achieved was within ≤0.02m/s across repetitions, an additional load (15-20 kg for males and 5-10 kg for females) was added, and participants performed another set of three repetitions with maximal intended lifting velocity. Once participants were familiarised with this lifting strategy, they were told to incorporate the BP into their own RT regimen and continue practicing with maximal intended lifting velocity until the commencement of the study.

In pre-visit one, after re-familiarisation with correct exercise technique, participants completed a 1-RM assessment for the BP. First, a warm-up consisting of one set of five repetitions was performed with the minimum possible load (20 kg). The load was then progressively increased (15-20 kg increments for males and 5-10 kg for females) until the lifting velocity was lower than 0.5 m·s^{-1}. Thereafter, the load was increased in smaller increments (2.5-10 kg for men, and 1.25-5 kg for females) until the 1-RM was determined, defined as the heaviest load with which a single repetition was possible with a full range-of-motion. For the lighter loads (> 1 m·s^{-1}), three repetitions were performed at each load, two repetitions were performed for the moderate loads, and a single repetition for the heavier loads (< 0.5 m·s^{-1}). Three minutes of passive recovery was allowed between sets for lighter and moderate loads, and approximately five minutes of passive recovery for heavier loads. If the participant was unable to complete a repetition at a given load, they were allowed one additional attempt at that load. If the second attempt was not successful or if the participant declined a second attempt, the load was either i) reduced to 50% of the difference between it and the last successful 1-RM attempt, or ii) the last successful repetition was confirmed as the 1-RM.

Once the 1-RM assessment was complete, and in pre-visit two after a standardised warm-up, participants were required to complete a repetitions-to-failure assessment that involved performing two sets to momentary muscular failure with the load corresponding to 75% of 1-RM. Participants were first briefed about subjective RIR prediction, and it was made clear that 0-RIR indicates the last full range-of-motion repetition possible before momentary muscular failure is reached (i.e., if a subsequent repetition was attempted, momentary muscular failure would occur). Before each set to momentary muscular failure, participants were given an RIR target (1- or 3-RIR in a randomised order) and were required to verbally indicate when they believed they had reached the RIR target during the set. After verbal indication, participants were required to continue performing repetitions until momentary muscular failure occurred to assess the accuracy of RIR prediction. The additional repetitions performed after the participant provided the verbal indication were counted to assess individual predictive ability and were recorded for future analysis. At no point were participants informed about the number of repetitions completed within a set, nor were the repetitions counted aloud throughout the set by the supervisors. Participants also rated their level of perceived discomfort after completing each set using the rating of perceived discomfort (RPD) scale. During pre-visit two, a velocity assessment was also conducted for familiarisation purposes, and upon completion of the familiarisation session participants were asked to rate their perceived exertion and general feelings associated with the RT performed.

5.3.3.4 Experimental Trials

The RT protocols (Figure 5.1) completed during each experimental trial consisted of the BP performed with 75% 1-RM. Three experimental trials were conducted, involving RT protocols performed in a randomised order: i) momentary muscular failure (FAIL), ii) 1-RIR, and iii) 3-RIR. A minimum of 96-h was allocated between each RT protocol to ensure adequate recovery and minimise the influence of residual fatigue on subsequent trials. Before the commencement of each RT protocol, four warm-up sets were performed, starting with the minimum load for each exercise and working up to 50%, 65%, and 85% of the 75% 1-RM load (for six, five, four and three repetitions, with 2-minute inter-set rest periods). A pre-exercise velocity assessment was then completed before six total sets were performed until the target proximity-to-failure of the protocol was reached (repetitions performed differed between participants). Set termination for the RIR protocols involved the participant subjectively terminating each set when they perceived they had reached the RIR target (1- or 3-RIR) with no physical or verbal assistance from the supervisors. Participants were therefore provided with the following standardised instruction: *"you will be required to stop the set when you perceive to have n (1 or 3, depending on the RIR target of the protocol) repetitions-in-reserve."* Conversely, during the FAIL protocol, set termination occurred when the supervisor was required to assist the participant in re-racking the barbell due to the participant being: i) unable to lift the barbell off their chest, despite attempting to do so, ii) unable to complete a full range-of-motion repetition despite being provided with two seconds to lift the bar beyond the sticking point (i.e., the point during the concentric phase where the barbell stopped moving upwards), or iii) the barbell started exhibiting downward motion during the concentric phase. Four minutes of passive recovery was allowed between sets, and upon completion of the sixth (and final) set, participants rested for another four minutes and repeated the velocity assessment to establish an immediate measure of acute neuromuscular fatigue. Participants were also required to rate their perceived discomfort after each set, and their perceived exertion and general feelings after completing each RT protocol. Participants also attended the training facility 24- and 48-hrs thereafter to rate their perceived recovery and perceived muscle soreness before completing another velocity assessment to assess the post-exercise recovery time-course of neuromuscular function.

5.3.4 Objective Outcome Measures

5.3.4.1 Assessment of Recovery Time-Course

Three BP repetitions were performed (with maximal intended lifting velocity) using 85% of the 75% 1-RM load before the commencement of each RT protocol (i.e., last warm-up set), and 4-min, 24-hrs, and 48-hrs following the completion of each RT protocol (a standardised warm-up was completed 24- and 48-hrs post-exercise) (Figure 5.1). The change in the mean lifting velocity of the three repetitions from pre-exercise to post-exercise was used as a surrogate measure of acute neuromuscular fatigue (4-min post-exercise) and the associated recovery time-course of neuromuscular function (24- and 48-hrs post-exercise). Strong verbal encouragement and velocity feedback was provided during each repetition to ensure participants were applying maximal intended lifting velocity.

5.3.4.2 Loss of Lifting Velocity from First to Final Set

The lifting velocity achieved in each set performed (i.e., mean lifting velocity of all repetitions completed within each set) was calculated to determine the decline in mean lifting velocity from the first to the final set, and was used as a surrogate measure of the acute neuromuscular fatigue incurred over the six sets.

5.3.4.3 Repetition Loss from First to Final Set

To determine the influence of proximity-to-failure on RT volume (calculated as: volume = sets * repetitions), the total number of repetitions achieved in each set was recorded to determine the volume accumulated within each RT protocol and the percentage decrease in repetitions performed from the first set to the final set.

5.3.5 Subjective Outcome Measures

5.3.5.1 Perceived Discomfort

Immediately after completion of each RT set, participants rated their perceived discomfort using a rating of perceived discomfort (RPD) scale [113]. Participants were asked*: "how much discomfort did you feel in that set?"* and to rate their perceived discomfort during the set on a 1-10 scale, whereby zero represents "no discomfort" and 10 "maximal discomfort".

5.3.5.2 Perceived Exertion and General Feelings

Up to 30-minutes after the cessation of each RT protocol, participants rated their perceived exertion and general feelings for the entire session (via Qualtrics) using the modified category-ratio rating of perceived exertion (RPE CR-10) scale [123, 124] and the feeling scale [125], respectively. Participants were asked "*how hard was your workout*?" and to rate their perceived exertion for the session on a 0-10 (CR-10) scale whereby zero represents "rest" and 10 "maximal exertion". Participants were also asked *"how do you currently feel"* and to assess their general feelings toward the session with the feeling scale, ranging from "+5", which refers to "very good", to "-5", which refers to "very bad" [125].

5.3.5.3 Perceived Recovery and Muscle Soreness

Participants rated their perceived level of recovery and muscle soreness 24- and 48-hrs after the completion of each experimental trial. The perceived recovery status (PRS) scale was used to assess the perceived level of recovery and involves a rating of perceived recovery between 0 and 10, with 0–2 representing very poor recovery with an expected decline in performance, 4–6 representing low-to-moderate recovery with an expected similar performance, and 8–10 representing high perceived recovery with an expected increase in performance [126, 127]. Participants were also asked to rate pain/soreness sensations in muscles of the chest (following three BP repetitions with the minimum possible load) from 0-10, whereby 0–1 represents little to no pain, 2 represents slight pain, 3–4 represents mild pain, 5–6 represents moderate pain, 7–8 represents severe pain, and 9–10 indicates the worst pain the individual has previously experienced following resistance training [126].

5.3.6 Statistical analysis

All statistical analyses were performed using 'R' software (v 4.0.2; R Core Team, https://www.r-project.org/). Two separate linear mixed models (with two-way interaction effects including 'protocol' and 'time' or 'sex', and 'participant' as a random effect) were generated (with the 'lme4' package in R) to first analyse differences between protocols at each timepoint (protocol x time), and secondly, differences between sexes for each protocol (protocol x sex), for the following outcome measures: i) change in lifting velocity from pre-exercise to post-exercise, ii) loss of lifting velocity (mean of entire set) from the first to the final set, and ii) decrease in the total number of repetitions performed from the first to the final set. A linear mixed model (with 'protocol' and 'time' as fixed effects, and 'participant' as a random effect) was also used to assess differences between each RT protocol for all subjective measures (i.e., perceived discomfort, recovery, muscle soreness, exertion, and general feelings) at each time point measured. Diagnostic tests for each linear mixed model were performed using the 'redres' package in R to assess the validity of the model results. If model assumptions were violated, data was either log-transformed or analysed using non-parametric alternatives (i.e., Friedman's test). Statistical significance was set at P = <0.05. Effect sizes (Cohen's d) for within-protocol changes in outcome measures, and between-protocol differences in these changes, were calculated using the 'effsize' package in R with a Hedge's g correction applied. The magnitude of effect size values was interpreted as <0.2 = trivial, 0.2 to <0.5 = small, 0.5 to <0.8 = moderate, and ≥0.8 = large [128]. Post-hoc analyses for pairwise comparisons were conducted when a main or interaction effect was statistically significant using Tukey's Test (or a Wilcoxon Rank-Sum test). To *complement* traditional null hypothesis significance testing, we also considered the outcomes based on the magnitude of effect size estimates and the associated 95% confidence interval width.

5.5 Results

Descriptive characteristics (including total repetitions and lifting velocities) for each RT protocol are reported in Table 5.2 for males and females separately. All participants completed 100% of the procedures required in each experimental trial.

5.5.1 Total Volume

A statistically significant effect of protocol on total volume (sets x reps) performed [F (2) = 12.32, P = < 0.001] was found, with greater total volume achieved in 1-RIR versus both FAIL

[ES = 0.18 (95% CI: 0.06, 0.30), *P* = 0.015] and 3-RIR [ES = 0.40 (95% CI: 0.21, 0.60), *P* = < 0.001], but there was no statistically significant difference between FAIL and 3-RIR [ES = 0.18 (95% CI: –0.03, 0.39), *P* = 0.117] (Figure 5.2). Further, there was a statistically significant effect of sex on total volume (mean of all protocols combined) [*F* (1) = 17.80, *P* = < 0.001], with females performing more total volume than males [ES = 1.58 (95% CI: 1.04, 2.11), *P* = < 0.001] (Table 5.2). No statistically significant interaction effect of protocol x sex was found (see Appendix B for all results).

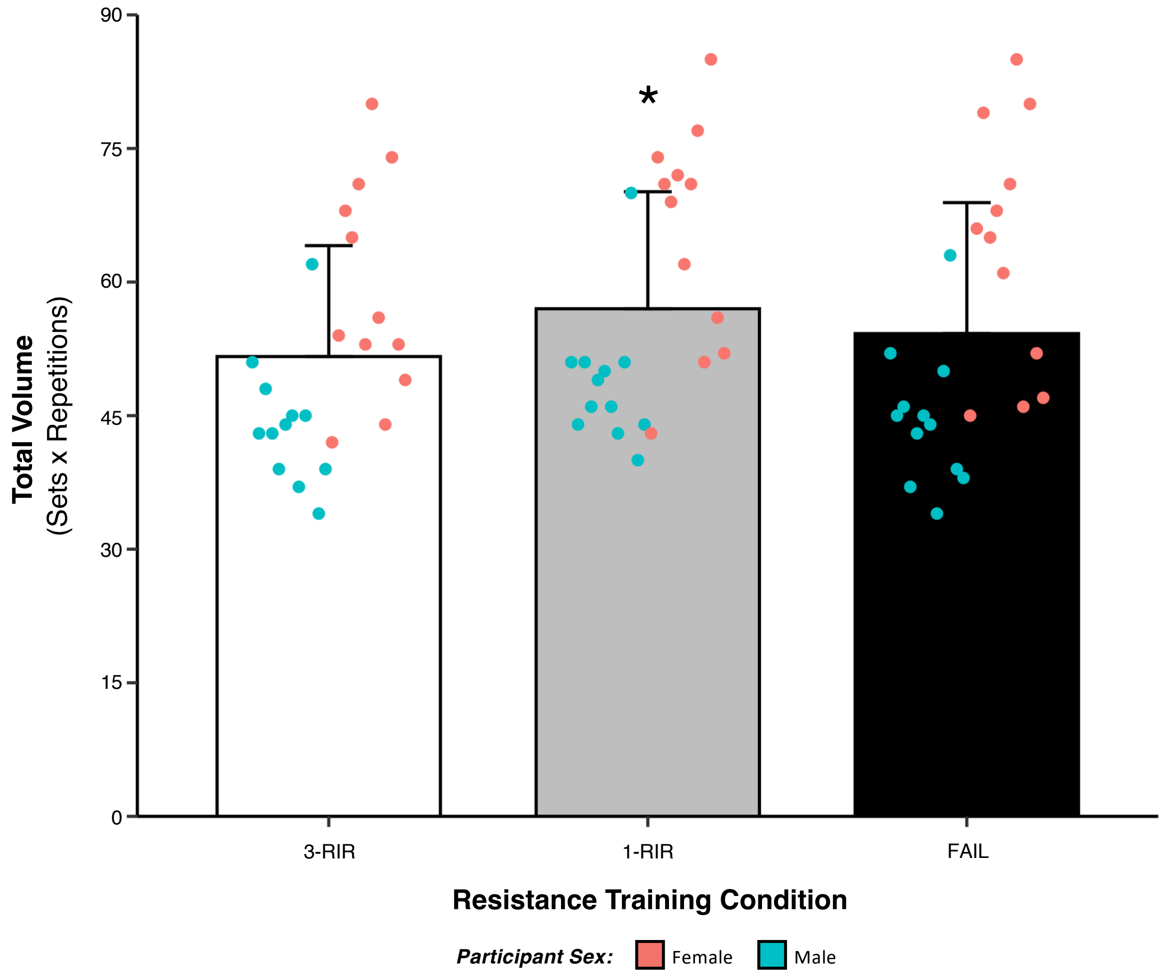

Figure 5.2. Influence of proximity-to-failure on total RT volume completed. Total volume calculated as the number of repetitions performed across six sets for each protocol (sets x repetitions). Data shown are presented as mean ± SD. **Denotes a statistically significant difference from FAIL and 3-RIR.*

Table 5.2. Descriptive characteristics for each RT protocol. Data shown are presented as mean ± SD. *Denotes a statistically significant within-protocol difference from the first set. *LV, lifting velocity; reps, repetitions.*

	Men (*n* = 12)			Females (*n* = 12)		
Variable	**3-RIR**	**1-RIR**	**FAIL**	**3-RIR**	**1-RIR**	**FAIL**
Total reps	44 ± 7	49 ± 8	45 ± 8	59 ± 12	65 ± 12	64 ± 14
Reps (first set)	9 ± 2	11 ± 2	12 ± 2	12 ± 3	14 ± 3	16 ± 3
Reps (final set)	6 ± 2*	6 ± 1*	5 ± 1*	9 ± 2*	9 ± 2*	8 ± 2*
% Decrease Reps	*29%*	*43%*	*59%*	*25%*	*37%*	*51%*
Mean LV (first set)	0.36 ± 0.05	0.33 ± 0.03	0.33 ± 0.04	0.35 ± 0.04	0.33 ± 0.04	0.32 ± 0.04
Mean LV (final set)	0.33 ± 0.05	0.30 ± 0.04*	0.23 ± 0.03*	0.34 ± 0.04	0.29 ± 0.05	0.26 ± 0.05*
% Decrease LV	*8.1%*	*11.3%*	*28.8%*	*1.1%*	*10.1%*	*19.6%*
Mean LV (last rep)	0.25 ± 0.04	0.19 ± 0.03	0.14 ± 0.03	0.23 ± 0.04	0.16 ± 0.03	0.12 ± 0.03

5.5.2 Recovery Time-Course (Changes in Lifting Velocity from Pre-Exercise to Post-Exercise)

Statistically significant main and interaction effects of protocol [F (2) = 52.81, P = < 0.001], time [F (2) = 229.58, P = < 0.001], and protocol x time [F (4) = 18.18, P = < 0.001] for the decrease in lifting velocity from pre-exercise to post-exercise were found (see Appendix B for all results). The greatest decreases in lifting velocity from pre-exercise to post-exercise were observed at the 4-min time point for FAIL versus 1-RIR [ES = 1.16 (95% CI: 0.68, 1.63), P = <0.001] and 3-RIR [ES = 1.87 (95% CI: 1.26, 2.47), P = <0.001], and for 1-RIR versus 3-RIR [ES = 1.26 (95% CI: 0.80, 1.73), P = < 0.001] (Table 5.3, Figure 5.3). Greater decreases in lifting velocity from pre-exercise to post-exercise were also identified at 24-hrs for FAIL versus 3-RIR [ES = 0.90 (95% CI: 0.47, 1.32), P = 0.001], and 1-RIR versus 3-RIR [ES = 1.02 (95% CI: 0.40, 1.64), P = 0.001], but no statistically significant differences were identified at 48-hrs (Table 5.3, Figure 5.3). To investigate sex differences at 4-min post-exercise, linear mixed modelling produced a statistically significant interaction effect of protocol x sex [F (2) = 7.14 P = 0.001], with post hoc analysis revealing a greater decrease in lifting velocity from pre-exercise to 4-min post-exercise in males versus females only when RT was performed to FAIL [ES = 0.82 (95% CI: –0.03, 1.67, P = 0.007], but no other statistically significant sex differences were found (Figure 5.4).

Table 5.3. Mean decreases in lifting velocity from pre-exercise to post-exercise. Mean change calculated as 'time point value' minus 'pre-exercise value', with positive numbers indicating increases in lifting velocity (m·s-1) from pre-exercise (and negative values indicate a decrease). Data shown are presented as mean ± SD. **Denotes a statistically significant within-protocol difference from pre-exercise to post-exercise.*

	Post-Exercise Time Point		
Protocol	**4-min**	**24-hrs**	**48-hrs**
3-RIR	–0.05 ± 0.03	0.01 ± 0.03	0.01 ± 0.02
1-RIR	–0.09 ± 0.03*	–0.02 ± 0.03	–0.01 ± 0.02
FAIL	–0.15 ± 0.06*	–0.02 ± 0.04	0.00 ± 0.04
Male Participants			
3-RIR	–0.04 ± 0.02	0.01 ± 0.02	0.01 ± 0.03
1-RIR	–0.08 ± 0.03*	–0.01 ± 0.02	–0.01 ± 0.03
FAIL	–0.17 ± 0.05*	–0.02 ± 0.03	0.00 ± 0.04
Female Participants			
3-RIR	–0.05 ± 0.03	0.01 ± 0.03	0.00 ± 0.02
1-RIR	–0.09 ± 0.03*	–0.03 ± 0.03	–0.01 ± 0.01
FAIL	–0.12 ± 0.06*	–0.02 ± 0.04	–0.01 ± 0.05

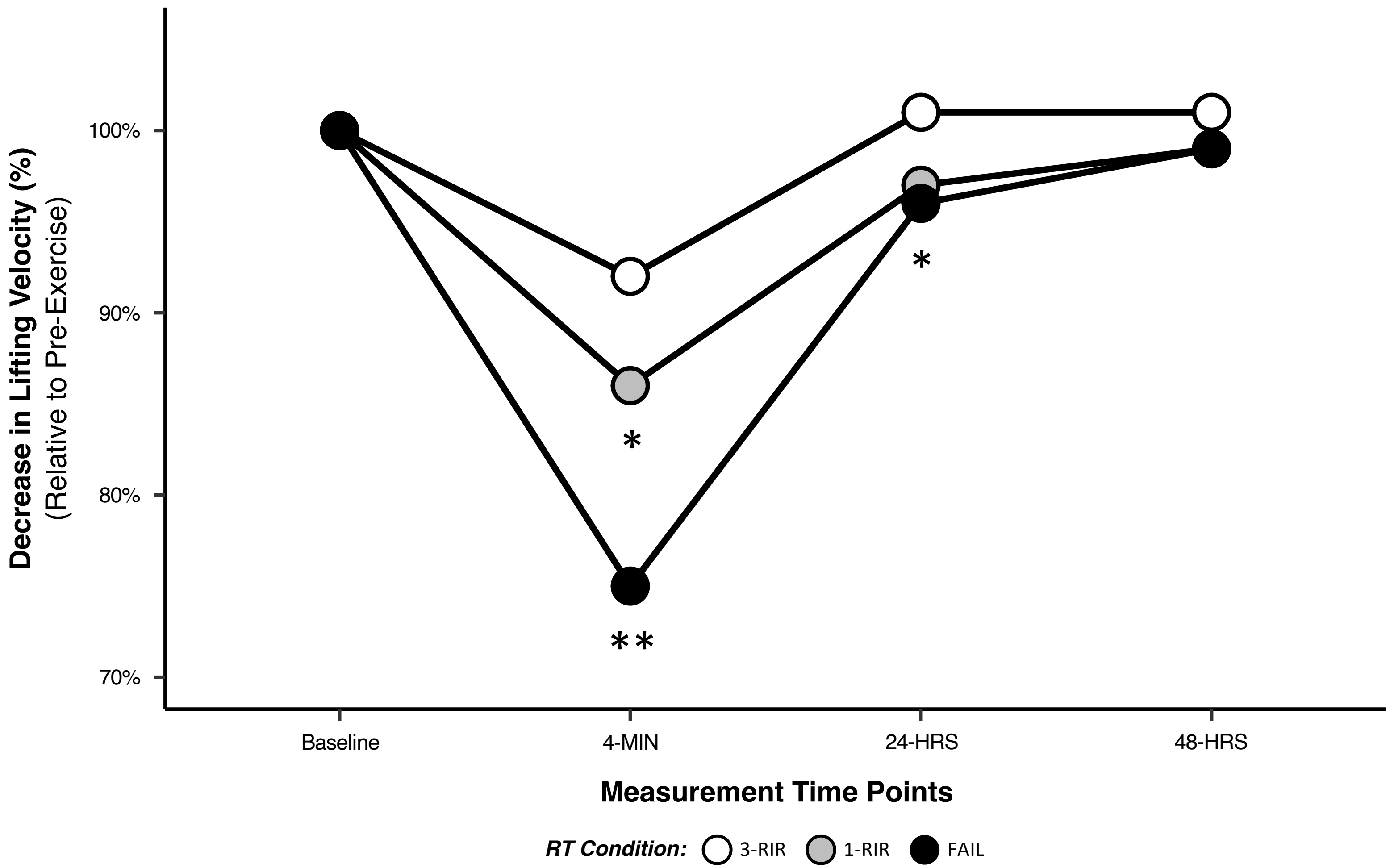

Figure 5.3. Post-exercise recovery time-course of neuromuscular fatigue for all participants (males and females combined). Changes in lifting velocity are expressed as percentage values relative to pre-exercise. Data shown are presented as mean values (accompanying SD values can be found in Table 5.3). **Denotes a statistically significant difference from 3-RIR. **Denotes a statistically significant difference from 1-RIR and 3-RIR.*

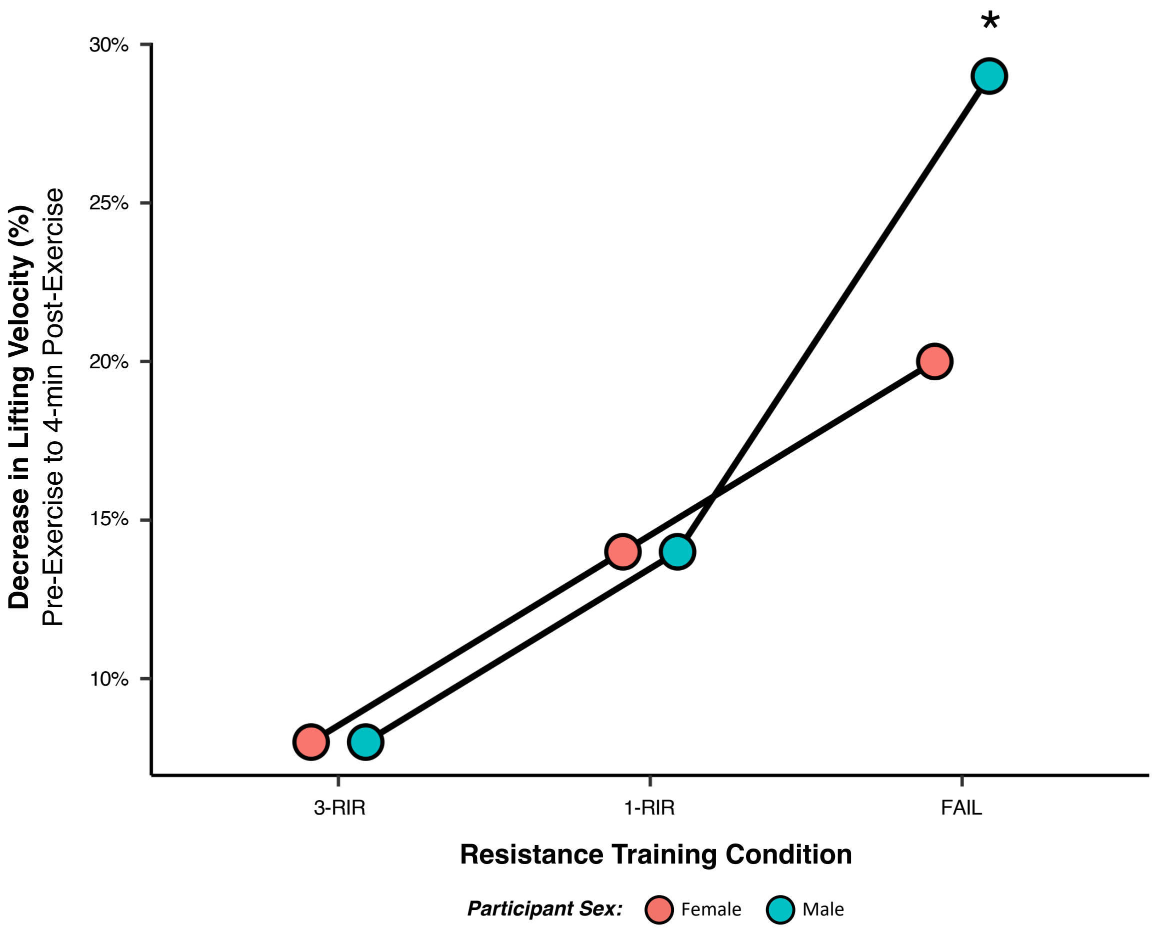

Figure 5.4. Relationship between proximity-to-failure and acute neuromuscular fatigue. Data shown are expressed as a percentage decrease in lifting velocity with a fixed load from pre-exercise to 4-min post-exercise (displayed as a positive value to indicate an increase in neuromuscular fatigue) in response to six sets performed on the barbell bench press exercise to either momentary muscular failure (FAIL), 1-RIR, or 3-RIR. Accompanying SD values can be found in Table 5.3. **Denotes a statistically significant difference from female participants.*

5.5.3 Loss of Lifting Velocity from First to Final Set

Statistically significant main effects of protocol [*F* (2) = 30.14, *P* = <0.001] and sex [*F* (1) = 6.33, *P* = 0.012] were found for the loss of lifting velocity from the first set to the final set, but there was no interaction effect of protocol x sex (see Appendix B for all results). Post hoc analysis of decreases in lifting velocity from the first set to the final set for each protocol (Mean ± *SD*: FAIL = –0.08 ± 0.03, 1-RIR = –0.03 ± 0.02, 3-RIR = –0.02 ± 0.04) revealed greater decreases for FAIL versus both 1-RIR [ES = 1.46 (95% CI: 0.63, 2.29), *P* = <0.001] and 3-RIR [ES = 1.59 (95% CI: 1.02, 2.16), *P* = <0.001] (Figure 5.5). Further post hoc analysis of sex also revealed a greater decrease in lifting velocity (mean of all protocols combined) from the first set to the final set (Mean ± *SD*: Male = –0.05 ± 0.04, Female = –0.03 ± 0.04) for male versus female participants [ES = 0.52 (95% CI: 0.06, 1.00), *P* = 0.020], with the largest effect size differences between male and female participants found for FAIL [ES = 1.09 (95% CI: 0.21, 1.96)] and 3-RIR [ES = 0.66 (95% CI: 0.18, 1.50)].

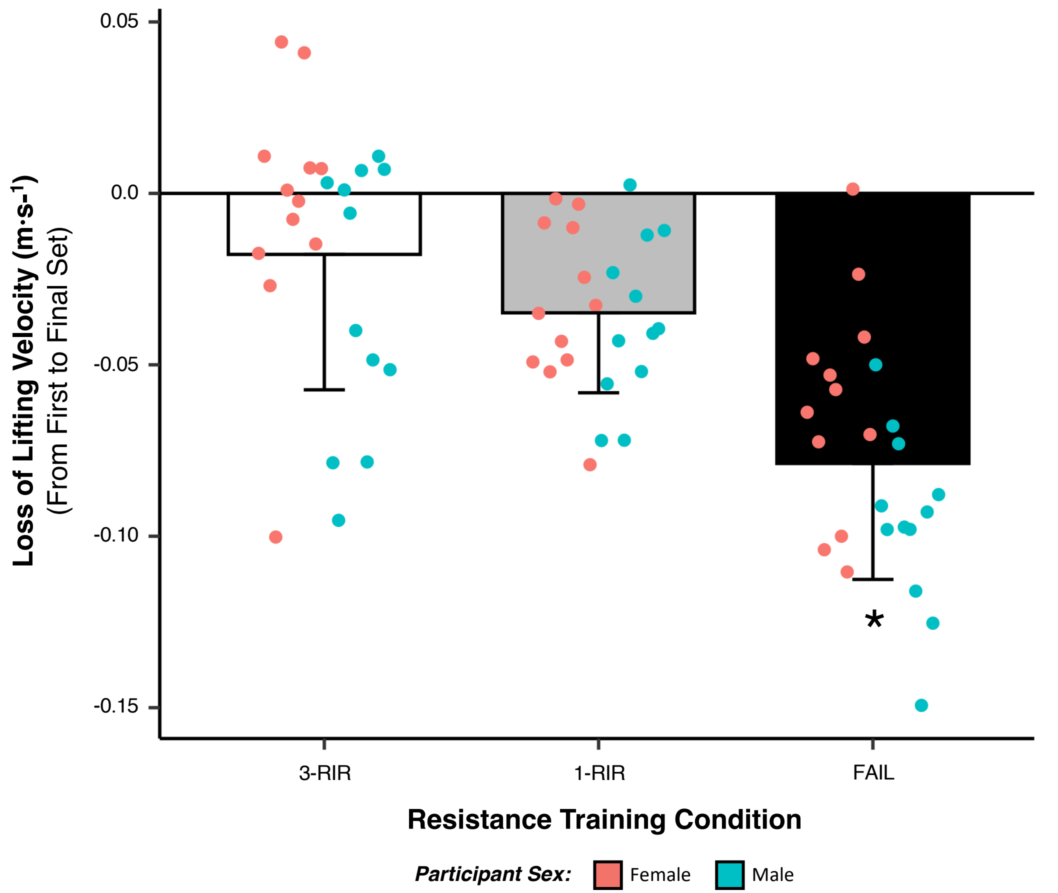

Figure 5.5. Loss of lifting velocity from first to final set. Data shown are presented as absolute values (m·s-1) and as both protocol means (± SD) and individual values. **Denotes a statistically significant difference from 1-RIR and 3-RIR.*

5.5.4 Repetition Loss from First to Final Set

A statistically significant main effect of protocol [F (2) = 64.96, P = <0.001] for repetition loss from the first set to the final set was found, but there was no main effect of sex or interaction effect of protocol x sex (see Appendix B for all results). Post hoc analysis of the decrease in repetitions performed from the first set to the final set for each protocol (Mean ± *SD*: FAIL = –7.58 ± 1.89, 1-RIR = –5.13 ± 1.73, 3-RIR = –2.79 ± 1.84) revealed greater decreases for FAIL versus both 1-RIR [ES = 1.31 (95% CI: –0.78, 1.84), P = <0.001] and 3-RIR [ES = 2.49 (95% CI: 1.67, 3.30), P = <0.001], and repetition loss was greater for 1-RIR versus 3-RIR [ES = 1.26 (95% CI: 0.56, 1.97), P = <0.001]. The decrease in repetitions from set-to-set for all protocols is shown in Figure 5.6.

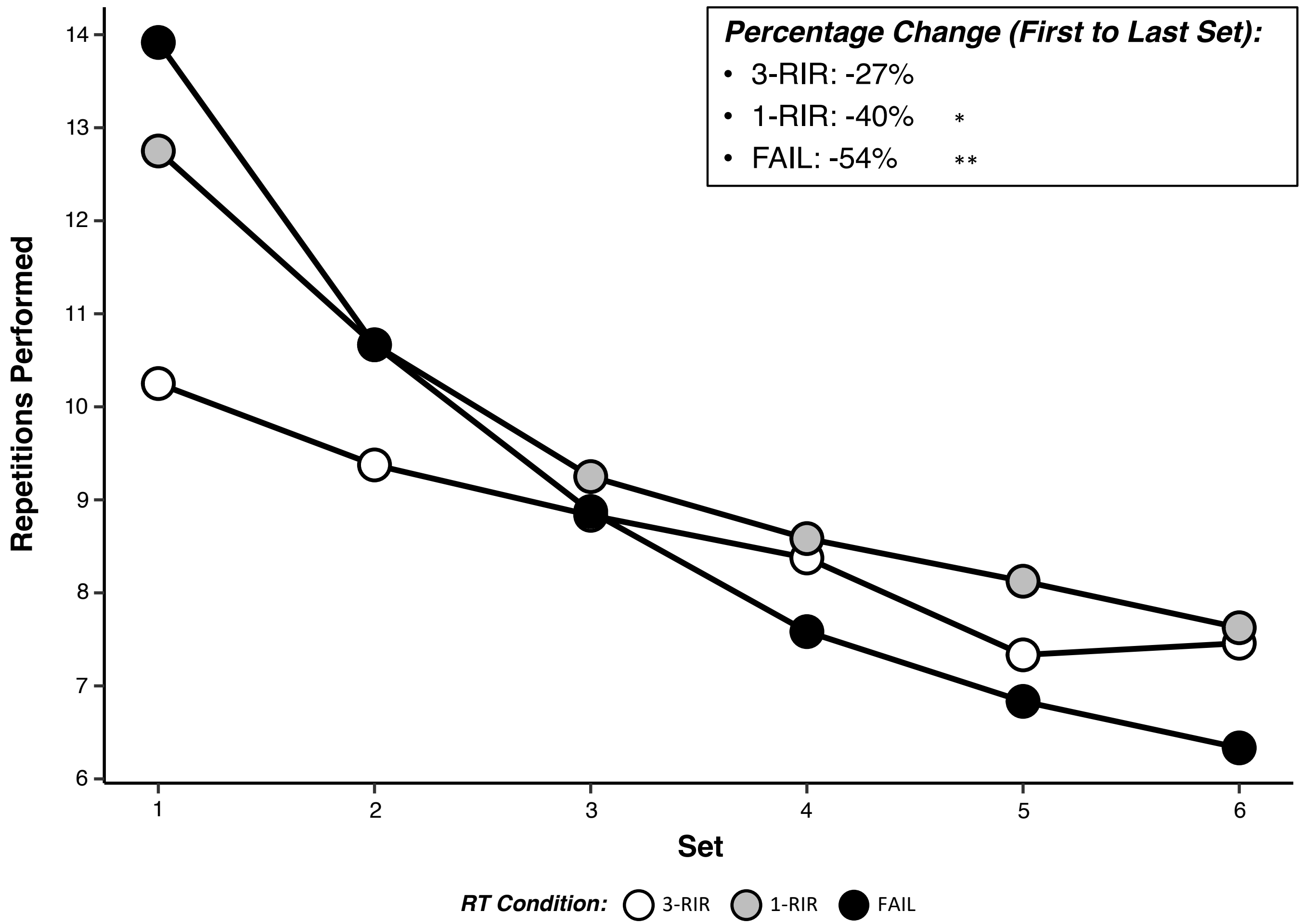

Figure 5.6. Number of repetitions performed in each set. Data shown are presented as mean (absolute) values (accompanying SD values can be found in Appendix B). *Denotes a statistically significant difference from 3-RIR. ***Denotes a statistically significant difference from 1-RIR and 3-RIR.*

5.5.5 Perceived Discomfort, Perceived Exertion, and General Feelings

A statistically significant main effect of protocol for rating of perceived discomfort [*Chi* (2) = 30.98, P = <0.001], rating of perceived exertion [*Chi* (2) = 35.89 P = <0.001], and general feelings using the feeling scale was found [*Chi* (2) = 17.13, P = <0.001]. Post hoc analysis revealed that ratings of perceived discomfort were greater for FAIL versus both 1-RIR [ES = 0.65 (95% CI: 0.36, 0.94), P = 0.001] and 3-RIR [ES = 1.50 (95% CI: 1.06, 1.93), P = <0.001], and greater for 1-RIR versus 3-RIR [ES = 0.62 (95% CI: 0.26, 0.99), P = 0.005]. Further, ratings of perceived exertion were greater for FAIL versus both 1-RIR [ES = 0.95 (95% CI: 0.37, 1.53), P = 0.003] and 3-RIR [ES = 1.85 (95% CI: 1.12, 2.57), P = <0.001], and greater for 1-RIR versus 3-RIR [ES = 1.14 (95% CI: 0.66, 1.63), P = <0.001]. Lastly, lower feeling scale ratings were observed for FAIL versus 3-RIR [ES = –1.19 (95% CI: –1.81, –0.58), P = 0.001], and for 1-RIR versus 3-RIR [ES = –0.56 (95% CI: –1.00, –0.12), P = 0.025]. Figure 5.7 displays mean, standard deviation, and individual values for perceived discomfort, perceived exertion, and feeling scale ratings (see Appendix B for all results).

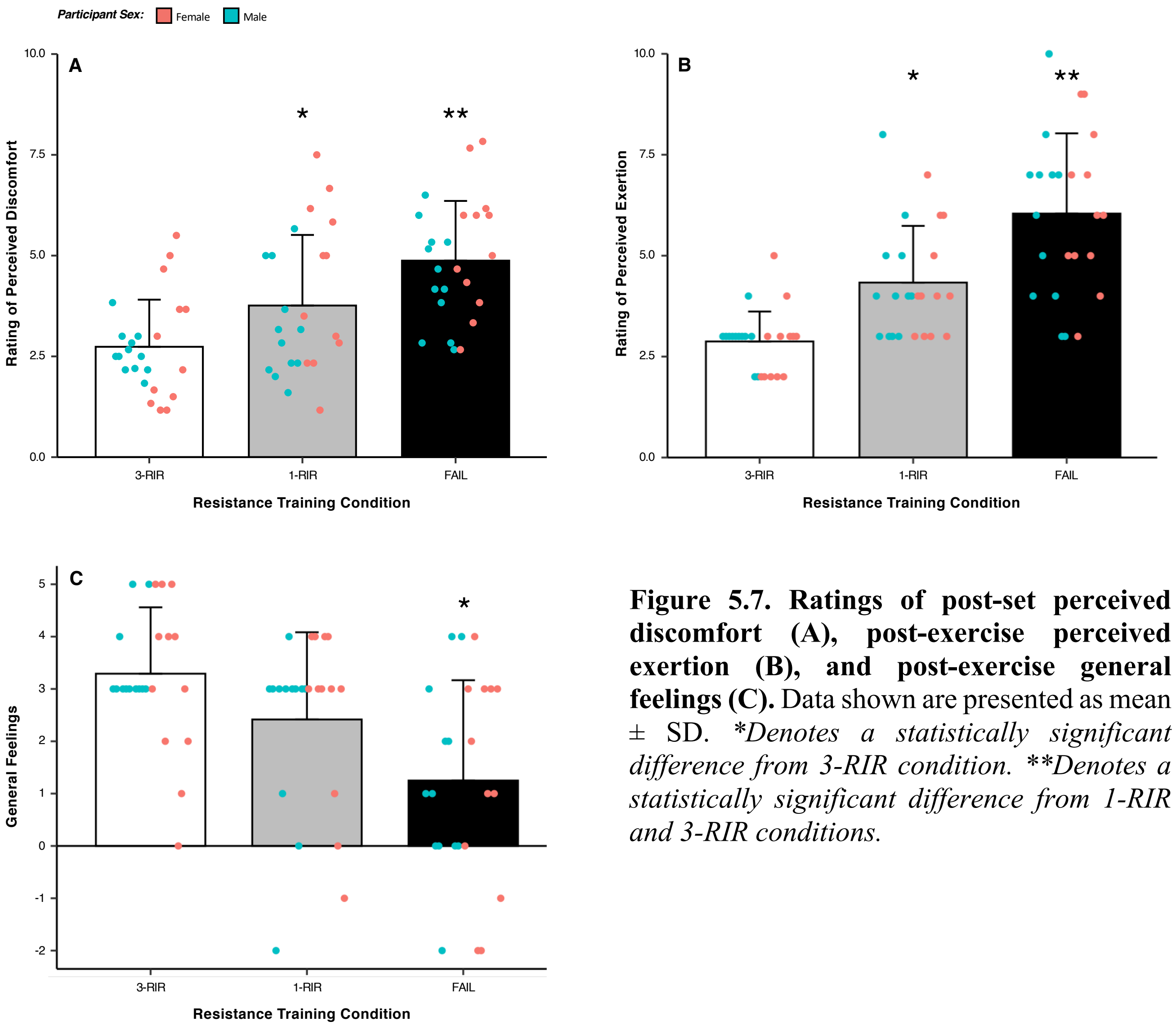

Figure 5.7. Ratings of post-set perceived discomfort (A), post-exercise perceived exertion (B), and post-exercise general feelings (C). Data shown are presented as mean ± SD. **Denotes a statistically significant difference from 3-RIR condition. **Denotes a statistically significant difference from 1-RIR and 3-RIR conditions.*

5.5.6 Perceived Recovery and Muscle Soreness

A statistically significant main effect of protocol for ratings of muscle soreness at 24- [*Chi* (2) = 18.40, *P* = <0.001] and 48-hrs [*Chi* (2) = 14.08, *P* = <0.001] and perceived recovery status at 24- [*Chi* (2) = 21.30, *P* = <0.001] and 48-hrs was found [*Chi* (2) = 12.83, *P* = 0.002]. Post hoc analysis revealed greater muscle soreness ratings at 24-hrs post-exercise for FAIL versus both 1-RIR [ES = 0.79 (95% CI: 0.19, 1.39), *P* = 0.023] and 3-RIR [ES = 1.16 (95% CI: 0.64, 1.68), *P* = < 0.001], and greater perceived recovery ratings at 24-hrs post-exercise for 3-RIR versus FAIL [ES = 1.55 (95% CI: 0.83, 2.27), *P* = <0.001], and for 3-RIR versus 1-RIR [ES = 0.75 (95% CI: 0.21, 1.29), *P* = 0.014]. Further post hoc analysis revealed greater muscle soreness ratings at 48-hrs post-exercise for FAIL versus 3-RIR [ES = 0.90 (95% CI: 0.31, 1.50), *P* = 0.004], and greater perceived recovery ratings at 48-hrs post-exercise for 3-RIR versus FAIL [ES = 1.02 (95% CI: 0.45, 1.58), *P* = 0.003] and for 3-RIR versus 1-RIR [ES = 0.66 (95% CI: 0.25, 1.06), *P* = 0.008]. Figure 5.8 displays mean and standard deviation values for muscle soreness and perceived recovery ratings at 24- and 48-hrs (see Appendix B for all results).

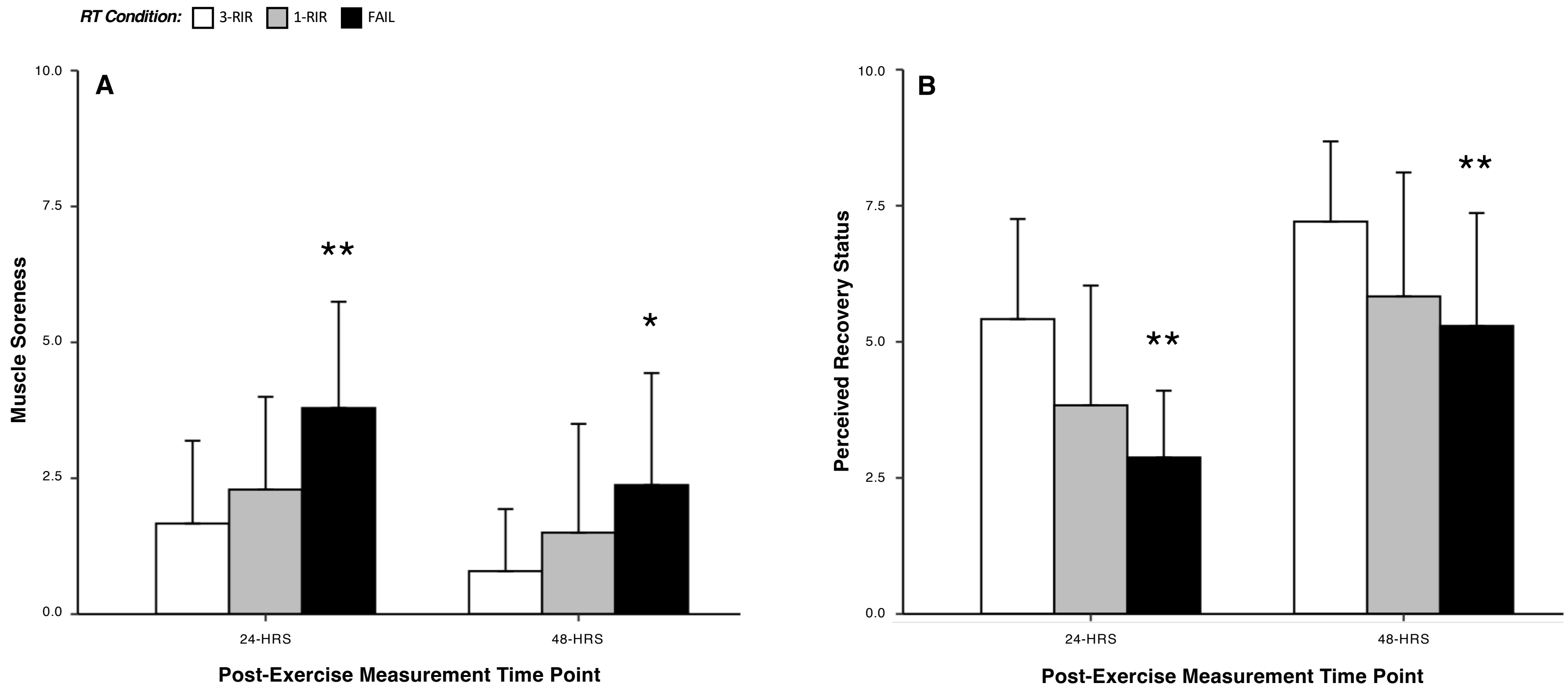

Figure 5.8. Ratings of muscle soreness (A) and perceived recovery status (B) at 24- and 48-hrs post-exercise. Data shown are presented as mean ± SD. *Denotes a statistically significant difference from 3-RIR. ***Denotes a statistically significant difference from 1-RIR and 3-RIR.*

5.6 Discussion

5.6.1 Influence of Proximity-to-Failure on Neuromuscular Fatigue

Our primary findings suggest that i) *acute* neuromuscular fatigue (i.e., decreases in lifting velocity from pre-exercise to 4-min post-exercise, and from the first to the final set) increases in resistance-trained males and females as proximity-to-failure nears and is greatest when momentary muscular failure is reached, providing evidence for a *linear* relationship between proximity-to-failure and acute neuromuscular fatigue, ii) 48-hrs is likely sufficient for complete recovery of neuromuscular function when RT is performed for six sets on the barbell bench press, independent of the proximity-to-failure reached, iii) performing RT to 3-RIR may be a viable strategy to minimise the neuromuscular fatigue incurred from RT and potentially improve RT performance at 24- and 48-hrs post-exercise, and iv) males experience greater acute neuromuscular fatigue than females when RT is performed to momentary muscular failure.

Although previous research suggests that neuromuscular fatigue is greater following RT performed to momentary muscular failure versus non-failure [14, 48-52], considering the ambiguity and variability in the proximity-to-failure achieved during non-failure RT protocols, these data are unable to inform the specific effect of different proximities-to-failure on neuromuscular fatigue. To address this research limitation, we employed subjective RIR prediction to control the proximity-to-failure reached by participants in our 1-RIR and 3-RIR protocols that were compared with RT performed to momentary muscular failure (FAIL). As proximity-to-failure neared, we observed a graded increase in acute neuromuscular fatigue at 4-min post-exercise (Figure 5.3) and from the first to the final set (Figure 5.5), with the highest levels of neuromuscular fatigue found when participants performed RT to FAIL versus 1-RIR and 3-RIR (FAIL > 1-RIR > 3-RIR). These results corroborate previous findings that showed greater decreases in lifting velocity immediately post-exercise as sets were terminated with higher magnitudes of velocity loss (and therefore as proximity-to-failure neared) [70]; however, the magnitude of velocity loss used to control set termination can't be accurately translated to RIR [97]. As such, our data provide novel insights into the specific effect of reaching different proximities-to-failure during RT, quantified via RIR, on neuromuscular fatigue. Of interest are the *central* (i.e., suppression of skeletal muscle excitation by the central nervous system) and *peripheral* (i.e., energy depletion and intramuscular perturbations in metabolite concentration and calcium (Ca^{+2}) kinetics that impair cross-bridge formation) mechanisms underpinning the neuromuscular fatigue observed [33, 34], which may supress i) force production by type II muscle fibres and their exposure to mechanical tension during RT (potentially explaining the non-linear relationship between proximity-to-failure and muscle hypertrophy [115]), and ii) the absolute load lifted on a given exercise, ultimately hampering muscle hypertrophy or maximal strength development, respectively. Our results also demonstrate that contrary to our hypothesis, the majority of participants experienced complete recovery of neuromuscular function at 24-hrs post-exercise, independent of the RT protocol completed (Table 5.3); however, it is possible that increasing the number of sets performed for a given exercise or muscle group may elongate the recovery time-course of neuromuscular function. Although not statistically significant ($P = >0.05$), we observed a slight increase in lifting velocity, and thus improvement in neuromuscular function, at 24-hrs post-exercise for 3-RIR (Figure 5.3), which was not evident for FAIL and 1-RIR. Overall, these data provide evidence for a linear relationship between proximity-to-failure and acute neuromuscular fatigue and suggest that performing RT to 3-RIR incurs low levels of neuromuscular fatigue that has minimal negative effects on force production 24- and 48-hrs post-exercise, while inducing a possible 'supercompensation' (or potential priming) effect.

To provide further insights into the neuromuscular fatigue incurred from each RT protocol, we also assessed the number of repetitions performed in each of the six sets completed and the total volume (sets x reps) achieved. Similar to previous research comparing RT performed to momentary muscular failure versus 20% velocity loss [14], we also found that FAIL resulted in the highest number of repetitions performed in the first set (14 ± 3) compared to 1-RIR (13 ± 3) and 3-RIR (10 ± 3), but fewer repetitions were performed in the final set (FAIL = 6 ± 2, 1-RIR = 8 ± 2, 3-RIR = 7 ± 2), leading to a percentage loss in repetitions from the first to the final set of 54% for FAIL versus 40% and 27% for 1-RIR and 3-RIR, respectively (Figure 5.6). While FAIL resulted in the most repetitions in the first set, decreases in repetitions performed with a given load likely reflect a supressed force production and overall decrease in the exposure of active muscle fibres to mechanical tension across the multiple subsequent sets, highlighting the possibility of a similar hypertrophic stimulus achieved between our RT protocols with differing levels of neuromuscular fatigue. Indeed, differences in repetitions performed per set across our RT protocols resulted in a similar total volume achieved for FAIL (54 ± 15) and 3-RIR (52 ± 12), with the greatest total volume observed for 1-RIR (57 ± 13), suggesting that RT volume may be maximised in multiple-set protocols when terminating sets close to (i.e., ~1-RIR), but prior to, momentary muscular failure (Figure 5.2). These data, in corroboration with similar results reported elsewhere (for example: Mangine et al. [52] showed no statistically significant difference in total volume achieved over five sets between RT performed to momentary muscular failure and '0-3-RIR'), suggest that the proximity-to-failure reached across multiple sets has a major influence on the total volume accumulated during RT, potentially influencing subsequent physiological adaptations that may be associated with the total RT volume achieved.

5.6.2 Role of Biological Sex in the Influence of Proximity-to-Failure on Neuromuscular Fatigue

To elucidate potential differences in neuromuscular fatigue between biological sexes, both male and female participants with a similar level of RT experience (Table 5.1) were recruited for this study. Our analysis of sex differences revealed that FAIL induced greater *acute* neuromuscular fatigue at 4-min post-exercise in males compared to females (Figure 5.4); however, no sex differences in neuromuscular fatigue were found for 1-RIR and 3-RIR. When analysing the mean of all RT protocols combined, we also found males experienced greater loss of lifting velocity from the first to the final set compared to females [with the greatest effect sizes observed for FAIL (ES = 1.09) and 3-RIR (ES = 0.66)], providing further evidence for the influence of biological sex on acute neuromuscular fatiguability during RT (Figure 5.5). Explaining these potential sex differences in neuromuscular fatiguability may be the greater absolute load lifted by males compared to females in our study [129], however, it is also possible that the degree of arterial occlusion experienced during RT contributed to sex differences in neuromuscular fatigability, with males possessing larger muscle mass than females and likely experiencing more arterial occlusion [130-132] throughout a RT set performed to momentary muscular failure. Further, females may have experienced more recovery in-between sets than males due to having a greater proportion of type I skeletal muscle fibres [133-135] comprising of a high capillary density and allowing for greater vasodilation and muscle perfusion [130-132]. Any of these factors, alone or in combination, could have ultimately resulted in the male participants experiencing greater acute neuromuscular fatigue over multiple sets when momentary muscular failure was reached and the inter-set recovery period was confined to 4-min. Similar to our results, recent research [136] found greater acute neuromuscular fatigue in males compared to females when RT was performed to a 40% versus 20% velocity loss threshold, although this sex difference was absent following completion of an 8-week RT intervention. In contrast, another study [51] found greater neuromuscular fatigue up to 72-hrs post-exercise in males compared to females when RT was performed for five repetitions with 80% 1-RM, but no sex differences were found when RT was performed to momentary muscular failure; however, considering inconsistencies in lifting velocity data, it is possible that participants in this study were not well-familiarised to performing RT with maximal intended lifting velocity, a necessary requirement to obtain reliable and valid measures of lifting velocity. Nonetheless, considering the set termination methods applied in these studies [51, 136] are unable to inform RIR values, the present findings provide unique insights into the potential interaction of proximity-to-failure with biological sex, revealing possible sex differences in neuromuscular fatigue.

5.6.3 Perceptual Measures of Neuromuscular Fatigue

To evaluate differences in perceptual responses between RT protocols, we assessed ratings of perceived discomfort immediately after each set performed, session ratings of perceived exertion, and general feelings within 30 minutes of exercise cessation, and ratings of perceived muscle soreness and recovery 24- and 48-hrs post-exercise. We found that i) perceived discomfort and exertion increased gradually as proximity-to-failure neared, ii) general feelings following RT were similar for FAIL and 1-RIR, but worse for FAIL and 1-RIR compared to 3-RIR, iii) perceived muscle soreness was greater for FAIL versus 3-RIR at both 24- and 48-hrs post-exercise, but was only greater for FAIL versus 1-RIR at 24-hrs post-exercise, and iv) perceived recovery was lower for FAIL versus both 1-RIR and 3-RIR at both 24- and 48-hrs post-exercise.

Perceptual responses are important considerations when prescribing RT as they may influence the affective response to RT and subsequent exercise adherence, and ultimately, physiological adaptations to RT. In support of previous research [14, 137], we found that perceived discomfort and exertion increased gradually as proximity-to-failure neared (Figure 5.7A and 5.7B), with the greatest ratings observed for FAIL (FAIL > 1-RIR > 3-RIR). Although ratings of perceived discomfort and exertion were 5 ± 1 and 6 ± 2 for FAIL, respectively, these results should be interpreted within the context of a RT session involving numerous exercises, whereby ratings of perceived discomfort and exertion may be even higher. It is also possible that perceived discomfort would be greater if the relative load lifted was lower (and thus the repetitions per set higher) [113] or the exercise performed involved a larger amount of active musculature (e.g., leg press versus bench press). Additionally, although general feelings following RT were similar for FAIL and 1-RIR, the ratings were lower compared to 3-RIR (Figure 5.7C), providing further support for the idea that exercise difficulty may be a primary influencer of the affective response to an exercise bout [18, 138], which may be linked to long-term exercise adherence [17]. There is, however, large intra-individual variability in feelings toward a given RT protocol; for example, feeling scale ratings ranged from -3 ('fairly bad') to +3 ('good') following RT to FAIL. As such, these results suggest that an individual's affective valence, along with their perceptions of discomfort and exertion, should be considered when prescribing proximity-to-failure during RT.

In combination with our objective measures of lifting velocity to assess neuromuscular fatigue, we also assessed perceptual measures of recovery 24- and 48-hrs post-exercise. Contrasting previous research [67] that found no significant difference in perceived muscle soreness between RT performed to set failure (definition other than momentary muscular failure) versus non-failure, we found perceived muscle soreness was greater for FAIL versus 3-RIR at both 24- and 48-hrs post-exercise, but was only greater for FAIL versus 1-RIR at 24-hrs post-exercise (Figure 5.8A). Although perceived muscle soreness was still present 48-hrs post-exercise for all RT protocols, this did not seem to negatively influence the recovery of neuromuscular function (assessed via changes in lifting velocity) at 48-hrs post-exercise (Figure 5.3). Similar results were also found for perceived recovery status, with lower ratings for FAIL versus both 1-RIR and 3-RIR at both 24- and 48-hrs post-exercise (Figure 5.8B); however, the level of perceived recovery did not always reflect lifting velocity outcomes. For example, five participants expected 'declined performance' 24-hrs following RT to 1-RIR, but instead experienced complete recovery of lifting velocity. Although our findings suggest perceptions of muscle soreness and recovery may not always reflect objective changes in lifting velocity in a research setting, in practice (when individuals may not be prompted to perform RT maximally by qualified supervisors), these perceptions may influence performance and should be considered during RT prescription. Given our previous scoping review [97] found only two studies [14, 67] investigating the influence of proximity-to-failure on perceptual responses to RT, the present findings provide unique insights into the influence of proximity-to-failure on these measures and may have important implications for enjoyment with, and potentially long-term adherence to, RT.

5.6.4 Limitations of Current Research

The present study assessed neuromuscular fatigue with the barbell bench press exercise, but whether our results can be generalised to other exercises and/or muscle groups is unclear. Considering our RT protocols involved subjective RIR prediction, whether participants terminated their sets accurately, as per the RIR target, is unknown. However, we employed an extended familiarisation that required participants to perform RT to momentary muscular failure and subjectively predict a 1- and 3-RIR on two separate occasions, to theoretically increase the accuracy of their RIR predictions. Previous research has also shown that the accuracy of RIR predictions increases with RT experience [81, 88], and a recent meta-analysis

[89] found individuals typically underpredict RIR by approximately one repetition, independent of RT experience. Finally, our analysis of neuromuscular fatigue is also limited to the outcome measure tested (e.g., changes in lifting velocity), and as such, future research should combine measures of lifting velocity with other objective measures of neuromuscular fatigue such as maximum voluntary isometric contraction and twitch interpolation to provide insight into both central and peripheral mechanisms of neuromuscular fatigue.

5.7 Conclusion

In resistance-trained males and females, we observed greater decreases in lifting velocity on the barbell bench press exercise from pre-exercise to 4-min post-exercise and from the first to the final set performed as proximity-to-failure neared (FAIL > 1-RIR > 3-RIR), providing evidence for a *linear relationship* between proximity-to-failure and *acute* neuromuscular fatigue. Further, when momentary muscular failure was reached (FAIL), males also experienced greater acute neuromuscular fatigue than females. A slight decrement in neuromuscular function when RT was performed to momentary muscular failure and 1-RIR was sustained at 24-hrs post-exercise versus 3-RIR, with 48-hrs of recovery post-exercise likely sufficient for complete recovery of neuromuscular function when RT is performed for six sets on the barbell bench press exercise, independent of the proximity-to-failure reached. Our assessments of the perceptual response to RT also showed that as proximity-to-failure neared, ratings of perceived discomfort, exertion, and muscle soreness increased, general feelings worsened, and perceived recovery decreased. Overall, proximity-to-failure not only influences the neuromuscular fatigue incurred from RT, but is also a key determinant of the perceptual responses to RT.

Chapter Six – Accuracy of Intra-Set Repetitions-in-Reserve Predictions During the Bench Press Exercise in Resistance Trained Males and Females

Please note, the following text in Chapter Six has been adapted from a peer-reviewed and published manuscript (DOI: 10.1519/JSC.0000000000004653).

6.1 Preface

Our previous works [115, 139] indicate that RIR may influence muscle hypertrophy and short-term responses to RT, and although RIR prescription seems a viable strategy to determine set termination, its effectiveness is contingent on the accuracy of individual RIR predictions. Given that true RIR accuracy can only be known if momentary muscular failure is reached following an intra-set RIR prediction, deriving RIR accuracy from non-failure RT interventions is challenging. As such, prior to conducting Study Two, each participant performed 'repetitions-to-failure' assessments to provide a baseline measure of RIR accuracy. The participants were all resistance-trained, with 96% reporting previous experience predicting RIR. To assess RIR accuracy comprehensively, we analysed the difference between predicted and actual RIR (i.e., 'absolute' accuracy) and the directionality of the error (i.e., did participants overpredict or underpredict), while accounting for potential moderating factors like the number of repetitions performed in the statistical analysis. Performing RIR accuracy assessments prior to RT interventions employing intra-set RIR predictions not only establishes the validity of such predictions, but also informs readers about the RIR accuracy of the sample. Further, these data provide valuable insights regarding the absolute RIR accuracy of resistance-trained individuals and the potential for inter-individual variability, informing both practical applications and future research.

6.2 Introduction

Proximity-to-failure during resistance training (RT) can be quantified as the number of 'repetitions-in-reserve' (RIR) before reaching momentary muscular failure (i.e., when completion of the concentric portion of a repetition is not possible with a full range-of-motion without deviation from the prescribed exercise form) [25, 26]. For example, a proximity-to-failure of 1-RIR indicates a single additional repetition could be completed, while 0-RIR indicates the next attempted repetition would result in momentary muscular failure. Importantly, the proximity-to-failure in which an RT set is terminated may influence long-term RT outcomes such as strength development [10] and muscle hypertrophy [115] along with the neuromuscular fatigue incurred from RT [13, 139].

Despite the importance of terminating RT sets at a given RIR to promote the desired physiological adaptations, common methods of RT prescription lead to uncertainties in the RIR achieved upon set termination [97]. For example, some studies have employed a predetermined repetition prescription with a given relative load [e.g., 3 sets of 5 repetitions with 75% of 1-repetition maximum (1-RM)], but considering the within- and between-individual variability in the maximum number of repetitions possible with the same relative load [76, 77], some individuals may reach momentary muscular failure, while others may have many RIR. Other studies [69, 71, 74] have also attempted to control set termination during RT by having an individual terminate a given set once a specific percentage of 'velocity loss' from the first (or fastest) repetition has been reached. However, velocity loss is not inherently individualised, is both exercise- and load-specific, and the velocity loss that corresponds to a given RIR varies from set-to-set [140]. Additionally, despite the objectivity of this velocity-based method of set termination, recent data [141] have found that percentage of velocity loss does not accurately predict repetitions performed in a set; thus, it cannot accurately quantify RIR.

To rectify the limitations of set prescriptions based on repetition maximum loads and percentage of velocity loss, an individual may control the proximity-to-failure reached by performing repetitions with a given load until they perceive a given RIR target has been reached, known as self-reported prediction of RIR. However, the utility of RIR-based set prescription (e.g., 3 sets of 10-15 repetitions with 2-RIR) is contingent upon the accuracy of the individual's RIR prediction. A recent meta-regression found that individuals under-predict RIR, on average, by ~1 repetition [89], and other research has found that RIR predictions may improve when RT sets are performed closer to momentary muscular failure [81, 87, 142], with higher relative loads and a greater number of successive sets performed [26, 82, 143], and in resistance trained versus untrained individuals [81, 88]. However, considerable heterogeneity exists between studies assessing the accuracy of RIR predictions. Specifically, studies may employ various definitions of 'set failure' (i.e., the set termination criteria for the definition of 'failure' used in a given study) when instructing individuals to predict RIR, which may render the true accuracy of the RIR prediction unclear [97]. In other words, if an individual gives an RIR prediction on a set that is terminated at volitional failure (i.e., when an individual perceives they have reached the prescribed set termination criteria), it cannot be known what the true RIR would be if the individual was told to terminate the set at momentary muscular failure. It is also possible that some individuals confuse proximity-to-failure with perceptions of discomfort, leading to an underestimation of RIR [87].

6.2.1 Objectives

Therefore, the purpose of this study was to assess the accuracy of intra-set RIR predictions (1- and 3-RIR) on the barbell bench press exercise (75% of 1-RM load) over two sessions in resistance-trained males and females who terminated each set at momentary muscular failure and were familiarised with the difference between perceived discomfort and proximity-to-failure. We also explored the relationship between RIR accuracy and i) years of RT experience, ii) biological sex, and iii) relative bench press strength. We hypothesised that RIR accuracy would be greater when participants were required to predict a 1-RIR versus a 3-RIR and we expected RIR accuracy to be greater in the second experimental session versus the first.

6.3 Methods

6.3.1 Experimental Approach to the Problem

This was a randomised cross-over trial whereby participants attended two experimental sessions at a local gymnasium (at JPS Health & Fitness, Melbourne) approximately 48 h apart. In the first experimental session, the 1-RM load was determined for the flat barbell bench press and used to calculate the 75% of 1-RM load for each participant. A repetitions-to-failure assessment was conducted for the bench press in both experimental sessions, involving two sets performed to momentary muscular failure. Participants were required to verbally indicate when they believed they had reached a 1- or 3-RIR (in a randomised order) during the set, and the difference between the predicted RIR and the actual RIR (i.e., number of repetitions performed after the prediction was given until momentary muscular failure was reached) was recorded to assess RIR accuracy.

6.3.2 Subjects

A total of 12 males and 12 females were recruited (Table 6.1). All participants: i) were between 18-40 years old, ii) reported no existing musculoskeletal injuries or neuromuscular disorders, iii) confirmed they had not used anabolic steroids, or any illegal agents known to increase muscle size for the previous year, and iv) had ≥3 yrs of RT experience with a minimum of ≥3 weekly RT sessions. The mean 1-RM for the bench press exercise was also greater than 120% and 80% of bodyweight for males and females, respectively, indicating an advanced RT status as specified by Santos Junior et al. [117]. All participants reported experience working with a private fitness coach in a face-to-face setting, 12 participants (50%) declared they had previously competed in strength or physique sports (e.g., powerlifting or bodybuilding), and 23 participants (96%) reported experience with intra-set RIR prediction. The study procedures were approved by the Deakin University Human Research Ethics Committee (reference number: 2021-407). Prior to the commencement of data collection, all participants were informed of the benefits and risks of the investigation (via plain language statement) prior to signing an institutionally approved informed consent from.

Table 6.1. Baseline participant characteristics. An overview of the relevant characteristics for each participant. Data shown are mean ± SD. Relative strength calculated as: barbell bench press 1-RM (kg) divided by bodyweight (kg). *1-RM, one repetition maximum; BP, bench press; kg, kilograms; p/w, per week; RT, resistance training; y, years.*

	Males (*n* = 12)		**Females (*n* = 12)**	
Variable	**Mean ± SD**	**Range**	**Mean ± SD**	**Range**
Age (y)	28.5 ± 5.3	19 - 39	31.6 ± 5.7	23 - 40
Bodyweight (kg)	85.1 ± 8.3	74 - 99	62.3 ± 11.0	52 - 90
RT experience (y)	8.3 ± 3.7	3 - 15	7.2 ± 2.3	4 - 13
RT frequency (p/w)	4.4 ± 0.7	3 - 5	4.4 ± 0.7	4 - 6

1-RM BP (kg)	116.0 ± 20.8	92.5 - 157.5	54.9 ± 13.0	35 - 77.5
Relative 1-RM BP strength (kg/kg bodyweight)	1.37 ± 0.26	1.14 - 1.93	0.88 ± 0.17	0.56- 1.08

6.3.3 Sample Size Justification

This study was based on a secondary analysis of another main study [139]. The target sample size of the main study (24 participants) was based on outcome measures other than RIR accuracy (e.g., neuromuscular fatigue) and the following pragmatic considerations: i) recruiting more than 24 participants was not feasible given resource constraints including the time and costs associated with data collection and subsequent analyses, and ii) the chosen sample size is greater than most published studies investigating the influence of RT proximity-to-failure on neuromuscular fatigue using similar research designs [32, 58, 61, 63, 69]. As α-priori sample size calculation was not performed, we conducted a sensitivity power analysis using G*Power software (Version 3.1.9.7) and calculated the minimum (critical) effect size (Cohen's d = 0.27) that could be statistically rejected based on a pre-specified sample size (n = 24) and both type I (0.05) and type II (0.20) error rates.

6.3.4 Procedures

The following protocols were part of the 'pre-testing' phase for an original research study designed to assess the influence of proximity-to-failure on neuromuscular fatigue and are extensively described elsewhere [139].

6.3.4.1 Pre-Study Familiarisation

Approximately one month before the commencement of the study period, participants underwent a pre-study familiarisation to establish appropriate exercise technique. Participants performed two sets of five repetitions with the minimum load on the BP exercise to ensure appropriate technique as follows: the advanced participants employed and replicated their own lifting grip based on their previous experience with the BP exercise (at minimum, the barbell had to be grasped slightly outside shoulder width) and lowered the barbell until it contacted their chest (below the nipple line) and then lifted it back to the starting position without excessive bouncing off the chest, or raising of the shoulders, trunk, or glutes off the bench. Participants were then familiarised with performing the concentric (lifting) phase of each repetition with maximal intended lifting velocity (i.e., as fast as possible), followed by a controlled eccentric (lowering) phase (~2 seconds). Once participants were familiarised with this lifting strategy, they were told to incorporate the BP into their own RT regimen and continue practicing with maximal intended lifting velocity until the commencement of the study.

6.3.4.2 One-Repetition Maximum Load Assessment

Upon commencement of the study, and after re-familiarisation with correct exercise technique, participants completed a 1-RM assessment for the BP. First, a warm-up consisting of one set of five repetitions was performed with the minimum possible load (20 kg). The load was then progressively increased (15-20 kg increments for males and 5-10 kg for females) until the lifting velocity was lower than 0.5 $m \cdot s^{-1}$. Thereafter, the load was increased in smaller increments (2.5-10 kg for men, and 1.25-5 kg for females) until the 1-RM was determined, defined as the heaviest load with which a single repetition was possible with a full range-of-motion. For the lighter loads (> 1 $m \cdot s^{-1}$), three repetitions were performed at each load, two repetitions were performed for the moderate loads, and a single repetition for the heavier loads (< 0.5 $m \cdot s^{-1}$).

6.3.4.3 Experimental Conditions and Repetitions-to-Failure Assessments

Participants completed two experimental sessions (48 h apart) involving a repetitions-to-failure assessment. A standardised warm-up was first completed, starting with 20kg, then 50%, 65%, and 85% of the 75% of 1-RM load (for six, five, four and three repetitions, respectively, with 2-minute inter-set rest periods). Participants were then briefed about intra-set RIR prediction, and it was made clear that 0-RIR indicates the last full range-of-motion repetition possible before momentary muscular failure is reached (i.e., if a subsequent repetition was attempted, momentary muscular failure would occur). Momentary muscular failure was defined as the point where despite attempting to do so, the individual was unable to complete the concentric portion of their current repetition with a full range-of-motion without deviation from the prescribed form of the exercise. Considering the possibility for participants to conflate RIR predictions with perceptions of discomfort [88], participants were also briefed about the difference between perceived discomfort and subjective perception of proximity-to-failure. Two sets to momentary muscular failure with the load corresponding to 75% of 1-RM were then performed. In a randomised order, participants verbally indicated when they believed they had reached 3-RIR during one of the sets and then indicated when they believed they had reached a 1-RIR during the other set, before continuing to perform repetitions to momentary muscular failure.

6.3.5 Objective Outcome Measures

The difference between the predicted RIR (i.e., 1- or 3-RIR) and the actual RIR (i.e., number of repetitions performed after the prediction was given until momentary muscular failure was reached) was defined as the RIR accuracy. This was calculated as both the *raw* RIR accuracy, which accounts for directionality of error (i.e., negative values indicate underestimation of RIR, and positive values indicate overestimation of RIR), and the *absolute* RIR accuracy, which is an absolute value (i.e., difference in predicted vs. actual RIR regardless of directionality) that represents the magnitude of error. For example, if a participant gave their 3-RIR prediction and completed five more repetitions, the raw RIR accuracy would be –2 repetitions (indicating the participant underestimated their capabilities by 2 repetitions) and the absolute RIR accuracy would be calculated as the absolute value of the raw RIR accuracy (i.e., 2 repetitions).

6.3.6 Statistical Analysis

6.3.6.1 Primary Outcomes

All statistical analyses were performed using 'R' software (v 4.0.2; R Core Team, https://www.r-project.4org/). In answering our research questions, we opted to avoid dichotomizing our findings and therefore did not employ traditional null hypothesis significance testing [144, 145]. Instead, we considered the outcomes based on the magnitude of effect estimates and associated confidence interval width, with greatest emphasis placed on the precision of point estimates. To investigate the accuracy of intra-set RIR predictions, separate mixed effects models were generated for raw and absolute RIR accuracy, respectively. Raw RIR accuracy was analysed with a linear mixed effects model using restricted maximum likelihood estimation (REML). Absolute RIR accuracy, however, was analysed with a generalized linear mixed effects model with a Poisson error distribution (specified with a log-link function and REML due to positively skewed count data of the dependent variable). Both models included fixed effects for i) the RIR target at which accuracy was evaluated, ii) the set number within each session, iii) the order of the experimental sessions, and iv) relevant interactions thereof (i.e., session × set, session × RIR, set × RIR). Random intercepts were included per participant to account for repeated measures and each model was adjusted for the number of repetitions performed per set, which was included as a covariate.

To address the primary research questions, estimated marginal means and their comparisons were produced with both 90% and 95% confidence intervals (CIs) within each fixed effect after adjusting for the other independent variables (i.e., session, set, and RIR) and the number of repetitions performed per set. Statistical equivalence was evaluated for each comparison including i) 1-RIR and 3-RIR conditions, ii) first set and second set, and iii) first session and second session [146]. Specifically, if the bounds of the confidence intervals for a given comparison are within the equivalence range set at the smallest effect size of interest, RIR accuracy is considered statistically equivalent (i.e., no meaningful difference). The smallest effect size of interest was set at ± 1 repetition (i.e., equivalence range), as recent meta-analytic data suggested a one repetition difference in proximity-to-failure is unlikely to influence long-term muscle hypertrophy outcomes with RT [115]. Further, the upper and lower bounds of the equivalence range, and their overlap with the estimated effect, were used to evaluate each comparison. Finally, interactions of fixed effects were evaluated visually and via model regression coefficients with their respective 95% CIs. All estimated marginal means from the Poisson model were back transformed to the response scale prior to marginal averaging using the "*emmeans*" package to allow for additive comparisons. Raw study data, model outputs, and visualizations are presented in Appendix C.

6.3.6.2 Secondary/Exploratory Outcomes

To explore the influence of RT experience (years), biological sex, and relative bench press strength on RIR prediction accuracy, multiple linear regression models were fit separately for raw and absolute RIR accuracy. Participant scores were averaged so that only one observation existed per participant for raw and absolute RIR accuracy, respectively. To eliminate unnecessary collinearity of model predictors, a correlation matrix was constructed with all candidate model predictors ($n = 4$) and only the strongest predictors were considered for further exploration (r = >0.20 with dependent variable). For raw RIR accuracy, the predictors included in the final models were biological sex and years of RT experience. For absolute RIR accuracy, the predictors included in the final model were biological sex and relative bench press strength. For both exploratory models, the reference level of biological sex was set to female.

6.4 Results

Overall, participants recorded a *raw* RIR accuracy of –0.23 ± 0.75 repetitions (range = 1 to –3 repetitions) for 1-RIR predictions, –0.10 ± 1.21 repetitions (range = 2 to –3 repetitions) for 3-RIR predictions, with a combined (1- and 3-RIR) raw RIR accuracy of –0.17 ± 1.00 repetitions (range = 2 to -3 repetitions) (Figure 6.1A). Further, an *absolute* RIR accuracy of 0.40 ± 0.68 repetitions (range = 0 to 3 repetitions) was recorded for 1-RIR predictions, 0.90 ± 0.81 repetitions (range = 0 to 3 repetitions) for 3-RIR predictions, and 0.65 ± 0.78 repetitions (range = 0 to 3 repetitions) for 1- and 3-RIR predictions combined (Figure 6.1B). Individual raw and absolute RIR accuracy for each participant is displayed in Figure 6.2.

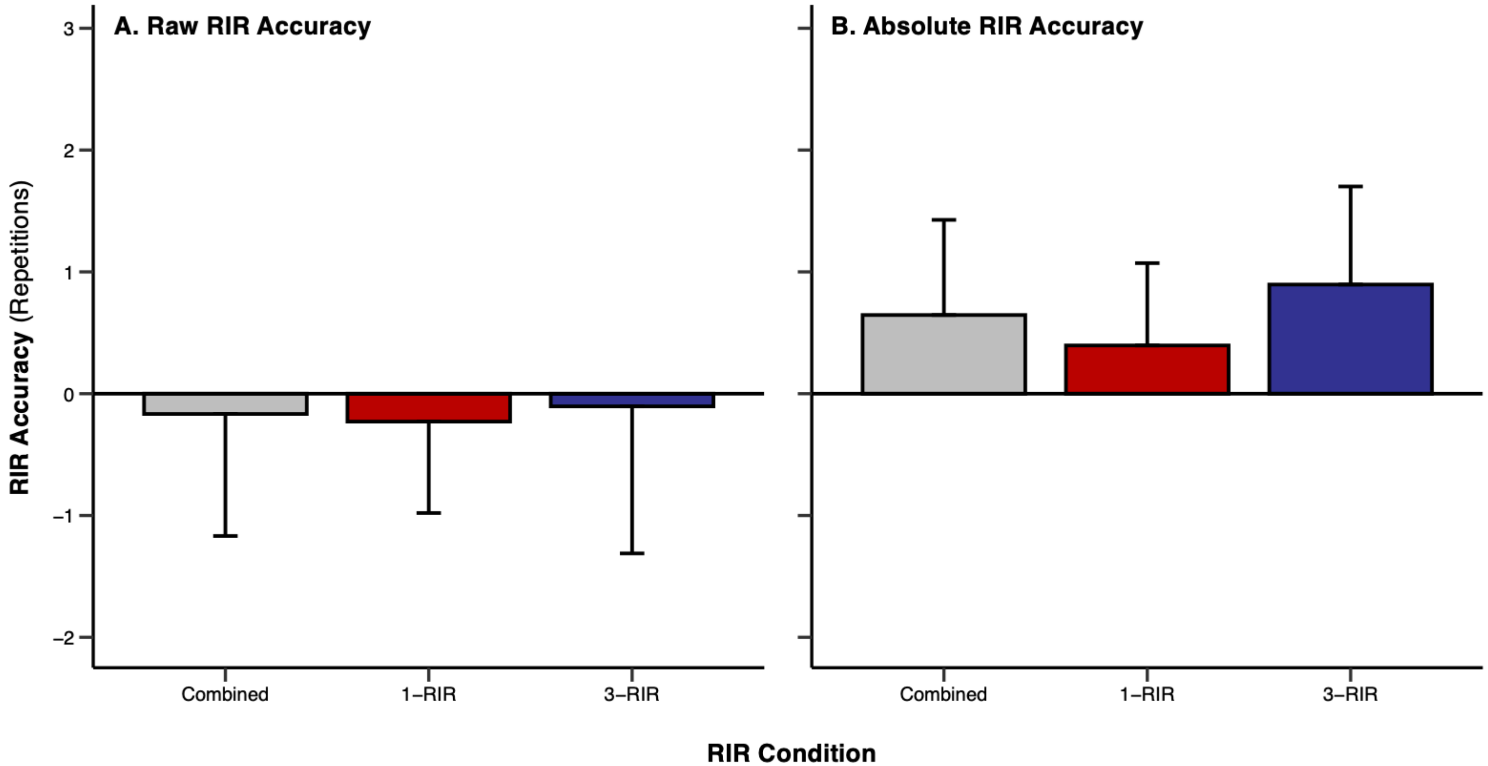

Figure 6.1. Raw (A) and absolute (B) mean RIR accuracy for combined (1- and 3-RIR) and individual 1-RIR and 3-RIR predictions. Data shown are presented as mean ± SD, averaged across all sets and sessions performed. Zero (on the y-axis) indicates accurate RIR predictions. Individual participant values are displayed in Figure 6.3 and Figure 6.4 to highlight inter-individual variability in RIR accuracy. *RIR, repetitions-in-reserve.*

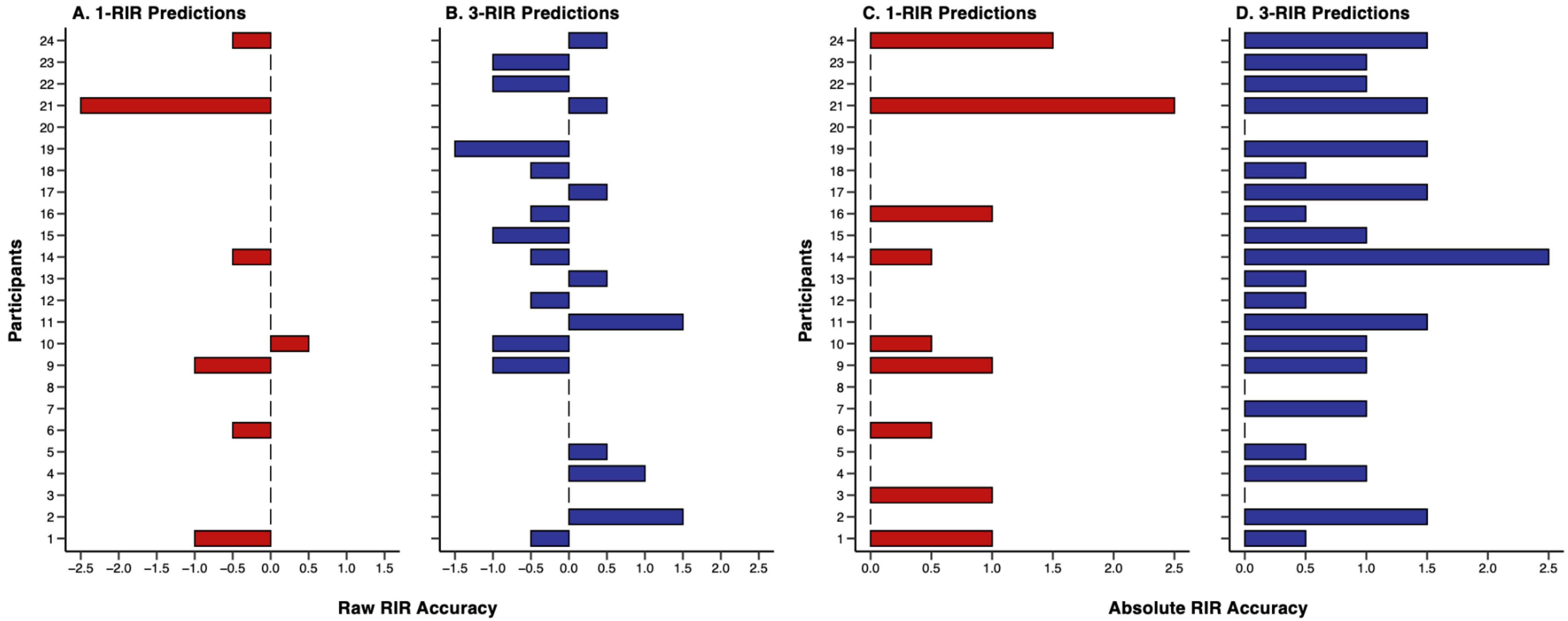

Figure 6.2. Individual participant values for the mean raw and absolute RIR accuracy of (A and C) 1-RIR, and (B and D) 3-RIR predictions. Data shown are presented as mean ± SD, averaged across all sets and sessions performed. RIR accuracy corresponding to zero (and shaded) indicates accurate RIR predictions. Positive RIR accuracy values indicate overprediction, and negative values indicate underprediction. *RIR, repetitions-in-reserve.*

6.4.1 Raw Repetitions-in-Reserve Accuracy

Raw RIR accuracy was comparable between RIR predictions made at 1-RIR [–0.23 repetitions (95% CI: –0.52, 0.06)] and 3-RIR [–0.15 repetitions (95% CI: –0.45, 0.14)], and between set one [–0.13 repetitions (95% CI: –0.43, 0.17)] and set two [–0.25 repetitions (95% CI: –0.56, 0.05)]. The 95% CIs of the comparisons in RIR accuracy between 1-RIR and 3-RIR [–0.08 repetitions (95% CI: –0.49, 0.33)] and between set one and set two [0.12 repetitions (95% CI: –0.31, 0.56)] indicated the data are compatible with a null-effect (i.e., no meaningful differences between 'RIR condition' and 'set number' were found). Conversely, slightly greater RIR underprediction was found in session two [–0.44 repetitions (95% CI: –0.73, –0.16)] compared to session one [0.06 repetitions (95% CI: –0.24, 0.36)] as the 95% CI of the comparison in RIR accuracy between session one and session two did not contain the null-point estimate [0.51 repetitions (95% CI: 0.09, 0.92)].

When evaluating statistical equivalence with an equivalence range of ± 1 repetition, raw RIR accuracy was considered statistically equivalent for all comparisons (Figure 6.3A); 1-RIR versus 3-RIR [–0.08 repetitions (90% CI: –0.42, 0.26)], set one versus set two [0.12 repetitions (90% CI: –0.24, 0.49)], and session one versus session two [0.51 repetitions (90% CI: 0.16, 0.85)]. Further, we found no evidence of interactions between variables (i.e., RIR, set, and session) (Appendix C); the 95% CIs for all model regression coefficients indicated the data were compatible with a null-effect and can be found within Appendix C.

6.4.2 Absolute Repetitions-in-Reserve Accuracy

Absolute RIR accuracy was comparable between RIR predictions made in session one [0.72 repetitions (95% CI: 0.42, 1.02)] and session two [0.60 repetitions (95% CI: 0.35, 0.86)], and between set one [0.60 repetitions (95% CI: 0.33, 0.86)] and set two [0.73 repetitions (95% CI:

0.43, 1.03)]. The 95% CIs of the comparisons in RIR accuracy between session one and session two [0.11 repetitions (95% CI: –0.24, 0.47)] and between set one and set two [–0.13 repetitions (95% CI: –0.50, 0.24)] indicated the data were compatible with a null-effect (i.e., no meaningful differences between ‘session number and ‘set number’ were found). Conversely, slightly less RIR prediction error was found for RIR predictions made at 1-RIR [0.39 repetitions (95% CI: 0.19, 0.59)] compared to 3-RIR [0.93 repetitions (95% CI: 0.59, 1.28)], as the 95% CI of the comparison in RIR accuracy between 1-RIR and 3-RIR did not contain the null point estimate [–0.54 repetitions (95% CI: –0.91, –0.18)].

When evaluating statistical equivalence with an equivalence range of ± 1 repetition, absolute RIR accuracy was considered statistically equivalent for all comparisons (Figure 6.3B); 1-RIR versus 3-RIR [–0.54 repetitions (90% CI: –0.85, –0.24)], set one versus set two [–0.13 repetitions (90% CI: –0.44, 0.18)], and session one versus session two [0.11 repetitions (90% CI: –0.18, 0.41)]. Further, we found one potential interaction between session and set (Appendix C) and the 95% CI of the model regression coefficient did not contain the null point estimate [β = 4.24 (95% CI: 1.38, 13.02), suggesting that RIR prediction error (for both 1- and 3-RIR predictions, combined) decreased in session one from set one [0.87 repetitions (95% CI: 0.43, 1.31)] to set two [0.57 repetitions (95% CI: 0.21, 0.93)], but in session two increased from set one [0.32 repetitions (95% CI: 0.08, 0.57)] to set two [0.89 repetitions (95% CI: 0.45, 1.32)]. The remaining 95% CIs for all model regression coefficients were compatible with a null-effect and can be found within Appendix C.

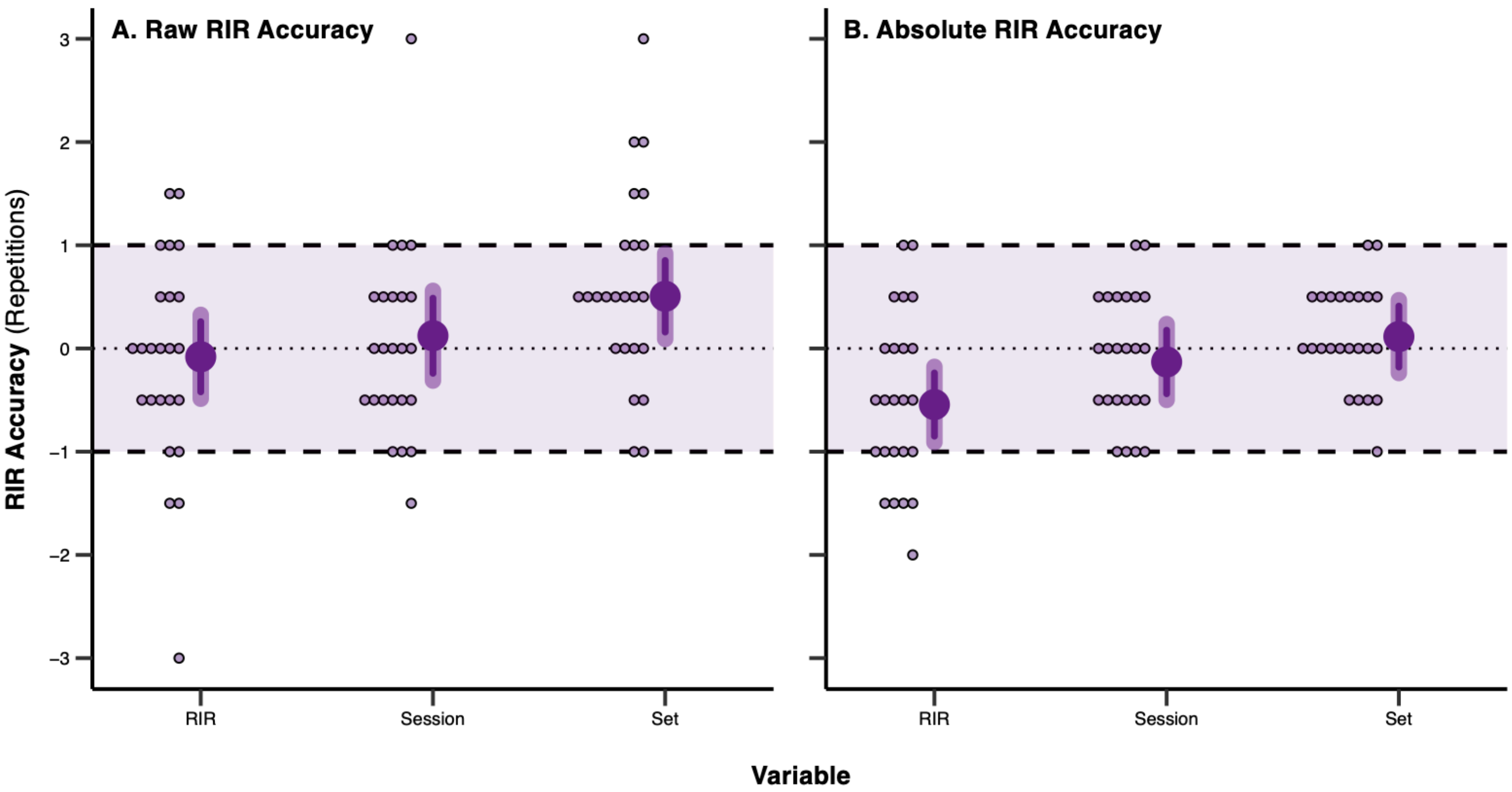

Figure 6.3. Estimated marginal mean values with equivalence range showing difference in raw (A) and absolute (B) RIR accuracy between RIR predictions (1- and 3-RIR), sessions (one and two), and sets (one and two). Point estimate presented as estimated marginal mean with 90% (darker coloured bands) and 95% CIs (lighter coloured bands). Smallest effect size of interest was set at ± 1 repetition, generating an equivalence range (indicated by the shaded area) with a lower equivalence bound of -1 repetition and upper equivalence bound of 1 repetition (indicated by the dotted lines). Neither of the point estimates (or their CIs) crossed the upper or lower equivalence bounds, demonstrating statistical equivalence between 1- and 3-RIR, session one and two, and set one and two. Individual participant values also displayed to highlight inter-individual variability in RIR accuracy for each comparison. *RIR, repetitions-in-reserve.*

6.4.3 Exploratory Predictors of Raw and Absolute Repetitions-in-Reserve Accuracy

The multiple regression model for raw [$R^2 = 0.22$, Adjusted $R^2 = 0.15$] and absolute [$R^2 = 0.08$, Adjusted $R^2 = 0.00$] RIR accuracy demonstrated weak predictive capacity [$R^2 = 0.22$, Adjusted $R^2 = 0.15$]. All visuals and summary outputs of the exploratory models can be found in the Appendix C.

6.5 Discussion

The purpose of this study was to examine the accuracy of intra-set RIR predictions (1- and 3-RIR) across multiple sets and sessions on the barbell bench press exercise in resistance-trained participants. High *raw* and *absolute* RIR accuracy (–0.17 ± 1.00 and 0.65 ± 0.78 repetitions, respectively) was observed (Figure 6.1) and based on our smallest effect size of interest (i.e., equivalence range of ± 1 repetition), we conclude statistically equivalent RIR accuracy between i) 1- and 3-RIR predictions, ii) set one and two, and iii) session one and two (Figure 6.5). Further, our exploratory analyses found a negligible impact of the variables of interest (i.e., years of RT experience, biological sex, and relative bench press strength) on RIR accuracy. Both hypotheses (i.e., RIR accuracy would be greater when participants were required to predict a 1-RIR versus a 3-RIR and would be greater in session two compared to session one) were thus not supported by our findings, likely due to the high RIR accuracy that participants achieved in each experimental session.

Our primary finding suggests that resistance-trained individuals can demonstrate high RIR accuracy on the barbell bench press exercise when instructed to subjectively predict 1- or 3-RIR during a set performed to momentary muscular failure. To our knowledge, we recruited one of the most highly resistance-trained samples of participants examined within the relevant literature [89] (RT experience: males = 8.3 ± 3.7 and females = 7.2 ± 2.3 years; relative bench press strength: males = 1.37 ± 0.26 and females = 0.88 ± 0.17 kg/kg bodyweight), of which 96% had previous experience employing RIR as a set termination method. Although it is likely that the extensive RT experience of our participants contributed to the high *absolute* RIR accuracy observed (0.65 ± 0.78 repetitions), with a minor trend for underprediction (raw RIR accuracy = –0.17 ± 1.00 repetitions), these findings are in line with meta-analytic data revealing that participants of *any* RT experience across 13 studies also achieved an absolute RIR accuracy of less than one repetition [0.95 repetitions (CI: 0.17 – 1.73)] [89]. Also likely influencing the high absolute RIR accuracy observed in the present study was our effort to brief participants about the difference between *perceived discomfort* (i.e., unpleasant sensations perceived during exercise [147]) and proximity-to-failure. Perceived discomfort increases as proximity-to-failure nears [97] due to multiple factors including elevated metabolite accumulation, breathing rate, and body temperature [148], ultimately increasing local pain perception (via group III/IV muscle afferent activation [148]) and requiring greater cognitive effort to complete further repetitions [149]. Although afferent feedback does not seem to contribute substantially to perception of effort during exercise [147], making it possible to differentiate between perceived discomfort and proximity-to-failure (i.e., perceived effort), it is likely that RIR predictions in previous research have been influenced by perceived discomfort [24, 88]. For example, one may confuse a given level of perceived discomfort with a specific proximity-to-failure, leading to erroneous RIR predictions that are based on individual tolerance to discomfort and not on perceptions of proximity-to-failure. This possibility highlights the importance of distinguishing between perceived discomfort and proximity-to-failure when employing RIR prediction as a set termination method in research and practice. Overall, although the RIR accuracy that should be deemed acceptable to employ RIR in RT prescription remains unclear, future research may consider employing extensive familiarisation (e.g., performing RT to momentary muscular failure, practicing intra-set RIR prediction, briefing on perceived discomfort) when using RIR as a set termination method.

Contrary to our findings that demonstrate similar accuracy between 1-RIR and 3-RIR predictions (Figure 6.2), previous research found that RIR accuracy improves when predictions are made closer to momentary muscular failure [81, 87, 142]. For example, one study [81] found that when participants verbally indicated a perceived 5-RIR, 3-RIR, and 1-RIR during a set to volitional failure at 70% 1RM on the barbell back squat exercise, RIR accuracy was greater as proximity-to-failure neared; specifically, RIR predictions were off by 5.15 ± 2.92, 3.65 ± 2.46, and 2.05 ± 1.73 repetitions, for 5-RIR, 3-RIR, and 1-RIR, respectively. Importantly, however, the exercise performed may influence the accuracy of RIR predictions (e.g., RIR predictions may be more accurate for upper body versus lower-body exercises [150]), possibly contributing to differences or lack thereof in RIR accuracy between RIR conditions across studies. The possibility also remains that meaningful differences in RIR accuracy between RIR conditions would have been evident if we had included RIR predictions even further from momentary muscular failure (e.g., 5-RIR). We also investigated differences in RIR accuracy between the first and second set performed and the first and second experimental session completed and found that neither variable (i.e., set and session number) meaningfully influenced RIR accuracy (Figure 6.2). These findings are in contrast with previous research suggesting that the accuracy of RIR predictions increases as successive sets are performed [82, 151], likely due to the lowered number of repetitions performed due to neuromuscular fatigue. Unlike our study, however, whereby participants were instructed to verbally indicate when they had reached the RIR target at any point during each set, previous studies [82, 151] required participants to predict RIR at the same point within each set (e.g., following the 10th repetition), ultimately prompting RIR predictions closer to momentary muscular failure due to neuromuscular fatigue, and as such, improved RIR accuracy. Overall, our findings provide evidence that i) resistance-trained individuals (with experience predicting RIR) can predict 1-RIR and 3-RIR with similar accuracy based on the equivalence range we deemed meaningful, and ii) improvements in RIR accuracy across successive sets and sessions are likely dependent on the initial RIR accuracy (i.e., lower RIR accuracy allows for greater improvements) and may not be observed in resistance-trained individuals.

Our exploratory multiple regression analysis found no evidence of a relationship between i) years of RT experience, ii) biological sex, or iii) relative bench press strength and RIR accuracy, likely due to the consistently high RIR accuracy that we observed; but considering the lack of previous research exploring the influence of these variables on RIR accuracy, future research is required to consolidate our findings.

The consistently high RIR accuracy of our resistance-trained participants likely influenced the statistically equivalent RIR accuracy detected between 1- and 3-RIR predictions, set one and two, and session one and two. Further, we only examined RIR accuracy on the barbell bench press exercise and whether our results can be generalised to other exercises and/or muscle groups is unclear and thus requires further research to elucidate. The qualified supervisors in the present study did not count the repetitions performed by the participants aloud during the experimental sessions and did not report the number of repetitions performed to the participants; but whether the participants kept track of the number of repetitions performed is unknown and whether our findings apply when repetitions are counted, and pacing strategies are implemented (as is common in practice) is unclear.

6.6 Conclusion

Our main findings show that resistance-trained individuals can demonstrate high *absolute* RIR accuracy when predicting 1- and 3-RIR (0.65 ± 0.78 repetitions), with a minor trend for underprediction indicated by the negative *raw* RIR accuracy observed (–0.17 ± 1.00 repetitions), on the barbell bench press exercise. Further, likely due to the consistently high RIR accuracy of our participants, we found statistically equivalent (within an equivalence range of ± 1 repetition) *raw* and *absolute* RIR accuracy between i) 1- and 3-RIR predictions, ii) set one and two, and iii) session one and two. Overall, these findings provide evidence that RIR can be consistently predicted within one repetition of the RIR target, which we deemed meaningful and practically important.

Chapter Seven – Similar Muscle Hypertrophy Following 8-Weeks of Resistance Training to Momentary Muscular Failure or with Repetitions-in-Reserve in Resistance-Trained Individuals

Please note, the following text in Chapter Seven has been adapted from a peer-reviewed and published manuscript (DOI: 0.1080/02640414.2024.2321021).

7.1 Preface

Study One (Chapter Four) reported little evidence that RT performed to momentary muscular failure is superior to non-failure RT for hypertrophy; however, due to the variability and ambiguity in the actual proximities-to-failure reached in non-failure groups, firm conclusions regarding the relationship between proximity-to-failure and muscle hypertrophy cannot be made [115]. Indeed, no studies in this meta-analysis employed an RIR-based approach to set termination, preventing precise estimates of the specific influence of RIR on hypertrophy. We therefore designed a within-participant unilateral study assessing changes in quadriceps thickness, whereby lower limbs were randomised to perform RT either to i) momentary muscular failure, or ii) a perceived 2-RIR and 1-RIR, respectively. Further, to expand on our understanding of the acute influence of RIR on neuromuscular fatigue (Study Two; Chapter Five), we examined surrogate measures of neuromuscular fatigue across multiple timepoints to assess whether repeated exposure to a given RT stimulus impacts these markers longitudinally. This final thesis study provides novel experimental evidence comparing the impact of RT performed to momentary muscular versus with RIR on muscle hypertrophy and neuromuscular fatigue not previously explored in prior literature (see Chapter Two), and subsequently, practical applications for practitioners who work with a wide demographic of individuals that regularly partake in RT. Finally, the methods we employed (e.g., within participant design, typical error calculation, assessing RIR accuracy etc.) can inform future research investigating RT proximity-to-failure and muscle hypertrophy.

7.2 Introduction

Skeletal muscle hypertrophy is a physiological adaptation to resistance training (RT), specifically driven by the repeated exposure of muscle fibres to mechanical tension [31]. To promote meaningful muscle hypertrophy, it is accepted that resistance-trained individuals should terminate RT sets with a close proximity-to-failure (defined as the number of repetitions remaining in a set prior to momentary muscular failure) [79, 115]. Whether closer proximities-to-failure during RT *always* promote greater muscle hypertrophy, however, is contentious. For example, RT sets to momentary muscular failure may incur high levels of i) neuromuscular fatigue that impair the level of mechanical tension within a RT session [116], and ii) muscle damage that compromises protein synthesis directed toward muscle hypertrophy [152]. Therefore, prescribing RT with a repetitions-in-reserve (RIR) scale to terminate sets close to, but not at momentary muscular failure has become common [26, 97]. The lack of research employing RIR prescription, however, and the uncertainties surrounding the relationship between proximity-to-failure, neuromuscular fatigue, and muscle hypertrophy, highlight key areas for future research to explore.

To investigate the influence of proximity-to-failure on muscle hypertrophy, previous research has compared either i) RT performed to momentary muscular failure versus non-failure [43-47], or ii) RT performed to different percentages of velocity loss from the first (or fastest) repetition [71-74, 98, 99]. Specifically, meta-analysis [115] of this relevant literature suggests there is no evidence to support that RT performed to momentary muscular failure is superior to non-failure RT for muscle hypertrophy, and that performing RT to high velocity loss thresholds (>25%) promotes similar muscle hypertrophy to moderate (20-25%) velocity loss thresholds (i.e., closer versus further proximities-to-failure). Although these data demonstrate that proximity-to-failure may influence muscle hypertrophy in a *non-linear* manner (i.e., as sets are terminated closer to momentary muscular failure, muscle hypertrophy increases, but only to a certain point), the specific RIR achieved in non-failure conditions is unclear [97, 140]. Nonetheless, Robinson et al. [153] conducted an *exploratory* analysis of the relationship between RIR and muscle hypertrophy by estimating specific RIR values for each non-failure RT group from the relevant literature [97, 140]. Muscle hypertrophy increased as sets were terminated closer to momentary muscular failure in the resulting meta-regression, but uncertainty surrounding i) the accuracy of RIR estimations of non-failure RT groups, and ii) the variability in RIR between participants and across sets within a given study [97, 140], renders the exact relationship between RIR and muscle hypertrophy, unclear. As a whole, the literature suggests that RT to momentary muscular failure is effective for promoting muscle hypertrophy (within the timeframes studied); however, reaching close proximities-to-failure may also be sufficient even in resistance-trained individuals [47, 71-74, 98]. Overall, deriving practical recommendations that inform the proximity-of-failure of set termination is challenging due to the limitations of the current literature.

To monitor and control the proximity-to-failure achieved during RT, sets can be terminated at specific RIR values (e.g., 3 sets x 10-15 repetitions at 2-RIR). Although RIR prescription is commonly used in practice, few studies [52, 84-86] have investigated the influence of intra-set RIR predictions on RT adaptations and short-term responses. This research gap may be due, in part, to concerns relating to individual RIR accuracy (i.e., the proximity of actual set termination from the target RIR). Consequently, most RIR-related research (to date) focuses on RIR accuracy [26, 81, 83, 154], with one meta-analysis concluding that individuals underpredict RIR by approximately one repetition on average [89] and a recent experimental trial observing resistance-trained individuals were within 0.40 (± 0.68) and 0.90 (± 0.81) repetitions from 1-RIR or 3-RIR targets, respectively [155]. These data indicate that RIR prescription may be an efficacious set termination strategy for controlling proximity-to-failure in RT interventions, at least in resistance-trained samples. Indeed, future research comparing RIR prescription with reaching momentary muscular failure during RT can advance the understanding of the relationship between proximity-to-failure and outcomes of interest (i.e., muscle hypertrophy and neuromuscular fatigue) and subsequently improve practical recommendations.

7.2.1 Objectives

Proximity-to-failure in RT is a continuous variable as RIR values range from 0-10+. However, proximity-to-failure has only been investigated dichotomously, with previous research comparing RT to 'set failure' versus non-failure. As such, previous research does not describe the relationship between RIR and muscle hypertrophy, and is therefore practically limited, as set termination does not have to be binary (i.e., set failure or non-failure). Therefore, the primary objective of this study was to examine the influence of RT proximity-to-failure, determined by RIR, on quadriceps hypertrophy following eight weeks of RT performed to either momentary muscular failure or with RIR in resistance-trained individuals. Importantly, only one [47] out of five [43-46] studies comparing RT performed to momentary muscular failure versus non-failure on muscle hypertrophy has been conducted in a resistance-trained sample. We employed a Bayesian approach for data analysis to directly model uncertainty and intuitively present the results through posterior probabilities to allow meaningful inferences to be made regarding the influence of proximity-to-failure on muscle hypertrophy [100]. We also explored changes in lifting velocity and repetitions performed during RT, and volume accumulation to quantify acute neuromuscular fatigue.

7.3 Methods

7.3.1 Experimental Approach

Resistance-trained participants completed an 8-week unilateral RT intervention (within-participant design), whereby each lower limb was randomised to perform the unilateral leg press and leg extension exercises either to i) momentary muscular failure (FAIL), or ii) a perceived 2-RIR and 1-RIR, respectively (RIR) (Figure 7.1). Prior to the RT intervention, two pre-testing sessions were conducted to obtain baseline measurements of muscle thickness, determine individual load selection, and familiarise participants with predicting intra-set RIR and reaching momentary muscular failure. Participants then commenced the 8-week intervention involving two RT sessions per week (with each lower limb performing RT to either FAIL or RIR) separated by ~72 hours (Figure 7.1). Muscle thickness of the quadriceps [rectus femoris (RF) and vastus lateralis (VL)] was assessed via ultrasound at baseline and following the 8-week RT intervention. To provide surrogate measures of neuromuscular fatigue, the change in lifting velocity (in weeks one, four, and eight) and repetitions performed from the first to final set, along with volume (i.e., volume load and repetition volume) accumulation were assessed.

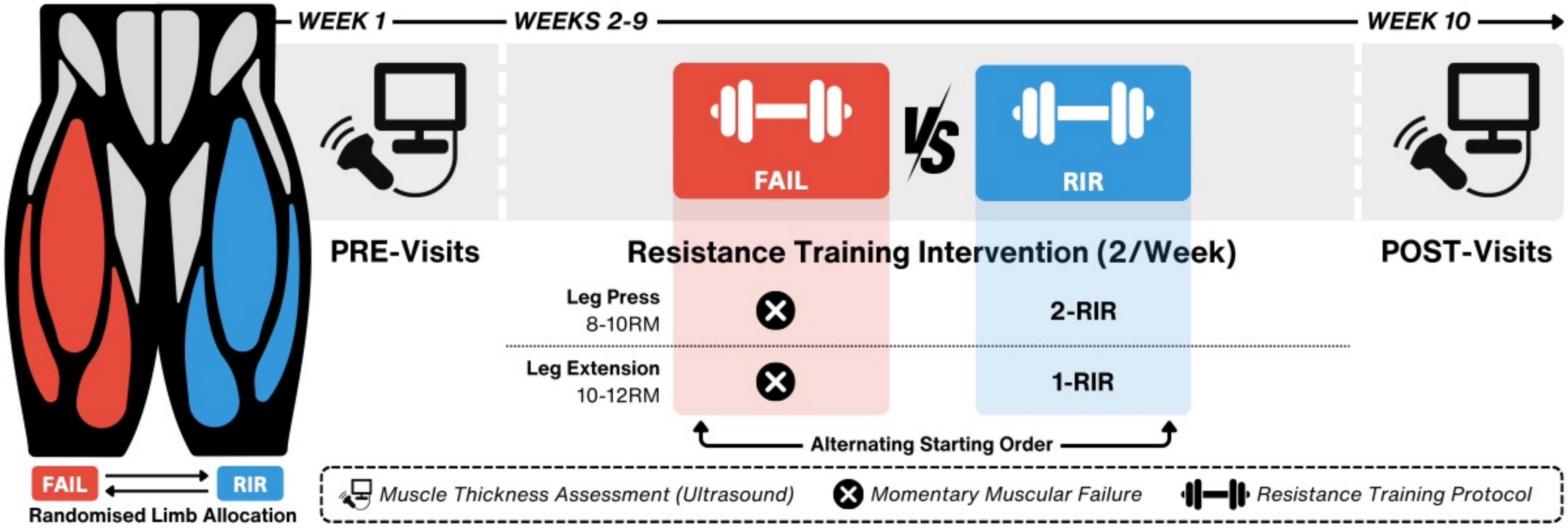

Figure 7.1. Schematic overview of study design and resistance training protocols. Participants completed two pre-testing sessions (involving two ultrasound assessments, and a repetitions-to-failure and repetition-maximum load assessment), 16 experimental sessions across the 8-week intervention (two times per week separated by ~72 hours), and two post-testing sessions (involving two ultrasound assessments). *RIR, repetitions-in-reserve. RM, repetition-maximum.*

7.3.2 Participants

Pre-exercise participant characteristics are presented in Table 7.1. Male (*n* = 12) and female (*n* = 7) participants were recruited i) between 18-40 years old, ii) with no existing musculoskeletal injuries or neuromuscular disorders, iii) who confirmed they had not used anabolic steroids, or illegal agents known to increase muscle size for the previous year, iv) with a minimum of three years RT experience (with at least three or more RT sessions per week) [117]. One female participant did not adhere to the nutritional requirements and was therefore not included in data analysis. However, a sensitivity analysis was conducted for our primary outcome measure (i.e., change in muscle thickness) with the full sample (*n* = 19) displayed in Appendix D. All 18 participants included in data analysis reported experience with intra-set RIR predictions, 16 (89%) had worked with a personal trainer face-to-face, and nine (50%) had previously competed in powerlifting or bodybuilding. Of the six female participants, four (67%) reported experiencing a regular menstrual cycle and five reported using oral contraceptives.

Table 7.1. Baseline participant characteristics. An overview of the relevant characteristics for each participant included in data analysis. Quadriceps set volume is reported as 20% higher than the initial volume that participants were assigned based on previous resistance training experience. *kg, kilograms; p/w, per week; y, years.*

	Males (*n* = 12)		**Females (*n* = 6)**	
Variable	**Mean ± *SD***	**Range**	**Mean ± *SD***	**Range**
Age (y)	26.9 ± 3.1	20 - 31	30.0 ± 5.8	24 - 38
Bodyweight (kg)	82.6 ± 6.0	75 - 94	62.8 ± 5.4	57 - 72
RT experience (y)	7.8 ± 2.6	4 - 13	7.5 ± 2.3	5 - 10
RT frequency (p/w)	4.8 ± 0.9	3 - 6	4.7 ± 0.8	4 - 6
Quadriceps set volume	12 ± 1	10 - 14	14 ± 2	12 - 17

7.3.2.1 Sample Size Justification

The target sample size for this study was 18 participants; however, to account for a 20% dropout rate, we aimed to recruit 20 participants. Sample size was based on the following pragmatic considerations: i) recruiting more than 20 participants was not feasible due to resource constraints (time and associated costs to complete data collection and analysis), and ii) this sample size is greater than similar within-subject unilateral pre-post studies investigating the influence of RT proximity-to-failure on muscle hypertrophy [43, 47, 74]. An α-priori sample size calculation was therefore not performed for this study and Bayesian statistical methods were employed.

7.3.3 Procedures

7.3.3.1 Exercise and Nutrition Control

Participants were asked to not perform i) any high-intensity aerobic exercise during the RT intervention, and specifically, ii) any lower-body RT or aerobic exercise in the 24 hour period before each study visit. Participants were allowed to perform additional moderate-intensity RT involving muscle groups other than the quadriceps, but exercise constraints were employed to minimise potential confounding influences (described in Appendix D). Participants were required to track their nutritional intake and bodyweight using a mobile application (MacroFactor; Stronger By Science Technologies LLC, Raleigh, NC, USA), which provided each participant individualised macronutrient (i.e., protein, carbohydrate, dietary fat) and energy (i.e., kilocalories) targets based on a monthly rate of weight gain equal to 1% of their starting body weight (kg) for the duration of the study period (10-weeks). Data retrieved from MacroFactor are reported in Table 7.2.

7.3.3.2 Menstrual Cycle Considerations

Considering that all female participants completed both unilateral protocols, thus acting as their own "controls", and that recent meta-analyses indicate that both i) menstrual cycle phase [122], and ii) modern oral contraceptive use [122], have at most trivial effects on exercise performance at the group level, females commenced the intervention period at any time-point throughout their menstrual cycle and no timing considerations were made for post-testing. If participants experienced menstrual symptoms during the study period that they believed affected RT performance, study visits were rescheduled as necessary.

7.3.3.3 Exercise Technique

For the leg press (Hammer Strength), participants were seated with one foot positioned on the plate whilst ensuring that the foot, knee, and hip were in line. Participants held the handles and maintained contact with the seat whilst lowering the plate until knee angle was less than 90 degrees and contact was made with the safety mechanism. The safety mechanism was individualised for each participant to standardise range-of-motion. For the leg extension, participants were seated with their back flush against the back rest and hands gripping the support handles. Toes were pointed upwards, and participants were required to reach full knee extension by ensuring their shin contacted - or was at least within sufficient proximity of - the standardised implement (see yellow dotted lines in Appendix D). Participants were instructed to perform the concentric (lifting) phase of each repetition with maximal lifting velocity (i.e., as fast as possible), followed by a controlled eccentric (lowering) phase (~2 seconds). See Appendix D for images of equipment and demonstration of exercise technique.

7.3.3.4 Repetition-Maximum Load Assessment

To determine starting loads, participants completed four repetition-maximum (RM) assessments (8-10-RM for the leg press and 10-12-RM for the leg extension per limb) in pre-visit one. To begin, a warm-up consisting of three sets of eight repetitions was performed on a randomly selected lower limb with the minimum load on the leg press exercise (55 kg) and with 70 and 80% of the approximate 8-10-RM load determined for the leg press based on participant training history. Participants then rested two minutes before attempting a set to momentary muscular failure with the predicted 8-10-RM load. If the participant appeared i) able to (as determined by an experienced supervisor) perform more than 10 repetitions without reaching momentary muscular failure, or ii) unable to complete eight repetitions, the set was immediately terminated. The load was then increased or decreased (5-10 kg on the leg press and 2.5-5 kg on the leg extension), and after a five-minute recovery period, another set was attempted. This was repeated until the participant reached momentary muscular failure on the 9^{th}, 10^{th}, or 11^{th} repetition. Once the 8-10-RM load was established on the leg press, the same procedures were used to determine the 10-12-RM load on the leg extension. This procedure was completed on both limbs. An experienced supervisor ensured participant safety and encouraged maximum lifting velocity with strong verbal encouragement.

7.3.3.5 Repetitions-to-Failure Assessment

In pre-visit two, participants completed two sets to momentary muscular failure with the loads determined in pre-visit one for the leg press and leg extension. An overview of the procedures and participant instructions can be found elsewhere [155]. All procedures were performed on both limbs, in a randomised manner.

7.3.3.6 Resistance Training Intervention

Participants performed both exercises in a unilateral manner on both lower limbs twice per week for eight weeks (Figure 1), with each limb randomly assigned to perform either the FAIL or RIR protocol. FAIL performed all sets to momentary muscular failure. Considering RT sets do not have terminated at the same proximity-to-failure, and that proximity-to-failure may be prescribed based on the complexity of the exercise performed [97], RIR performed the leg press to 2-RIR and leg extension to 1-RIR. For RIR, participants were provided the following standardised instruction: *"you will be required to stop the set when you perceive to have reached the RIR target."* Conversely, during FAIL, momentary muscular failure occurred when despite attempting to do so, participants were unable to complete the concentric portion of their current repetition with a full range-of-motion and without deviation from the prescribed form of the exercise [97] (participants had up to two seconds to progress past the 'sticking point' before sets were ceased). To explore individual responses and increase the precision of RT effects on muscle hypertrophy [156], set volume for each participant was equal to the weekly number of quadriceps sets they typically performed in their most recent training routine and was equally distributed between the leg press and leg extension. Where a participant was assigned ≥15 sets, a 20% decrease in volume was implemented (e.g., 16 sets – 20% = 13 sets) to mitigate potential injury risk, excessive fatigue, and prolonged session durations. Halfway through the intervention (commencement of week five), all participants increased set volume by 20%.

7.3.3.7 Resistance Training Protocol

Participants commenced the first RT session on a random limb, with the starting limb alternated each session. Both exercises were completed on the starting limb before training the alternate limb. Four warm-up sets were performed on the leg press, starting with the minimum load, working up to 50, 65, and 85% of the 8-10-RM load (for ten, eight, six and four repetitions, with two minute inter-set rest periods). Only two warm-up sets were performed on the leg extension (50 and 65% of the 10-12-RM load for five repetitions). Participants then performed their specified number of sets on each exercise with their individualised load. For both protocols, if the participants performed more repetitions than the RM load range, the load was adjusted on the subsequent set by 2.5-5 kg on the leg press and 1.25-2.5 kg on the leg extension. Four minutes rest was given between working sets on the leg press, two minutes for the leg extension, and five minutes between exercises. If a participant experienced musculoskeletal discomfort that prevented them from performing either exercise, if feasible, all sets were allocated to the exercise they could perform. For example, if a participant needed to complete 10 sets but was unable to perform the leg press, the FAIL protocol would perform all 10 sets to momentary muscular failure on the leg extension and the RIR protocol would perform the first five sets to 2-RIR (4 min rest) and the remaining five sets to 1-RIR (2 min rest) on the leg extension (for a total of 10 sets). To ensure recovery and minimise residual fatigue, ~72 hours was allocated between RT sessions; however, 48 to 96 hours were allowed for scheduling flexibility (in case participants were unable to schedule 72 hours between sessions). All RT sessions were monitored by a qualified exercise professional (MR) and strong verbal encouragement was provided during each working set. Participants that completed 90% of scheduled sessions (14 out of 16 RT sessions) were included in the final analysis.

7.3.4 Outcome Measures

7.3.4.1 Repetitions-in-Reserve Prediction Accuracy

The difference between the predicted (i.e., 1- or 3-RIR) and actual RIR (i.e., number of repetitions performed after the prediction was given until momentary muscular failure was reached) achieved during the repetitions-to-failure assessment was defined as RIR accuracy

[155]. This was calculated as both *raw* RIR accuracy, which accounts for directionality of error, and *absolute* RIR accuracy, an absolute value representing the magnitude of error [155].

7.3.4.2 Volume Accumulation

Volume of RT, measured as repetition volume (sets x repetitions) and volume load (sets x repetitions x load), was deliberately not equalised between FAIL and RIR. Volume completed in each protocol was recorded and the percentage decrease in repetitions performed from the first to final set was also calculated.

7.3.4.3 Change in Lifting Velocity from the First to Final Set

Mean concentric velocity (MV) for each repetition (described herein as 'lifting velocity') was measured (on the starting limb in both sessions in weeks one, four, and eight) using a linear position transducer (GymAware, Kinetic Performance Technology, Canberra, Australia) attached to the loading bar of the leg press. The mean lifting velocity of the first three repetitions completed in each of the leg press sets was used to determine the change in mean lifting velocity from the first to final set to investigate acute neuromuscular fatigue [65, 139]. The result was expressed as percentage change, with negative values (i.e., decreased lifting velocity from the first to final set) used to indicate acute neuromuscular fatigue.

7.3.4.4 Muscle Thickness

Ultrasound imaging [SONOSITE M-Turbo (probe size = 5 cm, scanning frequency = 15-16 MHz); FUGIFILM, Bothell, Western Australia] was used to determine left and right RF and VL thickness. Two separate scans were performed during both pre-testing and post-testing (separated by 48-72 hours) at least 72 hours after RT to assess the reliability of the measurement and minimise any confounding effect of residual intramuscular swelling. Participants lied in a supine position and images were obtained at 50% of the distance between the lateral epicondyle and greater trochanter for the vastus lateralis and 50% on the distance between the anterior spina iliaca superior (ASIS) and the superior part of the patella for the rectus femoris. Accurate repositioning of the probe in subsequent scans was ensured by marking measurement sites and transferring the markings to a transparent plastic sheet (when apparent, blemishes and tattoos were also marked to replicate its positioning). Scans were taken three times at the same site with the probe positioned longitudinally (i.e., lengthwise on the thigh, not perpendicular to it) with the skin layer located in the most superior portion of the image to standardise probe pressure. Images were transferred to a computer and analysed using open-source software (OsiriX, version 3.2.1; OsiriX Imaging Software, Geneva, Switzerland) by generating an average measurement (i.e., largest distance between the superficial and deeper aponeuroses) of the proximal, central, and distal portions of images [157] as shown in Appendix D. The average of the three images for each site was used for analysis. The typical error (TE) and intraclass correlation (ICC) of the two pre- and post-testing ultrasound assessments are summarised in Appendix D. As the same investigator (MR) supervised all RT sessions during the study, it was not possible to blind the ultrasound assessments and data analysis.

7.3.5 Statistical analysis

To provide a more flexible modelling approach and an intuitive results interpretation by reporting probabilities [100], we analysed data with Bayesian linear mixed-effect models using the “brms” (Bürkner, 2023) package in R (v 4.0.2; R Core Team, https://www.r-project.org/). Posterior draws were extracted using “tidybayes” (Kay, 2023), estimated marginal effects were calculated using “emmeans” (Lenth, 2023), and the probability (i.e., percentage value ranging from 0% to 100%) that an estimate was in favour of a given protocol was calculated manually by examining the proportion of posterior draws that met the criteria of interest (e.g., >0) and denoted as the probability of direction (*pd*). For our primary outcome (i.e., change in muscle thickness) a model was generated to assess mean differences in outcome measures between protocols for the quadriceps (average of RF and VL) and for the RF and VL individually. We also calculated the probability that a certain change in muscle thickness exceeded the TE and denoted it as "*pd* > TE". For change in lifting velocity, a model was generated to explore differences at three time points throughout the RT intervention between protocols. For change in repetitions performed, volume load, and repetition volume, models were generated to calculate the slopes for each protocol (i.e., change in the variable assessed per session) and explore differences in longitudinal trends between protocols. Further model details, population-level effects, and final group-level slope structures are displayed in Appendix D. Non-informative priors (i.e., default "brms" priors) were used for all model parameters across all outcome measures. Inferences from all analyses were made from posterior samples generated using the Hamiltonian Markov Chain Monte Carlo method and via the use of high-density credible intervals (HDI). Model diagnostics were conducted as per the WAMBS-Checklist [158] (Appendix D). All raw data of outcome measures (in text and figures) are presented as mean and standard deviation. A comprehensive overview of the statistical analysis along with the R code used can be found on the Open Science Framework (https://osf.io/34d92/).

7.4 Results

7.4.1 Intervention Adherence

Mean participant adherence was 97.5% (87.5-100%). In some instances, sessions were completed over 11 weeks instead of 10 due to scheduling constraints. No sessions had to be rescheduled due to menstrual symptoms in females. To maintain adherence, minor protocol modifications were made if a participant experienced musculoskeletal discomfort (e.g., muscular strains or knee joint pain) but was able to continue the study as mutually decided by the participant and supervisor. Eight participants experienced minor musculoskeletal discomfort (FAIL = 5, RIR = 3), with two of the eight unable to perform the leg press in some weeks (in which case the remaining set volume was allocated to the leg extension). One participant experienced a muscular strain (limb = RIR) in the second week and had to cease participation, but once recovered (~12-weeks), re-commenced the study from the start. All participants completed the study. Tracked nutritional variables and body weight change are reported in Table 7.2. Out of the 18 participants, 16 (89%) increased bodyweight, as intended by MacroFactor.

Table 7.2. Nutritional intake and bodyweight change. An overview of nutrition (energy, protein, carbohydrate, and dietary fat intake) and body weight data extracted from MacroFactor for males and females, separately. *BW, bodyweight; g, grams; kcal, kilocalories; kg, kilograms.*

	Males (*n* = 12)		**Females (*n* = 6)**	
Variable	**Mean ± *SD***	**Range**	**Mean ± *SD***	**Range**
BW change (kg)	3.1 ± 2.5	–0.2 - 9.3	2.2 ± 1.8	0 - 5.4
BW change (%)	3.6 ± 2.9	–0.3 - 10.2	3.5 ± 3	0 - 8.8
Energy Intake (kcal)	3149 ± 234	2722 - 3535	2523 ± 352	2102 - 3173
Protein (g)	208 ± 18	178 - 234	145 ± 24	111 - 173
Protein (g) per kg/BW	2.5 ± 0.3	2.1 - 3	2.3 ± 0.4	1.7 – 2.8
Carbohydrate (g)	390 ± 59	299 - 511	293 ± 81	217 - 440
Dietary fat (g)	86 ± 17	56 - 115	82 ± 19	62 - 119

7.4.2 Repetitions-in-Reserve Prediction Accuracy

Participants had a high absolute RIR accuracy; on average less than one repetition from the 1- and 3-RIR targets on both exercises (Table 7.3). There was a slight trend for overestimation on 1-RIR predictions (i.e., participants were more likely to predict RIR closer to momentary muscular failure) and underestimation on 3-RIR predictions (i.e., participants were more likely to predict RIR further from momentary muscular failure) excluding the left limb leg press.

Table 7.3. Repetitions-in-reserve prediction accuracy. Summary of absolute repetitions-in-reserve prediction accuracy (raw values) for both exercises on each lower limb. Arrow symbols inform the raw repetitions-in-reserve accuracy and indicate whether the average prediction was an overestimation (up arrow = ↑) or underestimation (down arrow = ↓). Data shown are presented as mean ± *SD*. *RIR, repetitions-in-reserve.*

	Leg Press		**Leg Extension**	
RIR Target	**Left**	**Right**	**Left**	**Right**
1-RIR	↑0.44 ± 0.51	↑0.44 ± 0.78	↑0.56 ± 0.51	↑0.44 ± 0.70
3-RIR	↑0.61 ± 0.70	↓0.94 ± 1.16	↓0.83 ± 0.99	↓0.89 ± 1.08

7.4.3 Resistance Training Variables

Average volume load and repetition volume across all sessions of the RT intervention were similar between FAIL and RIR (Figure 7.2). Table 7.4 displays a summary of all RT variables recorded for each week (average values from both sessions completed) across the intervention.

Table 7.4. Descriptive characteristics for each resistance training protocol. Repetition values are rounded to the nearest whole number. Percentage decrease from the first to final set is calculated from instances where the load was not adjusted across sets (i.e., not calculated from repetition data shown in table). Data shown are calculated as the average result from both resistance training sessions completed in each week and are presented as mean ± *SD*. *kg, kilograms; reps, repetitions.*

	Week 1				**Week 2**			
	FAIL		**RIR**		**FAIL**		**RIR**	
Variable	**LP**	**LE**	**LP**	**LE**	**LP**	**LE**	**LP**	**LE**
Total Reps	46 ± 10	57 ± 10	42 ± 7	63 ± 10	47 ± 8	59 ± 11	46 ± 9	63 ± 10
Reps (first set)	11 ± 3	11 ± 2	9 ± 2	12 ± 2	11 ± 2	12 ± 2	10 ± 2	12 ± 2
Reps (final set)	8 ± 2	8 ± 1	8 ± 1	9 ± 2	8 ± 2	8 ± 1	8 ± 2	10 ± 1
% Decrease Reps	*23.5%*	*32%*	*8.7%*	*23.5%*	*17.9%*	*32.4%*	*11.6%*	*19%*
Load Lifted (kg)	101 ± 45	32 ± 10	98 ± 43	31 ± 8	105 ± 44	31 ± 8	102 ± 42	31 ± 7
Volume Load (kg)	546 ± 289	254 ± 71	527 ± 273	253 ± 55	574 ± 268	244 ± 48	555 ± 254	246 ± 46

	Week 3				**Week 4**			
	FAIL		**RIR**		**FAIL**		**RIR**	
Variable	**LP**	**LE**	**LP**	**LE**	**LP**	**LE**	**LP**	**LE**
Total Reps	49 ± 11	60 ± 10	44 ± 9	64 ± 10	46 ± 8	63 ± 12	43 ± 8	63 ± 10
Reps (first set)	11 ± 4	12 ± 2	10 ± 2	13 ± 1	10 ± 2	13 ± 2	9 ± 2	13 ± 1
Reps (final set)	8 ± 2	8 ± 1	8 ± 2	10 ± 1	8 ± 2	9 ± 1	8 ± 2	9 ± 1
% Decrease Reps	*21.6%*	*29%*	*8.1%*	*22.3%*	*21.4%*	*28.5%*	*11%*	*25.4%*
Load Lifted (kg)	110 ± 46	31 ± 8	107 ± 43	31 ± 7	110 ± 47	32 ± 8	112 ± 44	32 ± 7
Volume Load (kg)	599 ± 282	248 ± 47	582 ± 266	252 ± 46	592 ± 266	257 ± 52	582 ± 255	264 ± 55

	Week 5				**Week 6**			
	FAIL		**RIR**		**FAIL**		**RIR**	
Variable	**LP**	**LE**	**LP**	**LE**	**LP**	**LE**	**LP**	**LE**
Total Reps	52 ± 11	63 ± 15	49 ± 11	66 ± 14	49 ± 12	65 ± 11	48 ± 10	65 ± 11
Reps (first set)	9 ± 2	12 ± 3	9 ± 1	12 ± 2	9 ± 2	13 ± 2	8 ± 2	12 ± 1
Reps (final set)	8 ± 1	8 ± 1	8 ± 1	9 ± 2	7 ± 2	8 ± 1	7 ± 1	9 ± 2
% Decrease Reps	*20.2%*	*28.9%*	*10.6%*	*21%*	*26.8%*	*31.5%*	*15.2%*	*20.1%*
Load Lifted (kg)	104 ± 41	34 ± 8	104 ± 42	34 ± 8	114 ± 45	34 ± 8	112 ± 43	35 ± 8
Volume Load (kg)	669 ± 225	303 ± 110	668 ± 227	313 ± 111	709 ± 237	300 ± 76	701 ± 219	307 ± 78

	Week 7				**Week 8**			
	FAIL		**RIR**		**FAIL**		**RIR**	
Variable	**LP**	**LE**	**LP**	**LE**	**LP**	**LE**	**LP**	**LE**
Total Reps	51 ± 8	67 ± 9	48 ± 10	69 ± 13	48 ± 10	68 ± 13	44 ± 9	73 ± 12
Reps (first set)	10 ± 2	13 ± 2	9 ± 2	12 ± 2	9 ± 3	13 ± 2	8 ± 2	13 ± 2
Reps (final set)	7 ± 2	8 ± 1	7 ± 2	9 ± 3	7 ± 2	8 ± 2	7 ± 2	9 ± 3
% Decrease Reps	*32%*	*33.7%*	*21.7%*	*23%*	*25.6%*	*35.4%*	*20.7%*	*24.3%*
Load Lifted (kg)	121 ± 45	36 ± 8	124 ± 44	37 ± 8	121 ± 48	37 ± 8	122 ± 47	37 ± 8
Volume Load (kg)	740 ± 274	344 ± 82	776 ± 253	331 ± 68	768 ± 287	330 ± 76	770 ± 277	338 ± 74

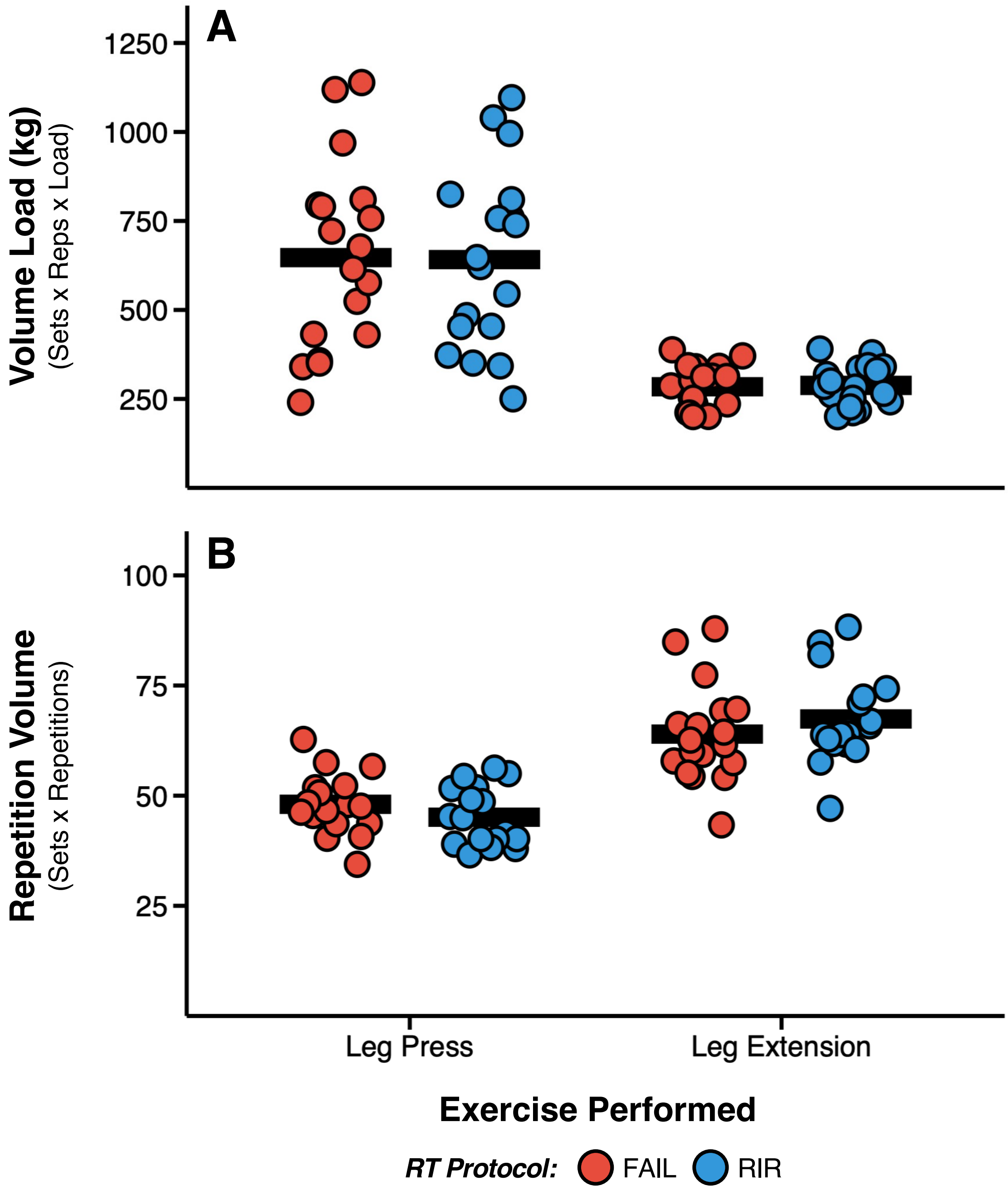

Figure 7.2. Volume load (A) and repetition volume (B) completed across the resistance training intervention for FAIL and RIR and for both exercises. Volume load calculated as: sets x repetitions x load. Repetition volume calculated as: sets x repetitions. Data shown are raw values presented as both protocol means (with individual values), and the *SD* of protocol means can be found in Appendix D.

7.4.4 Muscle Thickness

Raw quadriceps thickness (average of RF and VL) is displayed in Figure 7.3A/B. Similar increases in quadriceps thickness were estimated for FAIL [0.181 cm (HDI: 0.119 to 0.243); *pd* = 100%] and RIR [0.182 cm (HDI: 0.115 to 0.247); *pd* = 100%] from pre- to post-intervention (Figure 7.3C). The probability of change in quadriceps thickness above the TE of measurement (0.055 cm) was also similar between FAIL (*pd* > TE = 100%) and RIR (*pd* > TE = 100%). Raw measures of RF and VL thickness from pre- to post-intervention are displayed in Appendix D. Greater increases in RF thickness were estimated for RIR [0.193 cm (HDI: 0.114 to 0.264); *pd* > TE = 100%] versus FAIL [0.156 cm (HDI: 0.080 to 0.227); *pd* > TE = 100%] from pre- to post-intervention (Figure 7.4A). However, greater increases in VL thickness were estimated for FAIL [0.205 cm (HDI: 0.134 to 0.277); *pd* > TE = 100%] versus RIR [0.172 cm (HDI: 0.097 to 0.250); *pd* > TE = 100%] from pre- to post-intervention (Figure 7.4A). Estimates for between-protocol differences are shown in Table 7.5 and posterior distributions in Appendix D.

Table 7.5. Estimates of between-protocol differences (i.e., contrast between FAIL and RIR). Negative estimate values favour RIR, and positive estimate values favour FAIL. Probability that a certain estimate exceeded the typical error is only relevant for change in muscle thickness. *pd, probability of direction; TE, typical error.*

Outcome Measure	Estimate (Between-Protocol)	HDI	*pd*	*pd* > *TE*
Change in Muscle Thickness from Pre- to Post-Intervention				
Quadriceps Thickness	–0.001 cm	–0.063 to 0.058	48%	3%
Rectus Femoris	–0.036 cm	–0.113 to 0.047	81%	42%
Vastus Lateralis	0.033 cm	–0.046 to 0.116	79%	22%
Change in Lifting Velocity from the First to Final Set				
Week 1	–5.5%	–10.7% to –0.2%	98%	
Week 4	–6.8%	–12.4% to 1%	99%	
Week 8	–3.2%	–9.2% to 3.1%	85%	
Change in Repetitions Performed from the First to Final Set (Slope Estimates)				
Leg Press	0.3%	–0.2% to 0.8%	86%	
Leg Extension	0.1%	–0.4% to 0.5%	66%	
Volume Load (Slope Estimates)				
Leg Press	–0.83 kg	–1.67 to 0.07	97%	
Leg Extension	–0.11 kg	–0.78 to 0.55	63%	
Repetition Volume (Slope Estimates)				
Leg Press	0 repetitions	–0.17 to 0.19	49%	
Leg Extension	0.13 repetitions	–0.02 to 0.29	95%	

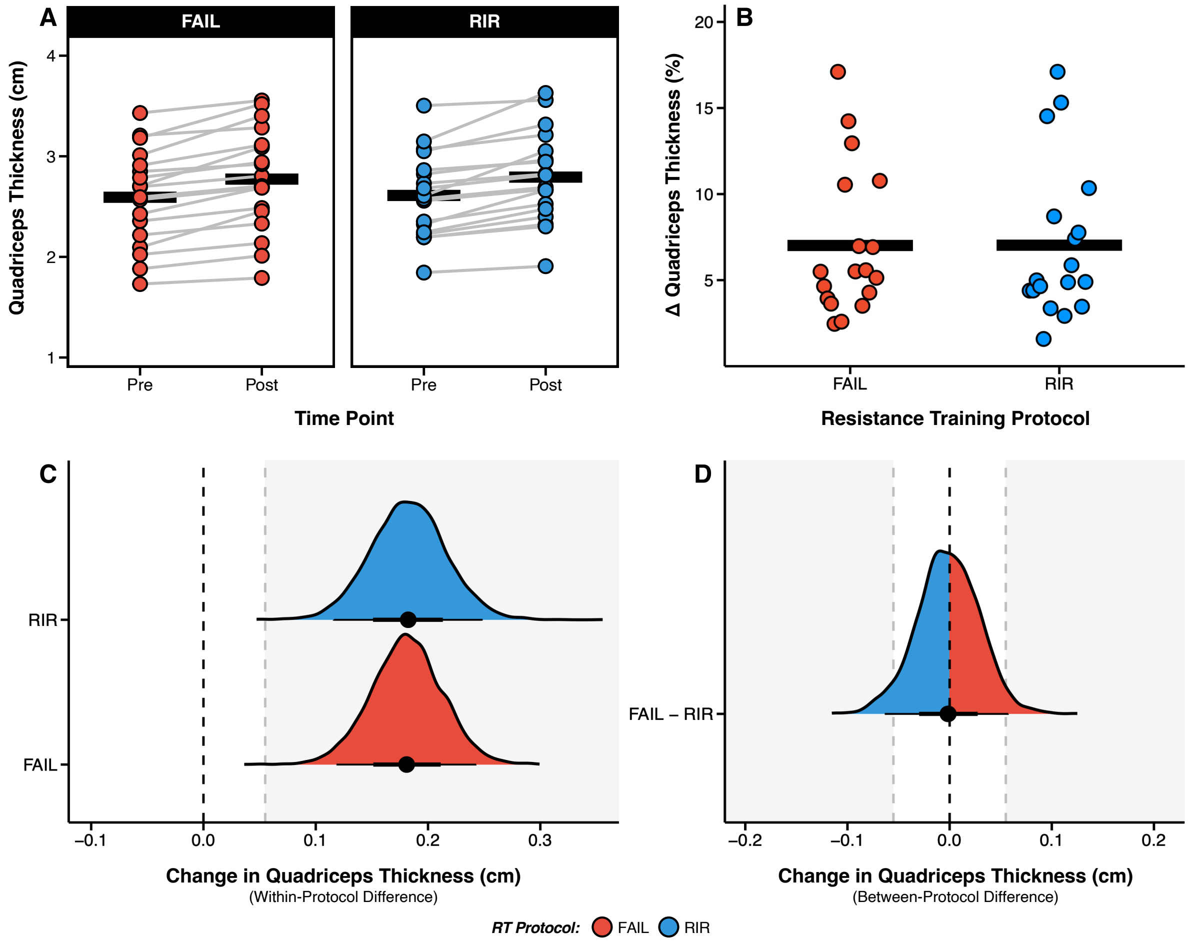

Figure 7.3. Quadriceps thickness at pre- and post-intervention for FAIL and RIR (A), percentage change (B), and with within-protocol (C) and between-protocol (D) posterior distributions. Quadriceps thickness calculated as the average result of raw rectus femoris and vastus lateralis measures. Data shown in Figure A/B are raw values presented as both protocol means and individual values. The SD of protocol means can be found in Appendix D. Figure C and D display posterior distributions that show the central tendency (i.e., point estimate = mean) and highest density credible intervals, with the grey dotted lines indicating the typical error of the measurement and the shaded grey area representing the proportion of the change in quadriceps thickness above the typical error.

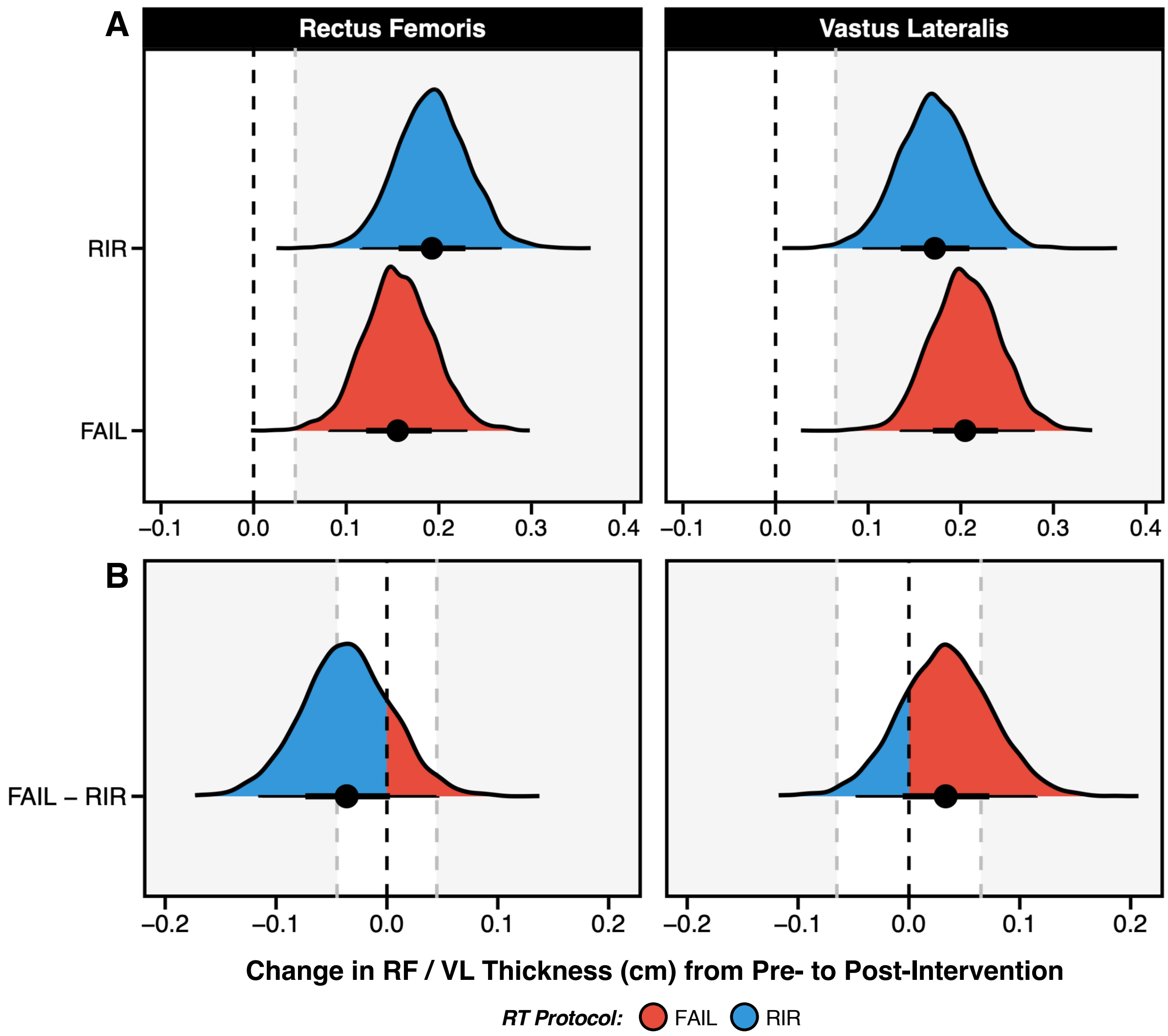

Figure 7.4. Posterior distributions of rectus femoris and vastus lateralis thickness for FAIL and RIR (A) along with between-protocol differences (B). Displayed are the posterior distributions for FAIL and RIR, along with the central tendency (i.e., point estimate = mean) and highest density credible intervals. Grey dotted lines indicate the typical error of the measurement, with the shaded grey area representing the proportion of the change in rectus femoris or vastus lateralis thickness above the typical error.

7.4.5 Change in Lifting Velocity from the First to Final Set

Raw measures of change in lifting velocity (as percentage change) from the first to final set for weeks one, four, and eight are displayed in Figure 7.5. Larger decreases in lifting velocity were estimated for FAIL [–9.9% (HDI: –14.8% to –5%); *pd* = 100%] versus RIR [–4.4% (HDI: –9.1% to 0.7%); *pd* = 98%] in Week 1, for FAIL [–12.6% (HDI: –18% to –7.2%); *pd* = 100%] versus RIR [–5.8% (HDI: –11.1% to –0.5%); *pd* = 99%] in Week 4, and for FAIL [–9.6% (HDI: –15.1% to –3.7 %); *pd* = 100%] versus RIR [–6.4% (HDI: –12% to 0.6%); *pd* = 99%] in Week 8. Estimates for between-protocol differences are shown in Table 7.5 and posterior distributions in Appendix D.

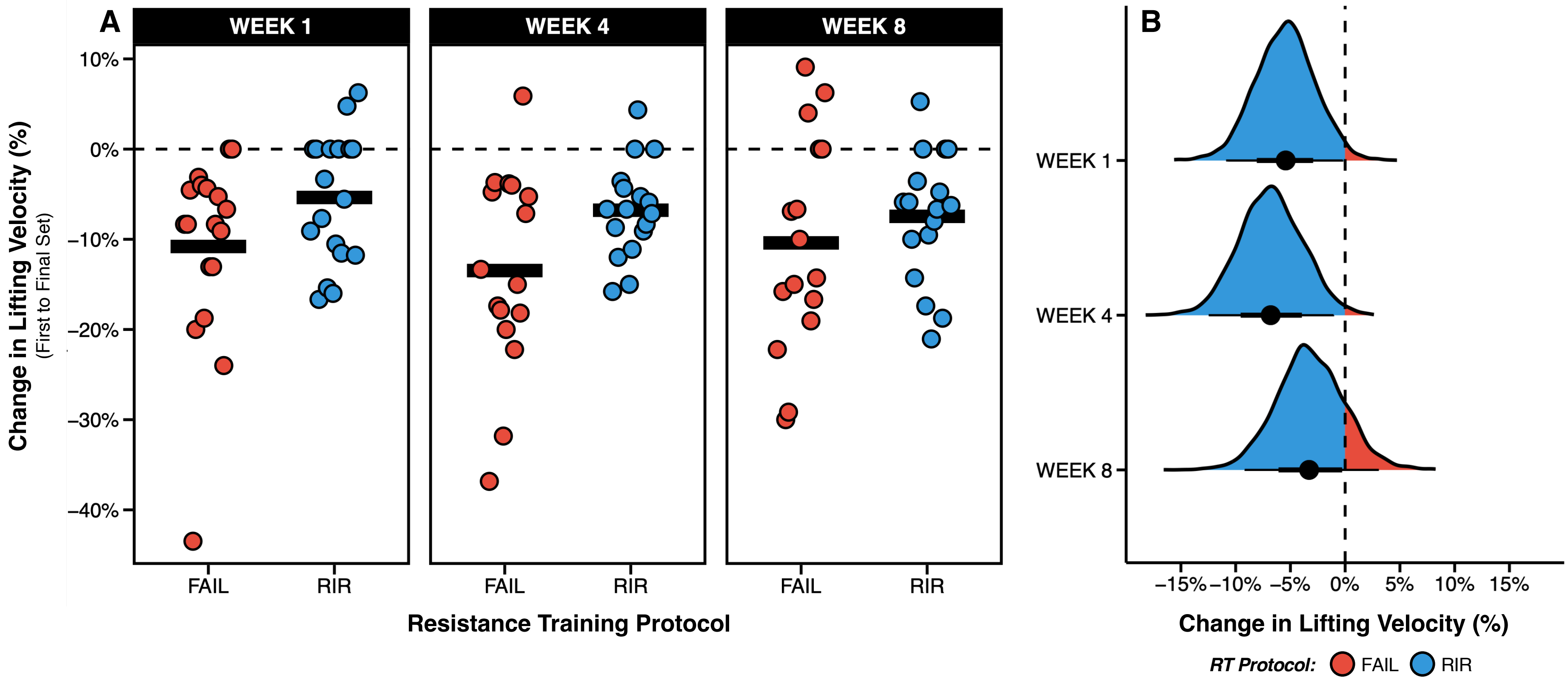

Figure 7.5. Change in lifting velocity (percentage) on the leg press from the first to final set for FAIL and RIR in weeks one, four, and eight (A) and posterior distributions of between-protocol differences (B). Percentage change in lifting velocity calculated as: first set lifting velocity – final set lifting velocity/first set lifting velocity. Data shown in Figure A are raw values presented as both protocol means (with individual values), and the *SD* of protocol means can be found in Appendix D. Figure B displays the posterior distributions for FAIL and RIR, along with the central tendency (i.e., point estimate = mean) and highest density credible intervals.

7.4.6 Change in Repetitions Performed from the First to Final Set

Predicted longitudinal trends for change in repetitions performed (as percentage change) from the first to final set for FAIL and RIR for each session and exercise are displayed in Figure 7.6. When averaged across all sessions, greater repetition loss was found for FAIL [–20.4% (HDI: –27% to –13.9%); *pd* = 100%] versus RIR [–15.8% (HDI: –22.8% to –9.3%); *pd* = 100%] on the leg press, and FAIL [–29.9% (HDI: –33.8% to –25.9%); *pd* = 100%] versus RIR [–21.4% (HDI: –25.8% to –17.6%); *pd* = 100%] on the leg extension. Slope estimates of the change in repetitions performed for each exercise were also calculated for FAIL [Leg Press = –0.3% (HDI: –1% to 0.2%); *pd* = 86%, Leg Extension = 0.4% (HDI: 0% to 0.7%); *pd* = 98%] and RIR [Leg Press = –0.6% (HDI: –1.2% to 0.1%); *pd* = 97%, Leg Extension = 0.3% (HDI: 0.1% to 0.7%); *pd* = 94%]. Posterior distributions for between-protocol differences are shown in Appendix D and estimates for between-protocol differences in Table 7.5.

7.4.7 Volume Load and Repetition Volume

Predicted longitudinal trends for volume load for FAIL and RIR for each session and exercise are displayed in Figure 7.6. When averaged across all sessions, similar mean volume load was found between FAIL [350 kg (HDI: 290 to 406); *pd* = 100%] and RIR [346 kg (HDI: 290 to 406); *pd* = 100%] on the leg press, and FAIL [129 kg (HDI: 114 to 143); *pd* = 100%] and RIR [131 kg (HDI: 116 to 145); *pd* = 100%] on the leg extension. Slope estimates of volume load for each exercise were also calculated for FAIL [Leg Press = 5.70 kg (HDI: 3.92 to 7.26); *pd* = 100%, Leg Extension = 0.71 kg (HDI: –0.12 to 1.47); *pd* = 96%] and RIR [Leg Press = 6.53 kg (HDI: 4.73 to 8.14); *pd* = 100%, Leg Extension = 0.81 kg (HDI: 0.02 to 1.63); *pd* = 97%].

Predicted longitudinal trends for repetition volume for FAIL and RIR for each session and exercise are displayed in Figure 7.6. When averaged across all sessions, similar mean repetition volume was found between FAIL [27 repetitions (HDI: 25 to 29); *pd* = 100%] and RIR [25 repetitions (HDI: 24 to 27); *pd* = 100%] on the leg press, and FAIL [31 repetitions (HDI: 29 to 32); *pd* = 100%] and RIR [32 repetitions (HDI: 31 to 34); *pd* = 100%] on the leg extension. Slope estimates of repetition volume for each exercise were also calculated for FAIL [Leg Press = –0.24 repetitions (HDI: –0.40 to –0.09); *pd* = 100%, Leg Extension = 0.25 repetitions (HDI: 0.13 to 0.37); *pd* = 100%] and RIR [Leg Press = –0.24 repetitions (HDI: –0.43 to –0.06); *pd* = 99%, Leg Extension = 0.13 repetitions (HDI: –0.04 to 0.30); *pd* = 94%]. Posterior distributions for between-protocol differences are shown in Appendix D and 4.3 and estimates for between-protocol differences in Table 7.5.

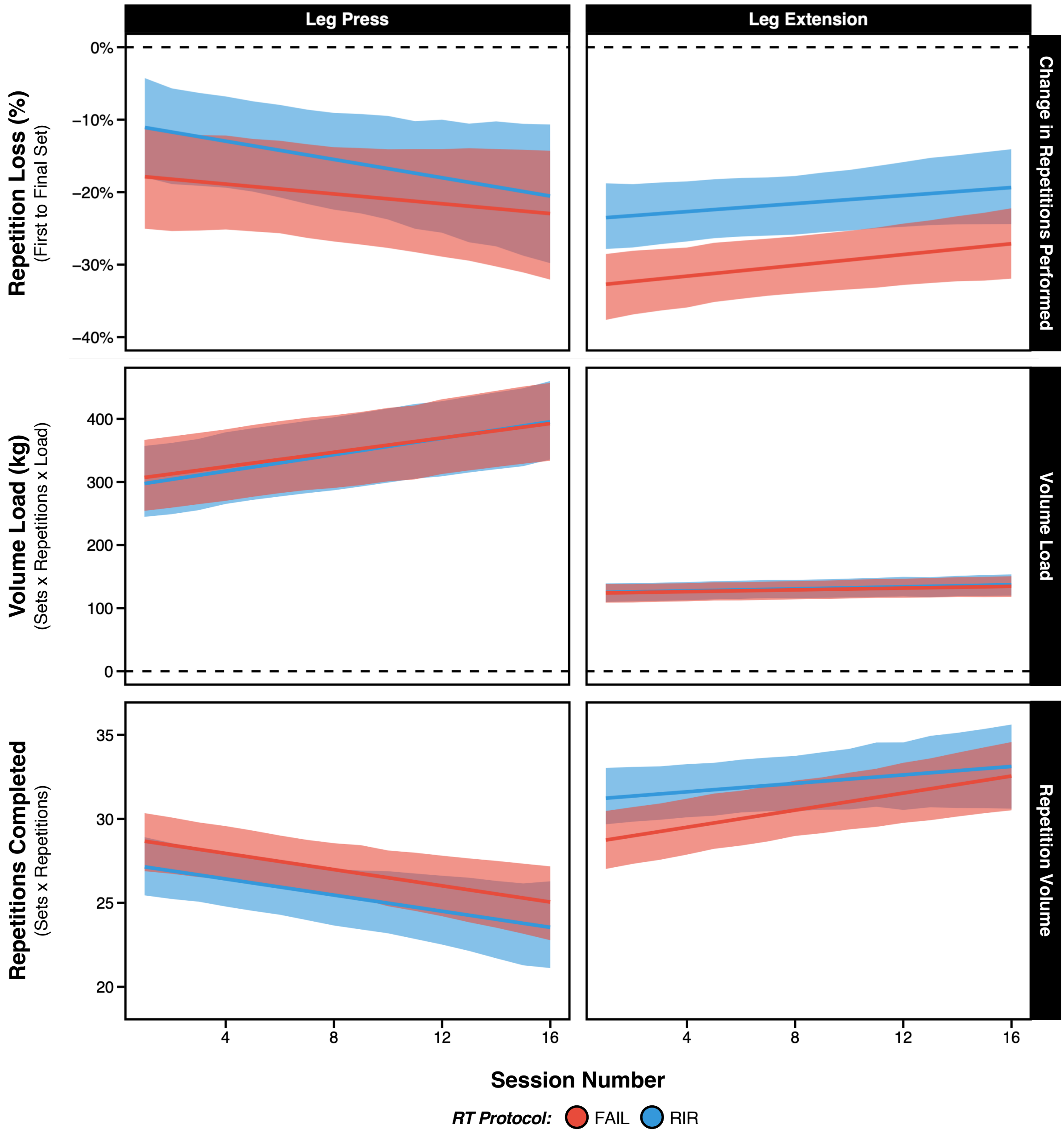

Figure 7.6. Predicted longitudinal trends for change in repetitions performed, volume load, and repetition volume on each exercise for FAIL and RIR across all sessions. Displayed are the predicted longitudinal trends (i.e., means marginalised across categorical variables) for each outcome measure analysed (i.e., indicated by the lines) and the highest density credible intervals (i.e., shaded area).

7.5 Discussion

7.5.1 Muscle Hypertrophy

We found a similar increase in quadriceps thickness (i.e., average of RF and VL) after eight weeks of RT performed to either FAIL (+6.96%) or RIR (+6.98%) in resistance-trained males and females, with a 48% probability ($pd > TE = 3\%$) that any potential difference between the protocols exists. These changes in quadriceps thickness were unlikely due to measurement error, but rather, hypertrophy of the targeted musculature (Figure 7.3C). Moreover, we found an 81% probability ($pd > TE = 42\%$) of slightly greater RF thickness when RT was performed to RIR (+7.38%) versus FAIL (+5.98%), but a 79% probability ($pd > TE = 22\%$) of slightly greater VL thickness when RT was performed to FAIL (+7.95%) versus RIR (+6.59%). Overall, these findings demonstrate that in resistance-trained males and females, terminating sets at 1- to 2-RIR promotes similar overall quadriceps hypertrophy to reaching momentary muscular failure over eight weeks of RT, but the influence of proximity-to-failure on muscle-specific hypertrophy may depend on other factors (e.g., muscle group measured, exercises performed etc.).

Our findings of similar quadriceps hypertrophy between FAIL and RIR (Figure 7.3) align with previous studies [47, 74] and meta-analyses [11, 12, 115] in resistance-trained individuals. For example, our meta-analysis [115] found no statistically significant difference between i) RT performed to momentary muscular failure versus non-failure across five studies (n = 3 untrained; n = 2 resistance-trained), or ii) between moderate and high velocity loss thresholds across six studies in resistance-trained individuals. However, ambiguity of the proximities-to-failure achieved in non-failure RT groups, and different definitions of set failure used across studies [97, 140, 141], makes it difficult to confidently infer the influence of specific RIR values on muscle hypertrophy from previous research. Indeed, a recent meta-regression of estimated RIR values highlights that greater muscle hypertrophy seems to occur when sets are terminated closer to momentary muscular failure [153], but whether closer proximities-to-failure are *always* better for muscle hypertrophy remains equivocal. For example, both Santanielo et al. [47] and Andersen et al. [74] reported similar quadriceps hypertrophy (RF and VL) following RT performed to momentary muscular failure versus non-failure or high versus moderate velocity loss thresholds (i.e., closer versus further proximities-to-failure), respectively, in resistance-trained individuals. Taken as a whole, we provide further evidence that an adequate set volume coupled with close proximities-to-failure, rather than reaching momentary muscular failure *per se*, are key stimulators of muscle hypertrophy in resistance-trained individuals.

Despite similar quadriceps hypertrophy observed between protocols, greater VL hypertrophy occurred in FAIL versus RIR while greater RF hypertrophy occurred in RIR versus FAIL (Figure 7.4). Similarly, Andersen et al. [74] observed that RT performed to a high velocity loss (~40%) promoted slightly greater VL versus RF hypertrophy, and a moderate velocity loss (~20%) promoted slightly greater RF versus VL hypertrophy, but no between-group differences were found. Considering that the leg press was performed before the leg extension in the present study and by Andersen et al. [74], it is possible that performing RT to, or very close to momentary muscular failure on the leg press maximised hypertrophy of the VL, but when the leg extension was subsequently performed in a fatigued state, hypertrophy of the RF was impaired. Conversely, performing RT further from momentary muscular failure on the leg press may have compromised hypertrophy of the VL but allowed for greater hypertrophy of the RF from the leg extension. Indeed, previous research has found that the RF is highly activated and subsequently hypertrophied from the leg extension compared to other quadricep exercises (e.g., squat and leg press) that involve simultaneous hip and knee flexion [159, 160].

The findings of the present study thus highlight that muscle-specific hypertrophy may be influenced by the proximity-to-failure reached in given exercises, their order within a RT session, and the subsequent musculature targeted.

Although proximity-to-failure is a key RT variable that influences muscle hypertrophy, other variables like total volume and load also need to be considered in RT prescription. The set volume for each participant was equal to what they habitually performed in their previous training [156] and was increased by 20% halfway through the RT intervention. Our results are therefore based on performing 10 to 17 sets for a given muscle group per week, indicating the relationship between proximity-to-failure and muscle hypertrophy may be stable across this range of set volumes, on average. This is an informative finding given set volumes employed in practice likely vary widely across individuals. Additionally, although a wide range of relative loads may induce muscle hypertrophy [161], we employed 8-12-RM loads to reduce perceived discomfort, neuromuscular fatigue, and muscle damage [63, 66, 69, 70], and improve individual RIR accuracy [81]. Whether similar muscle hypertrophy would be observed between FAIL and RIR if lower loads (>15-RM) were employed is unclear, as performing RT with closer proximities-to-failure may be more important for simulating muscle hypertrophy when lower versus higher loads are lifted [46]. Overall, the set volumes and loads we employed represent a practically-relevant RT intervention for resistance-trained individuals.

7.5.2 Neuromuscular Fatigue

We observed greater decreases in lifting velocity from the first to final set for FAIL versus RIR in weeks one, four, and eight, indicating acute neuromuscular fatigue is higher when terminating sets at momentary muscular failure versus 1- to 2-RIR. For example, FAIL experienced decreases in lifting velocity on the leg press that ranged from –9.6% to –12.6%, with lower decreases in lifting velocity in RIR from –4.4% to –6.4%. Similarly, greater repetition loss from the first to final set (when averaged across all sessions of the RT intervention) was observed for FAIL versus RIR on the leg press (–20.4% versus –15.8%) and leg extension (–29.9% versus –21.4%). Indeed, greater repetition loss for FAIL versus RIR was sustained on both exercises across the RT intervention, with repetition loss gradually increasing for both RT protocols on the leg press but decreasing on the leg extension (Figure 7.6). These findings corroborate previous research [13, 139] showing that proximity-to-failure influences acute neuromuscular fatigue, with FAIL experiencing greater decreases in lifting velocity and repetitions performed across sets compared to RIR. To our knowledge, this is the first study to assess neuromuscular fatigue longitudinally between RT protocols differing in proximity-to-failure.

Similar to the findings of the present study, we previously examined the influence of specific proximities-to-failure on neuromuscular fatigue by employing an RIR-based approach to set termination and found greater decreases in lifting velocity when momentary muscular failure was reached versus a perceived 1-RIR and 3-RIR [139]. Like much of the relevant literature, our previous study [139] was conducted acutely; this is relevant as the effect of proximity-to-failure on neuromuscular fatigue may be attenuated with repeated bouts of RT [96]. As such, the present study examined surrogate measures of neuromuscular fatigue across the whole RT intervention. Although loss of lifting velocity on the leg press was consistently greater for FAIL versus RIR, the difference between protocols was smaller in week eight (–3.2%; *pd* = 85%) compared to week four (–6.8%; *pd* = 99%) and week one (–5.5%; *pd* = 98%). Similarly, we observed larger differences in repetition loss on the leg press between FAIL and RIR in the earlier stages of the RT intervention versus the latter (FAIL > RIR); repetition loss increased further for RIR overtime versus FAIL, suggesting that some participants performing RT to

FAIL experienced improved intra-set fatigability or tolerance to the RT stimulus (i.e., fatigue resistance). Conversely, although repetition loss for the leg extension was consistently greater across the RT intervention for FAIL versus RIR, both FAIL and RIR experienced less repetition loss as the RT intervention persisted, providing evidence for improved fatigue resistance overtime. Indeed, the lower neuromuscular fatigue experienced by RIR (versus FAIL) on the leg press may have been inadequate to promote fatigue resistance, but allowed for fatigue resistance on the leg extension, which was performed in a fatigued state. Overall, our primary findings highlight that i) acute neuromuscular fatigue is consistently greater over eight weeks when momentary muscular failure is reached versus when sets are terminated at 1- to 2-RIR, and ii) acute neuromuscular fatigue can decrease across weeks of a RT intervention but this may depend on the exercises performed and the RT stimulus.

7.5.3 Volume Load and Repetition Volume

Repetition volume and volume load were deliberately not equalised to determine the potential influence of proximity-to-failure on volume accumulation. Nonetheless, we observed similar mean volume load and repetition volume for FAIL and RIR on both exercises with similar trends across the RT intervention (Figure 7.6). Although reaching momentary muscular failure theoretically maximises the RT stimulus experienced in a given set, the increased neuromuscular fatigue and muscle damage compared to non-failure RT [97] may reduce the volume completed across subsequent sets, and ultimately, the total RT stimulus experienced. Therefore, it is possible that the similar quadriceps hypertrophy observed between FAIL and RIR may be explained by the similar RT volumes achieved [112, 162], rather than differences in proximity-to-failure *per se*. Further, although we found similar repetition volume on both exercises, it is possible that repetition volume may depend on exercise order, particularly if more than two exercises for the same muscle group are performed consecutively; for example, performing sets to momentary muscular failure may maximise repetition volume in earlier exercises of a RT session, but compromise it in subsequent exercises. Considering that RT to momentary muscular failure results in similar volume load and repetition volume as a perceived 1- to 2-RIR, possibly influencing the overall RT stimulus achieved, the potential interaction between proximity-to-failure and other RT variables needs to be considered in RT prescription for muscle hypertrophy.

7.5.4 Strengths and Limitations of Current Research

Our sample of participants had the highest reported RT experience (7.8 ± 2.6 and 7.5 ± 2.3 years for males and females, respectively) of any study comparing RT to set failure versus non-failure or to different velocity loss thresholds [47, 53, 71-74, 98, 99]. This included an average RT frequency of 4.72 days per week, and 50% of participants having competed in strength and/or physique sports. Although muscle hypertrophy following RT is likely similar between sexes [163], measures of neuromuscular fatigue and volume accumulation may differ [139]. Thus, our statistical models included 'sex' as a population-level effect; however, we didn't specifically analyse sex differences as this was not a research question. To limit the potential influence of our unilateral design on the outcomes, we altered the starting limb of each session (i.e., the full RT protocol was completed on one limb, before the second RT protocol was completed on the following limb). This approach provided each limb an equal number of starting opportunities, as performance of the following limb may be impaired due to neuromuscular fatigue. Moreover, the change in lifting velocity was only measured on the starting limb to ensure standardised comparisons between RT protocols. Considering limb dominance may influence RT performance, we ensured an equal number of dominant limbs were assigned to each RT protocol. Our statistical models also accounted for dependency between observations (i.e., correlations between limbs), whereby observations for each limb were nested within each participant. Considering each participant's set volume varied and increased (by 20%) halfway through the intervention, we included 'number of sets performed' as a population-level effect in the relevant statistical models. Although RIR accuracy throughout the RT intervention is unclear, the results of our initial RIR accuracy assessment (Table 7.3) provide confidence that set termination regularly occurred close to the target 1- and 2-RIR. Finally, whether our results can be generalised to other exercises and/or muscle groups is unclear as it is possible that muscles may respond differentially. Our ultrasound scans only involved one measurement site on the RF and VL, respectively, and as such, we are also unable to discern regional changes in muscle thickness.

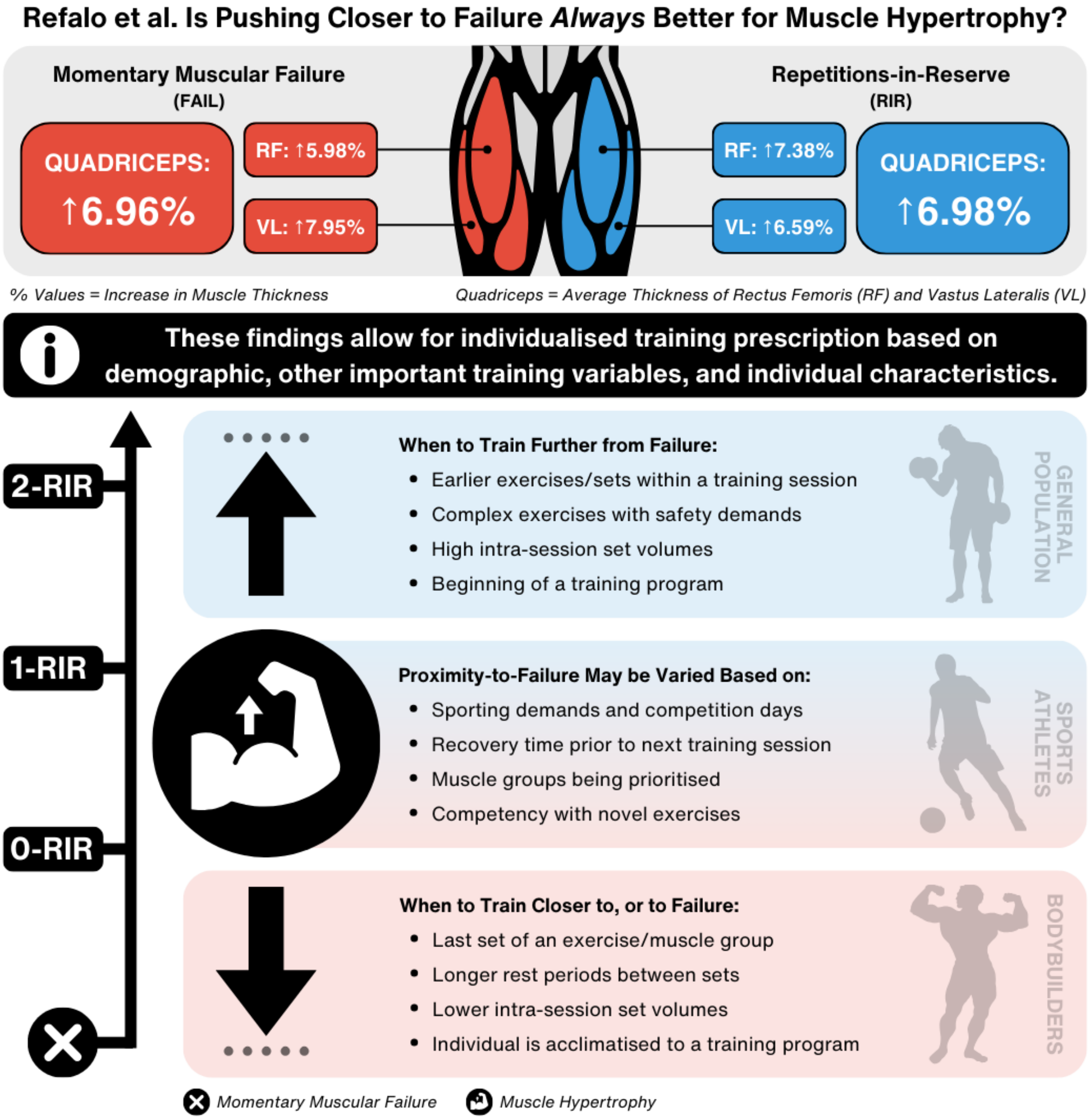

Figure 7.7. Graphical overview of key findings and practical applications. Resistance training variables (e.g., volume, load lifted, exercise order) other than proximity-to-failure that contribute to the resistance training stimulus, along with individual characteristics (e.g., fatigability), also need to be considered in resistance training prescription. Rather than being strict instructions, the demographic recommendations shown (via the silhouettes) are examples of how the target proximity-to-failure during resistance training may vary across individuals.

7.6 Conclusion

Overall, we observed that terminating sets with a perceived 1- to 2-RIR can be sufficient to promote similar hypertrophy of the quadriceps as reaching momentary muscular failure in resistance-trained individuals over eight weeks. Our findings also highlight that muscle-specific hypertrophy may depend on exercise selection, order, and subsequent musculature targeted. Importantly, our sample of participants were able to predict RIR within one repetition from the target RIR, and whether higher or lower RIR accuracy would influence our results is unclear. Performing RT with 1- to 2-RIR also allows for similar volume load and repetition volume accumulation as reaching momentary muscular failure, possibly influencing the overall RT stimulus achieved. Indeed, repetition loss from the first to the final set was greater when sets were terminated at momentary muscular failure versus with 1- to 2-RIR, likely contributing to the similar volume observed between protocols. Although performing RT to momentary muscular failure consistently induced higher levels of neuromuscular fatigue versus RT performed with 1- to 2-RIR, we observed improved fatigue resistance that may have attenuated neuromuscular fatigue and subsequent repetition loss across eight weeks. To our knowledge, the present study is the first to compare RT performed to momentary muscular failure versus with RIR on muscle hypertrophy and neuromuscular fatigue over an 8-week intervention period in resistance-trained males and females, further advancing the understanding of proximity-to-failure and providing practical recommendations that can be applied across different demographics (i.e., general population, sports athletes, bodybuilders).

Chapter Eight – General Discussion and Conclusions

8.1 Overview

The objective of this thesis was to explore the influence of RT proximity-to-failure on muscle hypertrophy and short-term responses to RT (i.e., neuromuscular fatigue and perceived discomfort, exertion, muscle soreness, and general feelings) while addressing critical research limitations and improving practical recommendations for RIR prescription. A comprehensive scoping review of the literature was conducted, followed by a meta-analysis and three experimental studies. The findings of each were used to inform the methods of subsequent studies and fill research gaps. For example, considering studies included in the scoping review and meta-analysis (Study One) did not employ RIR prescription, the subsequent experimental studies implemented RIR prescription as a set termination method to better inform practical applications. Studies Two and Three offered novel insights into the effect of RIR on neuromuscular fatigue and perceptual responses, and intra-set RIR prediction accuracy, whilst filling research gaps that were identified in the scoping review. Considering intra-set RIR prediction was deemed a valid set termination strategy (Study Three), Study Four compared the effect of RT to momentary muscular failure versus with 1- to 2-RIR on muscle hypertrophy over an 8-week intervention. Study Four therefore aimed to i) inform the influence of RIR on muscle hypertrophy, which Study One could not due to uncertainties in the RIR of non-failure RT groups, and ii) investigate neuromuscular fatigue across the intervention, not just acutely as in Study Two. This thesis provides comprehensive and novel insights into the influence of RT proximity-to-failure on relevant outcome measures.

8.2 Summary of Thesis Findings

8.2.1 State of Current Literature

Prior to this thesis, the impact of proximity-to-failure on muscle hypertrophy and short-term responses had been researched dichotomously, such that, RT performed to set failure was compared with non-failure. The scoping review found that proximity-to-failure in non-failure RT groups was ambiguous and varied widely across the literature, rendering the conclusions derived insufficient to offer practical set termination strategies to promote muscle hypertrophy and minimise neuromuscular fatigue. Further reducing the practical applicability of these research findings are conclusions based solely on statistical significance thresholds. When conclusions from previous research studies state that *"no difference between RT to failure versus RT not to failure is observed on muscle hypertrophy"* [12] or *"RT performed to failure leads to greater acute fatigue compared with RT not performed to failure"* [13], readers may i) interpret that RT should never be performed to momentary muscular failure, or ii) may dismiss the role of proximity-to-failure in promoting muscle hypertrophy. The definition of set failure also varies widely across the literature, with some studies explicitly reporting the definition used and others just stating 'failure' was reached. Therefore, whether momentary muscular failure (the most objective definition of set failure) is reached is at times unclear, further hindering practical interpretations. Moreover, the scoping review only retrieved one study that used RIR prescription to inform set termination [52]; this scarcity of RIR-related research is possibly due to the subjective nature of RIR predictions or their perceived inaccuracy that may lead researchers to choose other set termination methods.

8.2.2 Influence of Proximity-to-Failure on Muscle Hypertrophy

To address the research limitations identified in the scoping review, a meta-analysis (Study One) was conducted to extend the findings of previous meta-analyses [11, 12, 79] and improve subsequent interpretations. Instead of simply concluding that no statistically significant difference was found between RT groups, the meta-analysis concluded that it *"found no evidence to support that RT performed to momentary muscular failure is superior to non-failure RT for muscle hypertrophy."* Although inspection of effect sizes indicates a trivial advantage of performing RT to momentary muscular failure versus non failure on muscle hypertrophy [ES = 0.12 (95% CI: –0.13 to 0.37), P = 0.343], no statistically significant difference between groups was found. Importantly, studies meta-analysed within Theme A employed momentary muscular failure, but the proximity-to-failure reached in non-failure RT groups likely varied across studies, perhaps influencing the results. For example, performing RT to momentary muscular failure may be superior to ~5-RIR for muscle hypertrophy but may produce similar muscle hypertrophy to ~1-RIR. This highlights a potential non-linear relationship between proximity-to-failure and muscle hypertrophy, whereby muscle hypertrophy increases as sets are terminated closer to momentary muscular failure, but only to a certain point. However, the meta-analysis could not inform a potential non-linear relationship, requiring further research specifically investigating the RIR of set termination. The meta-analysis also compared studies that employed any definition of set failure (other than momentary muscular failure) versus non-failure (Theme B), and studies that compared different velocity loss thresholds to inform set termination (Theme C). These themes compared closer versus further proximities-to-failure, as not all definitions of set failure and nor all high velocity loss groups reached momentary muscular failure on every set performed. Although no statistically significant differences were identified between i) set failure versus non-failure [ES = 0.27 (95% CI: –0.03 to 0.57), P = 0.077], and ii) high versus moderate velocity loss thresholds [ES = 0.08 (95% CI: –0.16 to 0.32), P = 0.529], effect sizes favoured groups that performed RT closer to momentary muscular failure. Overall, despite the possibility of a trivial to small advantage of performing RT closer to momentary muscular failure, there is currently no statistically significant evidence to support a superior effect of RT to momentary muscular failure versus non-failure and to high versus moderate velocity loss thresholds.

Study Four was designed to better understand the difference between RT performed to momentary muscular failure versus 1- to 2-RIR on muscle hypertrophy. To our knowledge, this is the first study reporting the effect of specific RIR on muscle hypertrophy. Terminating sets with a perceived 1- to 2-RIR promoted similar hypertrophy of the quadriceps as reaching momentary muscular failure in resistance-trained individuals over eight weeks, however, performing RT to momentary muscular failure induced slightly greater changes in VL thickness whereas RF thickness was greater following RT with 1- to 2-RIR. Considering the leg press was performed before the leg extension, it is therefore possible that RT to (or close to) momentary muscular failure on the first exercise for a given muscle group promotes maximum muscle hypertrophy but may compromise muscle hypertrophy from subsequent exercises for the same muscle group (possibly due to neuromuscular fatigue lessening volume load on subsequent exercises). Overall, although similar muscle hypertrophy occurred following RT to momentary muscular failure and with 1- to 2-RIR, the influence of proximity-to-failure on muscle hypertrophy may depend on the specific muscles involved and other RT variables (e.g., relative load, volume load, exercise order etc.).

Importantly, only one [47] of five [43-46] studies analysed in Study One (Theme A) were conducted on resistance-trained individuals, making it unclear whether the findings apply to resistance-trained demographics. However, the Study Four sample had a higher RT experience than any study included in Study One, providing practical recommendations for athletes and bodybuilders. To better contextualise the findings of Study Four within the relevant literature, an updated meta-analysis of Theme A was performed including Study Four, which met Theme

A's inclusion criteria. This updated meta-analysis is shown in Figure 8.1 and summarised in Table 8.1 alongside the original [115] and previous [11, 12, 79] meta-analyses. After Study Four's inclusion, the ES still favoured RT to momentary muscular failure [ES = 0.09 (CI: –0.12 to 0.31); $P = 0.395$] but the ES was smaller [ES = 0.12 (95% CI: –0.13 to 0.37), $P = 0.343$] and still non-significant. One factor that may explain the ES values for muscle hypertrophy favouring RT performed to set failure across all relevant meta-analyses (Table 8.1) were the proximities-to-failure achieved in the non-failure RT groups. For example, the non-failure RT group in Martorelli et al. [44] performed seven repetitions with 70% of 1-RM. According to the National Strength & Conditioning Association [164], an average of 12 repetitions can be performed to momentary muscular failure with 70% of 1-RM, meaning participants in Martorelli et al. [44] likely terminated sets at ~5-RIR. Conversely, Study Four compared RT to momentary muscular failure versus with 1- to 2-RIR and observed similar muscle hypertrophy. Overall, despite a trivial effect size favouring RT to momentary muscular failure, the updated meta-analysis including Study Four also found no statistically significant evidence to support that performing RT to momentary muscular failure is superior to non-failure for muscle hypertrophy.

Table 8.1. Summary of original and previous meta-analyses comparing resistance training performed to set failure versus non-failure or to different velocity loss thresholds. Updated meta-analysis results of Study One (Theme A), including findings from Study Four, are shown in parentheses. *VeL, velocity loss; ↑ = increased; ↔ = no difference between groups.*

Study	Comparison	*N* Studies	RT Experience	Key Finding	ES	CI	*P*-Value
Grgic et al. 2021 [11]	Set failure vs. non-failure	7	Resistance-trained (*n* = 2) Untrained (*n* = 5)	↔ Muscle hypertrophy between set failure vs. non-failure.	0.22	–0.11 to 0.55	0.152
Vieira et al. 2021 [12]	Set failure vs. non-failure	4	Untrained (*n* = 4)	↑ Muscle hypertrophy for set failure vs. non-failure when volume was not equated.	0.82	0.09 to 1.56	0.028
				↔ Muscle hypertrophy between set failure vs. non-failure when volume was equated.	0.59	–0.39 to 1.58	0.239
Hickmott et al. 2022 [79]	Lower VeL (<25%) vs. higher VeL (>25%)	3	Resistance-trained (*n* = 3)	↑ Muscle hypertrophy for higher VeL vs. lower Vel.	0.28	0.05 to 1.16	0.03
Refalo et al. 2022 [115]							
Theme A	Momentary muscular failure vs. non-failure	5 (6)	Resistance-trained (*n* = 2) Untrained (*n* = 4)	↔ Muscle hypertrophy between momentary muscular failure vs. non-failure.	0.12 (0.09)	–13 to 0.37 (–0.12 to 0.31)	0.343 (0.395)
Theme B	Set failure vs. non-failure	4	Resistance-trained (*n* = 1) Untrained (*n* = 3)	↔ Muscle hypertrophy between set failure vs. non-failure.	0.27	–0.03 to 0.57	0.077
Theme C	Moderate VeL (20-25%) vs. high VeL (>25%)	6	Resistance-trained (*n* = 6)	↔ Muscle hypertrophy between moderate VeL vs. high VeL.	0.08	–0.16 to 0.32	0.529

Study	Measure	Non-Failure Mean	Non-Failure *SD*	Set Failure Mean	Set Failure *SD*	Weights	SMD [95% CI]
Lacerda et al. 2020.1	VL	11.40	12.54	8.54	12.12	5.66%	−0.22 [−1.10, 0.66]
Lacerda et al. 2020.2	RF	2.99	4.14	2.13	4.39	5.66%	−0.19 [−1.07, 0.69]
Lasevicius et al. 2019.1	Quads	6.40	7.55	6.70	8.33	7.34%	0.04 [−0.73, 0.81]
Lasevicius et al. 2019.2	Quads	2.20	10.36	6.60	10.30	6.66%	0.41 [−0.40, 1.22]
Martorelli et al. 2017.1	EF	1.57	4.38	3.29	6.81	16.55%	0.30 [−0.20, 0.80]
Martorelli et al. 2017.2	EF	0.45	6.20	3.29	6.81	15.13%	0.43 [−0.10, 0.95]
Nobrega et al. 2018.1	VL	1.50	4.03	1.60	3.50	7.60%	0.03 [−0.73, 0.78]
Nobrega et al. 2018.2	VL	1.40	3.64	1.70	3.89	7.59%	0.08 [−0.68, 0.83]
Santanielo et al. 2020	VL	5.50	4.47	4.30	3.86	7.80%	−0.28 [−1.02, 0.47]
Refalo et al. 2023.1	VL	0.17	0.46	0.20	0.53	10.02%	0.06 [−0.59, 0.72]
Refalo et al. 2023.2	RF	0.19	0.23	0.16	0.27	10.01%	−0.14 [−0.80, 0.51]
Total						100%	0.09 [−0.12, 0.31]

Heterogeneity: Q = 5.22, df = 10 (P = 0.876), I^2 = 4.5%

Test for overall effect: Z = 0.851 (P = 0.395)

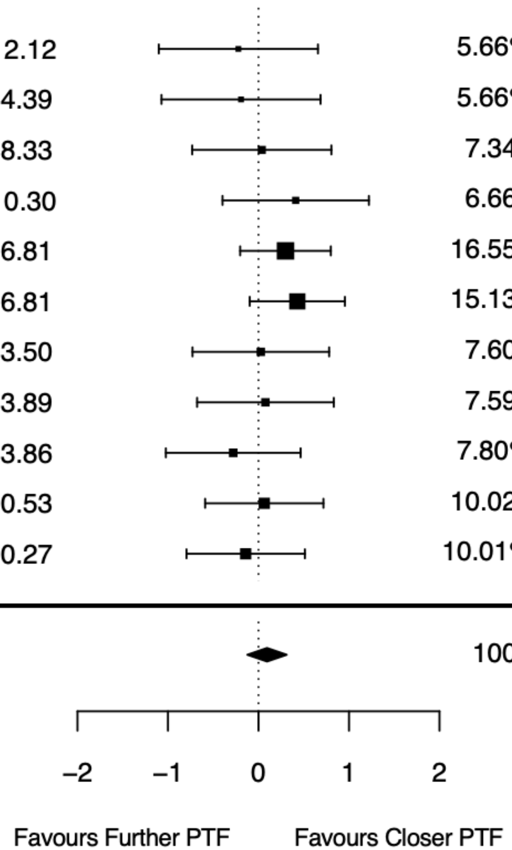

Figure 8.1. Updated meta-analysis of Theme A studies. Updated meta-analysis of studies in Theme A (presented in Study One) with the addition of Study Four data.

8.2.3 Influence of Proximity-to-Failure on Measures of Neuromuscular Fatigue

Study Two compared the barbell bench presses performed to momentary muscular failure versus 1-RIR and 3-RIR, allowing insight into the relationship between RT proximity-to-failure and neuromuscular fatigue. Because Study Two involved single sessions of RT, and fatigue responses are likely to change as individuals adapt to an exercise stimulus [136], acute neuromuscular fatigue was also assessed across the entire Study Four intervention. Data of lifting velocity and repetition loss from the first to final set from Studies Two and Four are reported in Table 8.2. For Study Four, data has been separated into weeks one and eight, to display possible differences from the start to the end of the RT intervention (Table 8.2). Taken together, these findings suggest acute neuromuscular fatigue increases linearly as sets are terminated closer to momentary muscular failure in upper- and lower-body muscle groups, as lifting velocity and repetition loss (from the first to final set) increase when RT is performed to momentary muscular failure versus 1-RIR, 2-RIR, and 3-RIR. However, the magnitude of repetition loss decreased longitudinally in Study Four on the leg extension exercise, suggesting that fatigue resistance may improve over time. The effect of proximity-to-failure on acute neuromuscular fatigue may also be influenced by biological sex, as greater acute neuromuscular fatigue occurred in males in Study Two when RT was performed to momentary muscular failure, but not with RIR. This thesis supports a linear relationship between proximity-to-failure and neuromuscular fatigue, whereby terminating sets closer to momentary muscular failure induces higher neuromuscular fatigue, likely more so in males versus females; however, resistance to fatigue may develop over time depending on the exercise performed, reducing its overall impact on repetition loss.

Table 8.2. Summary of results from measures of neuromuscular fatigue in Studies Two and Four. Changes in lifting velocity and repetitions performed are assessed from the first to the final set, of which the number of sets performed varied across the two studies. Study Two involved the bench press exercise, and Study Four involved the leg press and leg extension

exercises. Study Four displays data for weeks one and eight, separately, to highlight potential differences across the intervention period. Percentage values indicate the decrease in lifting velocity or repetitions performed. Values for Study Four are intervention averages. *W1, week one; W8, week eight.*

Study	Lifting Velocity Loss				Repetition Loss			
	3-RIR	2-RIR	1-RIR	FAIL	3-RIR	2-RIR	1-RIR	FAIL
All Participants (Males and Females Combined)								
2	–5.1%	-	–10.6%	–24.3%	–27.2%	-	–40.2%	–54.5%
4 (W1)	-	–5.4%	-	–10.8%	-	–15.6%	-	–27.6%
4 (W8)	-	–7.5%	-	–10.4%	-	–22.6%	-	–30.9%
Males								
2	–8.7%	-	–11.2%	–29%	–29.9%	-	–43.7%	–59.3%
4 (W1)	-	–7.5%	-	–12.4%	-	–16.7%	-	–30%
4 (W8)	-	–7.3%	-	–12.3%	-	–22.9%	-	–32.5%
Females								
2	–1.4%	-	–9.9%	–19.4%	–25.2%	-	–37.4%	–50.8%
4 (W1)	-	–1.1%	-	–7.5%	-	–13.6%	-	–23%
4 (W8)	-	–6.1%	-	–8.2%	-	–22%	-	–28%

8.2.4 Influence of Proximity-to-Failure on Perceptual Responses

Study Two also assessed the influence of proximity-to-failure on perceived discomfort, exertion, recovery, muscle soreness and general feelings. Perceptual responses to different proximities-to-failure are under researched, with only two studies [14, 67] in the scoping review assessing perceived discomfort. In line with previous research [14, 67], Study Two found that i) perceived discomfort and exertion increased gradually as proximity-to-failure neared, ii) general feelings following RT were similar for FAIL and 1-RIR, but worse for FAIL and 1-RIR compared to 3-RIR, iii) perceived muscle soreness was greater for FAIL versus 3-RIR at both 24- and 48-hrs post-exercise, but was only greater for FAIL versus 1-RIR at 24-hrs post-exercise, and iv) perceived recovery was lower for FAIL versus both 1-RIR and 3-RIR at both 24- and 48-hrs post-exercise. Importantly, however, lifting velocity may be maintained from the first to final set despite perceptions of poor recovery. Taken together, as proximity-to-failure nears, ratings of perceived discomfort, exertion, and muscle soreness increase, general feelings worsen, and perceived recovery decreases. Considering proximity-to-failure may influence affective responses during and following RT [18, 138], which may be linked to long-term exercise adherence [17], future research should focus on RT strategies that stimulate desired physiological adaptations but limit negative perceptual responses.

8.2.5 Intra-Set RIR Prediction Accuracy

Individual RIR accuracy was assessed prior to Studies Two (to develop Study Three) and Four by calculating participants' raw and absolute RIR accuracy. In Studies Three and Four, participants predicted RIR within one repetition of the prescribed RIR targets. These findings are in line with a recent meta-analysis [89] that found individuals typically underpredict RIR by approximately one repetition, independent of RT experience. Importantly, this evidence spans the bench press (Study Three), leg press, and leg extension (Study Four), which is important, as intra-set RIR prediction accuracy may be influenced by the exercise performed [90]. The RIR accuracy data in Study Four wasn't statistically analysed; however, Study Three suggests that 1- and 3-RIR targets can be predicted with similar accuracy. Although the RIR accuracy achieved in the experimental trials and intervention period of Study Three and Four, respectively, could not be calculated, these data confirm that set termination likely occurred at least within one repetition or RIR targets, on average. To our knowledge, these studies implementing RIR prescription are the first to assess participant RIR accuracy prior to their commencement. Ultimately, these findings provide important RIR accuracy information that informs future studies exploring the relationship between proximity-to-failure and relevant outcome measures.

8.3 Thesis Limitations

Study-specific limitations were reported in each chapter, so thesis-wide limitations are discussed here. Study One only included studies from the scoping review that assessed muscle hypertrophy and therefore did not investigate the influence of proximity-to-failure on other outcomes like neuromuscular fatigue and muscle damage. Further, although changes in lifting velocity are reliable and valid measures of neuromuscular fatigue [65], measurements of maximum voluntary isometric contraction and twitch interpolation in Studies Two and Four would have provided further insights into neuromuscular fatigue that are not possible with lifting velocity alone. High absolute RIR accuracy reported in Studies Three and Four, is only based on 1- and 3-RIR predictions, as such, the accuracy that would be observed with other RIR targets is unclear. The observed similar muscle hypertrophy between RT performed to momentary muscular failure versus with 1- to 2-RIR in Study Four were derived from ultrasound assessments of the rectus femoris and vastus lateralis. While additional ultrasound assessment sites, RIR targets to assess accuracy, and sophisticated measures of neuromuscular fatigue, would have been ideal, the present approach to Study Four was an important first step to improve the understanding of the relationship between proximity to failure, muscle hypertrophy and short-term responses to RT. Finally, 'research questions' that are subsequently answered using studies designed to isolate variables, may differ to 'practical questions' that are important outside of the research setting. For example, much of the research presented in this thesis was designed to compare RT performed to momentary muscular failure versus with RIR, however, in practice one may choose to perform RT to various proximities-to-failure, including to momentary muscular failure.

8.4 Contribution to the Literature/Significance

Despite the importance of proximity-to-failure in promoting muscle hypertrophy and influencing short-term responses to RT, no previous study had investigated the impact of RIR prescription on muscle hypertrophy, and only one assessed neuromuscular fatigue [52]. The combined findings in this thesis allow for the following novel points to be addressed in the general discussion (Chapter Eight):

- Critiquing previous research investigating proximity-to-failure, including the variability in definitions of set failure applied across studies and ambiguity in the proximity-to-failure reached in non-failure RT groups to inform and improve future research.
- Meta-analysing studies that investigated muscle hypertrophy based on the definition of set failure applied and the research question asked to provide more robust interpretations relevant to momentary muscular failure and therefore, improve practical recommendations.
- The specific effect of RIR on neuromuscular fatigue and perceptual responses to RT; identifying a linear relationship between RIR and outcomes of interest that ultimately allows for RIR prescription that limits excessive neuromuscular fatigue and negative perceptual responses.
- Possible biological sex differences in neuromuscular fatigue depending on the proximity-to-failure reached during RT, providing insights into the sex-specific response to RT and how RIR prescription may be employed differently between sexes.

- Assessing RIR accuracy of participants prior to the commencement of RT studies to provide information regarding initial RIR accuracy and improve subsequent interpretations about the relationship between RIR and outcome measures.
- The specific effect of RIR on muscle hypertrophy and neuromuscular fatigue over eight weeks of RT; identifying that similar quadriceps hypertrophy is achieved when RT is performed to momentary muscular failure versus with 1- to 2-RIR and that neuromuscular fatigue may be attenuated upon repeated exposure to the same RT stimulus.

8.5 Practical Application of Thesis Findings

Practical recommendations can be categorised based on outcome measure and may inform RIR prescription for promoting muscle hypertrophy and limiting negative short-term responses. A question of key practical importance is: *"How can proximity-to-failure maximise the RT stimulus (for a given muscle) across a whole session?"* To answer this question, aspects of the RT stimulus (e.g., volume, load lifted, exercise order) other than proximity-to-failure, along with individual characteristics (e.g., fatigability and perceptual responses), must be considered. For example, the linear relationship between proximity-to-failure and neuromuscular fatigue should be considered in RT prescription to limit intra-session neuromuscular fatigue and ensure post-exercise recovery is not impeded to an extent that negatively effects subsequent sessions. Further, the affective valence of an individual during and following exercise may be important for long-term adherence [16-18].

8.5.1 Muscle Hypertrophy

Given similar quadriceps hypertrophy between RT to momentary muscular failure and with 1- to 2-RIR in Study Four, RIR prescription can be individualised. For example: i) the general population may choose to perform RT further from momentary muscular failure to limit negative perceptual responses [139], ii) athletes may vary RIR based on the demands of their sport to maintain performance by limiting neuromuscular fatigue whilst stimulating muscle hypertrophy, and iii) bodybuilders and/or individuals looking to maximise muscle hypertrophy may prioritise set termination close to, or at momentary muscular failure. Study Four also suggested the possibility that performing RT to momentary muscular failure maximises the RT stimulus from the first exercise on the target musculature but may compromise the stimulus of the second exercise. As such, sets should be terminated closer to, or at momentary muscular failure with i) exercises at the end of a RT session or on the last set of an exercise or muscle group, ii) longer rest periods, iii) lower intra-session set volumes, and when iv) individual tolerance to fatigue is high. Moreover, considering the musculoskeletal complaints on the leg press in Study Four, the decision to reach momentary muscular failure should be based on safety and mostly used with single-joint versus multi-joint exercises, machines versus free-weights, and exercises involving lower cardiovascular demands to reduce injury risk. Overall, set failure or non-failure should not be treated dichotomously as a range of proximities-to-failure, including momentary muscular failure, can promote muscle hypertrophy. Although muscle hypertrophy is likely similar following RT to momentary muscular failure versus 1- to 2-RIR, this does not dismiss the potential utility of performing RT to momentary muscular failure in some circumstances (described above).

8.5.2 Neuromuscular Fatigue

When multiple exercises for a given muscle group are performed in a RT session, various proximities-to-failure should be employed to limit large decrements in force production that accumulate over multiple sets, possibly impeding subsequent physiological adaptations. For example, reduced volume or load lifted across sets and sessions may compromise muscle hypertrophy and strength development, respectively. Although repetition volume and volume load were deliberately not equalised in Study Four, each of the RT protocols achieved similar volume loads likely due to higher neuromuscular fatigue experienced when momentary muscular failure was reached. Considering the number of sets performed to, or close to, momentary muscular failure per muscle group per week [110] may influence neuromuscular fatigue, proximity-to-failure should depend on set-volume completed, with closer proximities-to-failure better suited to i) lower set-volumes, or ii) longer time courses of recovery between RT sessions (e.g., 48-72 hrs) involving the same muscle group. Potential sex differences in neuromuscular fatigability as observed in Study Two should also be considered when prescribing proximity-to-failure possibly indicating that males should i) not perform sets to momentary muscular failure as frequently as females, and ii) if momentary muscular failure is reached, employ longer inter-set rest periods than females. However, these recommendations are based on average responses and considering some females in Study Two had greater fatigability than some male participants, individual fatigability should primarily be considered. For example, highly fatigable participants experienced greater repetition loss from the first to final set, which can be used as an indicator of individual fatigability in practice. The findings from Study Four also highlight that repeated exposure to the same RT stimulus may generate less acute neuromuscular fatigue over time on certain exercises. As such, RT may be performed closer to, or to momentary muscular failure as an individual acclimates to a RT program.

8.5.3 Perceptual Responses

Given that perceptual responses like perceived discomfort and general feelings may be influenced by proximity-to-failure, they should be a key consideration in RT prescription. Although Study Two identified a linear relationship between proximity-to-failure and worsened perceptual responses, it was also observed that some individuals may experience a negative affective response or high levels of perceived discomfort and exertion when reaching momentary muscular failure, but other individuals may not. Understanding these individual factors is needed to uphold enjoyment and long-term adherence to RT, particularly within the general population. Perceptual responses like perceived recovery and muscle soreness, unlike measures of neuromuscular fatigue, are also practically feasible measurements which can inform individual fatigability and recovery. However, these perceptions may not always reflect the objective performance capabilities of an individual. Further, in relatively untrained individuals, these perceptual responses can be monitored overtime and used to adjust proximity-to-failure accordingly if they become undesirable.

8.5.4 Intra-Set RIR Prediction Accuracy

Considering the high absolute RIR accuracy observed in Study Three and Four, practitioners may prescribe a specific number of sets along with a repetition range and RIR target (e.g., 3 sets of 10-15 repetitions with 2-RIR). This prescription allows resistance-trained individuals to self-select loads that prompt set termination at the perceived RIR within the prescribed repetition range. Considering proximity-to-failure influences the stimulus achieved, employing an RIR prescription may be advantageous compared to a predetermined repetition prescription (e.g., 3 sets of 10 repetitions), whereby the proximity-to-failure upon set termination is unclear, and sets may be terminated with a potentially sub-optimal proximity-to-failure. However, RIR prescriptions may only be effective with a certain level of RIR accuracy and therefore be most suitable to resistance-trained individuals. For example, per Study Four, if an individual can predict RIR within one repetition, prescribing 0- to 2-RIR may be an effective approach to promote muscle hypertrophy. Further, before employing an RIR prescription, individuals should i) learn appropriate and safe exercise technique that can be sustained to momentary muscular failure, ii) understand the difference between perceived discomfort and proximity-to-failure to reduce inaccurate RIR predictions, and iii) practice reaching momentary muscular failure where safe to do so to improve perceptions of proximity-to-failure and 'anchor' RIR targets (e.g., if an individual performs 12 repetitions to momentary muscular failure, a 2-RIR is anchored to the perception of the 10th repetition). Finally, to assess whether RIR experience improves RIR prediction accuracy over time, individuals should periodically test their prediction accuracy when it is safe to reach momentary muscular failure.

8.6 Suggestions for Future Research

Firstly, to better standardise the RT stimulus in set failure groups, future studies should employ momentary muscular failure (or at least report the failure definition used) if safe and suitable to the study design (e.g., depending on exercise selection, training status etc.). Further, considering resistance-trained individuals' high absolute RIR accuracy, RIR prescription may be used to better standardise proximity to failure in non-failure groups. However, researchers should i) ensure participants are given clear RIR prediction instructions and are well familiarised before commencing experimental sessions (e.g., performing RT to momentary muscular failure, practicing intra-set RIR prediction, briefing on perceived discomfort), ii) higher-loads (e.g., >50% 1-RM) are used versus lower-loads, and iii) if safe to do so, momentary muscular failure is first experienced on a given exercise to 'anchor' subjective perceptions of proximity-to-failure [97].

To date, proximity-to-failure in RT has been largely considered in a binary fashion, with RT performed to set failure or non-failure for the duration of the intervention. Future research should therefore investigate various RIR targets to explore effective approaches to maximising muscle hypertrophy whilst limiting negative short-term responses. Moreover, neuromuscular fatigue should be assessed acutely and over a long-term intervention, with a combination of outcome measures that provide further insights regarding the relationship between proximity-to-failure and neuromuscular fatigue. Given the potential for muscle-specific differences in muscle hypertrophy and neuromuscular fatigue, exercises and/or muscle groups other than those investigated in this thesis should also be researched to provide further data that may improve practical RT prescription. More research is also required to elucidate any potential sex-based differences in the influence of proximity-to-failure on relevant outcome measures.

8.7 Thesis Conclusions

This thesis examined several previously under-investigated aspects of proximity-to-failure in RT and its influence on muscle hypertrophy and short-term responses to RT. The findings suggest that performing RT closer to momentary muscular failure is likely important for muscle hypertrophy, but reaching momentary muscular failure may not *always* have further benefit. For example, in resistance-trained males and females, terminating sets at 1- to 2-RIR promotes similar overall quadriceps hypertrophy to reaching momentary muscular failure over eight weeks of RT. The influence of proximity-to-failure on muscle-specific hypertrophy may also depend on other factors (e.g., muscle group measured, exercises performed etc.). Further, evidence from this thesis suggests a linear relationship between proximity-to-failure and acute neuromuscular fatigue, such that terminating sets closer to momentary muscular failure induces higher neuromuscular fatigue, however, improved fatigue resistance over time on certain exercises may reduce the magnitude of acute neuromuscular fatigue incurred. Perceptual responses to RT also seem to exhibit a linear relationship with proximity-to-failure; as proximity-to-failure nears, ratings of perceived discomfort, exertion, and muscle soreness increase, general feelings worsen, and perceived recovery decreases. Data from this thesis also indicate that RIR prescription may be a valid set termination strategy for controlling proximity-to-failure in RT interventions, at least in resistance-trained samples. Overall, this thesis has improved the understanding of proximity-to-failure and its role in promoting various important outcomes in RT, with many practical implications and directions for future research.

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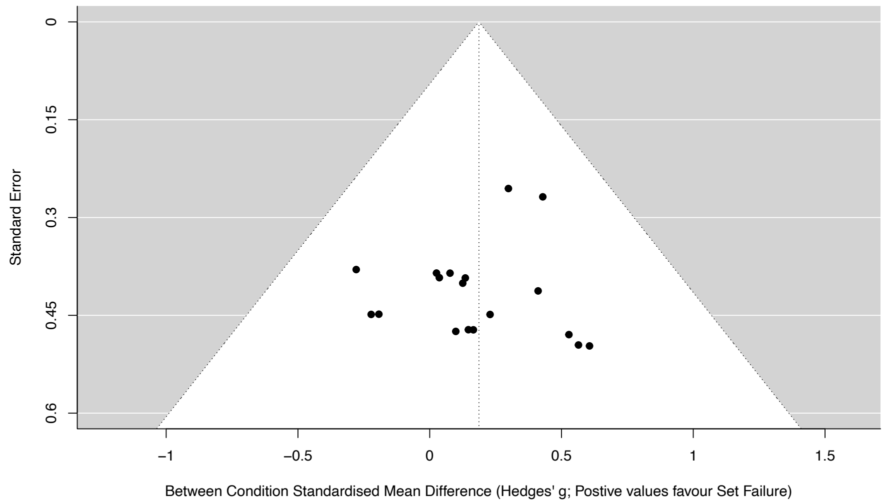
Appendices

Appendix A. Supplementary File for Study One

1. Publication Bias

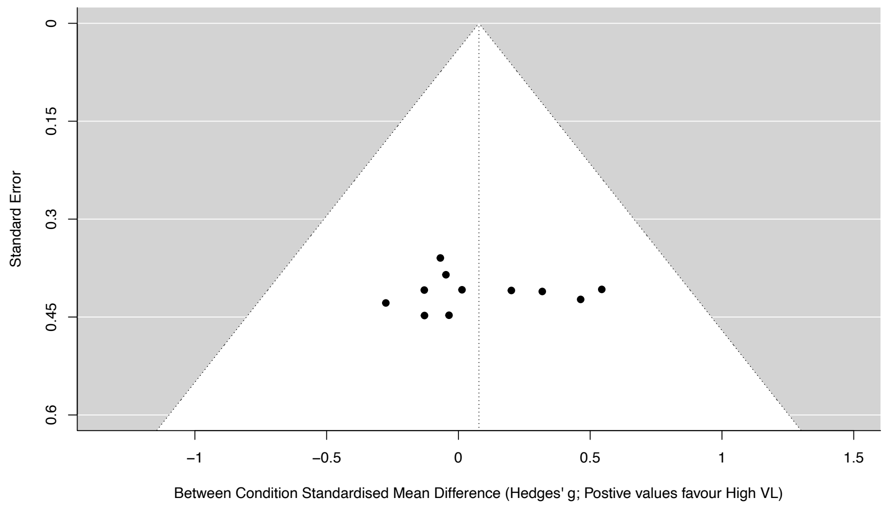
1.1 Studies Comparing Set Failure VS. Non-Failure (Theme A and B)

Figure 1. Funnel Plot of All Effects for Studies in Theme A and B



1.2 Studies Comparing High Velocity Loss VS. Moderate Velocity Loss (Theme C)

Figure 2. Funnel Plot of All Effects for Studies in Theme C



2. Sensitivity Analyses

2.1 Studies Comparing Set Failure VS. Non-Failure (Theme A and B)

Figure 3. Scatter Plot of P-Values Associated with r = 0.6 – 0.9

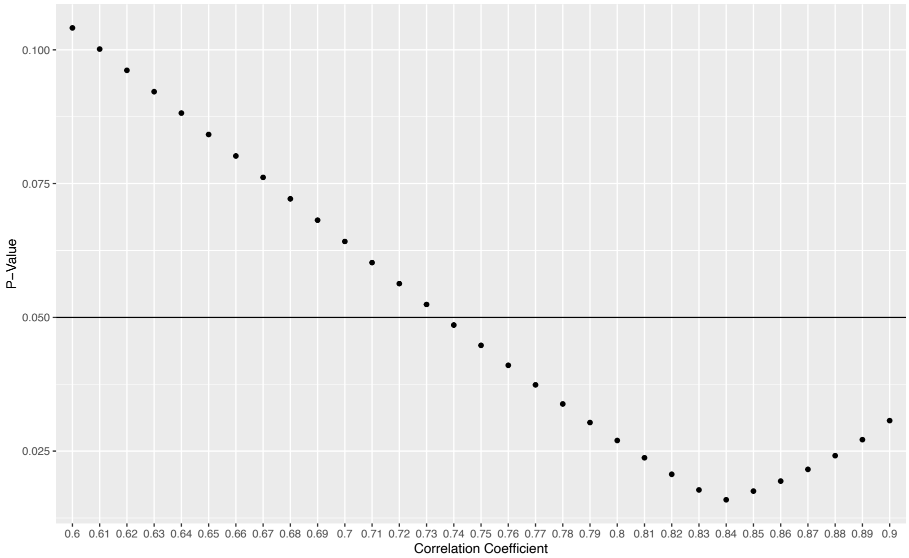
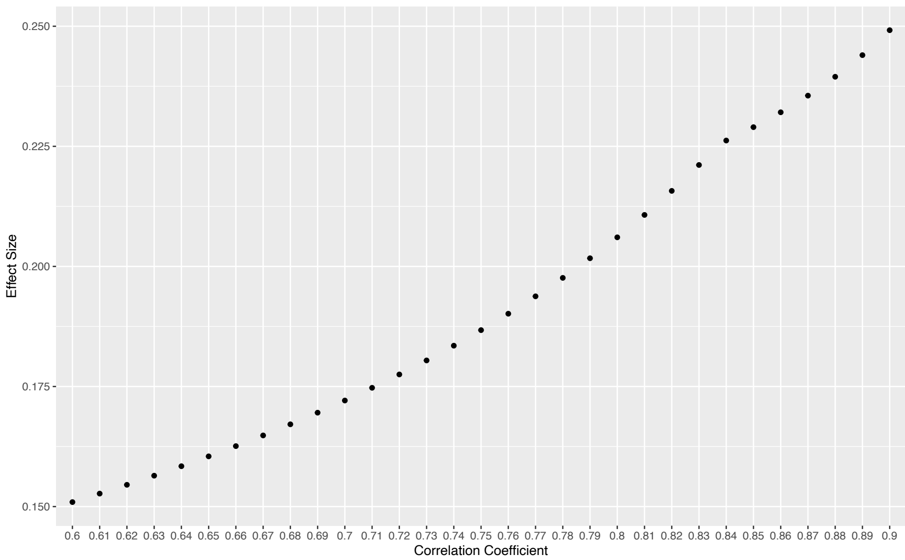


Figure 4. Scatter Plot of Effect Sizes Associated with r = 0.6 – 0.9



2.2 Studies Comparing High Velocity Loss VS. Moderate Velocity Loss (Theme C)

Figure 5. Scatter Plot of P-Values Associated with r = 0.6 – 0.9

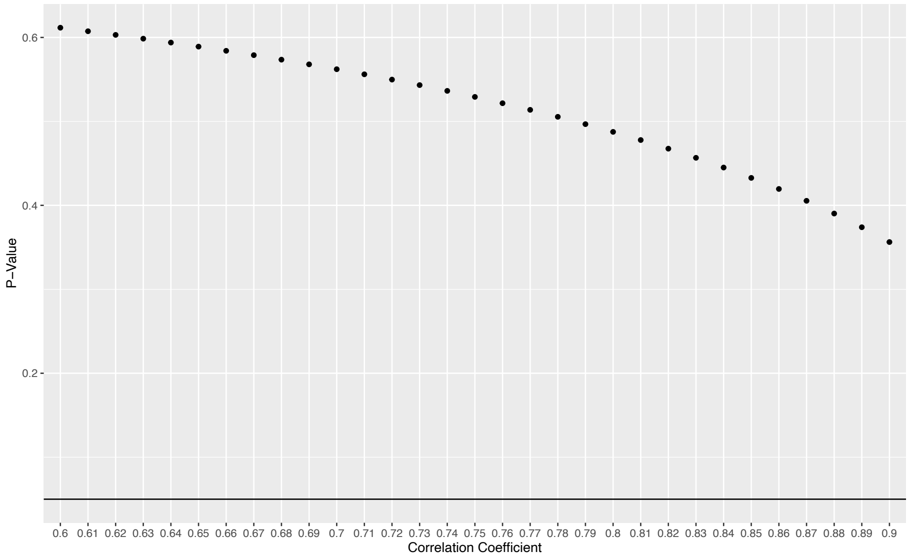
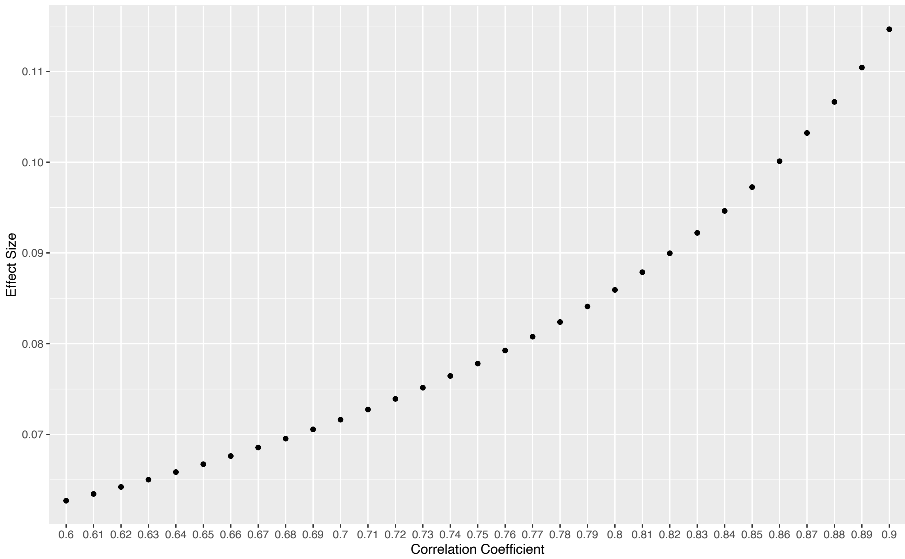


Figure 6. Scatter Plot of Effect Sizes Associated with r = 0.6 – 0.9



3. Methodological Quality Assessment

Table 1. Methodological quality for each included study assessed using the (TESTEX) scale.

Study	TESTEX Scale Item																
	1	**2**	**3**	**4**	**5a**	**5b**	**5c**	**6a**	**6b**	**6c**	**7**	**8**	**8**	**9**	**10**	**11**	**12**	**Total**
Andersen et al. 2021	1	1	0	1	No	No	0	0	1	1	0	1	1	1	0	1	1	10
Bergamasco et al. 2020	1	0	0	1	No	No	0	1	1	1	0	1	1	1	0	1	1	10
Karsten et al. 2021	1	0	0	1	No	No	0	1	1	1	0	1	1	1	0	1	1	10
Lacerda et al. 2020	1	1	0	1	No	No	1	1	1	1	0	1	1	1	0	1	1	12
Lasevicius et al. 2019	1	0	0	1	No	No	0	0	1	0	0	1	1	1	0	0	1	7
Martorelli et al. 2017	1	1	0	1	No	No	0	1	0	0	0	1	1	1	0	1	1	9
Nobrega et al. 2018	1	1	0	1	No	No	0	1	1	1	0	1	1	1	0	0	1	10
Pareja-Blanco et al. 2017	1	0	0	1	No	No	1	1	1	1	0	1	1	1	0	1	1	11
Pareja-Blanco et al. 2020a	1	0	0	1	No	No	1	0	1	0	1	1	1	1	0	1	1	10
Pareja-Blanco et al. 2020b	1	0	0	1	No	No	1	1	1	1	0	1	1	1	0	1	1	11
Rissanen et al. 2022	1	1	0	1	No	No	0	1	1	0	0	1	1	1	0	1	1	10
Rodiles-Guerrero et al. 2022	1	1	0	1	No	No	1	1	1	1	0	1	1	1	0	1	1	12
Sampson et al. 2020	1	1	0	1	No	No	0	1	1	1	0	1	1	1	0	1	1	11
Santanielo et al. 2020	1	0	0	1	No	No	1	0	1	1	0	1	1	1	0	0	1	9
Terada et al. 2021	1	0	0	1	No	No	0	1	1	0	0	1	1	1	0	0	1	8

Appendix B. Supplementary File for Study Two

S1. Total Volume

1.1 Linear Mixed Effects Model (Protocol x Sex)

Effect	DF	*F*-Value	*P*-Value
Protocol	2	12.32	<0.001
Sex	1	17.80	<0.001
Protocol x Sex	2	1.59	0.204

1.1.1 Tukey's Pairwise Comparisons

Protocol	ES (CI)	*P*-Value
1-RIR vs. 3-RIR	0.40 (0.21, 0.60)	<0.001
1-RIR vs. FAIL	-0.18 (-0.30, -0.06)	0.015
3-RIR vs. FAIL	0.18 (-0.03, 0.39)	0.117
Sex		
Male vs. Female	1.58 (1.05, 2.11)	<0.001

1.1.2 Descriptive Statistics [Total Volume (Sets x Repetitions)]

Protocol	Mean	*SD*
1-RIR	52	12
3-RIR	57	13
FAIL	54	15
Sex		
Males	46	7
Females	63	13
Protocol x Sex		
1-RIR *(Male)*	49	8
1-RIR *(Female)*	65	12
3-RIR *(Male)*	44	7
3-RIR *(Female)*	59	12
FAIL *(Male)*	45	8
FAIL *(Female)*	64	14

S2. Recovery Time-Course from Pre-Exercise to Post-Exercise

2.1 Linear Mixed Effects Model (Protocol x Time)

Effect	**DF**	***F*-Value**	***P*-Value**
Protocol	2	52.81	<0.001
Time	2	229.58	<0.001
Protocol x Time	4	18.18	<0.001

2.1.1 Tukey's Pairwise Comparisons

Protocol	**ES (CI)**	***P*-Value**
1-RIR vs. 3-RIR	0.66 (0.46, 0.85)	<0.001
1-RIR vs. FAIL	0.26 (0.10, 0.42)	<0.001
3-RIR vs. FAIL	0.58 (0.41, 0.74)	<0.001
Time		
24-hrs vs. 48-hrs	0.32 (0.11, 0.54)	0.067
24-hrs vs. 4-min	1.55 (1.24, 1.87)	<0.001
48-hrs vs. 4-min	1.83 (1.42, 2.25)	<0.001
Protocol x Time		
1-RIR vs. 3-RIR *(4-min)*	1.26 (0.80, 1.73)	<0.001
1-RIR vs. FAIL *(4-min)*	1.16 (0.68, 1.63)	<0.001
3-RIR vs. FAIL *(4-min)*	1.87 (1.26, 2.47)	<0.001
1-RIR vs. 3-RIR *(24-hrs)*	1.02 (0.40, 1.64)	0.001
1-RIR vs. FAIL *(24-hrs)*	0.01 (-0.52, 0.55)	0.998
3-RIR vs. FAIL *(24-hrs)*	0.90 (0.47, 1.32)	0.001
1-RIR vs. 3-RIR *(48-hrs)*	0.57 (0.08, 1.06)	0.189
1-RIR vs. FAIL *(48-hrs)*	-0.02 (-0.48, 0.43)	0.993
3-RIR vs. FAIL *(48-hrs)*	0.36 (-0.10, 0.83)	0.230

2.1.2 Descriptive Statistics (Decrease in Lifting Velocity from Pre-Exercise)

Protocol	**Mean**	***SD***
1-RIR	-0.04	0.04
3-RIR	-0.01	0.04

FAIL	-0.06	0.08
Time		
4-min	-0.09	0.06
24-hrs	-0.01	0.03
48-hrs	0.00	0.03
Protocol x Time		
1-RIR *(4-min)*	-0.09	0.03
3-RIR *(4-min)*	-0.05	0.03
FAIL *(4-min)*	-0.15	0.06
1-RIR *(24-hrs)*	-0.02	0.03
3-RIR *(24-hrs)*	0.01	0.03
FAIL *(24-hrs)*	-0.02	0.04
1-RIR *(48-hrs)*	-0.01	0.02
3-RIR *(48-hrs)*	0.01	0.02
FAIL *(48-hrs)*	0.00	0.04

2.2 Linear Mixed Effects Model [Protocol x Sex (4-min)]

Effect	DF	*F*-Value	*P*-Value
Protocol	2	89.57	<0.001
Sex	1	0.90	0.342
Protocol x Sex	2	7.14	0.001

2.2.1 Tukey's Pairwise Comparisons

Protocol x Sex	ES (CI)	*P*-Value
1-RIR *(Male vs. Female)*	0.10 (-0.72, 0.92)	0.834
3-RIR *(Male vs. Female)*	0.12 (-0.69, 0.94)	0.828
FAIL *(Male vs. Female)*	0.82 (-0.03, 1.67)	0.007

2.2.2 Descriptive Statistics (Decrease in Lifting Velocity from Pre-Exercise)

Protocol x Sex	Mean	*SD*
1-RIR *(Male)*	-0.08	0.03
1-RIR *(Female)*	-0.09	0.03
3-RIR *(Male)*	-0.04	0.02
3-RIR *(Female)*	-0.05	0.03
FAIL *(Male)*	-0.17	0.05
FAIL *(Female)*	-0.12	0.06

2.3 Within-Protocol Statistical Differences from Pre-Exercise

Protocol x Time	ES (CI)	*P*-Value
All Participants		
1-RIR *(4-min)*	0.87 (0.71, 1.02)	0.003
1-RIR *(24-hrs)*	0.21 (0.09, 0.33)	0.453
1-RIR *(48-hrs)*	0.05 (-0.04, 0.15)	0.847
3-RIR *(4-min)*	0.55 (0.40, 0.69)	0.056
3-RIR *(24-hrs)*	-0.10 (-0.23, 0.03)	0.717
3-RIR *(48-hrs)*	-0.10 (-0.22, 0.02)	0.712
FAIL *(4-min)*	1.59 (1.20, 1.98)	<0.001
FAIL *(24-hrs)*	0.25 (0.08, 0.43)	0.365
FAIL *(48-hrs)*	0.05 (-0.15, 0.25)	0.848
Male Participants		
1-RIR *(4-min)*	0.78 (0.57, 0.99)	0.046
1-RIR *(24-hrs)*	0.87 (0.71, 1.02)	0.003
1-RIR *(48-hrs)*	0.21 (0.09, 0.33)	0.453
3-RIR *(4-min)*	0.47 (0.31, 0.62)	0.219
3-RIR *(24-hrs)*	-0.14 (-0.29, 0.02)	0.725
3-RIR *(48-hrs)*	-0.15 (-0.33, 0.03)	0.693
FAIL *(4-min)*	1.83 (1.35, 2.30)	<0.001
FAIL *(24-hrs)*	0.26 (0.04, 0.48)	0.501
FAIL *(48-hrs)*	0.03 (-0.21, 0.27)	0.945
Female Participants		
1-RIR *(4-min)*	0.84 (0.62, 1.06)	0.036
1-RIR *(24-hrs)*	0.33 (0.15, 0.52)	0.387
1-RIR *(48-hrs)*	0.06 (-0.02, 0.13)	0.883
3-RIR *(4-min)*	0.56 (0.32, 0.81)	0.150
3-RIR *(24-hrs)*	-0.05 (-0.24, 0.14)	0.885
3-RIR *(48-hrs)*	-0.04 (-0.18, 0.11)	0.919
FAIL *(4-min)*	1.32 (0.77, 1.86)	0.001
FAIL *(24-hrs)*	0.20 (-0.05, 0.45)	0.560
FAIL *(48-hrs)*	0.07 (-0.23, 0.38)	0.839

S3. Lifting Velocity Loss from First to Final Set

3.1 Linear Mixed Effects Model (Protocol x Sex)

Effect	**DF**	***F*-Value**	***P*-Value**
Protocol	2	30.14	<0.001
Sex	1	6.33	0.012
Protocol x Sex	2	1.66	0.190

3.1.1 Tukey's Pairwise Comparisons

Protocol	**ES (CI)**	***P*-Value**
1-RIR vs. 3-RIR	0.50 (-0.05, 1.06)	0.101
1-RIR vs. FAIL	1.46 (0.63, 2.29)	<0.001
3-RIR vs. FAIL	1.59 (1.02, 2.16)	<0.001
Sex		
Male vs. Female	0.53 (0.06, 1.00)	0.020

3.1.2 Descriptive Statistics (Decrease in Lifting Velocity from First to Final Set)

Protocol	**Mean**	***SD***
1-RIR	-0.03	0.02
3-RIR	-0.02	0.04
FAIL	-0.08	0.03
Sex		
Males	-0.05	0.04
Females	-0.03	0.04
Protocol x Sex		
1-RIR *(Male)*	-0.04	0.02
1-RIR *(Female)*	-0.03	0.02
3-RIR *(Male)*	-0.03	0.04
3-RIR *(Female)*	0.00	0.04
FAIL *(Male)*	-0.10	0.03
FAIL *(Female)*	-0.06	0.03

3.2 Within-Protocol Statistical Differences from First Set to Final Set

Protocol	ES (CI)	*P*-Value
All Participants		
1-RIR	0.85 (0.58, 1.12)	0.003
3-RIR	0.39 (0.02, 0.76)	0.168
FAIL	1.88 (1.33, 2.43)	<0.001
Male Participants		
1-RIR	0.92 (0.50, 1.33)	0.015
3-RIR	0.58 (0.10, 1.06)	0.139
FAIL	2.32 (1.58, 3.05)	<0.001
Female Participants		
1-RIR	0.69 (0.35, 1.03)	0.076
3-RIR	0.11 (-0.41, 0.64)	0.766
FAIL	1.24 (0.71, 1.76)	0.003

S4. Repetition Loss from First to Final Set

4.1 Linear Mixed Effects Model (Protocol x Sex)

Effect	**DF**	***F*-Value**	***P*-Value**
Protocol	2	64.96	<0.001
Sex	1	0.76	0.382
Protocol x Sex	2	0.26	0.775

4.1.1 Tukey's Pairwise Comparisons

Protocol	**ES (CI)**	***P*-Value**
1-RIR vs. 3-RIR	1.26 (0.56, 1.97)	<0.001
1-RIR vs. FAIL	-1.31 (-1.84, -0.78)	<0.001
3-RIR vs. FAIL	2.49 (1.67, 3.30)	<0.001

4.1.2 Descriptive Statistics (% Change in Repetitions from First to Final Set)

Protocol	**Mean**
1-RIR	-40%
3-RIR	-27%
FAIL	-54%
Protocol x Sex	
1-RIR *(Male)*	-44%
1-RIR *(Female)*	-37%
3-RIR *(Male)*	-30%
3-RIR *(Female)*	-25%
FAIL *(Male)*	-59%
FAIL *(Female)*	-51%

4.2 Within-Protocol Statistical Differences from First Set to Final Set

Protocol	ES (CI)	*P*-Value
All Participants		
1-RIR	1.97 (1.50, 2.44)	<0.001
3-RIR	1.11 (0.73, 1.50)	<0.001
FAIL	2.64 (2.07, 3.22)	<0.001
Male Participants		
1-RIR	2.55 (1.59, 3.51)	<0.001
3-RIR	1.51 (0.63, 2.39)	<0.001
FAIL	3.72 (2.24, 5.20)	<0.001
Female Participants		
1-RIR	2.12 (1.28, 2.97)	<0.001
3-RIR	1.11 (0.54, 1.69)	0.008
FAIL	3.01 (1.93, 4.01)	<0.001

4.3 Repetitions Performed Per Set (Data Shown are Expressed as Mean ± *SD*)

Set	1	2	3	4	5	6
All Participants						
1-RIR	13 ± 3	11 ± 2	9 ± 2	9 ± 2	8 ± 2	8 ± 2
3-RIR	10 ± 3	9 ± 2	9 ± 2	8 ± 2	7 ± 2	7 ± 2
FAIL	14 ± 3	11 ± 3	9 ± 3	8 ± 3	7 ± 2	6 ± 2
Male Participants						
1-RIR	11 ± 2	9 ± 2	8 ± 2	7 ± 1	7 ± 1	6 ± 1
3-RIR	9 ± 2	8 ± 1	8 ± 2	7 ± 2	6 ± 1	6 ± 2
FAIL	12 ± 2	9 ± 2	7 ± 1	6 ± 2	5 ± 1	5 ± 1
Female Participants						
1-RIR	14 ± 2	12 ± 2	11 ± 2	10 ± 2	9 ± 2	9 ± 2
3-RIR	12 ± 3	11 ± 2	10 ± 2	10 ± 2	9 ± 2	9 ± 2
FAIL	16 ± 3	12 ± 3	11 ± 3	9 ± 3	8 ± 2	8 ± 2

S5. Perceived Discomfort

5.1 Friedman Test (Protocol)

Effect	**DF**	***Chi-Squared***	***P*-Value**
Protocol	2	30.98	<0.001

5.1.1 Tukey's Pairwise Comparisons

Protocol	**ES (CI)**	***P*-Value**
1-RIR vs. 3-RIR	0.62 (0.26, 0.99)	0.005
1-RIR vs. FAIL	0.65 (0.36, 0.94)	0.001
3-RIR vs. FAIL	1.50 (1.07, 1.93)	<0.001

5.1.2 Descriptive Statistics (Rating of Perceived Discomfort)

Protocol	**Mean**	***SD***
1-RIR	3.76	1.75
3-RIR	2.74	1.17
FAIL	4.88	1.48

S6. Perceived Exertion

6.1 Friedman Test (Protocol)

Effect	**DF**	***Chi-Squared***	***P*-Value**
Protocol	2	35.89	<0.001

6.1.1 Tukey's Pairwise Comparisons

Protocol	**ES (CI)**	***P*-Value**
1-RIR vs. 3-RIR	1.14 (0.66, 1.63)	<0.001
1-RIR vs. FAIL	0.95 (0.37, 1.53)	0.003
3-RIR vs. FAIL	1.85 (1.12, 2.57)	<0.001

6.1.2 Descriptive Statistics (Rating of Perceived Exertion)

Protocol	**Mean**	***SD***
1-RIR	4.33	1.40
3-RIR	2.88	0.74
FAIL	6.04	1.99

S7. General Feelings

7.1 Friedman Test (Protocol)

Effect	**DF**	***Chi-Squared***	***P*-Value**
Protocol	2	17.13	<0.001

7.1.1 Tukey's Pairwise Comparisons

Protocol	**ES (CI)**	***P*-Value**
1-RIR vs. 3-RIR	0.56 (0.12, 1.00)	0.025
1-RIR vs. FAIL	0.63 (0.08, 1.17)	0.071
3-RIR vs. FAIL	1.19 (0.58, 1.81)	0.001

7.1.2 Descriptive Statistics (Feeling Scale)

Protocol	**Mean**	***SD***
1-RIR	2.42	1.67
3-RIR	3.29	1.27
FAIL	1.25	1.92

S8. Muscle Soreness

8.1 Friedman Test (Protocol)

Effect	**DF**	***Chi-Squared***	***P*-Value**
Protocol *(24-hrs)*	2	18.40	<0.001
Protocol *(48-hrs)*	2	14.08	0.001

8.1.1 Tukey's Pairwise Comparisons

Protocol	**ES (CI)**	***P*-Value**
24-hrs		
1-RIR vs. 3-RIR	0.37 (-0.20, 0.94)	0.558
1-RIR vs. FAIL	0.79 (0.19, 1.39)	0.023
3-RIR vs. FAIL	1.16 (0.64, 1.68)	<0.001
48-hrs		
1-RIR vs. 3-RIR	0.40 (-0.06, 0.87)	0.316
1-RIR vs. FAIL	0.42 (-0.17, 1.00)	0.417
3-RIR vs. FAIL	0.90 (0.31, 1.50)	0.004

8.1.2 Descriptive Statistics (Rating of Muscle Soreness)

Protocol	**Mean**	***SD***
24-hrs		
1-RIR	2.29	1.71
3-RIR	1.67	1.52
FAIL	3.79	1.96
48-hrs		
1-RIR	1.5	2
3-RIR	0.79	1.14
FAIL	2.38	2.06

S9. Perceived Recovery

9.1 Friedman Test (Protocol)

Effect	**DF**	***Chi-Squared***	***P*-Value**
Protocol *(24-hrs)*	2	21.30	<0.001
Protocol *(48-hrs)*	2	12.83	0.002

9.1.1 Tukey's Pairwise Comparisons

Protocol	**ES (CI)**	***P*-Value**
24-hrs		
1-RIR vs. 3-RIR	0.75 (0.21, 1.29)	0.014
1-RIR vs. FAIL	0.52 (-0.05, 1.08)	0.204
3-RIR vs. FAIL	1.55 (0.83, 2.27)	0.001
48-hrs		
1-RIR vs. 3-RIR	0.66 (0.25, 1.06)	0.008
1-RIR vs. FAIL	0.24 (-0.33, 0.81)	0.659
3-RIR vs. FAIL	1.02 (0.45, 1.58)	0.003

9.1.2 Descriptive Statistics (Rating of Perceived Recovery Status)

Protocol	**Mean**	***SD***
24-hrs		
1-RIR	3.83	2.20
3-RIR	5.42	1.84
FAIL	2.88	1.23
48-hrs		
1-RIR	5.83	2.28
3-RIR	7.21	1.47
FAIL	5.29	2.07

Appendix C. Supplementary File for Study Three

Supplemental Digital Content 1

S1. RIR Accuracy – Mixed Effects Models

1.1 Raw RIR Accuracy Linear Mixed Effects Model Output

Predictors	**Estimates**	**Standard Error**	**95% CI**
(Intercept)	0.68	0.60	-0.51 – 1.88
RIR	0.12	0.36	-0.58 – 0.83
Session	0.02	0.34	-0.66 – 0.71
Set	-0.06	0.36	-0.79 – 0.66
Repetitions Per Set	-0.07	0.05	-0.16 – 0.02
RIR x Session	-0.51	0.41	-1.32 – 0.30
RIR x Set	0.42	0.41	-0.38 – 1.23
Session x Set	-0.54	0.41	-1.35 – 0.27
Random Effects			
σ^2	0.92		
$\tau_{00\ id}$	0.01		
ICC	0.01		
N_{id}	24		
Observations	90		
Marginal R^2	0.142		
Conditional R^2	0.155		

1.2 Absolute RIR Accuracy Generalised Linear Mixed Effects Model Output

Predictors	**Estimates**	**Standard Error**	**95% CI**
(Intercept)	0.58	0.53	0.10 – 3.49
RIR	2.34	1.05	0.97 – 5.64
Session	0.37	0.23	0.11 – 1.22
Set	0.62	0.36	0.20 – 1.93
Repetitions Per Set	0.99	0.07	0.86 – 1.14
RIR x Session	0.98	0.59	0.30 – 3.20
RIR x Set	1.07	0.65	0.33 – 3.50
Session x Set	4.24	2.43	1.38 – 13.02
Random Effects			

σ^2	0.95
$\tau_{00\ id}$	0.20
ICC	0.18
N $_{id}$	24
Observations	90
Marginal R^2	0.238
Conditional R^2	0.374

1.2.1 Untransformed Generalised Linear Mixed Effects Model Output

Predictors	**Estimates**	**Standard Error**	**95% CI**
(Intercept)	-0.55	0.92	-2.35 – 1.25
RIR	0.85	0.45	-0.03 – 1.73
Session	-0.98	0.60	-2.16 – 0.20
Set	-0.47	0.58	-1.60 – 0.66
Repetitions Per Set	-0.01	0.07	-0.15 – 0.13
RIR x Session	-0.02	0.60	-1.21 – 1.16
RIR x Set	0.06	0.61	-1.12 – 1.25
Session x Set	1.44	0.57	0.32 – 2.57
Random Effects			
σ^2	0.95		
$\tau_{00\ id}$	0.20		
ICC	0.18		
N $_{id}$	24		
Observations	90		
Marginal R^2	0.238		
Conditional R^2	0.374		

S2. RIR Accuracy – Unadjusted and Adjusted Means

2.1 Raw RIR Accuracy Means Separated by RIR, Set, and Session

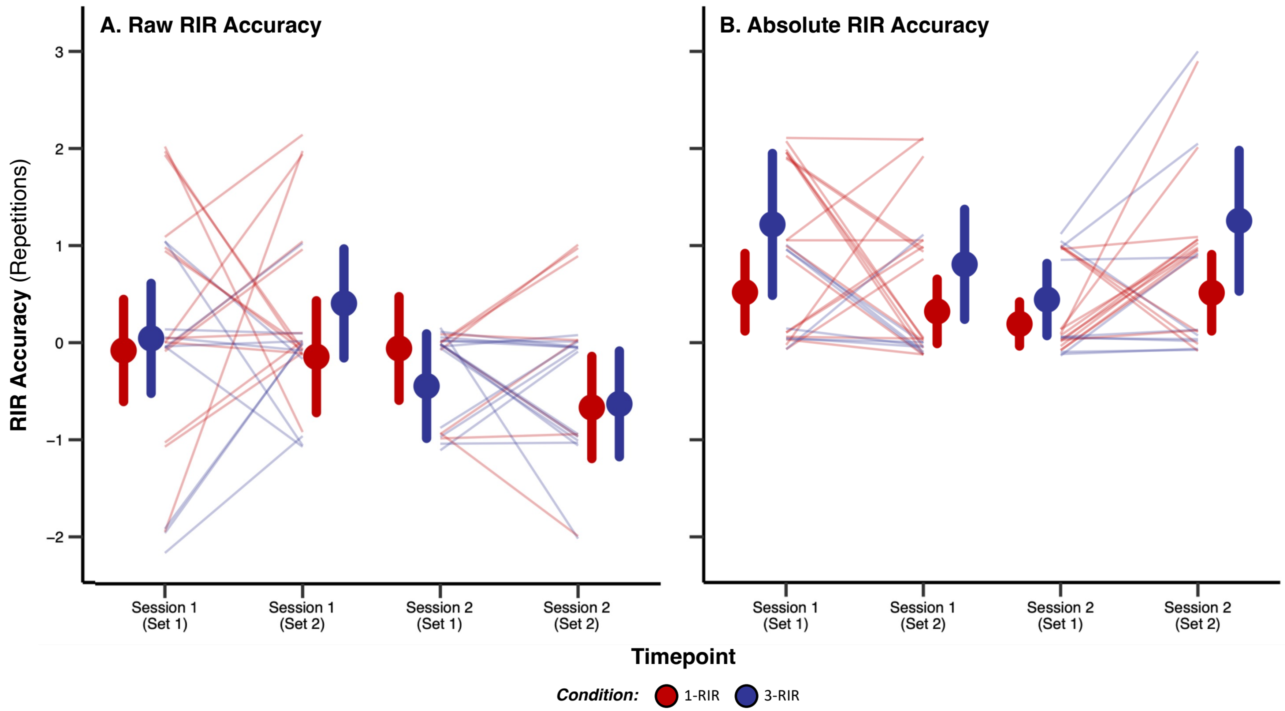
	1-RIR	Adjusted 1-RIR	3-RIR	Adjusted 3-RIR
Session 1				
Set 1	-0.08 ± 0.90	-0.07 [-0.6, 0.45]	0.17 ± 1.53	0.05 [-0.52, 0.61]
Set 2	-0.08 ± 0.51	-0.14 [-0.71, 0.44]	0.50 ± 1.09	0.41 [-0.15, 0.97]
Session 2				
Set 1	-0.17 ± 0.39	-0.05 [-0.59, 0.48]	-0.50 ± 0.52	-0.44 [-0.98, 0.1]
Set 2	-0.58 ± 1.00	-0.66 [-1.18, -0.14]	-0.58 ± 1.24	-0.62 [-1.17, -0.08]

2.2 Absolute RIR Accuracy Means Separated by RIR, Set, and Session

	1-RIR	Adjusted 1-RIR	3-RIR	Adjusted 3-RIR
Session 1				
Set 1	0.58 ± 0.67	0.52 [0.12, 0.92]	1.17 ± 0.94	1.22 [0.49, 1.95]
Set 2	0.25 ± 0.45	0.33 [-0.01, 0.66]	0.83 ± 0.83	0.81 [0.24, 1.38]
Session 2				
Set 1	0.17 ± 0.39	0.20 [-0.03, 0.42]	0.50 ± 0.52	0.45 [0.08, 0.82]
Set 2	0.58 ± 1.00	0.52 [0.12, 0.91]	1.08 ± 0.79	1.26 [0.53, 1.98]

Unadjusted means are presented as mean ± sd. Adjusted means are estimates extracted from the statistical modelling and are presented as estimated marginal means (95% confidence interval).

2.3 Parallel plot displaying raw (A) and absolute (B) RIR accuracy at several timepoints for 1- and 3-RIR.



Point estimates are presented as an estimated marginal mean with 95% CI. Zero (on the y-axis) indicates accurate RIR predictions. Individual participant values also displayed as part of the parallel plot to highlight change from set one to set two (for each session) and inter-individual variability in RIR accuracy. *RIR, repetitions-in-reserve.*

S3. RIR Accuracy – Exploratory Models

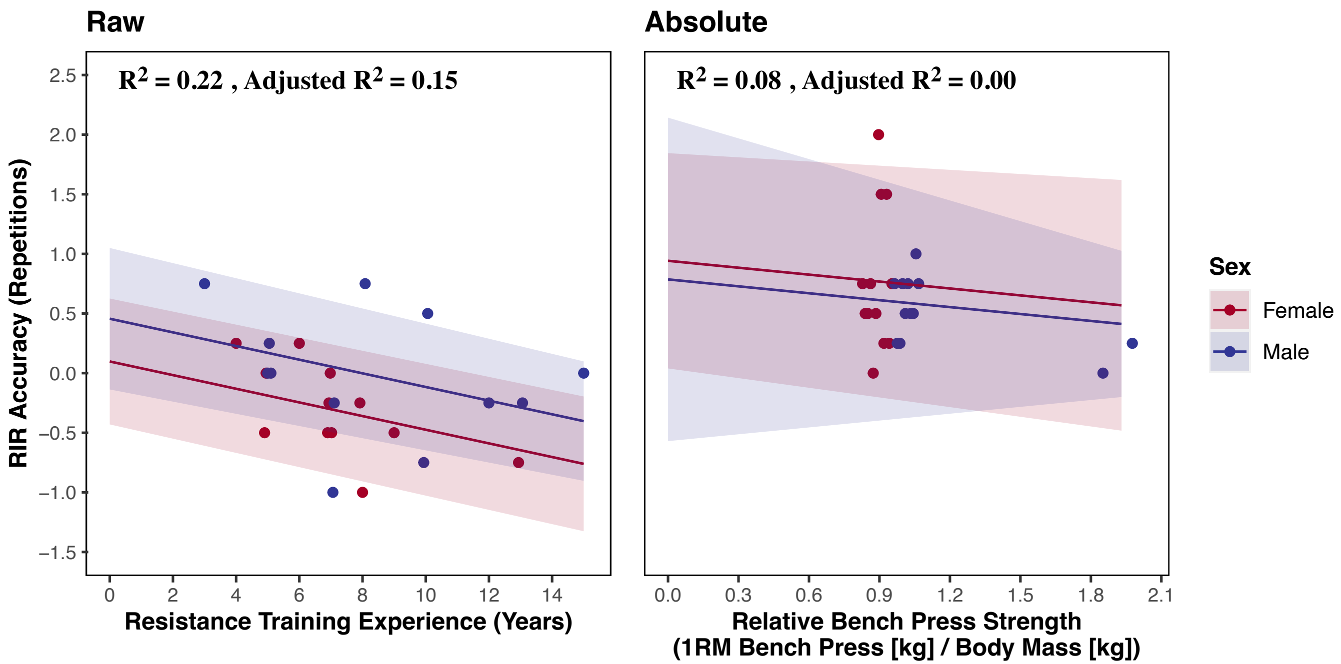
3.1 Raw RIR Accuracy Exploratory Multiple Regression Model Output

Predictors	Estimates	Standard Error	95% CI
(Intercept)	0.10	0.25	-0.43 – 0.63
Sex [Male]	0.36	0.18	-0.03 – 0.74
Resistance Training Experience (years)	-0.06	0.03	-0.12 – 0.01
Observations	24		
R^2	0.225		
Adjusted R^2	0.151		

3.2 Absolute RIR Accuracy Exploratory Multiple Regression Model Output

Predictors	Estimates	Standard Error	95% CI
(Intercept)	0.94	0.43	0.04 – 1.84
Sex [Male]	-0.16	0.30	-0.78 – 0.47
Relative Bench Press Strength (1RM/Body Mass)	-0.19	0.47	-1.16 – 0.77
Observations	24		
R^2	0.079		
Adjusted R^2	-0.009		

3.3 Exploratory Multiple Regression Model Plots



S4. Repetitions Performed Per Set

4.1 1-RIR Predictions

	Session 1	Session 2
Set 1	11.8 ± 2.2	12.3 ± 2.3
Set 2	9.9 ± 2.1	10.6 ± 2.4

4.2 3-RIR Predictions

	Session 1	Session 2
Set 1	11.2 ± 1.3	12.6 ± 2.6
Set 2	9.7 ± 2.5	10.8 ± 3.0

Appendix D. Supplementary File for Study Four

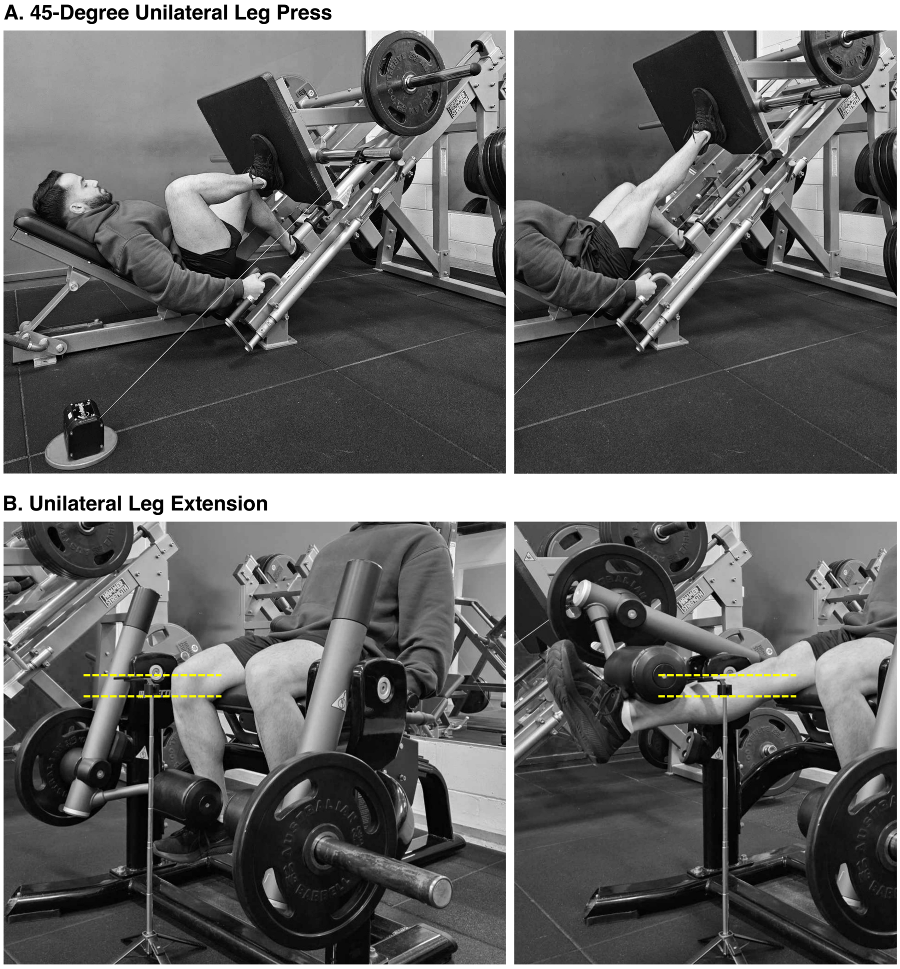
1. Additional Content

1.1 Exercise Control During Resistance Training Intervention

To minimise any potential confounding influences on outcome measures, participants were allowed to perform additional moderate-intensity RT involving muscle groups other than the quadriceps (i.e., the hamstrings, gluteals, calves, and upper-body muscles) for a maximum of 20 sets per muscle group per week, however, additional RT of the hamstrings and gluteals was limited to specific exercises to reduce quadriceps engagement.

Exercise Exclusions and Inclusions
Exercise Exclusions
All quadriceps exercises, including variations of: • Squat • Split squat • Lunge • Step up
All deadlift variations, including: • Conventional deadlift • Sumo deadlift • Stiff leg deadlift
Barbell hip thrust (full range-of-motion)
Exercise Inclusions
Romanian deadlift (without full knee extension)
Hamstring curl machines
Cable pull-through (without full knee extension)
Hip abduction
Glute cable kickback (straight leg)
Glute bridge
Barbell or machine hip thrust (short range-of-motion)
Back extension
Glute-ham raise

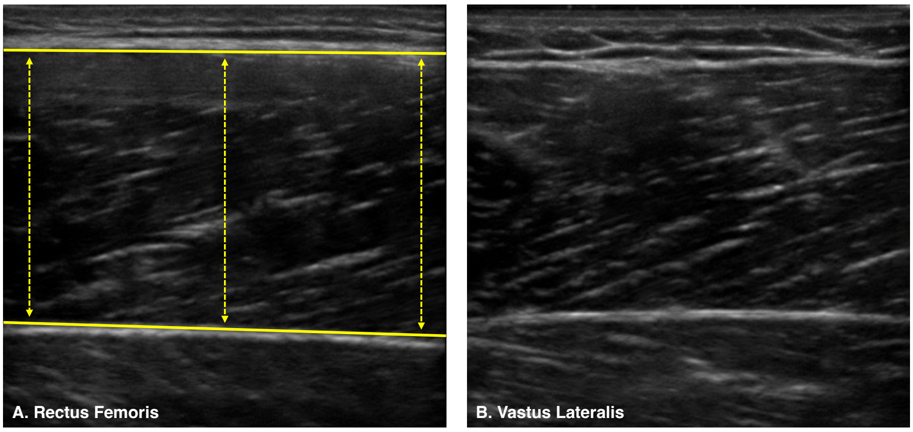
1.2 Visual Demonstration of Exercise Technique



Range-of-motion was individualised for each participant using the safety mechanism on the leg press machine and lifting velocity of repetitions on the leg press were tracked with a GymAware device as shown in Figure A. Yellow dotted lines in Figure B show an example of how range-of-motion was assessed on the leg extension using an external implement with upper and lower range-of-motion limits that were individualised for each participant.

1.3 Example Ultrasound Images and Reliability Scores

Test-retest reproducibility was carefully ensured by identifying structural patterns in the subcutaneous and connective tissues in the baseline scans (in subsequent scans, the baseline images were displayed next to the live view for direct comparison). Reliability of ultrasound imaging was assessed by generating the typical error (TE) and intraclass correlation (ICC) of the scans conducted in the pre- and post-testing weeks (two scans conducted 48-72 hours apart) using spreadsheets developed by Hopkins (Hopkins, Accessed September 2023). The reliability scores generated were similar to findings in previous research (Arruda et al., 2022) for the pre-testing (RF: TE = 0.05cm, ICC = 0.98; VL: TE = 0.07cm, ICC = 0.99) and post-testing (RF: TE = 0.04cm, ICC = 0.99; VL: TE = 0.06cm, ICC = 0.99) weeks. The same technician (MR) conducted and analysed all ultrasound scans to maximise the validity and reliability of the measurements.



Yellow arrows denote sites of measurement (cm) from the superficial aponeuroses to the deep aponeuroses (denoted by the horizontal yellow lines), with the average result of all three measurements used for further analysis.

2. Bayesian Data Analysis

The following supplementary information introduces the WAMBS (When to be concerned and how to prevent the misapplication of Bayesian Statistics) checklist as a diagnostic instrument employed to evaluate prior distributions, the estimation process, and the impact of priors on the analysis of outcome measures. The subsequent section provides a comprehensive explanation of the WAMBS checklist and its application.

THE WAMBS-CHECKLIST
When to worry, and how to Avoid the Misuse of Bayesian Statistics
DEPAOLI & VAN DE SCHOOT (2016)

	Did you show your supervisor…?	Should you worry?	Should you consult an expert?
TO BE CHECKED BEFORE ESTIMATING THE MODEL			
Point 1: Do you understand the priors?	Table 1	YES / NO	YES / NO
TO BE CHECKED AFTER ESTIMATION BUT BEFORE INSPECTING MODEL RESULTS			
Point 2: Does the trace-plot exhibit convergence?	Table 2, column 2	YES / NO	YES / NO
Point 3: Does convergence remain after doubling the number of iterations?	Table 4, columns 2, 3 (i) and akin to Table 3	YES / NO	YES / NO
Point 4: Does the histogram have enough information?	Table 2, column 3	YES / NO	n/a
Point 5: Do the chains exhibit a strong degree of autocorrelation?	Table 2, column 4	YES / NO	YES / NO
Point 6: Does the posterior distribution make substantive sense?	Table 2, column 5	YES / NO	YES / NO
UNDERSTANDING THE EXACT INFLUENCE OF THE PRIORS			
Point 7: Do different specifications of the multivariate variance priors influence the results?	Table 4, columns 2, 3 (ii)	YES / NO	YES / NO
Point 8: Is there a notable effect of the prior when compared with non-informative priors?	Table 4, columns 2, 3 (iii)	NEVER	n/a
Point 9: Are the results stable from a sensitivity analysis?	Sensitivity analysis akin to Table 5 or Figure 4	NEVER	YES / NO
AFTER INTERPRETATION OF MODEL RESULTS			
Point 10: Is the Bayesian way of interpreting and reporting model results used? *(a) Also report on: missing data, model fit and comparison, non-response, generalizability, ability to replicate, etc.*	Text – see Appendix	YES / NO	YES / NO

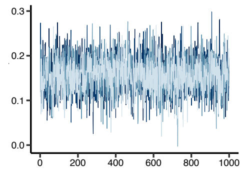
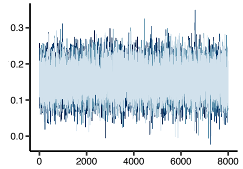
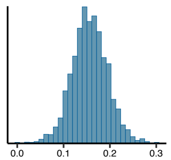
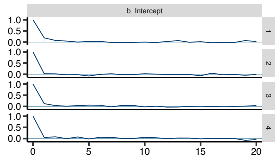
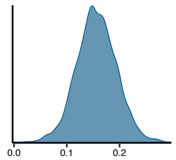
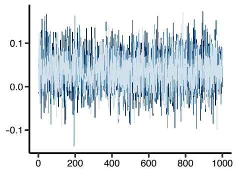
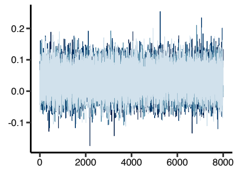
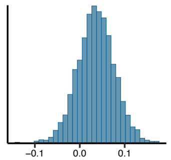
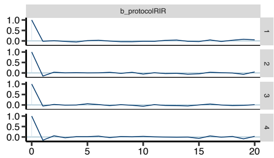
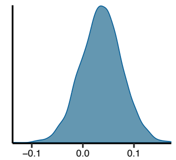
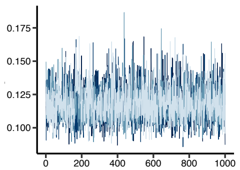
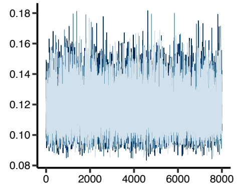
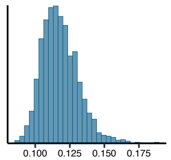
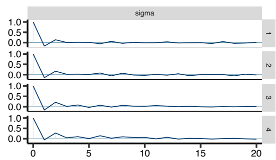
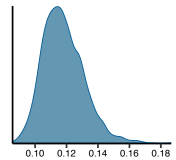
The WAMBS-checklist. Retrieved from Depaoli & Van De Schoot (Depaoli & van de Schoot, 2017) where further information about each point on the checklist can be found.

2.1 Bayesian Models (All Outcome Measures)

THE WAMBS-CHECKLIST
(Depaoli & Van De Schoot, 2016)

Prior to estimation	
1. Do you understand the priors?	Due to the uncertainty of the relevant literature, non-informative priors (i.e., default 'brms' priors) were used for this Bayesian analysis.
Estimation diagnosis	
2. Does the trace-plot exhibit convergence?	Yes, all trace-plots exhibit convergence.
3. Does convergence remain after doubling the number of iterations?	Yes, after doubling of iterations (from 10,000 to 20,000) the trace-plots still exhibit convergence as evidenced by our calculations of relative bias *[100 x (original estimate – new estimate / original estimate)]* that show the number of iterations did not meaningfully influence the posterior estimates.
4. Does the histogram have enough information?	Yes, histogram contains sufficient information, is smooth, and is absent of any gaps or other abnormalities.
5. Do chains exhibit autocorrelation?	Yes, autocorrelations plots exhibit appropriate dependence between samples.
6. Do posterior distributions make sense?	Yes, posterior distributions are clearly cantered around one value, display a realistic estimate, and make substantive sense based on our understanding.
Influence of priors	
7. Do different variance priors influence the results?	N/A
8. Is there a notable effect of the prior when compared with non-informative priors?	N/A
9. Are the results stable from a sensitivity analysis?	N/A
Interpretation of results	
10. Is the Bayesian way of interpretation and reporting model results used?	Yes, inferences from all the analyses were made from posterior samples generated using the Hamiltonian Markov Chain Monte Carlo method and via the use of high-density credible intervals (HDI). Interpretations were based on the estimate and associated HDI limits, along with the probability of direction (pd).

2.1.1 Model Diagnostics (Muscle Thickness)

Trace plot	Trace plot (double iterations)	Histogram	Autocorrelation	Kernel density
FAIL Parameter				
	 *Relative Bias = 0%*			
RIR Parameter				
	 *Relative Bias = 0%*			
Sigma Parameter				
	 *Relative Bias = 0%*			

NOTE: Diagnostics for all models (i.e., including outcomes other than muscle thickness) were also checked. See code: https://osf.io/34d92/

2.2 Population-Level Effects and Group-Level Slope Structures (All Outcome Measures)

To account for dependent observations in each model, group-level intercepts were included for each participant and each limb was nested within each participant. A maximal group-level slope structure (i.e., population-level effects as group-level slopes) was initially attempted, but then simplified until no errors were generated upon fitting the model (Barr et al., 2013; Oberauer, 2022).

Outcome	Population-Level Effects: Effects	Population-Level Effects: Interactions	Group-Level Slopes
Muscle thickness	• Protocol (FAIL or RIR) • Muscle (RF or VL) • Baseline muscle thickness	• Protocol x Muscle	• Protocol | id • 1 | id: limb
Δ Lifting velocity	• Protocol (FAIL or RIR) • Time (Weeks 1, 4, or 8) • First set LV (continuous) • Participant sex (male or female) • Number of sets performed (continuous)	• Protocol x Time	• Protocol x Time + First Set + Sets | id • 1 | id: limb
Δ Repetitions Performed	• Protocol (FAIL or RIR) • Time (continuous) • Exercise (leg press or leg extension) • Participant sex (male or female) • First set repetitions (continuous)	• Protocol x Time • Protocol x Exercise • Time x Exercise • Protocol x Time x Exercise	• Protocol x Time x Exercise + First Set + Sets | id • 1 | id: limb
Volume load	• Protocol (FAIL or RIR) • Time (continuous) • Exercise (leg press or leg extension) • Participant sex (male or female)	• Protocol x Time • Protocol x Exercise • Time x Exercise • Protocol x Time x Exercise	• Protocol x Time x Exercise + Sets | id • Time | id: limb
Repetition volume	• Protocol (FAIL or RIR) • Time (continuous) • Exercise (leg press or leg extension) • Participant sex (male or female)	• Protocol x Time • Protocol x Exercise • Time x Exercise • Protocol x Time x Exercise	• Protocol x Time x Exercise + Sets | id • Time + Exercise | id: limb

3. Additional Tables

3.1 Volume Load (Raw Values)

Protocol	Mean (kg)	*SD*
Leg Press		
FAIL	647	266
RIR	641	254
Leg Extension		
FAIL	284	61
RIR	288	58

Units = kilograms (kg)

3.2 Repetition Volume (Raw Values)

Protocol	Mean (Reps)	*SD*
Leg Press		
FAIL	48	7
RIR	45	7
Leg Extension		
FAIL	64	11
RIR	67	10

Units = repetitions

3.3 Quadriceps, Rectus Femoris and Vastus Lateralis Thickness (Raw Values)

Protocol	Mean (cm)	*SD*
Quadriceps (Combined Rectus Femoris and Vastus Lateralis)		
FAIL - Pre	2.593	0.477
FAIL - Post	2.773	0.511
RIR - Pre	2.611	0.419
RIR - Post	2.793	0.125
Rectus Femoris		
FAIL - Pre	2.610	0.366
FAIL - Post	2.766	0.393
RIR - Pre	2.603	0.287
RIR - Post	2.795	0.188
Vastus Lateralis		

FAIL - Pre	2.576	0.727
FAIL - Post	2.781	0.759
RIR - Pre	2.618	0.630
RIR - Post	2.791	0.663

Units = centimetres (cm)

3.4 Change in Lifting Velocity (Raw Values)

Protocol	Mean	*SD*
WEEK 1		
FAIL	–10.8%	10.5%
RIR	–5.4%	7.2%
WEEK 4		
FAIL	–13.5%	11.2%
RIR	–6.8%	5.3%
WEEK 8		
FAIL	–10.4%	12%
RIR	–7.5%	7.2%

Units = Mean concentric velocity (converted to percentage values)

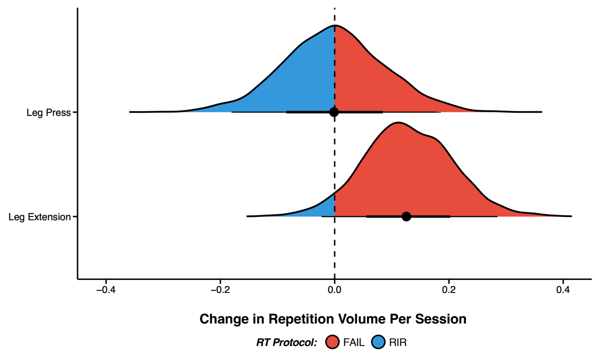
3.5 Sensitivity Analysis (with Full Sample)

Protocol	Estimated Mean (cm)	HDI
Within-Protocol		
FAIL	0.169	0.109 to 0.237
RIR	0.178	0.108 to 0.238
Between-Protocol		
FAIL vs RIR	-0.009	-0.065 to 0.052

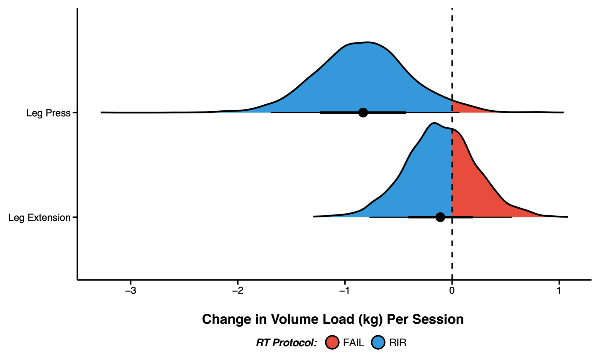
Units = centimetres (cm)
For between-protocol differences, negative estimates favour RIR, and positive estimates favour FAIL.

4. Additional Figures

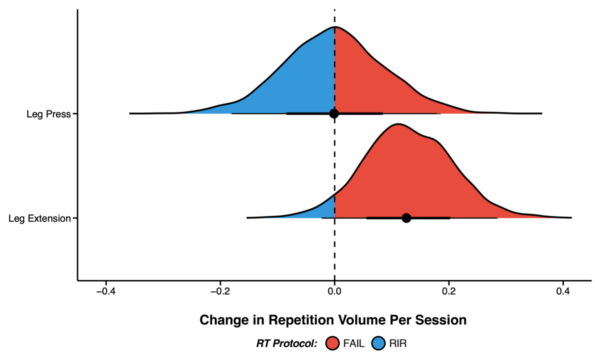
4.1 Contrast of Slopes for Change in Repetition Loss (%) Overtime



4.2 Contrast of Slopes for Volume Load (kg) Overtime



4.3 Contrast of Slopes for Repetition Volume Overtime



5. References

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Oberauer, K. (2022). The Importance of Random Slopes in Mixed Models for Bayesian Hypothesis Testing. *Psychol Sci*, *33*(4), 648-665. https://doi.org/10.1177/09567976211046884

Appendix E. Authorship Statement for Scoping Review

AUTHORSHIP STATEMENT

1. Details of publication and executive author

Title of Publication		Publication details
Towards an Improved Understanding of Proximity-to-Failure in Resistance Training and its Influence on Skeletal Muscle Hypertrophy, Neuromuscular Fatigue, Muscle Damage, and Perceived Discomfort: A Scoping Review		Journal of Sports Sciences
Name of executive author	School/Institute/Division if based at Deakin; Organisation and address if non-Deakin	Email or phone
Martin Refalo	School of Exercise and Nutrition Sciences	mrefalo@deakin.edu.au

2. Inclusion of publication in a thesis

Is it intended to include this publication in a higher degree by research (HDR) thesis?	Yes	If Yes, please complete Section 3 If No, go straight to Section 4.

3. HDR thesis author's declaration

Name of HDR thesis author if different from above. (If the same, write "as above")	School/Institute/Division if based at Deakin	Thesis title
As above	School of Exercise and Nutrition Sciences	Influence of Resistance Training 'Proximity-to-Failure' on Muscle Hypertrophy
If there are multiple authors, give a full description of HDR thesis author's contribution to the publication (for example, how much did you contribute to the conception of the project, the design of methodology or experimental protocol, data collection, analysis, drafting the manuscript, revising it critically for important intellectual content, etc.)		
The HDR thesis author contributed highly to all aspects and stages of this publication, including: Article conceptualisation, literature search, data extraction, drafted manuscript, critically revised manuscript.		
I declare that the above is an accurate description of my contribution to this paper, and the contributions of other authors are as described below.	Signature and date	8/12/23

4. Description of all author contributions

Name and affiliation of author	Contribution(s) (for example, conception of the project, design of methodology or experimental protocol, data collection, analysis, drafting the manuscript, revising it critically for important intellectual content, etc.)
Martin Refalo	Article conceptualisation, literature search, data extraction, drafted manuscript, critically revised manuscript.
Jackson Fyfe	Article conceptualisation, literature search, data extraction, drafted manuscript, critically revised manuscript.
Eric Helms	Article conceptualisation, critically revised manuscript.
Lee Hamilton	Critically revised manuscript.

5. Author Declarations

I agree to be named as one of the authors of this work, and confirm:

i. that I have met the authorship criteria set out in the Deakin University Research Conduct Policy,

ii. that there are no other authors according to these criteria,

iii. that the description in Section 4 of my contribution(s) to this publication is accurate,

iv. that the data on which these findings are based are stored as set out in Section 7 below.

If this work is to form part of an HDR thesis as described in Sections 2 and 3, I further

v. consent to the incorporation of the publication into the candidate's HDR thesis submitted to Deakin University and, if the higher degree is awarded, the subsequent publication of the thesis by the university (subject to relevant Copyright provisions).

Name of author	Signature*	Date
Jackson Fyfe		12/12/2023
Eric Helms		12/12/2023
Lee Hamilton		12/12/2023

6. Other contributor declarations

I agree to be named as a non-author contributor to this work.

Name and affiliation of contributor	Contribution	Signature* and date
N/A		

***** If an author or contributor is unavailable or otherwise unable to sign the statement of authorship, the Head of Academic Unit may sign on their behalf, noting the reason for their unavailability, provided there is no evidence to suggest that the person would object to being named as author

7. Data storage

The original data for this project are stored in the following locations. (The locations must be within an appropriate institutional setting. If the executive author is a Deakin staff member and data are stored outside Deakin University, permission for this must be given by the Head of Academic Unit within which the executive author is based.)

Data format	Storage Location	Date lodged	Name of custodian if other than the executive author
N/A			

This form must be retained by the executive author, within the school or institute in which they are based.

If the publication is to be included as part of an HDR thesis, a copy of this form must be included in the thesis with the publication.

Appendix F. Authorship Statement for Study One

AUTHORSHIP STATEMENT

1. Details of publication and executive author

Title of Publication		Publication details
Influence of Resistance Training Proximity-to-Failure on Skeletal Muscle Hypertrophy: A Systematic Review and Meta-Analysis.		Sports Medicine
Name of executive author	School/Institute/Division if based at Deakin; Organisation and address if non-Deakin	Email or phone
Martin Refalo	School of Exercise and Nutrition Sciences	mrefalo@deakin.edu.au

2. Inclusion of publication in a thesis

Is it intended to include this publication in a higher degree by research (HDR) thesis?	Yes	If Yes, please complete Section 3 If No, go straight to Section 4.

3. HDR thesis author's declaration

Name of HDR thesis author if different from above. (If the same, write "as above")	School/Institute/Division if based at Deakin	Thesis title
As above	School of Exercise and Nutrition Sciences	Influence of Resistance Training 'Proximity-to-Failure' on Muscle Hypertrophy
If there are multiple authors, give a full description of HDR thesis author's contribution to the publication (for example, how much did you contribute to the conception of the project, the design of methodology or experimental protocol, data collection, analysis, drafting the manuscript, revising it critically for important intellectual content, etc.)		
The HDR thesis author contributed highly to all aspects and stages of this publication, including: Article conceptualisation, literature search, data extraction, drafted manuscript, statistical analysis, critically revised manuscript.		
I declare that the above is an accurate description of my contribution to this paper, and the contributions of other authors are as described below.	Signature and date	 8/12/23

4. Description of all author contributions

Name and affiliation of author	Contribution(s) (for example, conception of the project, design of methodology or experimental protocol, data collection, analysis, drafting the manuscript, revising it critically for important intellectual content, etc.)
Martin Refalo	Article conceptualisation, literature search, data extraction, statistical analysis, drafted manuscript, critically revised manuscript.
Jackson Fyfe	Article conceptualisation, literature search, data extraction, drafted manuscript, critically revised manuscript.
Eric Helms	Article conceptualisation, critically revised manuscript.
Lee Hamilton	Critically revised manuscript.
Eric Trexler	Statistical analysis, critically revised manuscript.

5. Author Declarations

I agree to be named as one of the authors of this work, and confirm:

i. that I have met the authorship criteria set out in the Deakin University Research Conduct Policy,

ii. that there are no other authors according to these criteria,

iii. that the description in Section 4 of my contribution(s) to this publication is accurate,

iv. that the data on which these findings are based are stored as set out in Section 7 below.

If this work is to form part of an HDR thesis as described in Sections 2 and 3, I further

v. consent to the incorporation of the publication into the candidate's HDR thesis submitted to Deakin University and, if the higher degree is awarded, the subsequent publication of the thesis by the university (subject to relevant Copyright provisions).

Name of author	Signature*	Date
Jackson Fyfe		12/12/2023
Eric Helms		12/12/2023
Lee Hamilton		12/12/2023
Eric Trexler		12/12/2023

6. Other contributor declarations

I agree to be named as a non-author contributor to this work.

Name and affiliation of contributor	Contribution	Signature* and date
N/A		

***** If an author or contributor is unavailable or otherwise unable to sign the statement of authorship, the Head of Academic Unit may sign on their behalf, noting the reason for their unavailability, provided there is no evidence to suggest that the person would object to being named as author

7. Data storage

The original data for this project are stored in the following locations. (The locations must be within an appropriate institutional setting. If the executive author is a Deakin staff member and data are stored outside Deakin University, permission for this must be given by the Head of Academic Unit within which the executive author is based.)

Data format	Storage Location	Date lodged	Name of custodian if other than the executive author
Excel spreadsheets and R code	Deakin Research Data Store (RDS69939-PTF-Meta-Analysis)	12/12/2023	Martin Refalo

This form must be retained by the executive author, within the school or institute in which they are based.

If the publication is to be included as part of an HDR thesis, a copy of this form must be included in the thesis with the publication.

Appendix G. Authorship Statement for Study Two

AUTHORSHIP STATEMENT

1. Details of publication and executive author

Title of Publication		Publication details
Influence of Resistance Training Proximity-to-Failure, Determined by Repetitions-in-Reserve, on Neuromuscular Fatigue in Resistance-Trained Males and Females.		Sports Medicine - Open
Name of executive author	School/Institute/Division if based at Deakin; Organisation and address if non-Deakin	Email or phone
Martin Refalo	School of Exercise and Nutrition Sciences	mrefalo@deakin.edu.au

2. Inclusion of publication in a thesis

Is it intended to include this publication in a higher degree by research (HDR) thesis?	Yes	If Yes, please complete Section 3 If No, go straight to Section 4.

3. HDR thesis author's declaration

Name of HDR thesis author if different from above. (If the same, write "as above")	School/Institute/Division if based at Deakin	Thesis title
As above	School of Exercise and Nutrition Sciences	Influence of Resistance Training 'Proximity-to-Failure' on Muscle Hypertrophy
If there are multiple authors, give a full description of HDR thesis author's contribution to the publication (for example, how much did you contribute to the conception of the project, the design of methodology or experimental protocol, data collection, analysis, drafting the manuscript, revising it critically for important intellectual content, etc.)		
The HDR thesis author contributed highly to all aspects and stages of this publication, including: Article conceptualisation, data collection, drafted manuscript, statistical analysis, critically revised manuscript.		
I declare that the above is an accurate description of my contribution to this paper, and the contributions of other authors are as described below.	Signature and date	8/12/23

4. Description of all author contributions

Name and affiliation of author	Contribution(s) (for example, conception of the project, design of methodology or experimental protocol, data collection, analysis, drafting the manuscript, revising it critically for important intellectual content, etc.)
Martin Refalo	Data collection, article conceptualisation, drafted manuscript, statistical analysis, critically revised manuscript.
Jackson Fyfe	Article conceptualisation, drafted manuscript, statistical analysis, critically revised manuscript.
Eric Helms	Article conceptualisation, critically revised manuscript.
Lee Hamilton	Article conceptualisation, critically revised manuscript.

5. Author Declarations

I agree to be named as one of the authors of this work, and confirm:

i. that I have met the authorship criteria set out in the Deakin University Research Conduct Policy,

ii. that there are no other authors according to these criteria,

iii. that the description in Section 4 of my contribution(s) to this publication is accurate,

iv. that the data on which these findings are based are stored as set out in Section 7 below.

If this work is to form part of an HDR thesis as described in Sections 2 and 3, I further

v. consent to the incorporation of the publication into the candidate's HDR thesis submitted to Deakin University and, if the higher degree is awarded, the subsequent publication of the thesis by the university (subject to relevant Copyright provisions).

Name of author	Signature*	Date
Jackson Fyfe		12/12/2023
Eric Helms		12/12/2023
Lee Hamilton		12/12/2023

6. Other contributor declarations

I agree to be named as a non-author contributor to this work.

Name and affiliation of contributor	Contribution	Signature* and date
N/A		

***** If an author or contributor is unavailable or otherwise unable to sign the statement of authorship, the Head of Academic Unit may sign on their behalf, noting the reason for their unavailability, provided there is no evidence to suggest that the person would object to being named as author

7. Data storage

The original data for this project are stored in the following locations. (The locations must be within an appropriate institutional setting. If the executive author is a Deakin staff member and data are stored outside Deakin University, permission for this must be given by the Head of Academic Unit within which the executive author is based.)

Data format	Storage Location	Date lodged	Name of custodian if other than the executive author
Excel spreadsheets and R code	Deakin Research Data Store (RDS60538-PTF-and-Fatigue)	07/06/2022	Martin Refalo

This form must be retained by the executive author, within the school or institute in which they are based.

If the publication is to be included as part of an HDR thesis, a copy of this form must be included in the thesis with the publication.

Appendix H. Authorship Statement for Study Three

AUTHORSHIP STATEMENT

1. Details of publication and executive author

Title of Publication		Publication details
Accuracy of Intra-Set Repetitions-in-Reserve Predictions During the Bench Press Exercise in Resistance Trained Males and Females.		Journal of Strength and Conditioning Research
Name of executive author	**School/Institute/Division if based at Deakin; Organisation and address if non-Deakin**	**Email or phone**
Martin Refalo	School of Exercise and Nutrition Sciences	mrefalo@deakin.edu.au

2. Inclusion of publication in a thesis

Is it intended to include this publication in a higher degree by research (HDR) thesis?	Yes	If Yes, please complete Section 3 If No, go straight to Section 4.

3. HDR thesis author's declaration

Name of HDR thesis author if different from above. (If the same, write "as above")	School/Institute/Division if based at Deakin	Thesis title
As above	School of Exercise and Nutrition Sciences	Influence of Resistance Training 'Proximity-to-Failure' on Muscle Hypertrophy
If there are multiple authors, give a full description of HDR thesis author's contribution to the publication (for example, how much did you contribute to the conception of the project, the design of methodology or experimental protocol, data collection, analysis, drafting the manuscript, revising it critically for important intellectual content, etc.)		
The HDR thesis author contributed highly to all aspects and stages of this publication, including: Article conceptualisation, data collection, drafted manuscript, statistical analysis, critically revised manuscript.		
I declare that the above is an accurate description of my contribution to this paper, and the contributions of other authors are as described below.	Signature and date	8/12/23

4. Description of all author contributions

Name and affiliation of author	Contribution(s) (for example, conception of the project, design of methodology or experimental protocol, data collection, analysis, drafting the manuscript, revising it critically for important intellectual content, etc.)
Martin Refalo	Data collection, article conceptualisation, statistical analysis, drafted manuscript, critically revised manuscript.
Jackson Fyfe	Article conceptualisation, drafted manuscript, critically revised manuscript.
Eric Helms	Article conceptualisation, critically revised manuscript.
Lee Hamilton	Critically revised manuscript.
Jacob Remmert	Drafted manuscript, critically revised manuscript.
Zac Robinson	Drafted manuscript, statistical analysis, critically revised manuscript.
Joshua Pelland	Drafted manuscript, critically revised manuscript.
Michael Zourdos	Critically revised manuscript.

5. Author Declarations

I agree to be named as one of the authors of this work, and confirm:

i. that I have met the authorship criteria set out in the Deakin University Research Conduct Policy,

ii. that there are no other authors according to these criteria,

iii. that the description in Section 4 of my contribution(s) to this publication is accurate,

iv. that the data on which these findings are based are stored as set out in Section 7 below.

If this work is to form part of an HDR thesis as described in Sections 2 and 3, I further

v. consent to the incorporation of the publication into the candidate's HDR thesis submitted to Deakin University and, if the higher degree is awarded, the subsequent publication of the thesis by the university (subject to relevant Copyright provisions).

Name of author	Signature*	Date
Jackson Fyfe		12/12/2023
Eric Helms		12/12/2023
Lee Hamilton		12/12/2023
Jacob Remmert		12/12/2023
Zac Robinson	Zac Robinson	17/12/2023
Joshua Pelland		12/12/2023
Michael Zourdos		15/01/2024

6. Other contributor declarations

I agree to be named as a non-author contributor to this work.

Name and affiliation of contributor	Contribution	Signature* and date
N/A		

***** If an author or contributor is unavailable or otherwise unable to sign the statement of authorship, the Head of Academic Unit may sign on their behalf, noting the reason for their unavailability, provided there is no evidence to suggest that the person would object to being named as author

7. Data storage

The original data for this project are stored in the following locations. (The locations must be within an appropriate institutional setting. If the executive author is a Deakin staff member and data are stored outside Deakin University, permission for this must be given by the Head of Academic Unit within which the executive author is based.)

Data format	Storage Location	Date lodged	Name of custodian if other than the executive author
Excel spreadsheets and R code	Deakin Research Data Store (RDS69937-RIR-Accuracy)	12/12/2023	Martin Refalo

This form must be retained by the executive author, within the school or institute in which they are based.

If the publication is to be included as part of an HDR thesis, a copy of this form must be included in the thesis with the publication.

Appendix I. Authorship Statement for Study Four

AUTHORSHIP STATEMENT

1. Details of publication and executive author

Title of Publication		Publication details
Similar Muscle Hypertrophy Following 8-Weeks of Resistance Training to Momentary Muscular Failure or with Repetitions-in-Reserve in Resistance-Trained Individuals		In Peer Review
Name of executive author	**School/Institute/Division if based at Deakin; Organisation and address if non-Deakin**	**Email or phone**
Martin Refalo	School of Exercise and Nutrition Sciences	mrefalo@deakin.edu.au

2. Inclusion of publication in a thesis

Is it intended to include this publication in a higher degree by research (HDR) thesis?	Yes	If Yes, please complete Section 3 If No, go straight to Section 4.

3. HDR thesis author's declaration

Name of HDR thesis author if different from above. (If the same, write "as above")	School/Institute/Division if based at Deakin	Thesis title
As above	School of Exercise and Nutrition Sciences	Influence of Resistance Training 'Proximity-to-Failure' on Muscle Hypertrophy
If there are multiple authors, give a full description of HDR thesis author's contribution to the publication (for example, how much did you contribute to the conception of the project, the design of methodology or experimental protocol, data collection, analysis, drafting the manuscript, revising it critically for important intellectual content, etc.)		
The HDR thesis author contributed highly to all aspects and stages of this publication, including: Article conceptualisation, data collection, drafted manuscript, statistical analysis, critically revised manuscript.		
I declare that the above is an accurate description of my contribution to this paper, and the contributions of other authors are as described below.	Signature and date	21/01/2024

4. Description of all author contributions

Name and affiliation of author	Contribution(s) (for example, conception of the project, design of methodology or experimental protocol, data collection, analysis, drafting the manuscript, revising it critically for important intellectual content, etc.)
Martin Refalo	Data collection, article conceptualisation, drafted manuscript, statistical analysis, critically revised manuscript.
Jackson Fyfe	Article conceptualisation, drafted manuscript, critically revised manuscript.
Eric Helms	Article conceptualisation, critically revised manuscript.
Lee Hamilton	Article conceptualisation, critically revised manuscript.
Zac Robinson	Statistical analysis, critically revised manuscript.

5. Author Declarations

I agree to be named as one of the authors of this work, and confirm:

i. that I have met the authorship criteria set out in the Deakin University Research Conduct Policy,

ii. that there are no other authors according to these criteria,

iii. that the description in Section 4 of my contribution(s) to this publication is accurate,

iv. that the data on which these findings are based are stored as set out in Section 7 below.

If this work is to form part of an HDR thesis as described in Sections 2 and 3, I further

v. consent to the incorporation of the publication into the candidate's HDR thesis submitted to Deakin University and, if the higher degree is awarded, the subsequent publication of the thesis by the university (subject to relevant Copyright provisions).

Name of author	Signature*	Date
Jackson Fyfe		21/01/2024
Eric Helms		21/01/2024
Lee Hamilton		21/01/2024
Zac Robinson	Zac Robinson	21/01/2024

6. Other contributor declarations

I agree to be named as a non-author contributor to this work.

Name and affiliation of contributor	Contribution	Signature* and date
N/A		

***** If an author or contributor is unavailable or otherwise unable to sign the statement of authorship, the Head of Academic Unit may sign on their behalf, noting the reason for their unavailability, provided there is no evidence to suggest that the person would object to being named as author

7. Data storage

The original data for this project are stored in the following locations. (The locations must be within an appropriate institutional setting. If the executive author is a Deakin staff member and data are stored outside Deakin University, permission for this must be given by the Head of Academic Unit within which the executive author is based.)

Data format	Storage Location	Date lodged	Name of custodian if other than the executive author
Excel spreadsheets and R code	Deakin Research Data Store (RDS69941-PTF-and-Hypertrophy)	07/06/2022	Martin Refalo

This form must be retained by the executive author, within the school or institute in which they are based.

If the publication is to be included as part of an HDR thesis, a copy of this form must be included in the thesis with the publication.

Appendix J. Ethics Approval for Study Two

DEAKIN UNIVERSITY

Memorandum

To: Dr Jackson Fyfe
School of Exercise and Nutrition Sciences

B

cc: Mr Martin Charles Refalo
YUWEI XIE

From: Deakin University Human Research Ethics Committee (DUHREC)

Date: 06 April, 2022

Subject: 2021-407

Influence of Resistance Training Proximity-to-Failure on Acute and Delayed Neuromuscular Fatigue in Resistance-Trained Men and Women
Please quote this project number in all future communications

The DUHREC Executive has reviewed the modifications to this project received on 31/03/2022 and found them to comply with the National Statement on Ethical Conduct in Human Research 2007 (Updated 2018).

The DUHREC Executive has granted approval for Dr Jackson Fyfe, School of Exercise and Nutrition Sciences, to continue this project as modified to 6/01/2026.

The approval given by the Deakin University Human Research Ethics Committee is given only for the project and for the period as stated in the approval. It is your responsibility to contact the Human Research Ethics Unit immediately should any of the following occur:

- Serious or unexpected adverse effects on the participants
- Any proposed changes in the protocol, including extensions of time.
- Any events which might affect the continuing ethical acceptability of the project.
- The project is discontinued before the expected date of completion.
- Modifications are requested by other HRECs.
- Any complaints are received by the research team, an external HREC or, in the event of overseas research, an external complaints contact. In the case of overseas research, the local complaints contact should be aware that, where appropriate, they can directly contact DUHREC if they are unable to resolve a complaint or would like assistance in resolving a complaint.

In addition you will be required to report on the progress of your project at least once every year and at the conclusion of the project. Failure to report as required will result in suspension of your approval to proceed with the project.

DUHREC may need to audit this project as part of the requirements for monitoring set out in the National Statement on Ethical Conduct in Human Research 2007 (Updated 2018).

Please note: if you have indicated that your project will be conducted while COVID-19 restrictions are in place, approval has been granted in line with the current restrictions. It is the responsibility of the principal investigator to remain aware of any changes to the restrictions and in the event that such changes make the approved research non-compliant with the restrictions, to either seek approval for a further modification to the project, or postpone the research until the restrictions are lifted.

Human Research Ethics Unit
research-ethics@deakin.edu.au
Telephone: 03 9251 7123

Appendix K. Ethics Approval for Study Four

Memorandum

cc: Mr Martin Charles Refalo

To: Dr Jackson Fyfe

School of Exercise and Nutrition Sciences

B

From: Deakin University Human Research Ethics Committee (DUHREC)

Date: 01 March, 2023

Subject: 2022-329

Influence of Resistance Training Proximity-to-Failure, Determined by Repetitions-in-Reserve, on Skeletal Muscle Hypertrophy and Neuromuscular Fatigue in Resistance- Trained Males and Females.
Please quote this project number in all future communications

The DUHREC Executive has reviewed the modifications to this project received on 16/02/2023 and found them to comply with the National Statement on Ethical Conduct in Human Research 2007 (Updated 2018).

The DUHREC Executive has granted approval for Dr Jackson Fyfe, School of Exercise and Nutrition Sciences, to continue this project as modified to 13/12/2026.

The approval given by the Deakin University Human Research Ethics Committee is given only for the project and for the period as stated in the approval. It is your responsibility to contact the Human Research Ethics Unit immediately should any of the following occur:

- Serious or unexpected adverse effects on the participants
- Any proposed changes in the protocol, including extensions of time.
- Any events which might affect the continuing ethical acceptability of the project.
- The project is discontinued before the expected date of completion.
- Modifications are requested by other HRECs.
- Any complaints are received by the research team, an external HREC or, in the event of overseas research, an external complaints contact. In the case of overseas research, the local complaints contact should be aware that, where appropriate, they can directly contact DUHREC if they are unable to resolve a complaint or would like assistance in resolving a complaint.

In addition you will be required to report on the progress of your project at least once every year and at the conclusion of the project. Failure to report as required will result in suspension of your approval to proceed with the project.

DUHREC may need to audit this project as part of the requirements for monitoring set out in the National Statement on Ethical Conduct in Human Research 2007 (Updated 2018).

Please note: if you have indicated that your project will be conducted while COVID-19 restrictions are in place, approval has been granted in line with the current restrictions. It is the responsibility of the principal investigator to remain aware of any changes to the restrictions and in the event that such changes make the approved research non-compliant with the restrictions, to either seek approval for a further modification to the project, or postpone the research until the restrictions are

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