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Review

Responsiveness of functional performance and muscle strength, power, and size to resistance training: A systematic review

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ABSTRACT

There is a recent and growing interest in assessing differential responders to resistance training (RT) for diverse outcomes. Thus, the individual ability to respond to an intervention for a specific measurement, called responsiveness, remains to be better understood. Thus, the current study aimed to summarize the available information about the effects of RT on functional performance and muscle strength, power, and size in healthy adults, through the prevalence rate in different responsiveness classifications models. A systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) and was registered at the International Prospective Register of Systematic Reviews (PROSPERO, CRD42021265378). PubMed/MEDLINE, Scopus, and Embase databases were systematically searched in October 2023. A total of 13 studies were included, totaling 921 subjects. Only two studies presented a low risk of bias. Regarding the effectiveness of RT, the prevalence rate for non-responders ranged from 0% to 44% for muscle strength, from 0% to 84% for muscle size, and from 0% to 42% for functional performance, while for muscle power, the only study found showed a responsiveness rate of 37%. In conclusion, a wide range of differential responders is described for all variables investigated. However, the evidence summarized in this systematic review suggested some caution while interpreting the findings, since the body of evidence found seems to be incipient, and widely heterogeneous in methodological and statistical aspects.

1. Introduction

Resistance training (RT) is widely known for its applicability and efficiency in promoting functional performance and clinical improvements.[1,2] However, after the emergence of research associations and the growth of scientific investigations on the topic, mainly in the 2000s, the debate on the manipulation of RT variables has gained attention in the field.[2–4] In this context, over the last decade, evidence-based position standings and recommendations were proposed to guide RT prescription for different populations and goals such as healthy adults,[5] elderly,[6] trained individuals,[7] and athletes.[8]

However, as the premise of those guidelines is to propose general recommendations and most of the literature on RT is based on group responses, there is a growing interest regarding the effects of RT variable manipulation at the individual level. In this sense, when a group of subjects is submitted to the same training protocol, the individual responses for a particular measurement are specific and heterogeneous.[9] For example, there is evidence that individual changes in strength and muscle size can be widely variable (0%–250% and −2%–59%) in a group of subjects of the same age, in response to a 12-week RT intervention.[10] In studies that investigated changes in functional performance[11] and muscle power,[12] the inter-individual responses seem to be wide too (−141%–30% and 5%–22%, respectively). This phenomenon, which suggests that each individual has a particular ability to respond, or not, to a given training program is called responsiveness.[13]

Responsiveness can be influenced by extrinsic and behavioral factors such as sleep quality, psychological stress, habitual physical activity, and diet.[14] However, it is known that intrinsic and physiological factors such as the baseline phenotypic profile (homozygous myostatin mutation) and metabolic changes (ribosomal and mitochondrial biogenesis, increased ribonucleic acid [RNA] expression) may have a determinant role in the magnitude of individual responses to RT.[15–17] There is evidence that greater muscle size changes and ribosomal biogenesis were found in subjects with smaller muscle thickness and type II fibers cross-sectional area of the vastus lateralis before being exposed to RT.[17,18] On the

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Abbreviations

RT	Resistance Training
RoB 2	Cochrane risk of bias tool for randomized clinical trials
robvis	the Risk-of-bias VISualization
1RM	One repetition maximal
MRI	Magnetic Resonance Image
DXA	Dual-energy x-ray absorptiometry
TUG	Timed Up and Go Test
CV	Coefficient of variation
SPPB	Short Physical Performance Battery
MV	moderate volume
LV	low volume
MDC	minimal detectable change
RP	responders
NR	non-responders
LR	low responder
MR	moderate responder
HR	high responder
HP	muscle hypertrophy
CMJ	countermovement jump
VAR	RT protocol with overload variations
CSA	Cross-sectional area
US	ultrasound
TE	Typical error measurement
HF	high frequency
LF	low frequency
MT	Muscle thickness

other hand, greater activation of fast-contracting fibers and motor neuron excitability is associated with improvements in muscle power production and functional capacity.[19,20] However, it is necessary to ensure that the RT prescription was planned to achieve the specific outcome measured before inferring the impact of any intrinsic factor on responsiveness,[15] since the magnitude of changes in strength and muscle size appears to be highly affected by the manipulation of training volume and intensity.[21]

Despite the importance of intrinsic and extrinsic factors on RT responsiveness, the literature on this topic is still emerging, and methodological aspects need to be considered. Discussions have been raised about the study designs, the control of variables, and adequate statistical models applied to responsiveness investigations.[22–26] Dankel and Loenneke[23] point out that randomization error, sample homogeneity, biological and temporal variability, and the instrument's accuracy need to be controlled. Also, the authors highlight the need for a non-exercise control group, and the analysis of variance within and between groups to ensure that the effects were induced by the RT protocol applied.[23]

From this perspective, the magnitude of individual changes to training concerning the group mean and standard deviation or through response thresholds (highly, moderately, or low-responders) have been conducted to identify outliers and/or real effects of the intervention on each individual for a specific variable.[22,27] Another model often used in different study designs is based on the minimal detectable change, which establishes responsiveness thresholds (responders or non-responders) and minimizes the chances of measurement error.[28] Moreover, minimal detectable change has also been used to identify additional benefits when different protocols are applied to the same subject in a contralateral design.[24]

Thus, despite the main recommendations for RT prescription having a solid evidence-based background and having been widely disseminated for specific goals and different populations, the knowledge about the effects of RT variables manipulation on the variability of individual responses of functional performance and muscle strength, power, and size, is still lacking. Knowing the factors that may interfere with RT responses at the individual level, and the expected rates of responsiveness of different groups, can help trainers and coaches to better deal with real-life situations when facing high and non-responders. Also, progression strategies and variable manipulation can be proposed aiming to enhance the effectiveness of RT on the outcomes of interest. Therefore, this systematic review aims to summarize the responsiveness rates of functional performance, muscle strength, power, and size to RT in healthy adults. In parallel, to systematize discussions of RT variables manipulation, mechanistic factors, and methodological and statistical aspects related to responsiveness literature.

2. Methods

This review was registered in the International Prospective Register of Systematic Reviews (PROSPERO), identified by the code CRD42021265378, and followed the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).[29]

2.1. Eligibility criteria

Eligible studies were considered for inclusion if they met the following criteria: (i) be a study published in English in a refereed journal; (ii) participants were randomized to training and/or control group (s); (iii) interindividual response was measured directly from traditional dynamic exercise, on machines and/or free weights, plus concentric and eccentric actions simultaneously; (iv) responsiveness prevalence was presented; (v) measure of muscle hypertrophy or lean mass and/or power and/or strength and/or functional performance markers were described; (vi) with a minimum RT-intervention duration of four weeks; (vii) not involving any structured exercise other than RT. Furthermore, exclusion criteria considered studies with (i) non-healthy individuals; (ii) adolescents and children; (iii) that did not analyze responsiveness among the variables of interest; (iv) did not describe the volume and intensity variables in the intervention protocol; (v) analyzed muscle hypertrophy by skinfold estimation, and (vi) measured functional performance by scientifically non-validated tests.

2.2. Search strategy

To perform the systematic search, only studies indexed in PubMed/MEDLINE, Scopus, and Embase databases, published until October 2023, were considered. Thus, the search in the databases was conducted by combining two or more Boolean operators applied as follows: (“responders” OR “non-responders” OR “responsiveness” OR “individual responses” OR “inter-individual variation” OR “variability” OR “heterogeneity”) AND (“hypertrophy” OR “muscle size” OR “muscle thickness”) AND (“muscle strength” AND “muscle power”) AND (“functionality” OR “functional performance” AND “functional fitness”) AND (“resistance training” OR “strength training” OR “weight exercise”).

After the database search, the study selection process (mapping, exclusion of duplicated studies, exclusion, and inclusion of studies by titles and abstracts/abstracts) was performed using the Rayyan application (rayyan.ai).[30] Subsequently, at the end of the selection step, the reference lists of the selected papers were reviewed as part of a secondary search to discover any additional articles that met the inclusion criteria but were not found in the search strategy.[31] In addition, any studies found unintentionally in an unlisted source/database that met the eligibility criteria should be reported to be included. The entire search process was performed individually by two researchers and, if there was any disagreement between them, it was discussed to reach a final decision and, when necessary, a third researcher was consulted. PRISMA flow diagram was created by a specific online tool.[32] The complete search strategy is presented as a supplementary file.

2.3. Risk of bias assessment

The risk of bias was assessed according to the second version of the Cochrane risk of bias tool for randomized clinical trials (RoB 2),[33] focusing on different aspects of the trial design, conduct, and reporting. Each assessment is focused on the outcome level. The instrument is based on six domains used to assess the credibility which were: (i) randomization process; (ii) deviation from intended interventions; (iii) missing outcome data; (iv) outcome measurement; (v) reported outcome selection; and (vi) overall analysis. The overall risk of bias was expressed as "low risk of bias" if all domains were rated as low risk, "some concerns" if some concern was raised in at least one domain but not rated as high risk in any other, or "high risk of bias" if at least one domain was rated as high risk or has several domains with some concerns. Figures were created using the Risk-of-bias VISualization (robvis) tool.[34] The analysis was performed individually by two researchers and if there was any disagreement between them after the judgment of the studies, it was discussed to reach a final decision and, when necessary, a third researcher was consulted.

2.4. Data extraction

The studies were accessed and data extracted individually for the following variables: descriptive information of the subject (e.g., gender, training status [defined according to the concept of the original article], maturity level of the subjects [young adults 18–35 years, middle-aged adults 36–59 years, and older adults $\geq$ 60 years]); sample size in each group; RT intervention duration; training frequency (days per week); volume (number of sets and repetitions, amount of exercise per muscle group); exercise intensity (range of maximal repetitions and percentage of one-repetition maximum [1 RM]); type of morphological variables (lean mass, muscle thickness, muscle cross-sectional area); methods used to measure morphological variables (magnetic resonance imaging [MRI], ultrasound, dual-energy x-ray absorptiometry [DXA]), and/or bioimpedance); muscle power indicators (peak power, rate of force development, vertical jump height); methods used to measure muscle power (isokinetic dynamometry, and/or force platform); neuromuscular variables (maximal strength and/or maximal voluntary contraction); methods used to measure strength (maximal repetition tests and/or isokinetic dynamometry); tests used to measure functional performance (Timed Up and Go Test [TUG], Short Physical Performance Battery [SPPB], and/or any other scientifically validated functional test).

2.5. Weekly volume assessment

The included studies were classified by the weekly number of sets per muscle group as high ($>$ 9 sets) or low ($\leq$ 9 sets) volume.[35] For muscle hypertrophy, in the studies analyzing local muscle hypertrophy (cross-sectional area and muscle thickness), only the volume of the agonist muscle group in each training protocol was considered (e.g., for quadriceps cross-sectional area only the volume of the exercises that had this muscle group as agonist was analyzed). In the case of global muscle hypertrophy, it was considered the total set volume without discrimination of the muscle group. For strength, functional performance, and muscle power the volume of the segment involved in the test (e.g., for 1 RM in leg press, TUG, or countermovement jump, the volume measurement was specific to the lower body) was considered, except for tests that involved single-joint movements. Coding was cross-coded between reviewers, with any discrepancies resolved by mutual consensus.

3. Results

3.1. Search strategy

After the search strategy, 289 412 papers were mapped and, through filtering in each database by their automation tools, 15 062 studies were extracted for screening. Then, the filtering by titles and abstracts happened through the automation tools of the Rayyan app, manually edited and conducted by the researchers, which went through two steps: the first, exclude the articles based on eligibility exclusion criteria, added to additional criteria (systematic review, meta-analysis, animal studies, aerobic training, recommendations/positioning, etc.) that restricted to 1 434 studies; the second part of the screening was guided by the eligibility inclusion criteria. Thus, 157 potential studies were screened for eligibility, of which nine articles remained to be included in the present study. Furthermore, three papers that met the eligibility criteria were identified from the reference list of the previously selected articles. Another study on websites was identified, which totaled 13 articles included in this systematic review (Fig. 1).

3.2. Sample

As a result of the selection process, 921 subjects underwent 22 RT protocols, ranging from 6 to 24 weeks (Table 1). Among the included studies, 10 involved young people,[23,36–44] while two involved the elderly,[45,46] and one study included both populations.[9] Hence, regarding sex, three studies included only men,[36,43,44] two included only women,[37,42] seven involved both sexes,[9,23,38–41,45] and one did not describe the sex of the sample.[46] Regarding the level of experience with RT, only two studies enrolled trained subjects,[36,37] while the other eleven involved untrained subjects.[9,26,38–46]

3.3. Risk of bias

The risk of bias assessment showed that only two studies were classified as "low risk",[26,40] four studies were classified as "high risk",[9,38,46] and the remaining papers presented "some concerns".[36,37,39,41–45] Fig. 2 shows the weighted summary risk-of-bias plot. Additional data are given in Fig. 3.

3.4. Analytical model of responsiveness

Among the statistical models used to classify the individual responses (Table 1), two studies applied the typical error of measurement,[43,44] and two others used the minimal detectable change.[38,45] Two studies that were part of the same experimental design used the change from baseline ($\Delta\% > 0$).[39,41] One study[35] used the coefficient of variation, while the two studies ranked individual responses by percentage thresholds (cluster analysis).[37,42] The remaining studies combined two different responsiveness analysis models that did not follow a pattern.[9,26,40,46] Therefore, the classifications obtained through the all models used were: responders and non-responders[26,39,41,41–45]; high-responders, moderate responders, and low-responders[9,26,37,42,46]; and what the authors called "additional benefits".[36,38]

3.5. Analysis of strength, functional performance, and muscle power

Ten of the included studies analyzed the responsiveness of changes in muscle strength. Of those, one study used the five-repetition maximum test,[45] one study used only the maximal voluntary contraction (isokinetic dynamometer)[46] and seven studies used the 1 RM test.[9,36–39,42,44] On the other hand, only one study applied functional performance and muscle power analysis and used the TUG, stair ascent and descent tests, and countermovement jump, respectively.[45]

3.6. Muscle hypertrophy analysis

Five studies used muscle cross-sectional area measurements by ultrasound,[36,43,44] MRI,[38] or both.[9] Three studies analyzed lean mass through DXA[9,41] or bioimpedance.[40] Four studies evaluated muscle thickness by DXA,[38] ultrasound,[9,26] or MRI.[45] Other studies[9] involved all muscle hypertrophy analysis instruments and measurements reported above (Table 1).

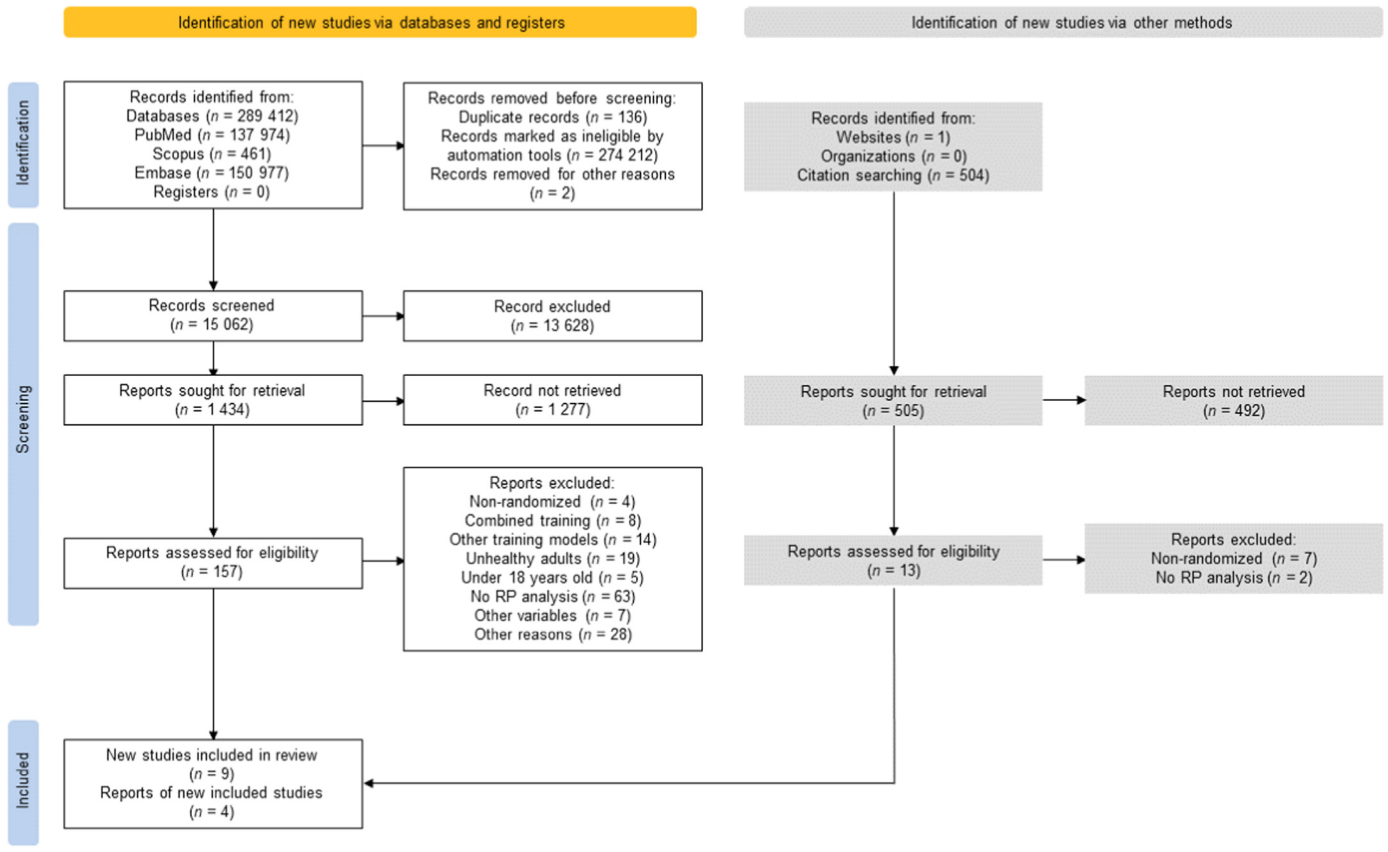

Fig. 1. Flowchart of the search process and study selection.

3.7. Responsiveness prevalence range

Regarding muscle strength (Table 2), the prevalence rate for the different classifications ranged from 0%[39] to 44%[46] for non-responders; from 12%[26] to 66%[37] for high-responders; from 10%[42] to 60%[37] for moderate-responders; from 7%[9] to 54%[42] for low-responders and from 3% to 47% to additional benefits from a contralateral protocol on the same individual.[38] Only one study applied responsiveness analysis for muscle power and indicated a 37% prevalence of non-responders.[45]

For muscle hypertrophy (Table 3), the prevalence ranged from 0%[43] to 84%[40] for non-responders; from 12%[9] to 50%[42] for high-responders; and from 29%[9] to 55%[42] for low-responders. Considering moderate responders, the prevalence ranged from 18% to 30%.[42] For protocols that generated additional benefits, the prevalence ranged from 0%[43] to 38%.[38,44]

For functional performance (Table 4), only the classification of non-responders was found in one study, at three different tests and the prevalence range was 37%–42%.[45] The range of non-responders for each outcome is summarized in Fig. 4.

3.8. Weekly volume

In the weekly volume per muscle group analysis (Tables 5–7), two studies involved protocols with only low RT volume,[45,46] while six were based on protocols with high RT volume,[26,36,37,39,41,47] and five covered both.[9,38,40,42,44]

3.9. Dose-response effect on responsiveness

The synthesis of the relationships identified between training variables manipulation and dosage of RT and responsiveness rates are presented in Tables 5–7. When directly compared, higher RT volume seems to induce more prominent muscle strength responsiveness than low volume (matched intensity) in trained and untrained youth, in all responsiveness classifications found.[38,42,43] However, when the low volume is associated with high intensity, the RT effectiveness can be greater than moderate intensity (99% and 81% responders, respectively).[26]

Regarding muscle hypertrophy, from studies that compared different RT dosages, two studies favored high-volume RT to responsiveness,[26,38] one study compared two protocols with high-volume RT and showed the same responsiveness rate,[43] and one did not find a difference between high and low volume.[44] Despite the differences in favor of the higher training volume in the responder's rate (80% vs 0%), the 1 RM group proposed by Dankel et al.[26] performed a very low training volume. On the other hand, Damas et al.[43] found that the variation in RT variables does not change the responsiveness rate, even with a higher total training volume. Also, Hammarström et al.[38] showed that higher training volumes may provide additional benefits for muscle hypertrophy than low volume (38% vs 9%, respectively), while Damas et al.[44] found the opposite (32% vs 37%, respectively). None of the included studies analyzed the dose-response effect on functional performance and muscle power.

4. Discussion

This systematic review aimed to describe the prevalence of responsiveness of functional performance and muscle strength, power, and size to resistance training in healthy adults. Specifically, considered dose-response characteristics in different age groups, experimental designs, analysis models, and responsiveness classifications were considered. Therefore, 13 articles were eligible after the search strategy, which involved 921 subjects, submitted to 22 intervention models. Of these studies, only two showed a low risk of bias, which impairs the ability to make consistent inferences based on the data obtained.

Table 1
Description of the studies according to the analytical model of responsiveness.

Author	Sample	Duration/ Weekly Frequency	RT Protocol	Weekly volume (sets/week)	Variables	Responsiveness Analysis	Main findings
Minimum Detectable Change							
Hammarström et al.[38]	Untrained youth (males; $n = 16$, [23 ± 4] years; females; $n = 18$; [22 ± 1] years)	12 weeks/2–3 sessions	MV (one thigh): 3 × (7–10) RM; LV (contralateral thigh): 1 × (7–10) RM; unilateral leg press, knee flexion, and knee extension	Lower limb strength: MV: 18–27 sets/week; LV: 6–9 sets/week; Quadriceps: MV: 12–18 sets/week; LV = 4–6 sets/week	1 RM (leg press); CSA – quadriceps (MRI)	MDC: mean baseline × 0.2 in favor of highest volume (RP)	HP: 13 participants showed additional benefits for moderate volume, while 3 participants showed an additional benefit from low volume; Strength: 16 participants showed additional benefits for moderate volume, while only one benefited more from low volume
Orssato et al.[45]	Untrained elderly (men; $n = 14$; women; $n = 5$; both [66 ± 4] years)	9 weeks/2 sessions	3 × (4–12) RM; leg press and knee flexion	Lower limb strength: 12 sets/week	5RM (leg press); CMJ; TUG and stairs ascent and descent	MDC: mean baseline × 0.2 (RP)	Strength: there were no NR subjects; Power: 7 subjects were NR for CMJ; Functionality: 12 subjects were RP for TUG and stair ascent, and 11 RP for stair descent
Typical Measurement Error							
Damas et al.[44]	Untrained youth (males; $n = 20$, [26 ± 3] years)	8 weeks/2 sessions	TR control: 4 × (9–12) RM vs VAR: (4–6) sets × (9–30) RM; leg press and knee extension	HP quadriceps: TR control: 16 sets/week VAR: 16–24 sets/week	CSA - vastus lateralis (US)	$TE = SD\ diff/\sqrt{2}$ RP = 2 × TE	HP: There were no NR subjects and no subjects gained additional benefit from either training protocol
Damas et al.[43]	Untrained youth (males; $n = 20$, [20 ± 4] years old)	12 weeks HF (one thigh): 5 sessions/week. LF (contralateral thigh): 2/3 session/week	RT: 3 × (9–12) RM; knee extension	Lower limb strength: HF:15 sets/week; LF: 6–9 sets/week	CSA - vastus lateralis (US); 1 RM knee extension	$TE = SD\ diff/\sqrt{2}$ RP = 2 × TE	HF 6 individuals responded more HF, 7 individuals responded more for LF, and the other 6 individuals were NR; Strength: 5 individuals increased more for HF, 3 for LF, and the other 11 showed similar responses between TR frequencies. There was no NR
Change from Baseline							
Marsh et al.[39]	Untrained youth (42 same-sex twin pairs; males; $n = 17$; females; $n = 25$; both genders 19–33 years)	12 weeks/3 sessions	RT: 3 × (5–15) RM (60%–90% 1 RM); press, bench press, squat, deadlift, and leg press	HP pectoral, deltoid and triceps: 12 sets/week; quadriceps and gluteus: 27 sets/week	1 RM (bench press and leg press)	RP: $\Delta\% > 0$ between pre- and post-intervention	Strength: no NR subjects
Thomas et al.[41]	Untrained youth (42 same-sex twin pairs; males; $n = 17$; females; $n = 25$; both genders 19–33 years)	12 weeks/3 sessions	RT: 3 × (5–15) RM (60%–90% 1 RM); 2 (lower limbs)-3 (lower limbs); press, bench press, squat, deadlift, and leg press	Full body HP: 45 sets/week	MM (DXA)	RP: $\Delta\% > 0$ between pre- and post-intervention	HP: 84% of the subjects were RP
Coefficient of Variation							
Angleri et al.[36]	Trained youth (male; $n = 31$; [27 ± 4] years)	12 weeks/2 sessions	TRAD (one thigh): 3 × (6–12) (75% 1 RM); CP (contralateral thigh): 3 × (5–15) (65%–85% 1 RM); DS (contralateral thigh): 3 × 15 (50%–75% 1 RM); leg press and knee extension	Quadriceps HP: 12 sets/week	CSA vastus lateralis (US); 1 RM (leg press and knee extension)	AB: Difference between TRAD and CP or TRAD and DS when this difference was greater than 2 × coefficient of variation	HP:1 subject obtained AB at DS > TRAD; F: For the leg press, 5 subjects obtained AB at TRAD > DS, 2 subjects obtained AB at DS > TRAD, 4 subjects obtained AB at CP > TRAD, 1 subject AB at TRAD > CP. For knee extension. Regarding

(continued on next page)

Table 1 (*continued*)

Author	Sample	Duration/ Weekly Frequency	RT Protocol	Weekly volume (sets/week)	Variables	Responsiveness Analysis	Main findings
							2 subjects got AB at DS > TRAD, 3 subjects got AB at TRAD > than DS, 2 subjects got AB at CP > TRAD, 2 others AB at TRAD > CP.
Groups by Response Percentage (Cluster)							
Marshall et al.[42]	Trained youth (female; $n = 32$, [27 ± 8] years)	6 weeks/2 sessions	1-SET vs 4-SET vs 8-SET × (4–12) reps; squat	Lower limb strength 1-SET: 2 sets/week 4-SET: 8 sets/week 8-SET: 16 sets/week	1 RM (squat and deadlift)	High responders (strength gains > 20%), moderate (10%–19%) and low responders (< 10%)	HR (1-SET $n = 3$; 4-SETS $n = 5$; 8-SETS $n = 5$) and LR (1-SET $n = 6$; 4-SETS $n = 5$; 8-SETS $n = 2$) were found in the training groups
Garcia et al.[37]	Trained youth (female; $n = 11$, [27 ± 8] years)	12 weeks/3 sessions	MS: 3 × (6–14) RM in each exercise; TS: 3 × (6-14 RM) in circuits of three exercises: squat, leg press, stiff and knee flexion, gluteus in smith, and plantar flexion	Lower limb strength: 54 sets/week	1 RM (squat)	High responders (strength gains > 20%), moderate (10%–19%) and low responders (< 10%)	HR were found in the training (MS $n = 4$ and TS $n = 1$), moderate (MS $n = 1$ and TS $n = 3$), and LR (MS $n = 1$ and TS $n = 1$) groups
Confidence Interval and/or The Standard Deviation of The Intervention Measure							
Ahtiainen et al.[9]	Untrained youth (males; $n = 61$; females; $n = 7$); Untrained middle-aged adults (men, $n = 55$; women, $n = 41$); Untrained elderly (men, $n = 67$; women, $n = 36$); Control (men, $n = 53$; women, $n = 19$)	24 weeks/2 sessions	RT: 3 × (5–12) (70%–90% 1 RM); 2 (quadriceps/triceps biceps),1 (hamstring/prices, dorsal, abdomen) exercises per muscle group. (Unilateral leg press, knee flexion, and knee extension). Control: no exercise	Quadriceps HP: 12, Lower limb strength: 18 sets/week	CSA - vastus (US and MRI); MT - vastus (US); MM - thigh (DXA); 1RM (leg press)	LR: higher CI threshold of the control group. HR 1 *SD* above the mean	HP: 84 subjects (29.3%) were defined as LR, and 35 subjects (12.2%) were defined as HR; Strength: 19 subjects (6.7%) were defined as LR, and 39 subjects (13.8%) were defined as HR
Dankel et al.[26]	Untrained youth (males; $n = 57$; females; $n = 94$)	6 weeks/3 sessions	RT group: (one arm) 6 × (9–12) RM, contralateral arm.; 1 RM test group: (1–5) × (1–2) RM; no exercise control group and no exercise control arm; elbow flexion	Biceps strength and HP: 18 sets/week	Proximal, medial, and distal MT(US); 1 RM (unilateral elbow flexion)	SDreal = $\sqrt{(\text{Intervention } SD^2 - \text{Control } SD^2)}$ LR < intervention mean - 1.96 × Control *SD* HR > intervention mean + 1.96 × Control *SD* MDC: baseline mean × 0.2 (PR)	HP: on the average of the 3 measurement points of the trained arm, 80% of the subjects were RP in the RT group. There were no changes in the untrained arm in any group. Strength: for the trained arm, 79% of subjects in RT and 99% of the 1 RM group were RP, in addition, 6 subjects were HR and 4 LR. For the control arm, 41% of the subjects in RT and 91% of the 1 RM group were PR
Typical Measurement Error and Minimum Detectable Change							
Ramírez-Vélez et al.[40]	Untrained youth (males; $n = 32$; females; $n = 23$)	12 weeks/3 sessions	4 × (20–30) RM (40%–80% 1 RM); squat, unilateral squat, lateral raise, unilateral curl, French triceps, development; Control group: no exercise	Biceps HP: 9 sets/week; Quadriceps, glutes, and ischiotibials: 18 sets/week; Deltoids and triceps: 18 sets/week	MM (bioimpedance)	$TE = SD\ diff/\sqrt{2}$ RP = 2 × TE MDC: mean baseline × 0.2 (RP)	Muscle hypertrophy: regarding the changes in the arms of the RT group, 4 subjects were RP. In the control group, 2 subjects were RP. Regarding the trunk, 5 subjects were RP. In the control group, 4 subjects were RP. Regarding the lower limbs, 4 subjects were RP in the RT group. In the control group, 2 subjects were RP

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Table 1 (*continued*)

Author	Sample	Duration/ Weekly Frequency	RT Protocol	Weekly volume (sets/week)	Variables	Responsiveness Analysis	Main findings
Coefficient of Variation and Response Threshold (Cluster)							
Tracy et al.[46]	Untrained elderly ($n = 21$)	16 weeks/3 sessions	RT: 3 × 10 Reps (30% 1 RM); Control group: no exercise; knee extension	Lower limb strength: 9 sets/ week	1 RM knee extension	Comparison of the individual percent change in coefficient of variation to the control group's percent change in the 1 RM test; *k*-mean cluster analysis of the change in 1-RM load from baseline to 16 weeks	Muscle strength: 14 subjects were RP, while 7 were NR after the intervention

MV: moderate volume; LV: low volume; MDC: minimal detectable change; RP: responders; NR: non-responders; LR: low responder; MR: moderate responder; HR: high responder; HP: hypertrophy; TUG: Timed Up and Go Test; CMJ: countermovement jump; TR Control: protocol of resistance training with overload fixed; VAR: resistance training protocol with overload variations; CSA: cross sectional area; US: ultrasound; TE: typical error measurement; HF: high frequency; LF: low frequency; MM: muscle mass; MT: muscle thickness; MS: multiple-set; TS: tri-set; TRAD: traditional resistance training; CP: crescent pyramid; DS: drop-set.

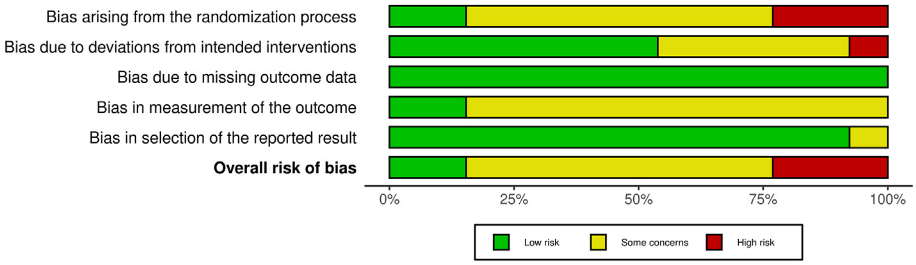

Fig. 2. Weighted summary risk-of-bias plot.

4.1. *Responsiveness of muscle strength and power to RT*

For muscle strength, a recent meta-analysis has indicated that the load is the primary mediator of changes in this component, so the greater the load applied in training, the greater the expected adaptation responses.[47] This idea is supported by our findings from the responsiveness perspective (Tables 1 and 2).[26,39,45] In this sense, even though high training volumes have shown to be more effective concerning responsiveness when intensity was equalized (Tables 5–7),[38,42,44] our results suggest that intensity manipulation can influence RT effectiveness independently of the volume dose for both young and older individuals.[26,39,45,46] Furthermore, a recent study, not randomized, showed that the duration of the RT protocol increased the responder's rate in the same elderly group (16 weeks > 8 weeks).[48] However, besides RT manipulation variables and dosage, other factors should be observed, considering the intrinsic effects of this training model.

Thus, a question has been raised related to a possible bias regarding neuromuscular adaptations and the test used. For example, if the 1 RM test is applied, individuals who experienced higher loads and lower repetition ranges would obtain better results than individuals who experienced a higher repetition range and moderate loads due to the specificity principle (Table 4).[49] In this context, the fundamentals of load dose-dependence and specificity in the test intended to be improved seem to be determinants of responsiveness and should be considered in the decision-making process regarding RT prescription.[26,46] On the other hand, specificity can also explain the lower efficiency of traditional RT in muscle power responsiveness.[45] However, it is likely that to increase positive rate responses of muscle power through RT, it is necessary to combine it with specific aspects of power training, as suggested by other authors,[13] in which the responsiveness rate of RT combined with plyometric training was higher than the RT traditional alone. It is noteworthy that, due to the limited data found regarding muscle power responses, caution is needed while interpreting our findings.

Regarding methodological issues, the randomization strategy may have influenced the reliability of the findings related to the responsiveness of muscle strength when the cross-effect phenomenon is not considered since it suggests that a trained limb can transfer neuromuscular adaptations to the contralateral limb regardless of its exposure to any of the investigated training protocols.[50] Experimental models that test different doses of RT in different limbs of the same subject, cannot infer (at least theoretically) the responsiveness results referring to a given training protocol, because it is not known how much of the magnitude of adaptations come from the protocol applied on the opposite limb.[26]

4.2. *Responsiveness of functional performance to RT*

Improvements in functional performance aspects may be interfered with by the load intensity and its association with muscle strength responsiveness.[47] In the study by Tracy et al.[46] elderly subjects submitted to low-intensity RT (30% 1 RM) obtained the lowest rate of responsiveness for muscle strength among all the studies selected in this review and did not show significant functional performance changes (Table 4). In contrast, Orssatto et al.[45] showed that high to moderate intensity RT (4–12 RM; ~90%–75% 1 RM) was highly effective for muscle strength (100% were responders) and induced a relevant rate of responders for functional performance (63% to TUG and Stair Ascent Test). Among unhealthy elderly subjects who experienced an RT protocol at 70% 1 RM, around 70% of the responders were subjects for muscle strength and functional performance.[51] Together, these findings reinforce the notion that changes in muscle strength may be significantly related to physical performance status and functional limitation.[52] Therefore, a protocol that does not positively change muscle strength may not transfer benefits to functional performance. However, future studies based on dose-response analysis of RT and functional performance, including the intrasubject analysis perspective, could better explain this phenomenon.

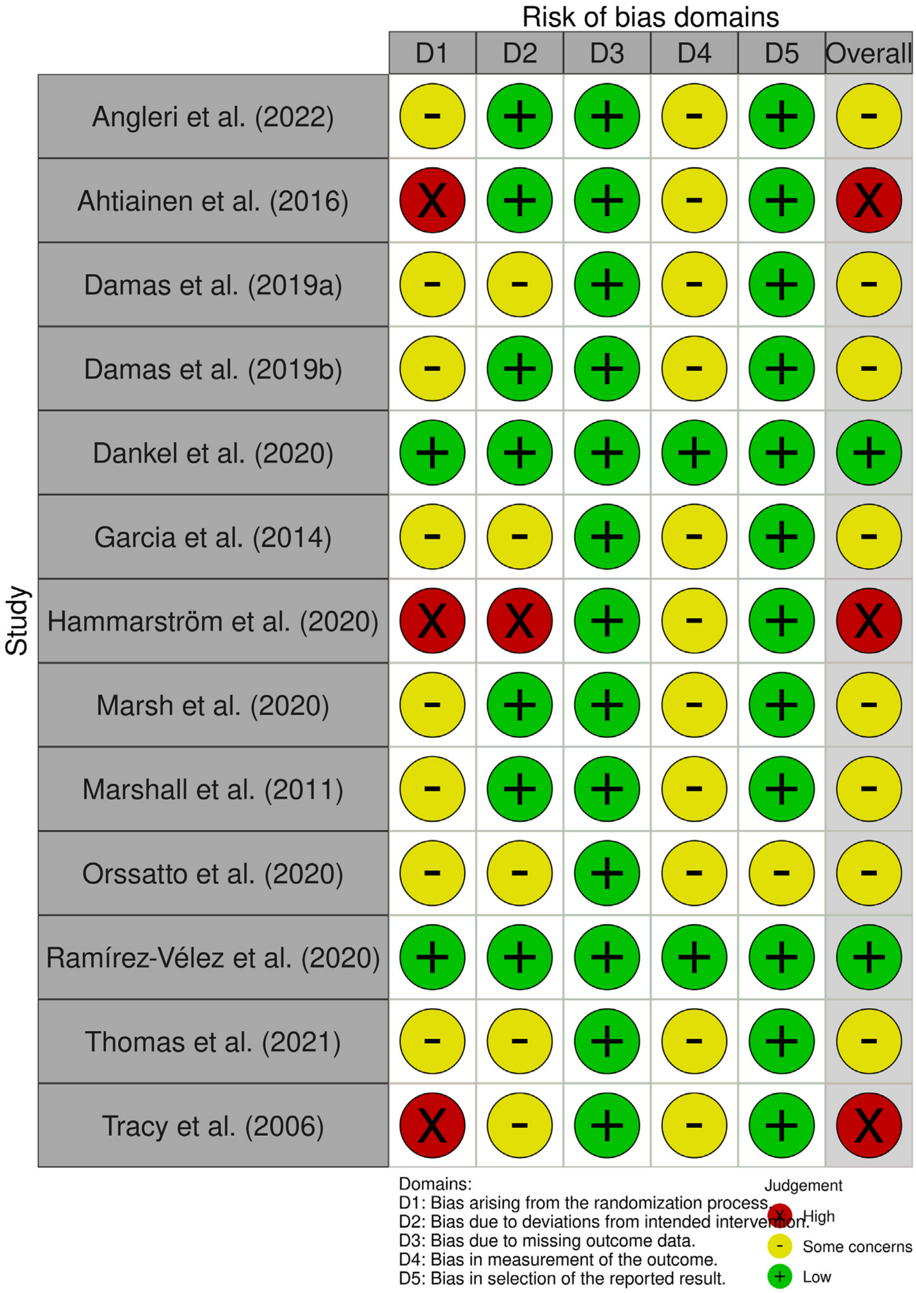

Fig. 3. Traffic light risk-of-bias plot.

4.3. *Responsiveness of muscle size to RT*

In general, for muscle size changes, a trend in favor of higher RT volume was found, however, it is noteworthy that evidence on hypertrophy responsiveness seems incipient, and specific research is needed.[26,38] In addition, the dose-response effect expected for hypertrophy has been proposed regarding the magnitude of changes in RT volume.[35] However, the prevalence of responders may not follow the same pattern since previous non-responders enrolled in a further 12-week RT program, with augmented volume, do not change their responsiveness status, at least in elderly women.[53] Thus, considering the suggestion of previous studies reinforcing high volume to muscle hypertrophy and the studies that shown greater effectiveness (80%–100% responders) in this present review, it is possible to suggest that a range between eight and 24 weekly sets per muscle group could be suggested as a range of RT volume to optimize responsiveness in muscle growth (Table 5).[26,38,43,44] Therefore, more evidence testing different RT doses from the perspective of responsiveness is needed.

The large variability in responsiveness for muscle hypertrophy found in this review can be explained by aspects other than the RT protocol. For example, the caloric deficit used in the study by Ramírez-Vélez et al.,[40] may have influenced the effectiveness range[54] and may have impaired the hypertrophic potential of RT.[55] In this sense, future studies seeking to investigate muscle hypertrophy optimization should control caloric intake. Another factor to be considered is the recruitment of subjects from previous studies, who had obtained excellent hypertrophic responses, therefore indicating that they were potentially better responders.[43] Nevertheless, the effectiveness of RT for muscle hypertrophy is still relatively high, even without considering the studies that may have influenced the range of results.[40,43]

From a physiological point of view, responders from higher RT volume for muscle hypertrophy showed higher phosphorylation of S6-

Table 2
The prevalence of responsiveness for muscle strength.

Author	Group	%HR (*n*)	%MR (*n*)	%LR (*n*)	%RP (*n*)	%NR (*n*)	%AB (*n*)
Marshall et al.[42]							
	Experimental	27 (3)	19 (2)	54 (6)	–	–	–
	Control 1	45 (5)	10 (1)	45 (5)	–	–	–
	Control 2	50 (5)	30 (3)	20 (2)	–	–	–
Garcia et al.[37]							
	Experimental	66 (4)	16 (1)	16 (1)	–	–	–
	Control	20 (1)	60 (3)	20 (1)	–	–	–
Ahtiainen et al.[9]							
	Experimental	14 (39)	–	7 (19)	–	–	–
	Control	–	–	–	–	–	–
Dankel et al.[26]							
	Experimental	12 (6)	–	8 (4)	81 (39)	19 (9)	–
	Control	–	–	–	99 (51)	1 (1)	–
Tracy et al.[46]							
	Experimental	–	–	–	66 (14)	44 (7)	–
	Control	–	–	–	–	–	–
Marsh et al.[39]							
	Experimental	–	–	–	100 (64)	0	–
	Control	–	–	–	–	–	–
Orssatto et al.[45]							
	Experimental	–	–	–	100 (19)	0	–
	Control	–	–	–	–	–	–
Damas et al.[43]							
	Experimental	–	–	–	100 (20)	0	25 (5)
	Control	–	–	–	100 (20)	0	16 (3)
Hammarström et al.[38]							
	Experimental	–	–	–	–	–	3 (1)
	Control	–	–	–	–	–	47 (16)
Angleri et al.[36] LP							
	Experimental	–	–	–	–	–	31 (5)
	Control 1	–	–	–	–	–	12 (2)
	Control 2	–	–	–	–	–	27(4)
Angleri et al.[36] EXT							
	Experimental	–	–	–	–	–	19 (3)
	Control 1	–	–	–	–	–	12 (2)
	Control 2	–	–	–	–	–	13 (2)

%RP(*n*): responders prevalence rate (number of subjects); %NR(*n*): non-responders prevalence rate (number of subjects); %HR(*n*): high responders prevalence rate (number of subjects); %MR(*n*): moderate responders prevalence rate (number of subjects); %LR(*n*): low-responders prevalence rate (number of subjects); AB: additional benefits; LP: leg press; EXT: knee extension.

kinase 1, ribosomal protein and myofibrillar protein fractional synthesis rate, higher resting total RNA, higher exercise-induced mRNA expression, and a gradual reduction in muscle damage.[38,43] Specifically, high responders may have a more expressive increase in the proliferation of satellite cells during training, besides presenting a larger mitochondrial volume. These factors may favor the anabolic potential[16,56] and further research would be of interest.

4.4. *Heterogeneity of studies*

To interpret the data on responsiveness, studies limitations and heterogeneity need to be considered, especially in statistical aspects. For example, it is suggested that studies in which a non-exercise control group is not present cannot sustain the inferences on the magnitude of individual changes since they did not account for the random error.[23] Thus, a misclassification of individual responses may occur in these studies regardless of the comparison between different protocols and the use of other statistical methods for responsiveness.[36–39,41–45] Also, the method of responsiveness analysis may have influenced the divergence of responses, mainly when a classification of subjects by different magnitudes of responses (high, moderate, and low responders) is used, based or not on the effect of the control group.[9,26,37,42]

Table 3
Prevalence of responsiveness for muscular hypertrophy.

Author	Group	%HR (*n*)	%PR (*n*)	%RP (*n*)	%NR (*n*)	%AB (*n*)
Ahtiainen et al.[9]						
	Experimental	12 (35)	29 (84)	–	–	–
	Control	–	–	–	–	–
Damas et al.[44]						
	Experimental	–	–	95 (19)	5 (1)	32 (6)
	Control	–	–	95 (19)	5 (1)	37 (7)
Damas et al.[43]						
	Experimental	–	–	100 (40)	0	0
	Control	–	–	100 (40)	0	0
Dankel et al.[26]						
	Experimental	–	–	80 (42)	20 (10)	–
	Control	–	–	0	100	–
Hammarström et al.[38]						
	Experimental	–	–	–	–	9 (3)
	Control	–	–	–	–	38 (13)
Ramirez-Velez et al.[40] ARM						
	Experimental	–	–	25 (3)	75 (9)	–
	Control	–	–	–	–	–
Ramirez-Velez et al.[40] TRUNK						
	Experimental	–	–	16 (2)	84 (10)	–
	Control	–	–	–	–	–
Ramirez-Velez et al.[40] TIGH						
	Experimental	–	–	16 (2)	84 (10)	–
	Control	–	–	–	–	–
Angleri et al.[36]						
	Experimental	–	–	–	–	0[a]
	Control 1	–	–	–	–	6 (1)
	Control 2	–	–	–	–	0
Thomas et al.[41]						
	Experimental	–	–	84 (54)	16 (10)	–
	Control	–	–	–	–	–

[a] Data refer to the same subjects; %RP(*n*): responders prevalence rate (number of subjects); %NR(*n*): non-responders prevalence rate (number of subjects); %HR(*n*): high responders prevalence rate (number of subjects); %MR(*n*): moderate responders prevalence rate (number of subjects); %LR(*n*): low-responders prevalence rate (number of subjects); AB: additional benefits.

Table 4
Prevalence of Responsiveness for functional performance tests.

Author	Group	%RP (*n*)	%NR (*n*)
Orssatto et al.[45] TUG			
	Experimental	63 (12)	37 (7)
	Control	–	–
Orssatto et al.[45] STA			
	Experimental	63 (12)	37 (7)
	Control	–	–
Orssatto et al.[45] STD			
	Experimental	58 (11)	42 (8)
	Control	–	–

TUG: Timed Up and Go test; STA: stair ascent test; STD: stair descent; %RP(*n*): prevalence rate of responders (number of subjects); %NR(*n*): non-responders prevalence rate (number of subjects).

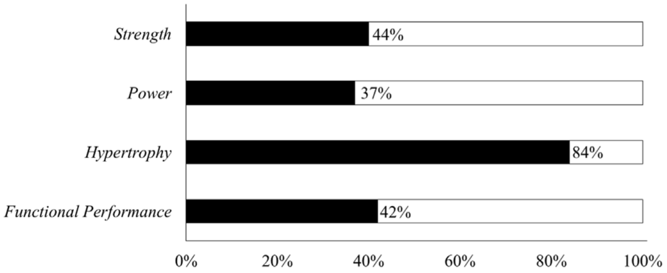

Fig. 4. Range of low responders for each outcome.

However, a recent study has pointed out that methods that cannot

Table 5
Relationship between intervention volume and effectiveness (responders).

Author	Hypertrophy		Strength		Power		Function	
	HV-RP (%)	LV-RP (%)	HV-RP (%)	LV-RP (%)	HV-RP (%)	LV-RP (%)	HV-RP (%)	LV-RP (%)
Dankel et al.[26]	80	0	81	99	–	–	–	–
Damas et al.[44]	95	95	100	100	–	–	–	–
Damas et al.[43]	100	–	–	–	–	–	–	–
Thomas et al.[41]	84	–	–	–	–	–	–	–
Ramírez-Vélez et al.[40]	19	–	–	–	–	–	–	–
Marsh et al.[39]	–	–	100	–	–	–	–	–
Tracy et al.[46]	–	–	–	66	–	–	–	–
Orssato et al.[45]	–	–	–	100	–	63	–	63

HV-RP (%): responders rate referring to the classification of high weekly volume per muscle group; LV-RP (%): prevalence rate referring to the classification of low weekly volume per muscle group.

Table 6
Relationship between volume and differential responders.

Author	Hypertrophy		Strength		
	%HR	%LR	%HR	%MR	%LR
Marshall et al.[42] 1SET (low volume)	–	–	27	19	54
Marshall et al.[42] 4SET (low volume)	–	–	45	10	45
Marshall et al.[42] 8SET (high volume)	–	–	50	30	20
Gargcia et al.[37] MT (high volume)	–	–	66	16	16
Gargcia et al.[37] TS (high volume)	–	–	20	60	20
Ahtiainen et al.[9] (high volume)	12	29	14	–	7
Dankel et al.[26] (high volume)	–	–	12	–	8

MS: multiple-set; TS: tri-set; %HR: prevalence rate of high responders; %MR: prevalence rate of moderate responders; %LR: prevalence rate of low responders.

Table 7
Relationship between training volume and additional benefits.

Author	Hypertrophy		Strength	
	HV-AB (%)	LV-AB (%)	HV-AB (%)	LV-AB (%)
Hammarström et al.[38]	38	9	47	3
Damas et al.[44]	32	37	25	16
Damas et al.[43]	–	–	0	0
Angleri et al.[36] TRAD vs. DS (leg press)	0	–	31	–
Angleri et al.[36] TRAD vs. CP (leg press)	–	–	7	–
Angleri et al.[36] DS (leg press)	6	–	12	–
Angleri et al.[36] CP (leg press)	0	–	27	–
Angleri et al.[36] TRAD vs. DS (knee extension)	–	–	19	–
Angleri et al.[36] TRA vs. CP (knee extension)	–	–	13	–
Angleri et al.[36] DS (knee extension)	–	–	12	–
Angleri et al.[36] CP (knee extension)	–	–	13	–

HV-AB (%): Rate of subjects who obtained additional benefits (AB) from a high-volume protocol; BV-AB (%): Rate of subjects who obtained additional benefits from a low-volume protocol; TRAD > DS (subjects who AB more from traditional TR than. Drop-set); TRAD > CP: (subjects who AB more from traditional RT than crescent pyramid); DS (subjects who AB more DS than traditional RT); CP (subjects who AB more from crescent pyramid than traditional RT).

isolate measurement error and random error, and that consider zero as the threshold for responsiveness for responders and non-responders, may overestimate the prevalence rates.[25] Thus, despite the heterogeneity of the studies, there was no evident divergence in the prevalence rates that could not be clearly explained by other factors.[26,39,43–46] However, in studies investigating responsiveness from additional benefits of one protocol over another,[36,38,43,44] it is not understudied whether the subjects are non-responders to the protocol or just did not get the benefits of the protocol without isolating the non-intervention effect.[24]

4.5. *RT effectiveness*

In general, the main findings highlighted that RT has a similar range of effectiveness in the variables of functional performance and muscle strength and size, showing the recurrence of a high prevalence of responders. However, when considering the probability of RT effectiveness, the comprehensive results show that strength and functional performance improvements are more likely to happen than hypertrophy and muscle power. However, the specificity principle mentioned to justify muscle power responsiveness may not be applied to muscle hypertrophy because it depends on other key factors that influence this phenomenon simultaneously, such as diet, sleep, recovery, age and level of training, and the magnitude of stimulus.[15]

Despite the positive potential of RT on the responsiveness of the analyzed variables,[9] reported that eight subjects (3%) showed null/-negative responses for both strength and hypertrophy. Furthermore, in the study by Carroll et al.[51] the authors found that four subjects (7%) showed negative responses to these two variables. In contrast, considering all variables of interest, two studies reported no individuals who responded negatively to all variables simultaneously.[11,12] In this sense, it is suggested that a universal non-responder subject is unlikely to exist, but one individual may not have the same responsiveness among different variables.

From another perspective, a recent review questioned that low and non-responses may represent only the response to the current training protocol applied. Still, if the training load was increased, the same subject would likely respond with a higher magnitude and become a responder.[57] In this context, the authors propose a novel term called “stubborn responders”, which describes individuals who need a higher training dosage than others.[57] According to the main findings of the present study, it is unclear how to specifically manipulate the RT to increase the rate of responders or high responders for all outcomes investigated. However, at least for muscle strength and hypertrophy, considering the manipulation of intensity[58] and volume,[59,60] respectively, are suggested. Also, keeping high specificity in mind while directing training variables to the primary outcome and the test chosen is highly encouraged.

4.6. *Perspectives*

In this systematic review, we report that a broader range of differential responders to RT should be expected for changes in muscle size compared to functional performance, muscle strength, and power. In this sense, this information is relevant to everyone involved in RT prescription and practice. More information about the causes of these differential responses is needed. However, the evidence summarized in this systematic review suggested some caution while interpreting the findings since the evidence is incipient and widely heterogeneous in methodological and statistical aspects.

4.7. *Study limitations and future studies*

The lack of studies investigating muscle power and functional performance was evident, as well as the heterogeneity regarding study designs, RT protocols, and responsiveness analysis models, as factors that limited better comparisons among the included studies, and these factors prevented the meta-analysis of the data to show the optimal volume dose to responsiveness in all outcomes and other subgroup analysis. Based on the questions raised, future studies should control factors that may interfere with the real effect of responsiveness and propose designs based on RT dose response. Also, the specificity and accuracy of the instrument/analysis method, the presence of a control group without intervention, and the statistical models that isolate the effect of the intervention are essential to understanding this phenomenon. In addition, designs with greater methodological rigor are needed. It is important to highlight that comparisons among responsiveness rates were only descriptive because the heterogeneity of the analysis found does not allow a metanalytical approach. Finally, based on the risk of bias analysis, future studies in this field must describe better the process of blinding and randomization of the groups.

5. Conclusion

In conclusion, the responsiveness of muscle strength and size to RT is better described and can be as effective as reaching 100% of responders. However, non-responders can reach 44% or 84% of a sample for strength and size, respectively. It suggests that some attention is needed to monitor muscle strength and size changes in response to a RT program. Regarding the dose-response effect, an increase in RT volume may enhance the effectiveness. Still, the intensity may be a critical factor in muscle strength and functional performance contexts. Furthermore, specific prescriptions for the intended benefits tend to provide satisfactory individual responses, considering characteristics such as dose dependence, the test used to measure changes, and the training model. However, it is essential to carefully analyze the studies due to their methodological limitations and statistical analysis to drive the decision-making in RT prescription.

Submission statement

All authors have read and agree with manuscript content. This manuscript is not being reviewed or submitted elsewhere.

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Authors' contributions

Tomé Edson dos Reis Moda: Writing – review & editing, Writing – original draft, Software, Project administration, Methodology, Formal analysis, Data curation, Conceptualization. **Ricardo Borges Viana:** Writing – review & editing, Writing – original draft, Methodology, Data curation. **Rayra Khalinka Neves Dias:** Writing – review & editing, Writing – original draft, Investigation, Data curation. **Eduardo Macedo Penna:** Writing – review & editing, Writing – original draft, Supervision, Methodology, Conceptualization. **Victor Silveira Coswig:** Writing – review & editing, Writing – original draft, Supervision, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization.

Conflict of interest

The authors state that they have no conflict of interest to declare.

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Appendix A. Supplementary data

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