Dose-response modelling of resistance exercise across outcome domains in strength and conditioning: A meta-analysis.

Review Article

Running head: S&C dose-response modelling

Paul Alan Swinton[1], **Brad J. Schonefeld**[2], **Andrew Murphy**[1,3]

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[1] School of Health Sciences, Robert Gordon University, Aberdeen, UK

[2] Department of Exercise Science and Recreation, CUNY Lehman College, Bronx, NY

[3] Greater Western Sydney Giants, Sydney, Australia

Corresponding Author

Dr. Paul Swinton

School of Health Sciences, Robert Gordon University

Garthdee Road

Aberdeen, UK,

AB10 7QG

p.swinton@rgu.ac.uk, +44 (0) 1224 262 3361

Abstract

Objectives

The aim of this meta-analysis was to use contemporary modelling techniques to investigate resistance-only and resistance-dominant training interventions, and explore relationships between training variables (frequency, volume, intensity), participant characteristics (training status, sex) and improvements across a range of outcome domains including maximum strength, power, vertical jump, agility, and sprinting performance.

Methods

Data were obtained from a database of training studies conducted between 1962-2018, which comprised healthy trained or untrained adults engaged in resistance-only or resistance-dominant interventions. Studies were not required to include a control group. Standardized mean difference effect sizes were calculated and interventions categorized according to a range of training variables describing frequency, volume, overall intensity, and intensity of load. Bayesian mixed effects meta-analytic models were fitted with predictors added sequentially and compared based on predictive accuracy.

Results

Data from a total of 295 studies comprising 535 groups and 6710 participants were included with analyses conducted on time points ≤26 weeks. The best performing model included: duration from baseline, average number of sets, and the main and interaction effects between outcome domain and intensity of load (%1RM) expressed non-linearly. Model performance was not improved by the inclusion of participant training status or sex.

Conclusions

The current meta-analysis represents the most comprehensive investigation of dose-response relationships across a range of outcome domains commonly targeted within strength and conditioning to date. Results demonstrate the magnitude of improvements are predominantly influenced by training intensity of load and the outcome measured. When considering the effects of intensity as a %1RM, profiles differ across outcome domains with maximum strength likely to be maximised with the heaviest loads, vertical jump performance likely to be maximised with relatively light loads (~30%1RM), and power likely to be maximised with low to moderate loads (40-70% 1RM).

1.0 Introduction

Resistance exercise is established as one of the most effective training modalities within strength and conditioning (S&C) [1,2]. Research has shown that improvements in strength and power can be transferred to a range of important activities including sprinting and jumping [1,3,4]. Results from a recent large meta-analysis also highlighted the importance of training specificity, with the greatest improvements made when matching the training stimulus and the outcomes assessed (e.g. traditional resistance exercise with heavy loads matched with 1RM assessment) [5]. Beyond specificity, appropriate prescription of resistance exercise requires consideration of a range of acute program variables including volume, intensity, frequency, and potentially more subtle variables including exercise selection, and exercise order [6]. There have been attempts to provide general recommendations of training dose to maximise a range of outcome domains including strength, hypertrophy, power, and muscular endurance [6]. Previous research has also indicated that the training status of participants may play an important role and interact with training dose [7,8]. Greater understanding of dose-response relationships across a range of factors including the training modality, outcome domain, participant characteristics (e.g. training status and sex) and length of intervention is key for continued development of resistance exercise and the desire to avoid over- or under-loading.

Several systematic reviews have investigated training dose within S&C, with most focusing on development of strength and hypertrophy [7-16]. Seminal research conducted by Rhea and colleagues [7-9] were among the first to use meta-analytic techniques to quantify dose-response relationships. Initial research from Rhea et al. [9] incorporated data from 16 studies to compare single versus multiple sets and concluded that performance of three sets was more effective than a single set. The authors' first large scale meta-analysis of dose-response relationships for strength development included data from 140 studies and provided further support for the superiority of multiple sets, with four sets per muscle group concluded to produce the greatest improvements [7]. The results from the comprehensive analysis indicated different dose-response relationships for trained and untrained participants, with a higher intensity of load (80% 1RM) and a frequency of two days per week judged most effective for trained participants; and lower intensity of load (60% 1RM) and a frequency of three days per week judged most effective for untrained participants. In a follow-up analysis of data from 37 studies restricted to competitive athletes, Peterson et al. [8] concluded higher volumes (8 sets per muscle group) and intensity of load intensities (85% 1RM) resulted in the largest effects with no differences found between frequencies of two or three days per week. Collectively, the work from Rhea and colleagues synthesised results from almost 200 studies and confirmed the existence of dose-relationships for the development of strength and the likely moderation by participant characteristics including training status [17].

Recent meta-analyses investigating dose-response relationships in S&C have tended to focus on the manipulation of a smaller number of program variables and restricting analyses to more homogenous studies [10-16]. Meta-analyses from Grgic et al. [12] and Ralston et al. [13] investigated the effects of manipulating training frequency on strength improvements and incorporated data from 22 studies directly comparing frequencies of one to four days per week, and from 12 studies directly comparing frequencies of one to three days per week, respectively. Grgic et al. [12] concluded that higher training frequencies resulted in greater improvements in strength, but that these increases appeared to be primarily mediated through increased weekly volume. Similar conclusions were presented by Ralston et al. [13] showing that when resistance volume was equated across low (1 day week^{-1}), medium (2 days week^{-1}) or high (≥3 days week^{-1}) frequencies, similar increases in strength were obtained for both isolation and multi-joint exercises. Investigating both strength and muscle hypertrophy, Schoenfeld et al. [15] meta-analysed results from 21 studies directly comparing low-load (≤60%1RM) versus high-load (>60%1RM) resistance training. Studies were relatively homogenous tending to focus on exercises including the bench press, knee extension, and leg press, all performed to momentary muscular failure. Results from the meta-analysis identified greater improvements in 1RM strength with high-load resistance training; however, the transfer of training to isometric strength testing showed marginally greater effects favouring higher versus lower loads (ES: 0.16; 95% CI: -0.06, 0.37) [15]. Moreover, similar improvements were observed in muscle hypertrophy across conditions. The results presented by Schoenfeld et al. [15] highlight the potential for different dose-response relationships across outcomes routinely targeted in S&C.

Whilst both large meta-analyses comprising heterogenous studies and smaller, more focussed meta-analyses present different strengths and weaknesses, there is likely a benefit in simultaneously modelling dose-response relations across a broader range of outcome domains than has been investigated previously. The response to any training program is ultimately a complex interaction of a range of variables and participant characteristics; however, large modelling analyses have the potential to identify general trends that provide researchers and practitioners with important information on which to design more specific programs. With this perspective in mind, the purpose of this encompassing meta-analysis was to use contemporary modelling techniques to investigate resistance training interventions and explore relationships between training variables (e.g. frequency, volume, overall intensity, and intensity of load), participant characteristics (training status, sex) and a range of outcome domains including maximum strength, power, vertical jump, agility and sprinting performance that are key targets in S&C program design.

2.0 Methods

2.1 Overview of meta-analysis

The meta-analysis was conducted on a database of S&C training studies with analyses restricted to interventions that comprised resistance training only, or combined interventions where resistance training accounted for the majority of the training volume (e.g. resistance combined with plyometrics, speed, agility or power training). The database included information describing outcome variables, participant characteristics, training dose parameters along with baseline and follow-up means and standard deviations, as has been described elsewhere [1]. The information was used to calculate intervention-only (e.g. non-controlled) effect sizes designed to draw inferences from indirect comparisons. To conduct the meta-analysis, sequential hierarchical models were fitted to account for dependencies (e.g. reporting of multiple outcomes at multiple time points from the same study) and structure within the data (e.g. time points nested in outcomes, nested in studies). Participant, training dose, and intervention characteristics were sequentially added to models to identify the most influential factors whilst monitoring changes caused by underlying associations among the variables. The focus of this meta-analysis was to quantify and describe the general influence of training dose across a range of outcomes commonly investigated in S&C studies.

2.2 Search strategy and reporting

The present review was conducted as a follow-up to a larger review that featured a broader range of training interventions [1]. The search for the original review was performed using Embase, Medline, Web of Science, Sport Discus and Google Scholar. Hand searching of relevant journals including Medicine and Science in Sports and Exercise, the Journal of Strength and Conditioning Research, and Research Quarterly was also conducted. Database search terms were included to identify various training modes and a range of outcome measures. The following keywords and phrases were combined with Boolean operators; “strength” OR “resistance” OR “sprint” OR “plyometric” OR “exercise” AND “intervention” OR “training” OR “program” OR “programme” AND “1RM” OR “repetition maximum” OR “speed” OR “velocity” OR “power” OR “jump” OR “change of direction” OR “agility” OR “acceleration” OR “rate of force development”. No restriction was placed on the date of the study with searching conducted in January 2018. Reporting of this review was guided by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 [18] statement with checklist included for transparency (Supplementary 1). Risk of bias assessment was not conducted.

2.3 Inclusion criteria and data extraction

Inclusion and exclusion criteria for the current meta-analysis were set to include as many relevant S&C training studies as possible. Inclusion criteria comprised: 1) any resistance training or majority resistant training-based study ≥ 4 weeks; 2) healthy trained or untrained participants with a mean age between 14 and 60; 3) training group with a minimum of 4 participants; 4) pre- and post-training means and standard deviations; and 5) sufficient information provided to quantify training intensity, volume, and frequency. Studies did not require a control or comparator group to be included. A standardised extraction codebook was developed using Microsoft Excel, with data extracted and coded independently by four researchers in duplicate with, one reviewer (AM) completing extraction for all studies to provide consistency. Data regarding the study (authors, year, total number of active intervention groups); participant characteristics (final study n, sex, training status, and age); outcome domain (maximum strength, power, jump performance, and sprinting performance); training dose (overall intensity, intensity of load, volume, frequency, number of exercises, number of sets, number of repetitions), and pre- and post-training means and standard deviations were obtained. The definitions used to categorise outcome domains included: 1) maximum strength: a measure of maximum force production where time was not limited (e.g. 1-6 repetition maximum, isometric mid-thigh pull, peak torque); 2) power: a direct measurement of power output measured in Watts (absolute and normalised relative to body mass); 3) jump performance: measure of jump height or distance; 4) sprint performance: a measurement of the time to complete a specified linear distance or the velocity achieved; and 5) agility performance: a measurement of the time to complete a change of direction or reactive task. Training status was categorised based on the mean S&C training experience as untrained (<1 year), recreationally trained (1-5 years), or highly trained (>5 years). If the mean S&C training experience was not stated, the minimum required experience was used for categorisation. Sex of the groups were categorised as male-only, female-only, or mixed sex. Criteria used to quantify overall intensity and volume for each training mode can be found in Table 1. In brief, overall intensity was categorised specific to each domain and considered both intensity of effort and mechanical factors. In addition, intensity of load was also quantified based on the mean percentage of one repetition maximum (%1RM) used in the resistance training. In cases where %1RM was not explicitly stated, %1RM values were estimated based on the number of repetitions performed per set using methods outlined by Haff and Triplett [**Error! Reference source not found.**] (Supplementary 2). Training frequency was classified as the average number of sessions per week throughout the intervention.

Table 1: Criteria used to categorise overall intensity and volume of each training mode included.

Training Mode	***Intensity Categorisation***	***Volume Categorisation***
Resistance Training	Coding based on %1RM 1 = Low 0-59.9%1RM 2 = Moderate 60-84.9%1RM 3 = High ≥85%1RM In cases where %1RM was not explicitly stated, %1RM value and category were estimated based on the number of repetitions performed per set using methods outlined by Haff and Triplett [19] (Supplementary 2)	Average number of repetitions performed per set in key exercises 1: Low - 1-5 2: Mid - 6-10 3: High - 11+
Plyometric	Based on the exercises included, for example: 1 = Low – low amplitude hopping, box jumps, squat jumps 2 = Moderate – bounding, lateral jumps, hurdle jumps, countermovement jump, drop jump with <30cm drop 3 = High – drop jump with >30cm drop, multidirectional bounding, single leg jumps, rebounding jumps	Average number of foot contacts per session 1: Low - <80 2: Mid - 80-120 3: High - 120>
Ballistic	Always categorised as high intensity due to high levels of relative effort required, unless it was explicitly stated sub-maximal effort was used	Average number of repetitions performed per set 1: Low - 1-3 2: Mid - 4-6 3: High - 7+
Sprint	Always categorised as high intensity due to high levels of relative effort required, unless it was explicitly stated sub-maximal effort was used (e.g. skipping, marching sub-maximal runs)	Average number of runs per session 1: Low - 1-4 2: Mid - 5-9 3: High 10+
Agility	Based on exercises included: 1 = Low – ladder drills, footwork drills, single turn run with <90^0 change of direction (COD), 2 = Moderate – lateral movement drills, single turn with >90^0 COD, 3 = High – multiple sharp COD's, 505 drills, reactive drills	Average number of runs per session 1: Low - 1-5 2: Mid - 6-9 3: High 10+
Combined	Combinations of resistance, sprint, ballistic, plyometric and agility training. To be considered a combined training mode, the secondary mode must account for at least 30% of total lower body training volume Categorisation of 1 = Low, 2 = Mid, 3 = High, based on categorisation of included training types	Categorisation of 1 = Low, 2 = Mid, 3 = High, based on categorisation of included training types

2.4 Statistical analysis

Effect sizes and their sampling variance were calculated using group mean and standard deviation values calculated pre-intervention and at any subsequent time-point. $\mathrm{SMD_{pre}}$ was calculated by dividing the relevant mean difference by the pre-intervention standard deviation. The sampling variance $\sigma_e^2(\mathrm{SMD_{pre}})$ of the effect size [20] was calculated with the following formula:

$$\sigma_e^2(\mathrm{SMD_{pre}}) = \frac{n-1}{n(n-3)}\left(2(1-r) + n\mathrm{SMD_{pre}^2}\right) - \frac{\mathrm{SMD_{pre}^2}}{c(n-1)^2}$$

where n is the sample size, r is the correlation between repeated measures, and $c(n-1)$ is the bias function which was approximated by $1 - \frac{3}{4n-5}$ [21]. To account for the small sample sizes generally used in S&C, a bias correction was applied to the effect size and sampling variance by multiplying by the approximated bias function and its square, respectively.

All meta-analyses were conducted using a nested four-level mixed effects meta-analytic model. The series of nestings included the individual study (level 4), the outcome (level 3), the measurement occasion (level 2) as many studies included more than just pre- and post-intervention assessments, and the within study sampling variance (level 1). A representation of the meta-analyses conducted includes:

$$\text{Level1: } d_{ijk} = \beta_{0ijk} + e_{ijk}, \qquad e_{ijk} \sim N(0, \sigma_e^2)$$

$$\text{Level2: } \beta_{0ijk} = \eta_{0jk} + \beta_{2,1}x_{2,1ijk} + r_{ijk}, \qquad r_{ijk} \sim N(0, \sigma_r^2)$$

$$\text{Level3: } \eta_{0jk} = \theta_{0k} + \beta_{3,1}x_{3,1jk} + \beta_{3,2}\left(x_{3,1jk} * x_{4,1k}\right) + u_{0jk}, \quad u_{0jk} \sim N(0, \sigma_u^2)$$

$$\text{Level4: } \theta_{0k} = \gamma_0 + \beta_{4,1}x_{4,1k} + s\left(x_{4,2k}\right) + v_{0k}, \qquad v_{0k} \sim N(0, \sigma_v^2)$$

where d_{ijk} is the observed effect size at measurement occasion i $(i = 1,2,\ldots,I_{jk})$, from outcome j $(j = 1,2,\ldots,J_k)$ and from study k $(k = 1,2,\ldots,K)$. The indexing I_{jk} denotes that the number of measurement occasions may vary across outcomes and studies, and J_k denotes the number of outcomes may vary across studies. The random effects across the different levels ($v_{0k}, u_{0jk}, r_{ijk}, e_{ijk}$) were assumed to be independent. β terms represent regression coefficients for the predictor variables x included at levels 2 to 4. Cross-level interactions are denoted by $*$ and for some continuous predictors, smooth functions (simple basis functions) were used to model non-linear effects of the predictor and are denoted by $s(x)$.

Predictors were added at level 2 (time of measurement from baseline), level 3 (outcome domain as a categorical predictor [strength, power, sprint, vertical jump, agility]) and level 4 (number of repetitions as a categorical predictor [low<8, high≥8]; number of repetitions as a smooth predictor; number of sets; number of sets as a smooth predictor; number of sets as a categorical predictor [low<4, high≥4]; number of sessions per week as a categorical predictor [low<3, high≥3]; number of sessions per week as a smooth predictor; number of exercises as a categorical predictor [low<4, high≥4]; number of exercises as smooth predictor; volume as a categorical predictor [low< 2, mid=2, high>2]; overall intensity as a categorical predictor [low < 2, mid = 2, high >2]; intensity of load (%1RM) as a categorical predictor [low<80; high≥80]; intensity of load (%1RM) as a smooth predictor; sex as a categorical variable [males, females, mixed]; and training status as a categorical predictor [untrained, recreationally trained, highly trained].

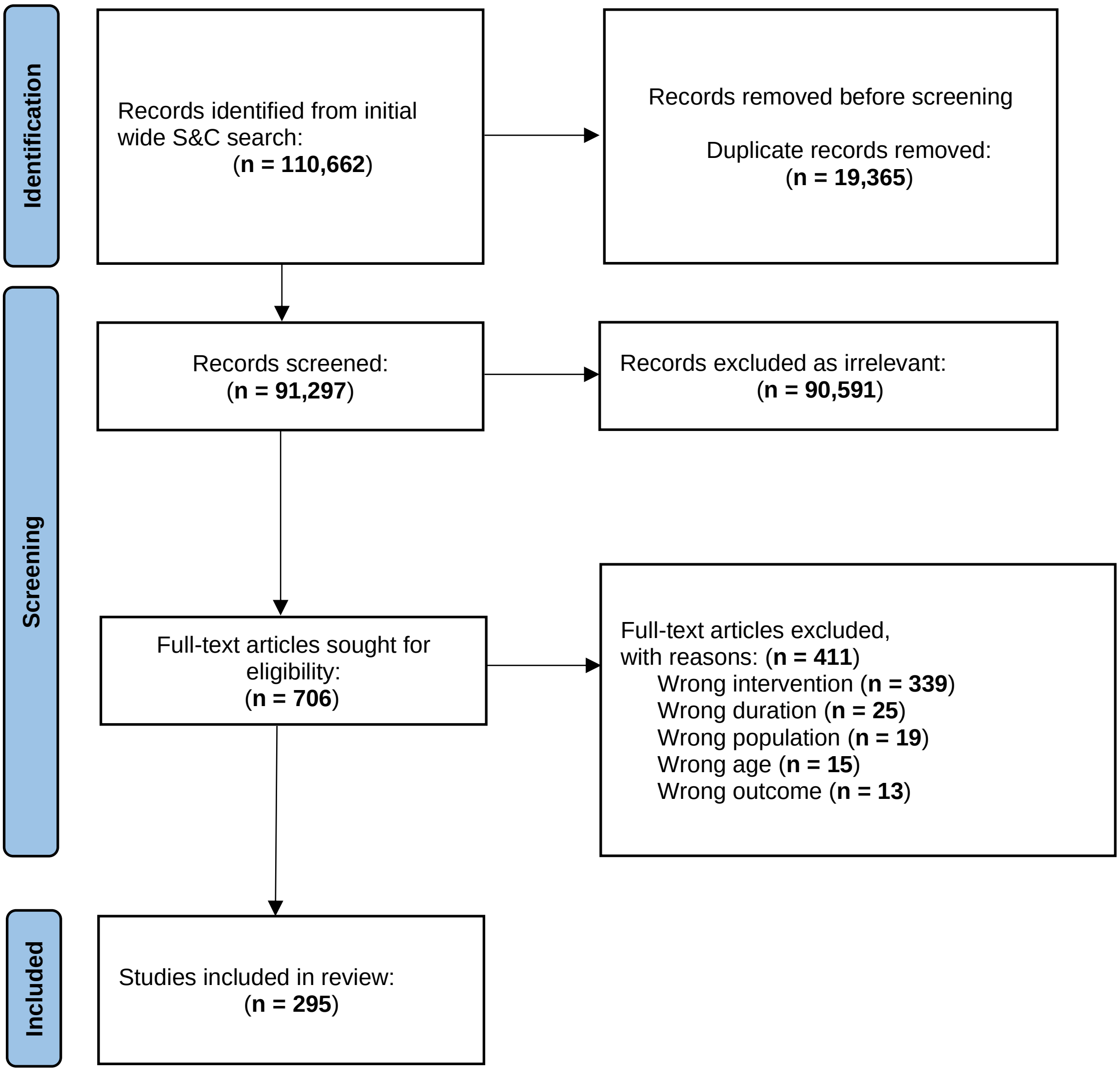
Candidate models were fitted and compared based on predictive accuracy using the theoretical expected log pointwise predictive density (ELPD) for a new dataset that was estimated with leave-one-out cross validation (ELPD-LOO) [22]. The ELPD-LOO generates a standard error that describes the uncertainty in the predictive performance for unknown future data. Candidate models were fit gradually increasing the number of predictors starting at level 2 and progressing to level 4. The ELPD-LOO difference between a new and previous model was calculated and addition of the predictor judged as an improvement and maintained in subsequent models if the value was at least two times the standard error. Median values and 95% credible intervals were presented for regression coefficients where predictors were found to improve the previous model, with the marginal effect of smooth terms visualised using plots and illustrating uncertainties. All analyses were conducted in R [23], with models fit using the brms package interfaced with Stan [24] to perform sampling, and leave-one-out cross validation performed using the loo package [25]. Analyses were completed across the entire data set including both resistance-only and resistance-dominant training interventions, with a sensitivity analysis completed with resistance-only training interventions. Outlier SMD_{pre} values were identified by adjusting the distribution by a Tukey g-and-h distribution and obtaining the 0.0035- and 0.9965-quantiles, with values beyond these points removed prior to further analysis [26]. Convergence of parameter estimates were obtained for all models with Gelman-Rubin R-hat values below 1.1 [27]. No attempts were made to assess certainty in the body of evidence for an outcome.

3.0 Results

3.1 Descriptions of data

Data from a total of 295 studies comprising 535 groups and 6710 participants were obtained (Figure 1 and reference list provided in Supplementary 3). Of the 535 groups, 372 comprised resistance training only (n=4664), and 163 comprised resistance training combined with other training modalities (n=2046). Sixty-five percent of groups were categorised as male-only, 23% were categorised as mixed sex, and 12% were categorised as female-only. Fifty-four percent of groups were categorised as untrained, 41% were categorised as recreationally trained, and 5% were categorised as highly trained. The duration of interventions ranged from 4 to 208 weeks with 97% of the data obtained from interventions ≤26 weeks. Analyses were thus restricted to time points ≤26 weeks following baseline, which provided data from 3065 outcomes (maximum strength: 1546 [50%]; power: 550 [18%]; jump performance: 512 [17%]; sprint performance: 370 [12%]; agility performance 87 [3%]). Results presented in text are from the complete data set comprising both resistance-only and resistance-dominant training interventions. Sensitivity analyses conducted with resistance-only training interventions were consistent with the larger data set. Full details of the best predictor models at each level for both resistance-only and resistance-dominant training interventions are presented in Tables 2 and 3.

Figure 1: Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram for included studies.



3.2 Null model

A total of 61 outliers were removed from the analysis such that effects sizes ranged from -0.83 to 4.7. For the null model the pooled mean effect size was $\mathrm{SMD}_{0.5}$ =0.55 [95%CrI: 0.51 to 0.60], with between-study standard deviation $\tau_{0.5}$=0.33 [75%CrI: 0.31 to 0.36] (Table 2).

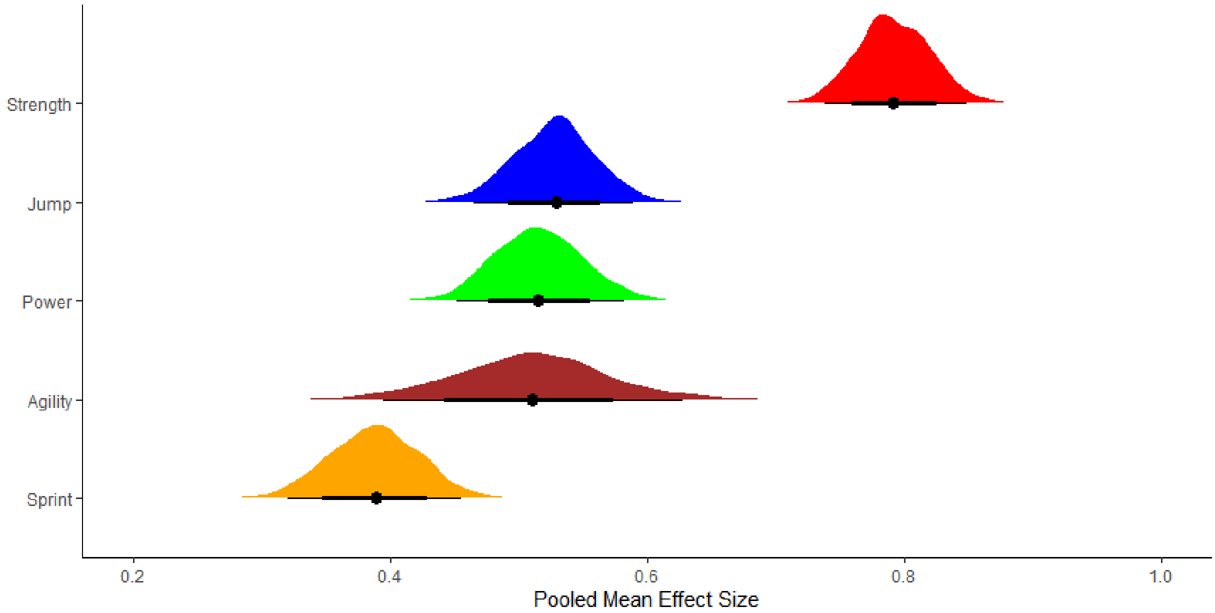
3.3 Level 2 predictors

The only level 2 predictor included was time of measurement following baseline. The median time of measurement was 8 weeks (IQR: 6-12), with binary (short: ≤8 weeks, long: >8 weeks) and linear predictors investigated. Binary categorisation showed an increase in mean pooled effect size with longer interventions ($\mathrm{SMD}_{\mathrm{short:long},0.5}$=0.17 [95%CrI: 0.11 to 0.23]), and for the continuous linear predictor the weekly increase was estimated as $\mathrm{SMD}_{\beta_{\mathrm{Time},0.5}}$=0.03 [95%CrI: 0.02 to 0.04]. The ELPD-LOO difference comparing the null model and inclusion of categorical time or continuous time showed improved model performance and was equal to -11.9 [se: 5.2] and -12.1 [se: 4.2], respectively. All subsequent models including those assessed as part of the sensitivity analysis featured time as a linear predictor (Tables 2 and 3).

3.4 Level 3 predictors

The only level 3 predictor assessed was the outcome domain measured (Figure 2). Using maximum strength as the reference level, the mean pooled value was higher in this domain compared to all others ($\mathrm{SMD}_{\mathrm{strength:agility},0.5}$=-0.28 [95%CrI: -0.39 to -0.17]; $\mathrm{SMD}_{\mathrm{strength:jump},0.5}$=-0.26 [95%CrI: -0.32 to -0.21]; $\mathrm{SMD}_{\mathrm{strength:power},0.5}$=-0.28 [95%CrI: -0.33 to -0.23]; $\mathrm{SMD}_{\mathrm{strength:sprint},0.5}$=-0.40 [95%CrI: -0.47 to -0.34]). The effect of time remained positive after including outcome domain ($\mathrm{SMD}_{\beta_{\mathrm{Time},0.5}}$=0.03 [95%CrI: 0.02 to 0.03]), with a large improvement in model performance (ELPD-LOO difference: -46.8 [se: 12.0]). All subsequent models including those assessed as part of the sensitivity analysis featured time as a continuous predictor and outcome domain (Tables 2 and 3).

Figure 2: Posterior distributions of pooled mean effect sizes across outcome domains.



Values represent shrunken values after fitting meta-analytic model also accounting for time of measurement. Black lines represent 75 and 95% Credible intervals.

3.5 Level 4 predictors

Initial analyses were conducted using the categorical volume and overall intensity predictors. No improvement in model performance relative to inclusion of time and outcome domain was obtained for volume (ELPD-LOO difference: +5.2 [se: 4.6]). In contrast, improvement was observed for overall intensity (ELPD-LOO difference: -6.6 [se: 2.2]) with evidence of greater mean pooled values for medium ($\text{SMD}_{\text{low:medium},0.5}$= 0.07 [95%CrI: 0.00 to 0.15]) and high categories ($\text{SMD}_{\text{low:high},0.5}$= 0.10 [95%CrI: 0.01 to 0.19]). The inclusion of smooth terms showed no improvement in model performance when adding the number of sessions per week (ELPD-LOO difference: +3.4 [se: 2.0]) or the average number of exercises per session (ELPD-LOO difference: +1.0 [se: 2.6]). Limited evidence of model improvement was obtained with inclusion of smooth terms for the average number of repetitions per session (ELPD-LOO difference: -6.4 [se: 3.7]). The marginal effect illustrated a consistent decrease in effect size with greater number of repetitions that slowed after 10 repetitions. Stronger evidence of model improvement using smooth terms was obtained for intensity of load with values expressed as percentage of maximum (ELPD-LOO difference: -18.0 [se: 4.5]) and the average number of sets per session (ELPD-LOO difference: -17.5 [se: 4.4]) Marginal smooths illustrated that the relationship was monotonic but non-linear for intensity of load with a reduced incline between 65 and 100% of maximum. The relationship was found to be linear for the average number of sets per session, with an increasing mean effect size association with a greater number of sets ($\mathrm{SMD}_{\beta_{\mathrm{Sets},0.5}}=$ 0.05 [95%CrI: 0.03 to 0.07]).

No improvement in model performance was obtained for the addition of sex (ELPD-LOO difference: +2.9 [se: 2.3]) or training status (ELPD-LOO difference: +0.2 [se: 2.3]). The same lack of improvement in model performance was obtained with sensitivity analyses conducted with resistance-only interventions. A final best performing model including both the average number of sets per session ($\mathrm{SMD}_{\beta_{\mathrm{Sets},0.5}}=$ 0.05 [95%CrI: 0.03 to 0.07]) and smoothed intensity of load was obtained for the complete data set and for resistance-only training interventions (Tables 2 and 3).

3.6 Cross-level interactions between levels 3 and 4

Potential cross-level interactions were investigated separately between outcome domain and both average number sets per session and intensity of load. No improvement in model performance was obtained for the cross-level interaction between outcome domain and average number of sets per session (ELPD-LOO difference: -0.6 [se: 3.5]). In contrast, model performance was increased for the cross-level interaction between outcome domain and intensity of load (ELPD-LOO difference: -0.6 [se: 3.5]), with spline modelled intensity showing markedly different relationships across the different outcome domains (Table 2 and Figure 3).

Table 2: Best performing models at each stage of analysis for complete data set comprising both resistance-only and resistance-dominant training interventions.

Level	Included data	Additional Included variables [95%CrI]	ELPD-LOO [Standard error]	ELPD-LOO difference	Level 2 standard deviation [75%CrI]	Level 3 standard deviation [75%CrI]	Level 4 standard deviation [75%CrI]
1	291 studies 3004 outcomes	Null model; Mean: 0.55 [0.51 to 0.60]	-1805 [60.9]		0.33 [0.31 to 0.36]	0.25 [0.24 to 0.26]	0.05 [0.02 to 0.07]
2	291 studies 3004 outcomes	Time (Weeks): 0.03 [0.02 to 0.04]	-1792 [61.2]	-12.1 [4.2]	0.33 [0.32 to 0.35]	0.24 [0.22 to 0.25]	0.05 [0.02 to 0.08]
2+3	291 studies 3004 outcomes	Outcome domain: Strength: 0.79 [0.74 to 0.84] Jump: 0.53 [0.47 to 0.59] Power: 0.52 [0.45 to 0.58] Agility: 0.51 [0.39 to 0.63] Sprint: 0.39 [0.32 to 0.46]	-1728 [62.0]	-46.8 [12.0]	0.33 [0.31 to 0.36]	0.20 [0.19 to 0.22]	0.05 [0.02 to 0.08]
2+3+4	265 studies 2795 outcomes	Average number sets 0.05 [0.03 to 0.07] Smooth(Intensity value %1RM)	-1600 [59.9]	-12.8 [3.8]	0.33 [0.31 to 0.36]	0.21 [0.20 to 0.22]	0.04 [0.01 to 0.07]
2+3*4	265 studies 2795 outcomes	Interaction between Outcome domain and Smooth(Intensity value %1RM)	-1588 [59.8]	-11.7 [4.8]	0.33 [0.31 to 0.36]	0.20 [0.19 to 0.22]	0.05 [0.02 to 0.08]

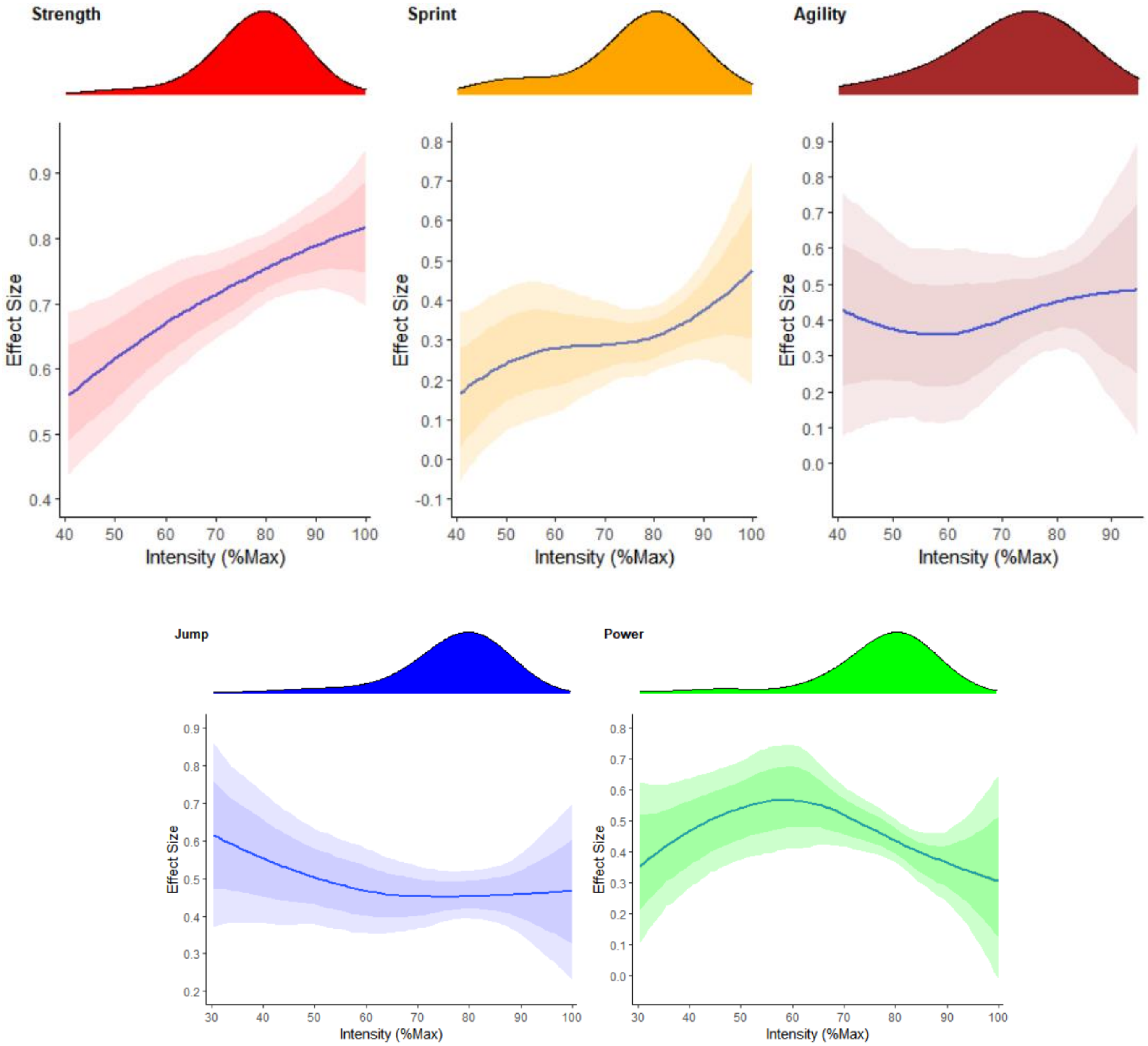
CrI: Credible interval. Table shows the additional variables included at each stage of the sequential process along with posterior estimates of model parameters, except for variables where smooth terms were added. At each stage, models also include variables identified as providing the best performance at the preceding stage.

Table 3: Best performing models at each stage of analysis for resistance-only training interventions.

Level	Included data	Additional Included variables [95%CrI]	ELPD-LOO [Standard error]	ELPD-LOO difference	Level 2 standard deviation [75%CrI]	Level 3 standard deviation [75%CrI]	Level 4 standard deviation [75%CrI]
1	197 studies 1876 outcomes	Null model; Mean: 0.58 [0.52 to 0.64]	-1197 [45.8]		0.36 [0.33 to 0.39]	0.26 [0.24 to 0.27]	0.10 [0.08 to 0.13]
2	197 studies 1876 outcomes	Time (Weeks): 0.03 [0.02 to 0.04]	-1189 [45.7]	-8.3 [3.3]	0.36 [0.34 to 0.39]	0.24 [0.22 to 0.26]	0.11 [0.08 to 0.13]
2+3	197 studies 1876 outcomes	Outcome domain: Strength: 0.79 [0.74 to 0.85] Jump: 0.54 [0.46 to 0.62] Power: 0.50 [0.42 to 0.58] Agility: 0.58 [0.42 to 0.70] Sprint: 0.45 [0.36 to 0.55]	-1162 [62.0]	-18.4 [6.5]	0.34 [0.32 to 0.38]	0.22 [0.20 to 0.23]	0.10 [0.08 to 0.13]
2+3+4	177 studies 1714 outcomes	Average number sets: 0.07 [0.04 to 0.09] Smooth(Intensity value %1RM)	-1077 [41.6]	-8.5 [3.1]	0.36 [0.33 to 0.40]	0.22 [0.20 to 0.24]	0.11 [0.09 to 0.13]
2+3*4	177 studies 1714 outcomes	Interaction between Outcome domain and Smooth(Intensity value %1RM)	-1061 [41.8]	-12.0 [4.2]	0.35 [0.31 to 0.39]	0.23 [0.20 to 0.25]	0.10 [0.08 to 0.13]

CrI: Credible interval. Table shows the additional variables included at each stage of the sequential process along with posterior estimates of model parameters, except for variables where smooth terms were added. At each stage, models also include variables identified as providing the best performance at the preceding stage.

Figure 3: Marginal effects of smooth terms illustrating interactions between intensity of load expressed as percentage of maximum and outcome domain.



Density plots at the top of each figure illustrates the distribution of the load intensity variable for the given outcome domain. Solid lines represent the best estimate of the smooth relationship and shaded regions represent intervals of uncertainty (75 and 95%).

4.0 Discussion

The primary aim of this meta-analysis was to produce a comprehensive modelling of the dose-response relationships between resistance exercise and commonly used measures of physical performance within S&C. The analyses identified that a range of factors are associated with the magnitude of change across resistance-only and resistance-dominant training interventions. These factors include the length of the intervention, outcome type, volume, overall intensity of training, and the intensity of load. The analyses also identified important interactions between loading intensity and outcome domain, such that some outcomes are more likely to experience greater improvements with sub-maximum loads.

Length of intervention has generally not been explored in dose-response modelling due to most reviews focusing on a smaller number of homogenous studies with a restricted range of durations. Across the studies included in this meta-analysis, durations were found to be relatively short, with the median duration equal to 8 weeks and 97% of interventions lasting less than 26 weeks. Despite the relatively short intervention durations, the results show that substantive improvements can be made, and that longer durations within these time frames creates greater mean improvements. The effect of duration remained consistent throughout the model-building process with standardised mean differences estimated to increase by approximately 0.03 for each additional week of training. Given the relatively short and homogenous durations included, there was limited ability to explore the functional form of changes over time. In a recent large modelling study investigating the time-course of strength adaptations, Steele et al. [28] showed that linear-log growth models were appropriate to describe improvements of relatively untrained participants over the course of almost seven years, with improvements tending to plateau after approximately one year. The training stimulus investigated by Steele et al. [28], focused on minimal dose resistance training (1x/week, single sets to momentary failure of six exercises), which is likely to have influenced the parameters obtained. Our analysis was limited to durations of no more than 26 weeks and thus we cannot draw inferences as to how results might change over longer time frames. Further research is required to better understand the influence of duration of an intervention and likely interactions between participant characteristics, the specific outcome, the training stimulus, and changes in the training stimulus following for example different periodized approaches.

The manipulation of acute program variables within resistance training interventions is often focused on the development of a single outcome domain. Previous meta-analyses investigating dose-response relationships have predominantly focused on the development of muscular strength and or hypertrophy [7-16]. The current meta-analysis was able to demonstrate varying effects across multiple outcome domains commonly targeted with the greatest effect sizes obtained for strength, and the lowest obtained for sprint performance. Resistance training for the purpose of improving maximum strength is arguably the most well understood area within S&C, and greater effect sizes may reflect this increased refinement and specificity between traditional resistance training methods and maximum strength outcomes. In addition, researchers frequently test maximum strength using the same exercises included in the training intervention further increasing specificity and potentially the improvements measured [29]. Results from a previous meta-analysis indicates that the dose-response relationship between the %1RM and strength gains diminishes when testing is carried out isometrically [15]. Further study is needed to provide greater context to the transfer of strength from varied magnitudes of load to neutral testing modalities.

Following maximum strength, jump performance and power generated the next largest effects. Similar magnitude improvements in jump performance and power may be expected given the well-established relationship between the two factors [30-33]. In addition, many of the studies measured power during loaded and unloaded jumps, further increasing associations and similar magnitude improvements. Outcomes relating to sprint performance demonstrated the lowest magnitude improvements. Sprinting comprises a substantial and complex technique element [34-38] and given the relatively low number of studies (~12%) that included sprint specific interventions, a lower effect size distribution may be expected. More broadly, the lower effect size distribution for sprint outcomes may also reflect a lack of specificity with regards to development of relevant physical outputs. Transference between improvements and long-term adaptations in S&C are dependent primarily on the training principles of specificity and progressive overload, respectively [39,40]. Most training methods included in the meta-analysis focused on bilateral production of maximum vertical forces over long durations. In contrast, sprinting activities require high forces produced over short ground contact times that are predominantly unilateral with substantive horizontal components [35,36,41]. In a recent meta-analysis, Murphy et al. [4] showed moderate to strong relationships between improvements in strength, power and sprint performance in team sport athletes, concluding that greater development of physical capacities may result in further improvements in sprint performance. Despite these correlations, however, research also shows that large increases in maximum strength (~12-18%) translate into only small decreases in sprint times (~-2-8%) [42-44]. Collectively, there appears to be scope for future research to investigate why improvements in sprint performance are generally much smaller than other outcome domains and whether this difference can be ameliorated with a focus on certain training practices.

Movements associated with change of direction and agility could be considered even more complex than sprinting due to the high acceleration and deceleration demands, the ability to rapidly alter body position, combined with the need in some activities to react to an external stimulus. The results of the current meta-analysis suggest improvements in agility are likely to be of similar magnitude to those measured during vertical jump and tasks focusing on the development of power, albeit with a greater level of uncertainty. Outcomes measuring agility and the related construct of change of direction speed represent a developing area within S&C [45,46] with only ~3% of outcomes assessing agility performance. Whilst reasons for the larger effect size distribution in comparison to linear sprinting requires further study, potential explanations include the complex, multifaceted nature of the tasks and the scope for multiple limiting factors to be addressed. Additionally, it is recognised that many agility and change of direction tasks include substantive skill elements [46], such that failure to appropriately familiarize participants could lead to systematic biases in regard to learning effects and subsequent overestimations of effect sizes.

The results of the current meta-analysis demonstrate the importance of training intensity. Previous research investigating dose-response relationships have tended to contextualise and quantify intensity based on load and thereby %1RM. This approach works best when considering traditional strength or hypertrophy focused interventions comprising large compound movements where 1RMs can be measured and appropriately summarise a relevant feature of intensity. An aim of the current meta-analysis was to investigate dose-response relationships across a range of resistance-based training modalities and outcomes; therefore, in addition to intensity of load expressed as a %1RM, a more general categorisation scheme was included. Interventions comprising predominantly ballistic, loaded jumping or sprinting exercises were always considered high intensity, due to the high mechanical loads and assumption that they are conducted with maximal intent, unless stated otherwise. Across all outcomes, evidence was obtained that greater overall intensity was associated with increased effect sizes, with interventions judged to be of medium and high overall intensity expected to increase effect sizes by approximately 0.10 relative to low overall intensity.

Additional detailed information on the dose-response relationship of intensity was obtained when investigating potential interaction effects between outcome and intensity of load measured by

%1RM. The results identified a range of different profiles, with no clear pattern for agility, monotonic increases for strength and speed, a monotonic decrease for jump performance, and a parabolic profile for power. The best estimate profile for maximum strength appeared non-linear with an inflection point ~70%1RM where increases started to slow. The results of the present meta-analysis are consistent with previous reviews, where Peterson et al. [8] identified increased effects with heavier %1RM loads but diminishing effects, particularly with untrained participants [17]. The results also align with previous research indicating that heavy load training may increase muscle activation by up to 30% [47], conceivably providing a stronger stimulus for adaptation. Some authors have also suggested, however, that improvements in strength with greater loads may be inflated due to high specificity of task and outcome, given that strength testing is often conducted performing the 1RM of the movement being trained [15].

Analysis of sprint performance also identified a monotonic increase in effect with the greatest increases obtained with the heaviest loads. The most common sprint outcomes investigated in S&C research include the time to sprint between 5 and 50 m, with the most frequent intervals comprising 10, 20 and 30 m. Most studies have been conducted with either team sport or untrained participants that achieve maximum velocity between 15 to 40 m, in comparison to trained sprinters that require distances of 40 to 80 m to achieve maximum velocity [34,41,48,49]. Consequently, sprint data collected over 10 to 30 m may provide researchers with divergent outcomes describing both acceleration and maximum velocity. Previous studies have reported strong associations with outcomes designed to assess acceleration (e.g. 10 m) and horizontal force, power and relative strength with longer duration ground contact times (approx. 200 ms) [35,36]. In contrast, maximum velocity sprinting has been shown to be dependent on the ability to maintain large horizontal and vertical forces whilst minimizing braking forces with reduced ground contact time (approx. 100ms) [36,37,49]. Previous meta-analyses have concluded that high intensity nonspecific resistance exercise is among the most effective training methods to improve sprint performance in team sport athletes [4,34,50]. Neural and morphological adaptations associated with high-load resistance exercise and improved force output may provide a mechanism for positive transfer to the high levels of horizontal force required during early phase acceleration to improve sprint performance. Highly trained individuals may require more specific training methods, however, that target improvements in physical qualities while matching the kinematic demands of sprinting [1,4].

In contrast to the increasing dose-response relationships with intensity for strength and sprint performance, results identified monotonic decreases for jump performance with the largest effects obtained at ~30% 1RM. Jump performance is dependent on net impulse and take-off velocity such that %1RM loads lifted with maximum intent provide sufficient stimulus but do not limit velocity to a large extent may provide the greatest transfer to improvements in jump performance [30,51]. Previous research has also demonstrated that jump squat training with low (<30%1RM) or no additional load can produce velocity specific adaptations associated with improvements jump performance [52]. The intensity profile for outcomes measuring power production was parabolic, with the greatest improvements obtained between ~40-70% 1RM. These results support the hypothesis that performing resistance exercise with loads that elicit the largest power outputs is the most effective method to improve power and that for most exercises power is maximised between 30 and 70% 1RM [53]. During Olympic weightlifting exercises (clean, snatch, hang and pull variations), power is maximised with heavier loads of (≥70% 1RM), whereas loads of 0-30%1RM maximise power during jump squat exercises [53].

The influence of training frequency and volume on strength and hypertrophy has been assessed in several previous meta-analyses [10-12,16]. The results obtained herein were mixed but showed limited evidence that these factors were influential. No improvement in model performance was obtained when including the number of sessions per week as a categorical or continuous predictor, or the average number of exercises per session. Only limited evidence of model improvement was obtained for the average number of repetitions per set, with the marginal effect showing declines as the number of repetitions increased. In contrast, evidence was obtained for greater effect sizes with increasing number of sets per session. Seminal research by Rhea et al. [9] was the among the first, within S&C, to use meta-analytical techniques to assess the use of single versus multiple sets in RE for strength development. The authors concluded multiple sets were more beneficial than single set training. Follow up meta-regression from Krieger et al. [54] found a 46% increase in muscular strength when completing two to three sets, in comparison to single sets, although no further difference was found for RE with more than four sets. More recently, research has concluded that increasing weekly training volume through increased number of sets can produce similar results to increasing training frequency [11,12]. The current meta-analysis demonstrates that focussing on a smaller number of key exercises while completing multiple sets at an appropriate intensity for a targeted outcome may be more beneficial than attempting to perform many exercises with an increased frequency.

The training status of participants is a key consideration when designing and implementing resistance exercise. Previous meta-analyses have demonstrated rank-order effects, with the largest improvements obtained by untrained participants [1,7] followed by recreationally trained and then highly trained participants. In contrast, the current meta-analysis found a lack of evidence to support different effects across the training status categories. Differences in results obtained in the present versus previous meta-analyses may be due to several reasons. Previous analyses have been less formal than the ones conducted herein, with authors identifying differences based primarily on point estimates. In contrast, participant training status was assessed in the present study with predictor variables for lower levels already included in the model and addition of the factor was assessed based on ability to improve model performance. The lack of data from highly trained participants, disproportionate inclusion of untrained participants, combined with short duration (≤26 weeks) interventions which are known limitation within S&C research [55], may have also influenced the results obtained and discordance with what is generally believed in the field. With advancements in technology and ability to collect valid and reliable high-frequency data over longer periods across all levels of sport and recreation, there is the potential for future research to more effectively investigate potential differences in dose-responses relative to participant training status.

In addition to training status, the current meta-analysis found a lack of evidence to support different effects between sexes. Although, males exhibit greater levels of baseline strength and muscle mass, the current meta-analysis results are consistent with previous research that has failed to identify any difference in effects between sexes in improvements in strength or hypertrophy [10,56]. A previous meta-analysis conducted by de Villareal et al, [57], however, reported greater improvement of males following plyometric training relative to females. The authors were unable to provide a strong rationale for the finding and speculated that large differences in sample sizes between the sexes may have confounded results. Research has shown that stronger individuals are able to produce greater rate of force development and power during time restricted tasks [3] and so there is the potential that increased strength at baseline may be advantageous for plyometric training. Further research is required to identify potential differences in the dose-response relationship between sexes and more complex sport specific outcomes. Female participants are largely under-represented in S&C research with only 12% of the studies included here conducted with female-only groups. In addition, research suggests that only 39% of all published sport science data is collected with female participants [58]. To better address the question of potential differences in dose-response relationships, more female participant data is required.

Whilst this is the most comprehensive meta-analysis to date investigating dose-response relationships between resistance and resistance-dominant interventions, there are multiple limitations that should be considered when interpreting the findings. There are clear limitations in summarising different dose components from a training intervention based on for example the average number of sets, where this variable may change substantially depending on the periodization or progression model. In addition, for variables such as overall training volume and intensity, there was a high degree of subjectivity and challenge in obtaining a single value, particularly when considering different training modes. The current meta-analysis was intended to uncover general relationships but the extensive heterogeneity across the data set limits nuance and there are limitations in drawing strong inferences from pooling of indirect data. It is expected that there will be many instances where factors such as training frequency and volume strongly influence the effectiveness of an intervention; however, variables quantifying frequency and volume in the present study lacked predictive power across this large and heterogenous data set. Despite these results and considering the limitations of the meta-analysis, practitioners are still recommended to implement periodized training interventions that include appropriate manipulations in intensity, volume, and frequency over time to try and maximise a given outcome. Overall, the results of the present meta-analysis suggest that practitioners should focus first on overall intensity and intensity of load with the appropriate target outcomes in mind.

5.0 Conclusion

The current meta-analysis is the most comprehensive to date to investigate dose-response relationships of resistance and resistance-dominant training with respect to a range of commonly studied outcome domains in S&C research. The findings are that resistance exercise is effective over relatively short durations (~8 weeks) and extending a single intervention over longer periods is likely to result in further improvements. The expected magnitude of improvement appears to be predominantly influenced by intensity and the outcome domain measured. Performance of resistance training with a higher intensity as measured by a composite of the effort applied, the difficulty of the exercise, and maximising target biomechanical quantities results in greater improvements. When considering the magnitude of the load lifted as a %1RM, the profile that creates the greatest improvements is dependent on the outcome domain. Improvements in strength are likely to be maximised with the heaviest loads, whereas vertical jump performance may be maximised with relatively light loads (~30%1RM), and power with low to moderate loads (40-70% 1RM). Sprinting performance represents the most difficult outcome domain to improve with resistance and resistance-dominant training and this may be influenced lower specificity.

Disclosure statement

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Supplementary File 1: Checklist of Preferred Reporting items for Systematic Review and Meta-Analysis

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Reported as a meta-analysis. Search is not exhaustive and does not include all relevant research.
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	4-6
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	6,7
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	8
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	7.8
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Not included.
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	8
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	8
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	8.9
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	9
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Stated that risk of bias was not assessed on pg 8
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of	11

Section and Topic	Item #	Checklist item	Location where item is reported
		results.	
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	11,12
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	12
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	12
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	12
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	13
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	13
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	Stated that risk of bias was not assessed on pg 8
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	Stated that no methods were used to assess certainty in the body of evidence for an outcome on pg 13
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	15
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	15
Study characteristics	17	Cite each included study and present its characteristics.	Citations for included studies presented in supplementary 3.
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Stated that risk of bias was not assessed on pg 8
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	15-21
Results of	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	15-21

Section and Topic	Item #	Checklist item	Location where item is reported
syntheses	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	15-21
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	15-21
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	16-20
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	Stated that risk of bias was not assessed on pg 8
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Stated that no methods were used to assess certainty in the body of evidence for an outcome on pg 13
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	22-30
	23b	Discuss any limitations of the evidence included in the review.	30
	23c	Discuss any limitations of the review processes used.	30
	23d	Discuss implications of the results for practice, policy, and future research.	31
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	Stated that this is a follow-on review from a previous review.
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	No protocol was prepared.
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	No protocol was prepared.
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	31
Competing interests	26	Declare any competing interests of review authors.	31
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	Supplementary files include checklist, conversion chart, and included references.

Supplementary File 2: Table outlining %1RM estimation based on repetitions performed, adapted from Haff and Triplett [19].

Repetitions Performed	%1RM
1	100
2	95
3	93
4	90
5	87
6	85
7	83
8	80
9	77
10	75
11	70
12	67
15	65

Supplementary File 3: Reference list of included studies

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