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The influence of specific resistance training methodological prescription variables on strength development under hypoxic conditions: A systematic review and meta-analysis.

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ABSTRACT

A systematic review and meta-analysis were conducted focused on the impact of specific methodological prescription variables in resistance training (R_T) programming on muscle strength under hypoxic conditions. Searches of Pubmed-Medline, Web of Science, Sport Discuss and the Cochrane Library compared the effect of R_T on strength development under hypoxic (RTH) vs. normoxic (RTN) conditions through the 1-repetition maximum (1RM) test. Apart from the overall meta-analysis, several R_T methodological prescription variables available in the included studies (set end point, total weekly training volume, type of exercise, region of the body measured or type of routine) were analysed. Thirteen studies met the inclusion criteria. The overall analyses showed trivial differences in 1RM favouring RTH over RTN (SMD = 0.18 [CI: 0.04; 0.31]; p = 0.030). Sub-analyses revealed that a R_T program of a non-full-body routine, including 9 or more sets per exercise/week of multi-joint exercises performed to non-failure, favoured RTH for enhancing 1RM ($p<0.10$). In conclusion, evidence ratified a trivial benefit of RTH over RTN for muscle strength gains after a R_T period. However, the handling of specific R_T methodological prescription variables can slightly improve strength development outcomes in hypoxia.

Keywords: altitude, performance, normobaric hypoxia, prescription variables

INTRODUCTION

Resistance training under hypoxic conditions (RTH) has become a potential strategy athletes use to improve muscular adaptations. The mechanisms by which RTH potentially improves muscle size and strength compared to the same training in normoxia (RTN) have been widely described in the literature [1,2]. However, the divergent methodologies employed in the studies make it difficult to draw firm conclusions on the potential benefit of RTH compared to RTN [3,4]. For this reason, the proper handling of the resistance training (R_T) methodological prescription variables (such as training load, number of sets, repetition sets, training load, inter-set rest intervals, velocity of movement, exercise selection, set end point, exercise order or training frequency, among others) has developed into a topic of great interest when optimizing muscle mass and strength development [5]. The level of impact these variables may have on the result of a RTH is a subject of great relevance that has not been studied to date due to the lack of a sufficient mass of publications. The last meta-analysis conducted on this topic [4] revealed that a particular combination of training loads between 60–80% of 1-repetition maximum (1RM), inter-set rest intervals ≤ 60 s during the R_T at moderate hypoxia benefit muscle mass gain, while training loads between 60–80% of 1RM, inter-set rest intervals ≥ 120 s, regardless of the severity of the hypoxia, favoured strength development. Nevertheless, the recent narrative reviews [6,7] and meta-analyses [3,4] agree that the changes detected in the benefit of RTH over RTN do not allow firm conclusions to be drawn due to the disparity of training methodologies used among the studies.

Even though the impact of handling methodological R_T prescription variables on RTH results has not been studied in depth, it still constitutes an extensive discussion topic in the literature under normoxic conditions [8]. For example, training frequency (i.e., the number of training sessions performed per muscle group per week) does not impact muscle hypertrophy [9] or strength [10] when the total weekly training volume is equated. Thus, R_T volume (i.e., number of sets) reaches a significant effect when more than 10 sets per week are performed for hypertrophy [11], while only 2-3 sets per session are needed for strength targets [12]. Regarding training to muscle failure versus non-failure, research suggests similar increases in muscle strength and mass in both cases [13]. Moreover, some studies and systematic reviews speculate on the role that the R_T experience of the participants may play when planning the R_T program [9,10] suggesting different program design recommendations for the participant's type [14]. For example, training with high loads (≥ 60% of 1RM) seems to result in even more maximal strength gains in trained participants [15] than in untrained ones.

Although the literature contains several meta-analyses and systematic reviews that analyse the overall impact of RTH on strength gains, the effect of training prescription variables on its outcome has yet to be analysed. Furthermore, since the last published meta-analysis [4], two new studies on the topic have become available [16,17], providing the opportunity to strengthen the findings. Therefore, the aim of the current systematic review and meta-analysis was to determine the impact individual R_T prescription variables may have on hypoxia-induced gains in strength. The analysis could enhance the ability to improve R_T programming results under hypoxic conditions and detect gaps in the literature that will hopefully encourage future research on the topic.

METHODS

Study design.

This meta-analysis was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [18] (see Supplementary Tables 1 and 2).

Literature search

Based on the previous meta-analysis conducted [4], we updated the database up to July 1, 2024, and performed a systematic search of relevant studies using Scopus, PubMed/MEDLINE (main collections), Sport Discus and the Cochrane Library. The following combination of terms was used for the search: ("strength training" OR "resistance training" OR "weight training") AND ("hypoxia" OR "altitude" OR "hypoxic training"). The first pre-selection of the manuscripts and data extraction was carried out individually by two authors (CB and BF). To ensure the reliability of this process, each author performed the data extraction of all studies included in the meta-analyses and separately entered the data into a spreadsheet. The data were then crosschecked and combined into a single spreadsheet for analysis. Any discrepancies were resolved through discussion.

Inclusion criteria

We included the studies that met the following criteria in the analysis: (1) examined the effect of R_T under intermittent terrestrial or simulated hypoxia for at least 3 weeks [19] on strength development (via 1RM) in healthy individuals between 18 and 65 years of age using a randomized design; (2) included a normoxic control group; (3) were published in English-language peer-reviewed journals; and (4) provided

information about outcomes both at baseline and post-study. Research studies were excluded if they (1) were not original investigations published in full; (2) did not specify the evaluation procedure of the variable selected for analysis (1RM); (3) applied hypoxia via local techniques, such as blood flow restriction; (4) did not provide or specify numerical or graphic data; and (5) examined only the acute effects of interventions.

Data encoding

Studies were read and individually coded by two of the authors (CB and BF) for the following prescription variables: set end point (failure or non-failure); total weekly training volume per muscle group (number of sets per muscle group per session × number of weekly sessions); exercise selection (single-joint or multi-joint); region/muscle of the body measured (upper or lower limbs); type of routine (full-body [all muscle groups are trained in the same session] or non-full-body [one or two muscle groups are trained in each session] routine). The type of 1RM measurement (direct or indirect procedure) was also assessed. It was not possible to classify the participants' training level due to the disparity in the terminology between studies. The encoding files were collated between the authors to refine the criteria and cross-checked between reviewers, with any discrepancies resolved by mutual consensus.

Risk of Bias Assessment

Two independent reviewers (CB and BF) determined the risk of bias of the included studies in this systematic review by using specific scales depending on the type of study, following the instructions given by the Cochrane's risk of bias tool [20] and the PEDro scale [21].

The assessment of the selected studies included specification of eligibility criteria, random sequence generation, allocation concealment, inter-group similarity in main study outcomes at baseline, blinding of participants, blinding of outcome, incomplete outcome data and selective reporting. Details of this quality assessment can be found in Supplementary Table 3.

Statistical analysis

All studies were independently analysed for the main outcome (maximal dynamic strength [1RM]) using pre- and post-study results under hypoxic or normoxic conditions with values expressed as standardised mean differences (SMD) and their 90% confidence intervals (CIs). Subgroup analyses were performed to determine possible confounding effects of set end point, total weekly training volume per

muscle group (<9 or ≥9 sets), type of 1RM test, exercise selection, region/muscle of the body measured and the type of routine. Standardised effect size coefficients from randomized control trials (RCTs) were computed as the mean differences between the mean change in hypoxia and normoxia groups from baseline to post-intervention, divided by the mean pooled baseline standard deviation ($\bar{S}$pre) [22]:

$$d = c(dfH, N) \cdot [((\bar{X}pre, H - \bar{X}pos, H) - (\bar{X}pre, N - \bar{X}pos, N))/(\bar{S}pre)].$$

$$\bar{S}pre = \sqrt{(((n, \mathrm{N}H - 1) \cdot S\hat{}2\ pre, H + (n, N - 1) \cdot S\hat{}2\ pre, N)/(n, \mathrm{N}H + n, N - 2))}$$

$$S\hat{}2\ (d) = [c(dfH, N)]\hat{}2 \cdot 2(1 - r) \cdot ((n\_H + n\_N)/(n\_H\ n\_N)) \cdot ((n\_H + n\_N - 2)/(n\_H + n\_N - 4)) \cdot [1 + (n\_H\ \llbracket \cdot n \rrbracket\ \_N \cdot d\hat{}2)/2(1 - r)(n\_H + n\_N)] - d\hat{}2$$

The coefficient included a correction factor for small samples $\mathrm{c}(\mathrm{dfH}, \mathrm{N})$ [23] and according to the standard r value recommended by Rosenthal, it was set as r=0.7 [24].

$$c(dfNH, N) = 1 - 3/(4(n, NH + n, N - 2) - 1)$$

The inverse variance method was used in both cases for the weighting of studies. Additionally, we calculated the raw (unstandardised) mean difference for RCTs $(\bar{X}pre, H - \bar{X}pos, H) - (\bar{X}pre, N - \bar{X}pos, N)$ by using the weights from our standardised meta-analysis to estimate the pooled mean difference in each outcome.

Data were analysed using a multi-level random effects model to account for multiple effects nested within groups, studies, and participants (three-level analysis) [25]. This approach allows for control for the bias of combining several measures from the same study. According to DerSimonian and Laird [26], independent effect size coefficients and their results were combined and analysed using the random effects model. The weighted standardized mean change from baseline to the end of the intervention was the pooled effect size for the outcome.

Consistent with previous meta-analytic approaches [27], we chose to avoid drawing binary conclusions via traditional null-hypothesis significance testing given the documented issues with this statistical method [28,29]. Although a null-hypothesis testing approach is still used and provided, we considered the spectrum of possible estimates from the lower to upper limits of compatibility, placing the greatest inferential emphasis on the point estimate. The SMD value was interpreted as: "trivial" (≤ 0.20); "small" (0.21–0.50); "medium" (0.51–0.80); "large" (> 0.80); and "very large" (>1.20) [30]. If the SMD had a positive value, the result favours RTH; conversely, if the results had a negative value, the result favours RTN. To estimate statistical heterogeneity, the Q test and the I^2 index were calculated; heterogeneity was

considered moderate if I^2 = 30–60% ($p < 0.1$). Potential publication bias was also tested using Egger's test [31] using the standard errors of the effect size, as estimated from a funnel plot. Statistical analysis was conducted using the Metafor package [32] of the R statistical program [33].

RESULTS

Study selection and characteristics

Since the publication of the last meta-analysis [4], two additional studies have been carried out [16,17] and met the inclusion criteria. However, they were found to be redundant since they came from the same experiment; thus, one of them was excluded from the analysis [17]. Finally, 13 studies [16,34–45] were incorporated in the meta-analysis to determine the impact of specific methodological prescription variables of a R_T period in hypoxia on muscle strength development. The impact of the RTH on muscle hypertrophy was not included in this study due to the lack of research measuring muscle growth in each sub-analysed category. A PRISMA flowchart of the search process is shown in Figure 1.

[Insert Figure 1 about here]

[Insert Table 1 about here]

Table 1 presents general characteristics and classification in accordance with the categories defined in the included studies. The pooled number of participants across all referred studies was 256 males (n = 119 for RTN and n = 137 for RTH), and the median number of participants per study was nine.

All the included studies employed a live low-train high (live in normoxia-train in hypoxia) strategy. Only one study was conducted under terrestrial altitude [16], while the rest of them used a normobaric hypoxic condition.

Six studies developed a training program using muscle failure[35,39,41–43,45], while the remainder used a non-failure method[16,34,36–38,40,44]. Only two studies included less than 9 sets per muscle group/week[36,39], while the rest included 9[16,35,41–43] or more sets per muscle group/week[34,37,38,40,44,45]. The threshold of 9 or more sets was stated according to the codification of the weekly training frequency previously established [46]. Nine studies used multi-joint exercises[16,34,35,37,38,40,43–45] during the R_T program, two studies used single-joint exercises[36,42] and two studies combined multi- and single-joint exercises[39,41]. Only two studies included exercises focused on the upper body[36,42], five studies included lower limb exercises[34,35,37,43,45], and six studies included both[16,38–41,44] in their program. Four studies employed a full-body routine[16,39,41], while

the remainder applied a non-full-body routine[34–38,40,42–45]. Seven studies measured the 1RM through a direct method[34,37,38,40,43–45], and six studies used an indirect procedure[16,35,36,39,41,42].

Meta-analyses

The final global analysis comprised 31 1RM assessments from different exercises from 13 studies (Figure 2). Results displayed trivial differences in strength development favouring RTH over RTN (SMD = 0.18 [CI: 0.04; 0.31]; p = 0.030).

[Insert Figure 2 about here]

Set end point

Table 2 shows the results for the set end point. There was a significant small effect on strength development favouring RTH when participants trained to non-failure in the set (SMD = 0.35 [0.13; 0.56]; p = 0.010) (Supplementary Figure 1).

[Insert Table 2 about here]

Total weekly training volume per muscle group

The outcomes for weekly sets per muscle as a two-level categorical variable are shown in Table 2. There was a significant trivial effect in strength gains favouring RTH when the participants trained for 9 or more sets/week (SMD = 0.18 [0.05; 0.31]; p = 0.030), while a small but non-significant effect favouring RTH was shown when training for less than 9 sets/week (SMD = 0.31 [-0.39; 1.02]; p = 0.470) (Supplementary Figure 2).

Type of 1RM test

Table 2 shows the outcomes for measuring strength development through a 1RM test. Strength development was favoured in RTH when direct versus indirect 1RM testing was used (SMD = 0.20 [0.02; 0.39]; p = 0.070) (Supplementary Figure 3).

Exercise selection

Outcomes for single-joint or multi-joint exercises are shown in Table 2. Strength outcomes significantly improved after a RTH period over RTN when training included multi-joint exercises (SMD = 0.15 [0.01; 0.29]; p = 0.080) (Supplementary Figure 4).

Region/muscle of the body measured

Table 2 shows the outcomes for the region of the body measured. There was a small significant effect favouring strength development in RTH when lower limb muscles were trained (SMD = 0.21 [0.03; 0.40]; p = 0.060) (Supplementary Figure 5).

Type of routine

Table 2 includes the outcomes for the type of routine used. Full-body routines reduced strength development in hypoxia compared with to non-full-body routines (SMD = 0.26 [0.09; 0.43]; p = 0.010) (Supplementary Figure 6).

Heterogeneity and risk of bias assessment.

Heterogeneity between studies was found to be low for 1RM between environmental conditions (I^2 = 8.8%), and none of the sub-analyses presented high heterogeneity (I^2 < 25.3%). The risk of bias/methodological quality in primary studies ranged from medium to high quality (mean quality scores = 5.2/5.4) (Table S4). The risk of bias was unclear for the concealment of participant randomization and the blinding of outcome data. All the included studies in this meta-analysis indicated random sequence generation but did not describe the method used. Egger's test suggested a risk of small study bias (p = 0.014) (Supplementary Figure 7).

DISCUSSION

This systematic review and meta-analysis comprised data from 13 studies to determine the impact of specific methodological prescription variables during RTH on strength development in healthy adults. Apart from the load, inter-set rest interval and severity of hypoxia assessed in a previous meta-analysis [4], this proposal delves into all the possible R_T available prescription variables in the included studies (set end point, total weekly training volume per muscle group, exercise selection, region/muscle of the body measured and type of routine) were sub-analysed. The pooled results, without controlling for covariates, provide a trivial global significant benefit of RTH over RTN on strength development. The use of a direct test in determining 1RM favours this result. The sub-analysis of the studied R_T prescription variables for strength development suggests that the handling of each of them is susceptible to further positively benefit outcomes in hypoxia. However, their impact only ranged from trivial (on total weekly training volume per

muscle group of 9 or more sets of multi-joint exercises) to small (on sets performed to non-failure during a non-full-body routine). A paucity of data in some categories limited our ability to shed insight into the impact of several R_T variables.

According to previous research [3,4,7,47], the pooled analysis without covariate adjustment yielded only trivial findings regarding the potential benefits of RTH on muscle strength gains. The recent meta-analysis by Benavente et al.[4] pooled 17 studies comparing the effects of RTH vs. RTN on muscle and strength gains. Since then, two new investigations were carried out on the topic [16,17], although just one [16] was considered. Finally, only 13 of the 19 available studies evaluated 1RM and met the criteria established. Including new data and the sub-analysis of R_T prescription variables should have allowed us to improve the knowledge of the biases accompanying the use of RTH for muscle strength development. However, a notable disparity in the training procedure continues to persist, which limits the scope of the results. Further standardization of protocols should be considered in future research on the topic.

Our results showed a small benefit of RTH on muscle strength development when a direct test was applied in the 1RM evaluation (Table 2; Supplementary Figure 3). The analysed studies assessed muscular strength under normoxic conditions using either the 1RM test directly or indirectly through Brzycki's equation, the 6RM test, or the 10RM test. Most of the studies (19 out of 31 comparisons) employed indirect methods, which likely reduced measurement precision and slightly diminished the magnitude of the observed effect. Although evidence suggests that using a direct 1RM test favours the impact of RTH over RTN, the SMD and CI were quite similar between the testing modalities. Brzycki's equation has proved to satisfy the validation criteria for determining 1RM in exercises such as bench press [48] or squat, while others, like deadlift [49], could underestimate the results. This result underscores the importance of using direct measurements when assessing muscle strength outcomes. Other variables, such as the specificity of the training program to the test evaluation exercise [50], could also have influenced the findings. Nevertheless, all the studies included in this meta-analysis have employed the same exercise for testing and training, which strengthens the results.

Under normoxic conditions, performing resistance exercises to muscle failure is posited as an important factor for increasing muscle strength [51]. Theoretically, training to muscle failure increases the recruitment of the higher threshold motor units to maintain force production [52], although it also may lead to neuromuscular fatigue and discomfort and pose safety risks. Nevertheless, training to muscle failure

under normoxic conditions does not seem to be required for gains in strength, and it does not have detrimental effects on this outcome [53]. Conversely, when exercise is combined with hypoxia, there seems to be a small significant benefit if subjects train to non-failure (SMD= 0.35; p = 0.010). Considering that the favourable effects of RTH are thought to be mediated in part by increases in metabolic stress [54], likely inducing higher motor unit recruitment [55], training to failure could cause extra fatigue that may increase the risks of overtraining and overuse injuries [56] while compromising training volume.

When considering weekly sets per muscle group as a two-level categorical variable (<9 vs. ≥9 sets per week), our findings revealed a trivial but significant effect when 9 or more sets/week were performed under hypoxic conditions (Table 2; Supplementary Figure 2). In a similar way, non-full-body routines also displayed a RTH benefit in 1RM development. Nonetheless, the results exposed a disparity between studies involving fewer than 9 sets per muscle group per week and those involving 9 or more sets (8 out of 31 comparisons, respectively). The codification of the weekly training frequency was established in accordance with a previous meta-analysis focused on the dose-response relationship between R_T weekly frequency and volume in muscle growth [46]. Available research conducted under normoxic conditions suggests that higher training frequencies (i.e., 3 days per week) result in greater strength gains than lower frequencies [10]. However, a negligible impact on muscular strength improvement is also depicted when the training volume is equated [57]. Therefore, it seems that increasing training frequency can allow for higher total weekly volume and subsequent muscle mass and strength improvements [10]. However, the result of our meta-analysis could be influenced by the low number of studies involving routines with <9 sets/week. In a complementary way, we also analysed weekly sets as a three-level categorical variable (<9 vs. 9 vs. ≥10 sets per week), which allowed for a more balanced distribution of data volume between categories (Supplementary Figure 8). This new result appears to reveal a strength plateau when comparing RTH vs. RTN for 9 or more sets per week. Nonetheless, separating the studies analysed into additional categories beyond 10 sets/week was unfeasible, limiting the detection of the potential strength plateau at some point during RTH. Future research is needed to determine the existence of an upper threshold in R_T volume and frequency at which point strength development no longer significantly improves under hypoxic conditions.

Finally, the type of exercise and the region/muscle of the body measured denoted a trivial to small significant effect favouring RTH when multi-joint exercises performed within a non-full-body routine were used. The reviewed studies primarily employed multi-joint exercises (23 out of 31 comparisons). This type of exercise recruits large amounts of muscle mass that are related to post-exercise hormonal elevations [58].

This fact, along with the hypoxia-induced metabolic stress [2,36,59] and, therefore, the potential improvement in motor unit recruitment [60], could make routines that involve larger muscle groups, more efficient for strength gains [61]. Additionally, while we found a balance between exercises targeting the upper and lower body, results revealed that 1RM improvements slightly favoured strength gains in RTH-involved lower body exercises. Conversely, a previous meta-analysis [3] that sub-analysed the impact of RTH comparing lower vs. upper body exercises, detecting no differences in strength development. The favouring trend of the lower body over the upper body observed in our analysis is attributable to the predominance of single-joint exercises when targeting the upper body (mainly biceps and triceps; Table 1), which could partially explain the discrepancy observed between the two sub-categories. Moreover, some of the studies included in the current meta-analysis comprised, in the same routine, both multi- and single-joint lower and upper body exercises with a training frequency and volume not compatible with any of the categories used, making it difficult to achieve clear results. Therefore, it is still needed to elucidate the impact of the RTH concerning the type of exercise and routine used.

This meta-analysis has some potential limitations: (1) Although most of the studies assessed muscle strength outcomes, we could not sub-analyse individual R_T prescription variables on muscle hypertrophy due to the lack of research measuring this outcome on each sub-category; (2) Only one study was conducted under terrestrial altitude. Although the weight of the study was not sufficient to influence the global result, research suggests physiological differences and muscle strength adaptations between both types of hypoxia. And finally, (3) none of the studies included women as participants. Gender bias in research conducted under hypoxic conditions is still evident today and must be solved in the future.

CONCLUSION

Evidence corroborates a global trivial positive effect of using RTH compared to RTN for muscular strength and highlights the impact of handling certain R_T prescription variables in the results. However, although this meta-analysis shows some benefits of RTH on strength adaptations, it is necessary to highlight that these are generally trivial/small. More benefits in RTH can be seen by altering some exercise/programming variables appropriately (i.e., using a program comprised of 9 or more sets/week of multi-joint exercises performed to non-failure during a non-full-body routine).

REFERENCES

1. Scott BR, Slattery KM, Dascombe BJ. Intermittent hypoxic resistance training: does it provide added benefit? *Front Physiol*. 2014;5:397. doi:10.3389/fphys.2014.00397

2. Schoenfeld BJ. Potential Mechanisms for a Role of Metabolic Stress in Hypertrophic Adaptations to Resistance Training. *Sports Medicine*. 2013;43(3):179-194. doi:10.1007/s40279-013-0017-1

3. Ramos-Campo DJ, Scott BR, Alcaraz PE, Rubio-Arias JA. The efficacy of resistance training in hypoxia to enhance strength and muscle growth: A systematic review and meta-analysis. *Eur J Sport Sci*. 2018;18(1):92-103. doi:10.1080/17461391.2017.1388850

4. Benavente C, Schoenfeld BJ, Padial P, Feriche B. Efficacy of resistance training in hypoxia on muscle hypertrophy and strength development: a systematic review with meta-analysis. *Scientific Reports 2023 13:1*. 2023;13(1):1-15. doi:10.1038/s41598-023-30808-4

5. Schoenfeld B, Grgic J, Van Every D, Plotkin D. Loading recommendations for muscle strength, hypertrophy, and local endurance: a re-examination of the repetition continuum. *Sports*. 2021;9(2):32.

6. Gamonales JM, Rojas-Valverde D, Vásquez J, et al. An Update to a Comprehensive Assessment of the Methods and Effectiveness of Resistance Training in Normobaric Hypoxia for the Development of Strength and Muscular Hypertrophy. *Applied Sciences*. 2023;13(2):1078. doi:10.3390/APP13021078

7. Deldicque L. Does Normobaric Hypoxic Resistance Training Confer Benefit over Normoxic Training in Athletes? A Narrative Review. *Journal of Science in Sport and Exercise 2022*. 2022;1:1-9. doi:10.1007/S42978-021-00159-5

8. Mcleod J, Currier B, Lowisz C, Phillips S. The influence of resistance exercise training prescription variables on skeletal muscle mass, strength, and physical function in healthy adults: An umbrella. *J Sport Health Sci*. 2023;13:47-60.

9. Schoenfeld BJ, Grgic J, Krieger J. How many times per week should a muscle be trained to maximize muscle hypertrophy? A systematic review and meta-analysis of studies examining the effects of resistance training frequency. *J Sports Sci*. 2019;37(11):1286-1295. doi:10.1080/02640414.2018.1555906

10. Grgic J, Schoenfeld BJ, Davies TB, Lazinica B, Krieger JW, Pedisic Z. Effect of resistance training frequency on gains in muscular strength: a systematic review and meta-analysis. *Sports Medicine*. 2018;48(5):1207-1220. doi:10.1007/s40279-018-0872-x

11. Schoenfeld B, Ogborn D, Krieger J. Dose-response relationship between weekly resistance training volume and increases in muscle mass : A systematic review and meta- analysis. *J Sports Sci*. 2017;35(11):1073-1082. doi:10.1080/02640414.2016.1210197

12. Krieger J. Single versus multiple sets of resistance exercise: a meta-regression. *The Journal of Strength & Conditioning Research*. 2009;23(6):1890-1901.

13. Grgic J, Schoenfeld BJ, Orazem J, Sabol F. Effects of resistance training performed to repetition failure or non-failure on muscular strength and hypertrophy: a systematic review and meta-analysis. *J Sport Health Sci*. 2021;11(2):202-211. doi:10.1016/j.jshs.2021.01.007

14. American College of Sports Medicine. American College of Sports Medicine position stand. Progression models in resistance training for healthy adults. *Med Sci Sports Exerc*. 2009;41(3):687-708. doi:10.1249/MSS.0B013E3181915670

15. Schoenfeld BJ, Grgic J, Ogborn D, Krieger JW. Strength and hypertrophy adaptations between low- vs. High-load resistance training: A systematic review and meta-analysis. *J Strength Cond Res*. 2017;31(12):3508-3523. doi:10.1519/JSC.0000000000002200

16. Rodríguez-Zamora L, Benavente C, Petrer I, et al. Hypoxia matters: comparison of external and internal training load markers during an 8-week resistance training program in normoxia, normobaric hypoxia and hypobaric hypoxia. *Eur J Appl Physiol*. Published online March 6, 2024:1-11. doi:10.1007/S00421-024-05442-1/FIGURES/2

17. Benavente C, Padial · P, Scott · B R, et al. Strength and muscle mass development after a resistance-training period at terrestrial and normobaric intermittent hypoxia. *Pflügers Archiv-European Journal of Physiology*. Published online 2024:1-13. doi:10.1007/s00424-024-02978-1

18. Page M, McKenzie J, Bossuyt P. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *Syst Rev*. 2021;10(1):1-11. doi:10.1136/bmj.n71

19. Damas F, Phillips SM, Libardi CA, et al. Resistance training-induced changes in integrated myofibrillar protein synthesis are related to hypertrophy only after attenuation of muscle damage. *J Physiol*. 2016;594(18):5209-5222. doi:10.1113/JP272472

20. Higgins J, Altman D, Gøtzsche P. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *BMJ*. 2011;343. doi:10.1136/bmj.d5928

21. Maher C, Sherrington C, Herbert RD, Moseley AM, Elkins M. Reliability of the PEDro scale for rating quality of randomized controlled trials. *Phys Ther*. 2003;83(8):713-721.

22. Morris SB. Estimating effect sizes from pretest-posttest-control group designs. *Organ Res Methods*. 2008;11(2):364-386. doi:10.1177/1094428106291059

23. Hedges LV, Olkin I. *Statistical Methods for Meta-Analysis.* Orlando FL: Academic Press; 1985.

24. Rosenthal R. Meta-Analytic Procedures for Social Science Research Sage Publications. *Educational Researcher*. 1986;15(8):18-20. doi:10.3102/0013189X015008018

25. Harrer M, Cuijpers P, Furukawa TA, Ebert DD. *Doing Meta-Analysis With R: A Hands-On Guide*. 1st ed. Chapman & Hall/CRC Press; 2021.

26. DerSimonian R, Lair N. Meta-analysis in clinical trials. *Control Clin Trials*. 1986;7(3):177-188.

27. Steele J, Plotkin D, Van Every D, et al. Slow and Steady, or Hard and Fast? A Systematic Review and Meta-Analysis of Studies Comparing Body Composition Changes between Interval Training and Moderate Intensity Continuous Training. *Sports*. 2021;9(11):155. doi:10.3390/SPORTS9110155

28. Amrhein V, Greenland S, McShane B. Scientists rise up against statistical significance. *Nature*. 2019;567(7748):305-307. doi:10.1038/d41586-019-00857-9

29. McShane BB, Gal D, Gelman A, Robert C, Tackett JL. Abandon Statistical Significance. *Am Stat*. 2019;73(sup1):235-245. doi:10.1080/00031305.2018.1527253

30. Cohen J. A power primer. *Psychol Bull*. 1992;112(1):155-159. doi:10.1037//0033-2909.112.1.155

31. Egger M, Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. *BMJ*. 1997;315(7109):629-634.

32. Viechtbauer W. Conducting Meta-Analyses in R with the metafor Package. *J Stat Softw*. 2010;36(1):1-48. doi:10.18637/JSS.V036.I03

33. R Development Core Team. R: A Language and Environment for Statistical Computing. Published online 2012. http://www.r-project.org.

34. van Doorslaer de ten Ryen S, Warnier G, Gnimassou O, et al. Higher strength gain after hypoxic vs normoxic resistance training despite no changes in muscle thickness and fractional protein synthetic rate. *The FASEB Journal*. 2021;35(8):e21773. doi:10.1096/FJ.202100654RR

35. Fashi M, Ahmadizad S. Short-term hypoxic resistance training improves muscular performance in untrained males. *Sci Sports*. 2021;36(4):312. doi:10.1016/j.scispo.2020.10.003

36. Nishimura A, Sugita M, Kato K, Fukuda A, Sudo A, Uchida A. Hypoxia Increases Muscle Hypertrophy Induced by Resistance Training. *Int J Sports Physiol Perform*. 2010;5(4):497-508. doi:10.1123/ijspp.5.4.497

37. Inness MW, Billaut F, Walker EJ, Petersen AC, Sweeting AJ, Aughey RJ. Heavy Resistance Training in Hypoxia Enhances 1RM Squat Performance. *Front Physiol*. 2016;7:502. doi:10.3389/fphys.2016.00502

38. Mayo B, Miles C, Sims S, Driller M. The effect of resistance training in a hypoxic chamber on physical performance in elite rugby athletes. *High Alt Med Biol*. 2018;19(1):28-34. doi:10.1089/ham.2017.0099

39. Martínez-Guardado I, Ramos-Campo DJ, Olcina GJ, et al. Effects of high-intensity resistance circuit-based training in hypoxia on body composition and strength performance. *Eur J Sport Sci*. 2019;19(7):941-951. doi:10.1080/17461391.2018.1564796

40. Honda A, Kon M, Matsubayashi T, Suzuki Y. Short-Term Intermittent Hypoxic Resistance Training Does Not Impair Osteogenic Response in Sea Level Residents. *High Alt Med Biol*. 2020;21(2):160-166. doi:10.1089/ham.2019.0089

41. Martínez-Guardado I, Sanchez-Ureña B, Camacho-Cardenosa A, Camacho-Cardenosa M, Olcina G, Timón R. Effects of strength training under hypoxic conditions on muscle performance, body composition and haematological variables. *Biol Sport*. 2020;37(2):121-129. doi:10.5114/biolsport.2020.93037

42. Kurobe K, Huang Z, Nishiwaki M, Yamamoto M, Kanehisa H, Ogita F. Effects of resistance training under hypoxic conditions on muscle hypertrophy and strength. *Clin Physiol Funct Imaging*. 2015;35(3):197-202. doi:10.1111/cpf.12147

43. Ho JY, Kuo TY, Liu KL, Dong XY, Tung K. Combining Normobaric Hypoxia With Short-term Resistance Training Has No Additive Beneficial Effect on Muscular Performance and Body Composition. *J Strength Cond Res*. 2014;28(4):935-941. doi:10.1519/JSC.0000000000000289

44. Kon M, Ohiwa N, Honda A, et al. Effects of systemic hypoxia on human muscular adaptations to resistance exercise training. *Physiol Rep*. 2014;2(6). doi:10.14814/phy2.12033

45. Yan B, Lai X, Yi L, Wang Y, Hu Y. Effects of five-week resistance training in hypoxia on hormones and muscle strength. *The Journal of Strength & Conditioning Research*. 2016;30(1):184-8011.

46. Schoenfeld BJ, Ogborn D, Krieger JW. Dose-response relationship between weekly resistance training volume and increases in muscle mass: A systematic review and meta-analysis. *J Sports Sci*. 2017;35(11):1073-1082. doi:10.1080/02640414.2016.1210197

47. Gamonales JM, Rojas-Valverde D, Vásquez J, et al. An Update to a Comprehensive Assessment of the Methods and Effectiveness of Resistance Training in Normobaric Hypoxia for the Development of Strength and Muscular Hypertrophy. *Applied Sciences*. 2023;13(2):1078. doi:10.3390/APP13021078

48. Nascimento M, Cyrino E, Nakamura F, Romanzini M, Pianca H, Queiroga M. Validation of the Brzycki equation for the estimation of 1-RM in the bench press. *Revista Brasileira de Medicina do Esporte*. 2007;13:47-50.

49. LeSuer D, McCormick J, Mayhew J, Wassertein R, Arnold M. The accuracy of prediction equations for estimating 1-RM performance in the bench press, squat, and deadlift. *J Strength Cond Res*. 1997;11:211-213.

50. Baechle T, Earle R, Wathen D. Resistance training. In: *Essentials of Strength Training and Conditioning*. 3rd Edition. Human kinetics; 2008:381-412.

51. Fisher J, Steele J, Bruce-Low S, Smith D. Evidence based resistance training recommendations. *Medicina Sportiva*. 2011;15(3):147-162. doi:10.2478/v10036-011-0025-x

52. Fisher J, Steele J, Smith D. Evidence-based resistance training recommendations for muscular hypertrophy. *Mdicina Sportiva*. 2013;17(4):217-235. doi:10.5604/17342260.1081302

53. Grgic J, Schoenfeld B, Orazem J, Sabol F. Effects of resistance training performed to repetition failure or non-failure on muscular strength and hypertrophy: A systematic review and meta-analysis. *J Sport Health Sci*. 2022;11(2):202-211.

54. Scott BR, Goods PSR, Slattery KM. High-intensity exercise in hypoxia: Is increased reliance on anaerobic metabolism important. *Front Physiol*. 2016;7:238425. doi:10.3389/FPHYS.2016.00637

55. Scott B, Slattery K, Sculley D, Lockhart C, Sacombe B. Acute physiological responses to moderate-load resistance exercise in hypoxia. *The Journal of Strength & Conditioning Research*. 2017;31(7):1973-1981.

56. Willardson JM, Norton L, Wilson G. Training to failure and beyond in mainstream resistance exercise programs. *Strength Cond J*. 2010;32(3):21-29. doi:10.1519/SSC.0B013E3181CC2A3A

57. Ralston GW, Kilgore L, Wyatt FB, Buchan D, Baker JS. Weekly Training Frequency Effects on Strength Gain: A Meta-Analysis. *Sports Med Open*. 2018;4(36). doi:10.1186/s40798-018-0149-9

58. Hansen S, Kvorning T, Kjær M, Sjøgaard G. The effect of short-term strength training on human skeletal muscle: The importance of physiologically elevated hormone levels. *Scand J Med Sci Sports*. 2001;11(6):347-354. doi:10.1034/J.1600-0838.2001.110606.X

59. Kon M, Ikeda T, Homma T, Suzuki Y. Effects of low-intensity resistance exercise under acute systemic hypoxia on hormonal responses. *J Strength Cond Res*. 2012;26(3):611-617. doi:10.1519/JSC.0b013e3182281c69

60. Alix-Fages C, Del Vecchio A, Baz-Valle E, Santos-Concejero, J., Balsalobre-Fernández C. The role of the neural stimulus in regulating skeletal muscle hypertrophy. *Eur J Appl Physiol*. 2022;122:1111-1128. doi:10.1007/s00421-022-04906-6

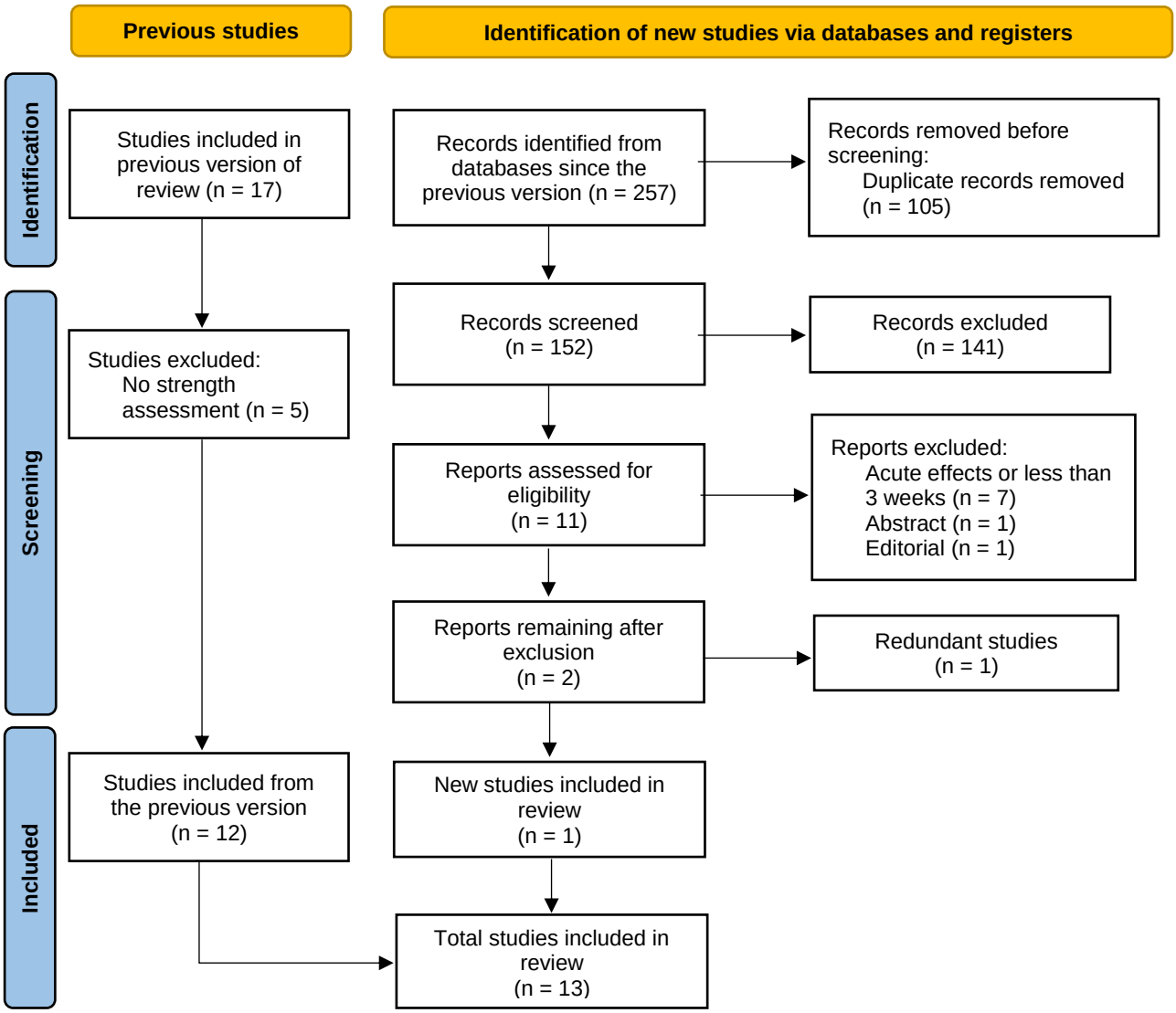
61. Kraemer W, Ratamess N. Fundamentals of resistance training: progression and exercise prescription. *Med Sci Sports Exerc*. 2004;36(4):674-688. doi:10.1249/01.MSS.0000121945.36635.61

FIGURE LEGEND

Figure 1. Flow diagram of the search and selection of studies.

Figure 2. Forest plot of the standardized mean differences of the final global analysis of the resistance training program between-conditions (hypoxic [H] group vs. normoxic [N] group) on 1-repetition maximum (1RM).

Δ: mean differences between post-pre in H and N or between H-N; n: sample size; Spre: mean baseline standard deviation; Std. MD: standard mean difference; Random: random effect's model; CI; confidence interval; HH: hypobaric hypoxia; NH: normobaric hypoxia; High: severe hypoxia; Moderate: moderate hypoxia; Q: test statistic for the test of heterogeneity; df: degrees of freedom; p; p value; I^2: I^2 test; Z: z value.


Previous studies
Identification of new studies via databases and registers
Identification
Screening
Included
Studies included in previous version of review (n = 17)
Records identified from databases since the previous version (n = 257)
Records removed before screening:
Duplicate records removed (n = 105)
Records screened (n = 152)
Records excluded (n = 141)
Studies excluded:
No strength assessment (n = 5)
Reports assessed for eligibility (n = 11)
Reports excluded:
Acute effects or less than 3 weeks (n = 7)
Abstract (n = 1)
Editorial (n = 1)
Reports remaining after exclusion (n = 2)
Redundant studies (n = 1)
Studies included from the previous version (n = 12)
New studies included in review (n = 1)
Total studies included in review (n = 13)

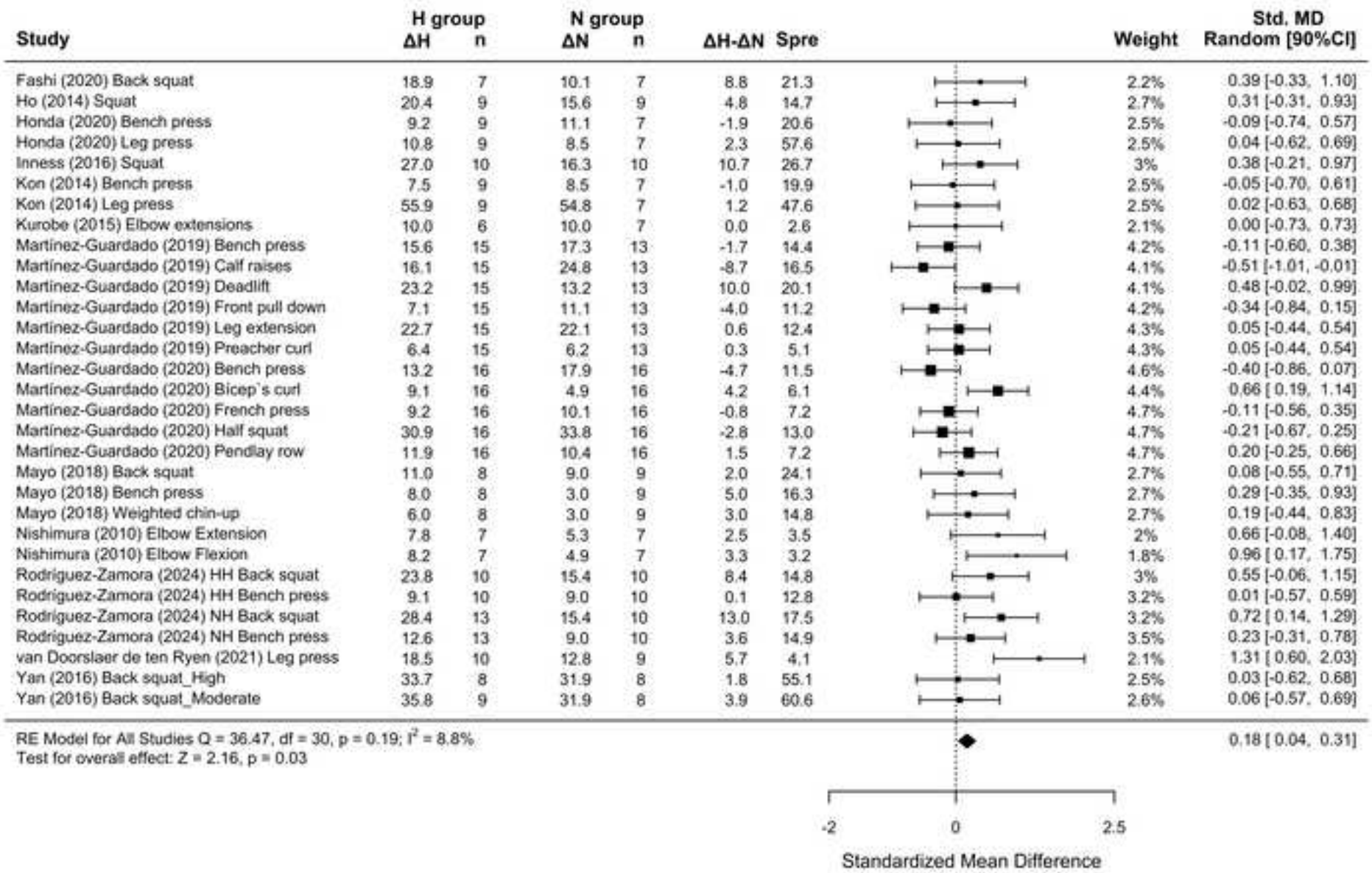

Study
H group
ΔH n
N group
ΔN n
ΔH-ΔN Spre
Weight
Std. MD
Random [90%CI]
Fashi (2020) Back squat 18.9 7 10.1 7 8.8 21.3 2.2% 0.39 [-0.33, 1.10]
Ho (2014) Squat 20.4 9 15.6 9 4.8 14.7 2.7% 0.31 [-0.31, 0.93]
Honda (2020) Bench press 9.2 9 11.1 7 -1.9 20.6 2.5% -0.09 [-0.74, 0.57]
Honda (2020) Leg press 10.8 9 8.5 7 2.3 57.6 2.5% 0.04 [-0.62, 0.69]
Inness (2016) Squat 27.0 10 16.3 10 10.7 26.7 3% 0.38 [-0.21, 0.97]
Kon (2014) Bench press 7.5 9 8.5 7 -1.0 19.9 2.5% -0.05 [-0.70, 0.61]
Kon (2014) Leg press 55.9 9 54.8 7 1.2 47.6 2.5% 0.02 [-0.63, 0.68]
Kurobe (2015) Elbow extensions 10.0 6 10.0 7 0.0 2.6 2.1% 0.00 [-0.73, 0.73]
Martínez-Guardado (2019) Bench press 15.6 15 17.3 13 -1.7 14.4 4.2% -0.11 [-0.60, 0.38]
Martínez-Guardado (2019) Calf raises 16.1 15 24.8 13 -8.7 16.5 4.1% -0.51 [-1.01, -0.01]
Martínez-Guardado (2019) Deadlift 23.2 15 13.2 13 10.0 20.1 4.1% 0.48 [-0.02, 0.99]
Martínez-Guardado (2019) Front pull down 7.1 15 11.1 13 -4.0 11.2 4.2% -0.34 [-0.84, 0.15]
Martínez-Guardado (2019) Leg extension 22.7 15 22.1 13 0.6 12.4 4.3% 0.05 [-0.44, 0.54]
Martínez-Guardado (2019) Preacher curl 6.4 15 6.2 13 0.3 5.1 4.3% 0.05 [-0.44, 0.54]
Martínez-Guardado (2020) Bench press 13.2 16 17.9 16 -4.7 11.5 4.6% -0.40 [-0.86, 0.07]
Martínez-Guardado (2020) Bicep`s curl 9.1 16 4.9 16 4.2 6.1 4.4% 0.66 [0.19, 1.14]
Martínez-Guardado (2020) French press 9.2 16 10.1 16 -0.8 7.2 4.7% -0.11 [-0.56, 0.35]
Martínez-Guardado (2020) Half squat 30.9 16 33.8 16 -2.8 13.0 4.7% -0.21 [-0.67, 0.25]
Martínez-Guardado (2020) Pendlay row 11.9 16 10.4 16 1.5 7.2 4.7% 0.20 [-0.25, 0.66]
Mayo (2018) Back squat 11.0 8 9.0 9 2.0 24.1 2.7% 0.08 [-0.55, 0.71]
Mayo (2018) Bench press 8.0 8 3.0 9 5.0 16.3 2.7% 0.29 [-0.35, 0.93]
Mayo (2018) Weighted chin-up 6.0 8 3.0 9 3.0 14.8 2.7% 0.19 [-0.44, 0.83]
Nishimura (2010) Elbow Extension 7.8 7 5.3 7 2.5 3.5 2% 0.66 [-0.08, 1.40]
Nishimura (2010) Elbow Flexion 8.2 7 4.9 7 3.3 3.2 1.8% 0.96 [0.17, 1.75]
Rodriguez-Zamora (2024) HH Back squat 23.8 10 15.4 10 8.4 14.8 3% 0.55 [-0.06, 1.15]
Rodriguez-Zamora (2024) HH Bench press 9.1 10 9.0 10 0.1 12.8 3.2% 0.01 [-0.57, 0.59]
Rodriguez-Zamora (2024) NH Back squat 28.4 13 15.4 10 13.0 17.5 3.2% 0.72 [0.14, 1.29]
Rodriguez-Zamora (2024) NH Bench press 12.6 13 9.0 10 3.6 14.9 3.5% 0.23 [-0.31, 0.78]
van Doorslaer de ten Ryen (2021) Leg press 18.5 10 12.8 9 5.7 4.1 2.1% 1.31 [0.60, 2.03]
Yan (2016) Back squat_High 33.7 8 31.9 8 1.8 55.1 2.5% 0.03 [-0.62, 0.68]
Yan (2016) Back squat_Moderate 35.8 9 31.9 8 3.9 60.6 2.6% 0.06 [-0.57, 0.69]
RE Model for All Studies Q = 36.47, df = 30, p = 0.19; I² = 8.8%
Test for overall effect: Z = 2.16, p = 0.03
0.18 [0.04, 0.31]
-2
0
2.5
Standardized Mean Difference

Table 1. Main characteristics of included studies in the meta-analysis.

Study	n	H condition (FiO_2)	Participants' training level	Weeks (s/w)	Training	Training to muscle failure	1RM test	Weekly sets per muscle	Exercises
Fashi (2021)	7 (M) 7 (M)	NH (12.7%) N (20.9%)	Untrained	4 (3)	3 sets x reps. to failure. 50% 10RM (~37% RM) (Rest 60 s)	Yes	Indirect (AMRAP + Brzycki's equation)	9	Back squat
Ho (2014)	9 (M) 9 (M)	NH (15%) N (21%)	Untrained and recreationally active	6 (3)	3 sets x 10 RM (75% RM) (Rest 120 s) a 10 RM	Yes	Direct (1RM test)	9	Squat
Honda (2020)	9 (M) 7 (M)	NH (14.4%) N (21%)	Untrained and recreationally active	8 (2)	5 sets x 10 reps. 70%RM (Rest 90 s)	No	Direct (1RM test)	10 10	Bench press Leg press
Inness (2016)	10 (M) 10 (M)	NH (14.3%) N (20%)	Strength trained	7 (3)	2-4 sets x 3-6 reps. 75%RM (Rest 180 s)	No	Direct (1RM test)	18	Squat Lunge Deadlift
Kon (2014)	9 (M) 7 (M)	NH (14.4%) N (21%)	Recreationally resistance trained	8 (2)	5 sets x 10 reps. 70% RM (Rest 90 s)	No	Direct (1RM test)	10 10	Bench press Leg press
Kurobe (2015)	6 (M) 7 (M)	NH (12.7%) N (20.9%)	Physically active	8 (3)	3 sets x reps. to failure. 10RM (75% RM) (Rest 60 s)	Yes	Indirect (10 RM test)	9	Elbow extensions
Martínez-Guardado (2019)	15 (M) 13 (M)	NH (15%) N (20.9%)	Strength trained	8 (2)	3 rounds x 2 blocks x 3x6RM (85%RM) (Rest 35s between exercises, 180s between sets, 5 min between blocks)	Yes	Indirect (6RM test)	6 6 6 6 6 6	Bench press Leg extension Front pull down Deadlift Preacher curl Calf raises
Martínez-Guardado (2020)	16 (M) 16 (M)	NH (13%) N (21%)	Untrained	7 (3)	3 sets x reps. to failure. 65-75-80%RM (Rest 90s)	Yes	Indirect (3RM test + Brzycki's equation)	9 9 9 9 9	Bench press Bicep's curl French press Pendlay row Half squat
Mayo (2018)	8 (M) 9 (M)	NH (14.4%) N (20.9%)	Elite rugby athletes	3 (4)	1-12 sets x 2-4 reps. 85-92.5%RM (Rest 180 s between. super sets)	No	Direct (1RM test)	12 16 16	Back squat Bench press Weighted Chin-up
Nishimura (2010)	7 (M) 7 (M)	NH (16%) N (21%)	Untrained	6 (2)	4 sets x 10 reps. 70% RM (Rest 60 s)	No	Indirect (10RM test)	8 8	Elbow flexion Elbow extension
Rodríguez-Zamora (2024)	10 (M) 13 (M) 10 (M)	HH (2320 m asl) NH (15.9%) N (21%)	Resistance trained	8 (3)	3 sets x 8-12 reps. 65-80% RM (Rest 90 s)	No	Indirect (2-3RM test + Brzycki's equation)	9 9	Back squat Deadlift Lat pulldown Barbell row Bench press Shoulder press

van Doorslaer de ten Ryen (2021)	10 (M) 9 (M)	NH (13.5%) N (21%)	Physically active	4 (3)	6 sets x 10 reps. 80% RM (Rest 120 s)	No	Direct (1RM test)	18	One leg extension
Yan (2016)	8 (M) 9 (M) 8 (M)	NH (12.6%) NH (16%) N (21%)	Recreationally active	5 (2)	5 sets x 10 reps. 70% RM (Rest 60 s)	Yes	Direct (1RM test)	10	Back squat

n: sample size; H: hypoxia; N: normoxia; NH: normobaric hypoxia; HH: hypobaric hypoxia; FiO_2: fraction of inspired oxygen; s/w: sessions per week; reps.: repetitions; RM: repetition maximum; M: male; asl: above sea level; AMRAP: as many repetitions as possible.

Table 2. Results of the subgroup meta-analyses.

Subgroup analysis	n	Classification	SMD (90% CI)	*p value*
Outcome: muscular strength	31	Overall	**0.18 [0.04; 0.31]**	**0.030**
Set end point	16	Failure	0.02 [-0.13; 0.16]	0.860
	15	Non-Failure	**0.35 [0.13; 0.56]**	**0.010**
Total weekly training volume per muscle group	8	<9 sets	0.31 [-0.39; 1.02]	0.470
	23	≥9 sets	**0.18 [0.05; 0.31]**	**0.030**
Type of 1RM test	12	Direct	**0.20 [0.02; 0.39]**	**0.070**
	19	Indirect	0.17 [-0.04; 0.38]	0.170
Exercise selection	23	Multi-joint	**0.15 [0.01; 0.29]**	**0.080**
	8	Single-joint	0.20 [-0.14; 0.54]	0.330
Region/muscle of body measured	16	Upper limbs	0.09 [-0.06; 0.23]	0.330
	15	Lower limbs	**0.21 [0.03; 0.40]**	**0.060**
Type of routine	18	Full-body routine	0.08 [-0.11; 0.26]	0.510
	13	Non-full-body routine	**0.26 [0.09; 0.43]**	**0.010**

n: number of outcomes; 90% CI = 90% confidence interval; SMD = standardized mean difference; p-value (text in bold denotes $p < 0.10$). Negative values denote favoring normoxia training and positive values indicate favouring hypoxic training.

The influence of specific resistance training methodological variables on strength development in hypoxic conditions: A systematic review and meta-analysis.

Supplementary materials

Supplementary Table 1. PRISMA for abstract checklist.

Section and Topic	Item #	Checklist item	Reported (Yes/No)
TITLE			
Title	1	Identify the report as a systematic review.	Yes
BACKGROUND			
Objectives	2	Provide an explicit statement of the main objective(s) or question(s) the review addresses.	Yes
METHODS			
Eligibility criteria	3	Specify the inclusion and exclusion criteria for the review.	Yes
Information sources	4	Specify the information sources (e.g. databases, registers) used to identify studies and the date when each was last searched.	Yes
Risk of bias	5	Specify the methods used to assess risk of bias in the included studies.	Yes
Synthesis of results	6	Specify the methods used to present and synthesise results.	Yes
RESULTS			
Included studies	7	Give the total number of included studies and participants and summarise relevant characteristics of studies.	Yes
Synthesis of results	8	Present results for main outcomes, preferably indicating the number of included studies and participants for each. If meta-analysis was done, report the summary estimate and confidence/credible interval. If comparing groups, indicate the direction of the effect (i.e. which group is favoured).	Yes
DISCUSSION			
Limitations of evidence	9	Provide a brief summary of the limitations of the evidence included in the review (e.g. study risk of bias, inconsistency and imprecision).	Yes
Interpretation	10	Provide a general interpretation of the results and important implications.	Yes
OTHER			
Funding	11	Specify the primary source of funding for the review.	Yes
Registration	12	Provide the register name and registration number.	N/A

Supplementary Table 2. PRISMA checklist.

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Title
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	Table S1 Abstract
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Pages 3-4
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Page 4
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Pages 4-5
Information sources	6	Specify all databases, registers, websites, organizations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Page 4
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Page 4
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.	Pages 4-5 Figure 1
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.	Pages 4-5 Figure 1
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.	Table 1
	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.	Pages 4-5
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.	Supp. Table 3
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	Pages 6-7
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)).	Pages 4-5
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	Pages 4-5
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Pages 4-5
	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.	Pages 4-5

Section and Topic	Item #	Checklist item	Location where item is reported
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	Pages 7-8
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	Page 7
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	Page 5
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	Page 6
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.	Page 7
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Page 7
Study characteristics	17	Cite each included study and present its characteristics.	Pages 7-8
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Supp. Table 3
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.	Pages 8-10
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Pages 9-10
	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.	Pages 8-10
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	Page 9
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	Pages 9-10
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	N/A
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Pages 9-10
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Pages 10-12
	23b	Discuss any limitations of the evidence included in the review.	Page 12
	23c	Discuss any limitations of the review processes used.	Page 12
	23d	Discuss implications of the results for practice, policy, and future research.	Page 12
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.	N/A
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	N/A
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	N/A
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Page 13

Section and Topic	Item #	Checklist item	Location where item is reported
Competing interests	26	Declare any competing interests of review authors.	Page 13
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 material

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372: n71. doi:10.1136/bmj.n71

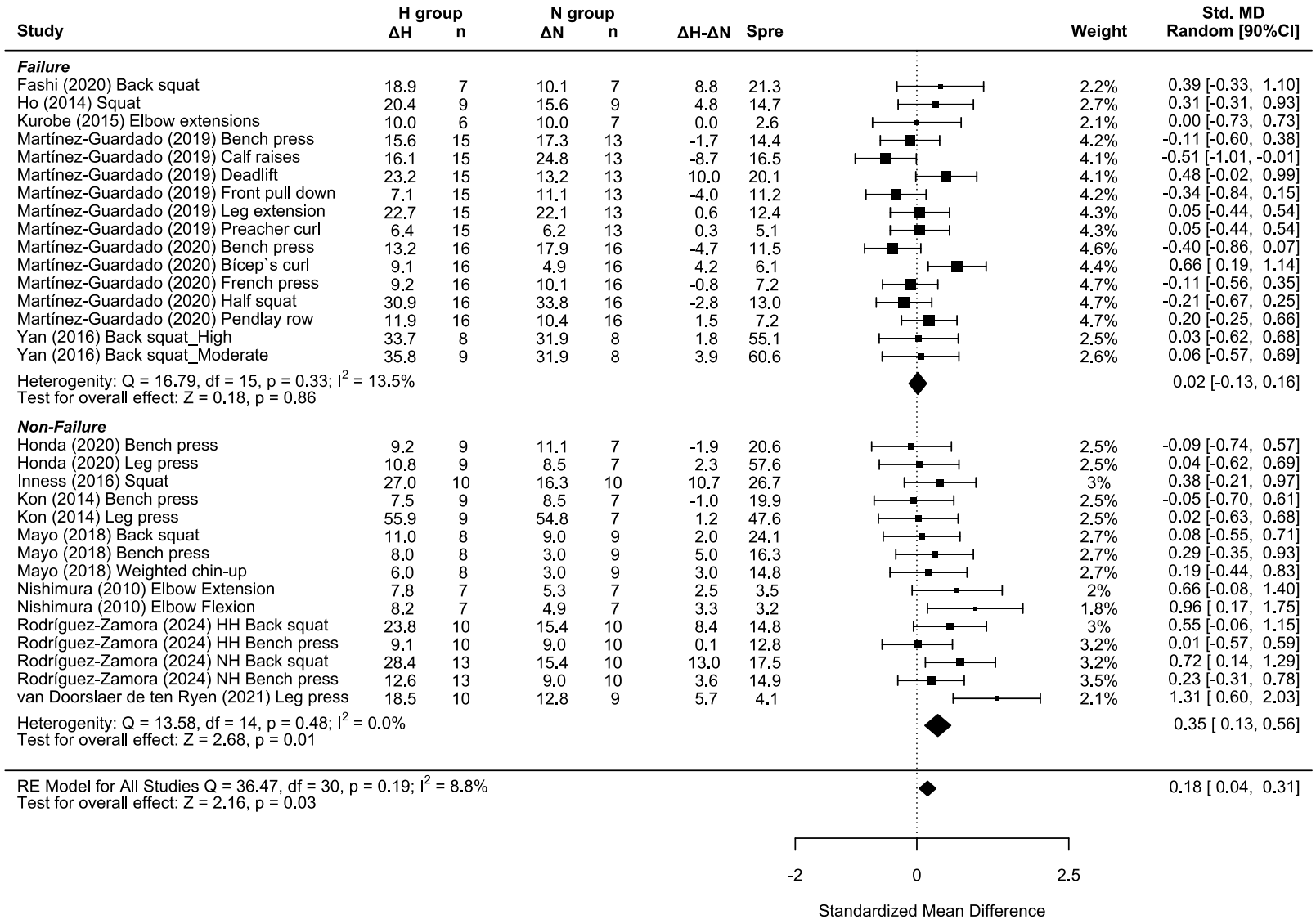
Supplementary Table 3. Risk of bias and quality assessment.

Study	Specification of eligibility criteria	Random sequence generation	Allocation concealment	Inter-group similarity at baseline	Blinding of participants	Blinding of outcome data	Incomplete outcome data	Selective reporting	Total quality score
Fashi (2020)	Low	Low	N/A	N/A	Low	N/A	Low	Low	5/5
Ho (2014)	Low	N/A	N/A	Low	Low	N/A	Low	Low	5/5
Honda (2020)	Low	Low	N/A	Low	N/A	N/A	Low	Low	5/5
Inness (2016)	Low	N/A	N/A	N/A	Low	N/A	Low	High	3/4
Kon (2014)	Low	Low	N/A	Low	N/A	N/A	Low	Low	5/5
Kurobe (2015)	Low	Low	N/A	Low	Low	N/A	Low	Low	6/6
Martínez-Guardado (2019)	Low	Low	N/A	Low	Low	N/A	Low	Low	6/6
Martínez-Guardado (2020)	Low	Low	N/A	N/A	Low	N/A	Low	Low	5/5
Mayo (2018)	Low	Low	N/A	Low	Low	N/A	Low	Low	6/6
Nishimura (2010)	Low	Low	N/A	Low	High	N/A	Low	Low	5/6
Rodríguez-Zamora (2024)	Low	Low	N/A	Low	High	N/A	Low	Low	5/6
van Doorslaer de ten Ryen (2021)	Low	Low	N/A	Low	Low	N/A	Low	Low	6/6
Yan (2016)	Low	Low	N/A	N/A	Low	N/A	Low	Low	5/5

Low: Low risk of bias; High: High risk of bias; Unclear: unclear risk of bias. N/A: not applicable.

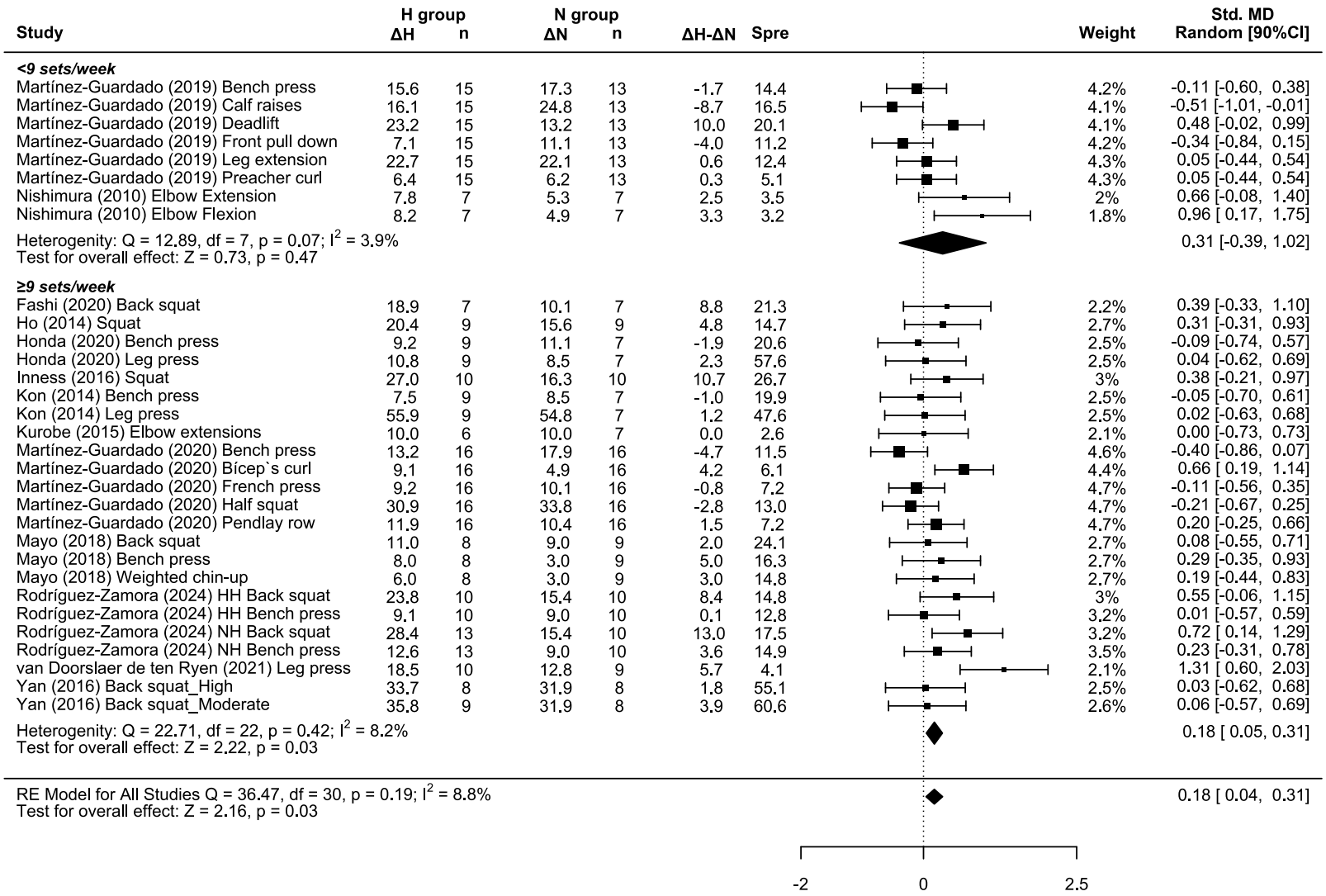
Supplementary Figure 1. Forest plot of the standardized mean differences of the resistance training program between-conditions (hypoxic [H] group vs. normoxic [N] group) on 1-repetition maximum (1RM) sub-analysed by set end point.

Δ: mean differences between post-pre in H and N or between H-N; n: sample size; Spre: mean baseline standard deviation; Std. MD: standard mean difference; Random: random effect's model; CI; confidence interval; HH: hypobaric hypoxia; NH: normobaric hypoxia; High: severe hypoxia; Moderate: moderate hypoxia; Q: test statistic for the test of heterogeneity; df: degrees of freedom; p; p value; I^2: I^2 test; Z: z value.



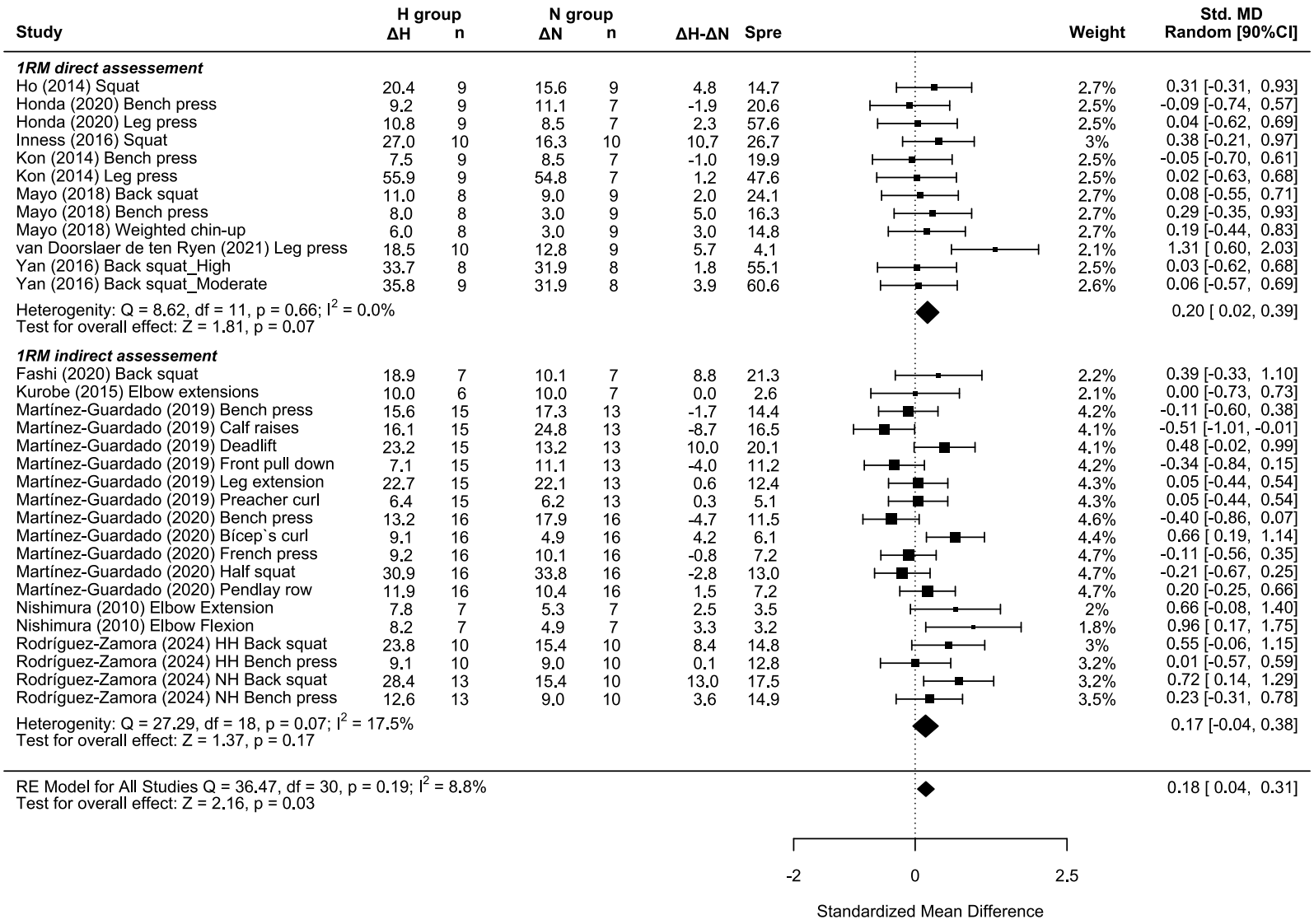
Supplementary Figure 2. Forest plot of the standardized mean differences of the resistance training program between-conditions (hypoxic [H] group vs. normoxic [N] group) on 1-repetition maximum (1RM) sub-analysed by total weekly training volume per muscle group as a two-level categorical variable.

Δ: mean differences between post-pre in H and N or between H-N; n: sample size; Spre: mean baseline standard deviation; Std. MD: standard mean difference; Random: random effect's model; CI; confidence interval; HH: hypobaric hypoxia; NH: normobaric hypoxia; High: severe hypoxia; Moderate: moderate hypoxia; Q: test statistic for the test of heterogeneity; df: degrees of freedom; p; p value; I^2: I^2 test; Z: z value.



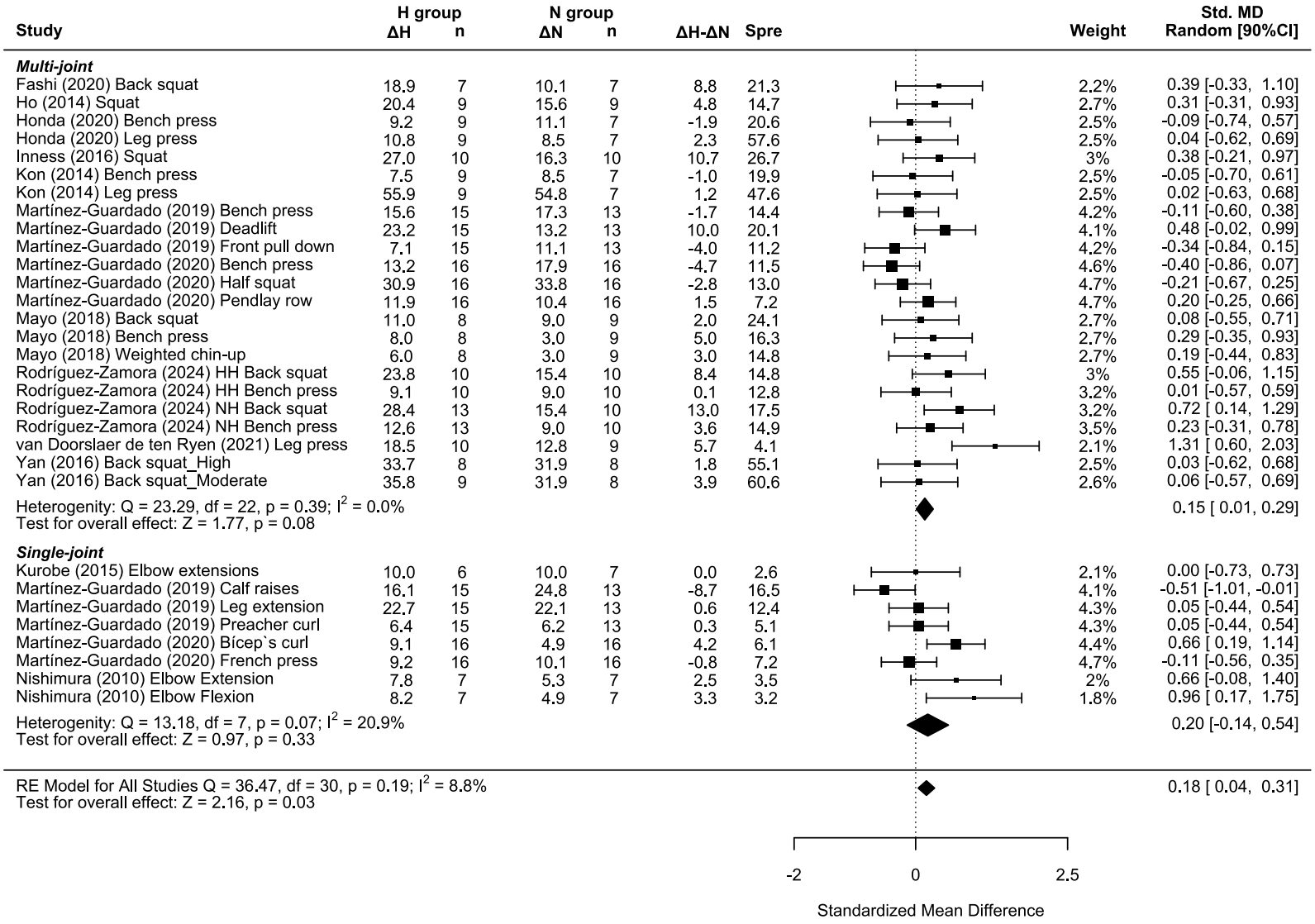
Supplementary Figure 3. Forest plot of the standardized mean differences of the resistance training program between-conditions (hypoxic [H] group vs. normoxic [N] group) on 1-repetition maximum (1RM) sub-analysed by type of 1RM test.

Δ: mean differences between post-pre in H and N or between H-N; n: sample size; Spre: mean baseline standard deviation; Std. MD: standard mean difference; Random: random effect's model; CI; confidence interval; HH: hypobaric hypoxia; NH: normobaric hypoxia; High: severe hypoxia; Moderate: moderate hypoxia; Q: test statistic for the test of heterogeneity; df: degrees of freedom; p; p value; I^2: I^2 test; Z: z value.



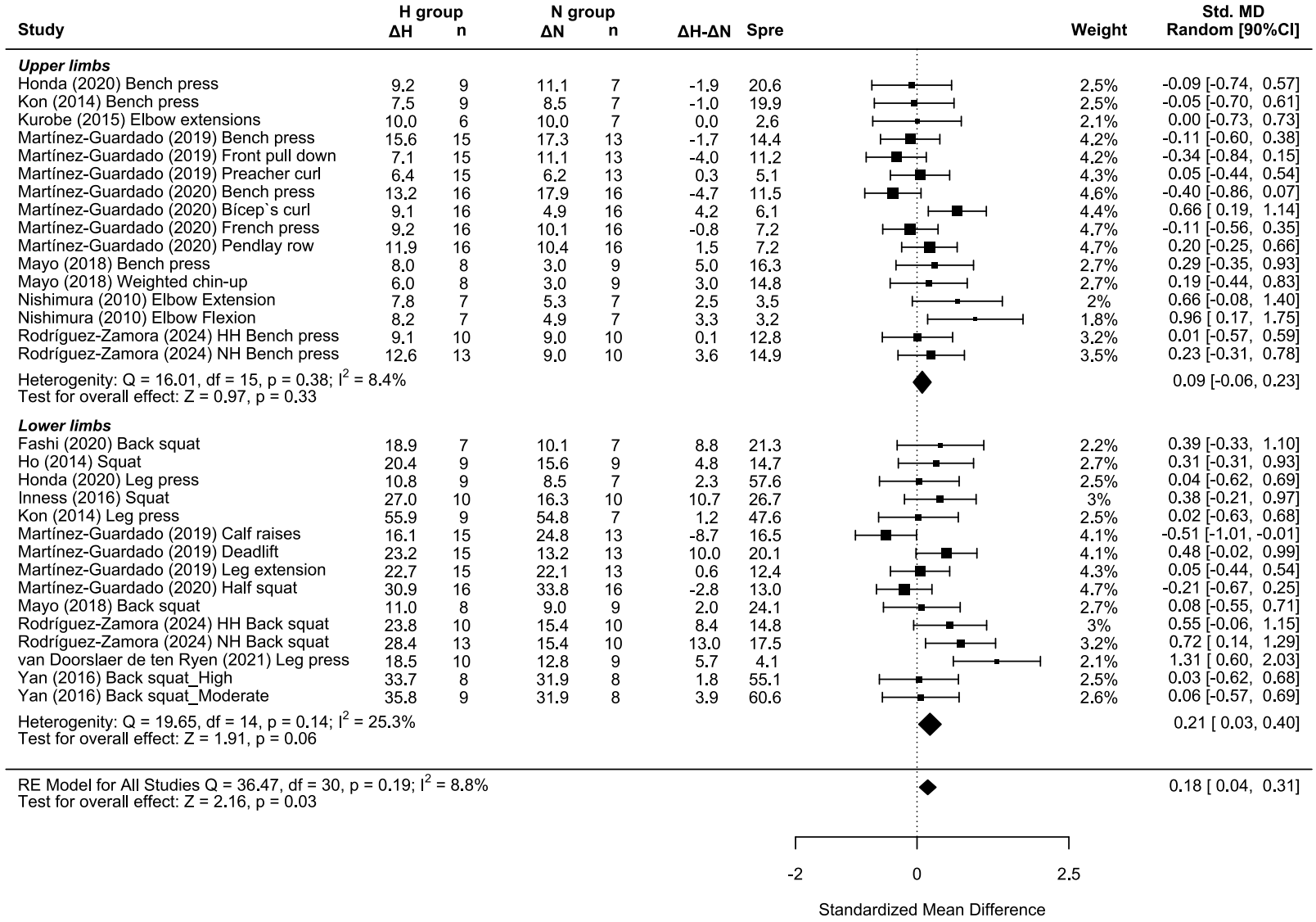
Supplementary Figure 4. Forest plot of the standardized mean differences of the resistance training program between-conditions (hypoxic [H] group vs. normoxic [N] group) on 1-repetition maximum (1RM) sub-analysed by exercise selection.

Δ: mean differences between post-pre in H and N or between H-N; n: sample size; Spre: mean baseline standard deviation; Std. MD: standard mean difference; Random: random effect's model; CI; confidence interval; HH: hypobaric hypoxia; NH: normobaric hypoxia; High: severe hypoxia; Moderate: moderate hypoxia; Q: test statistic for the test of heterogeneity; df: degrees of freedom; p; p value; I^2: I^2 test; Z: z value.



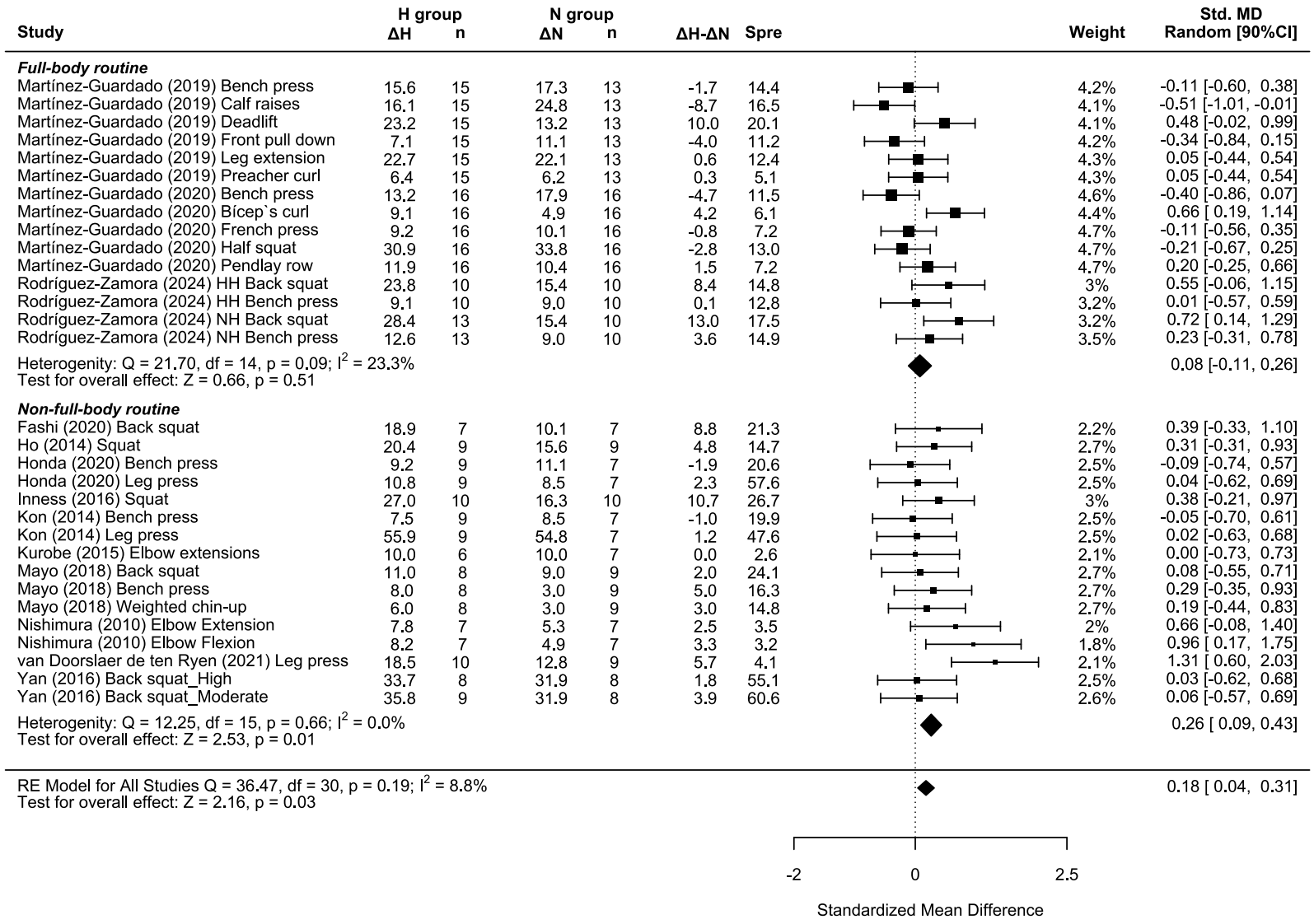
Supplementary Figure 5. Forest plot of the standardized mean differences of the resistance training program between-conditions (hypoxic [H] group vs. normoxic [N] group) on 1-repetition maximum (1RM) sub-analysed by region/muscle of the body measured.

Δ: mean differences between post-pre in H and N or between H-N; n: sample size; Spre: mean baseline standard deviation; Std. MD: standard mean difference; Random: random effect's model; CI; confidence interval; HH: hypobaric hypoxia; NH: normobaric hypoxia; High: severe hypoxia; Moderate: moderate hypoxia; Q: test statistic for the test of heterogeneity; df: degrees of freedom; p; p value; I^2: I^2 test; Z: z value.

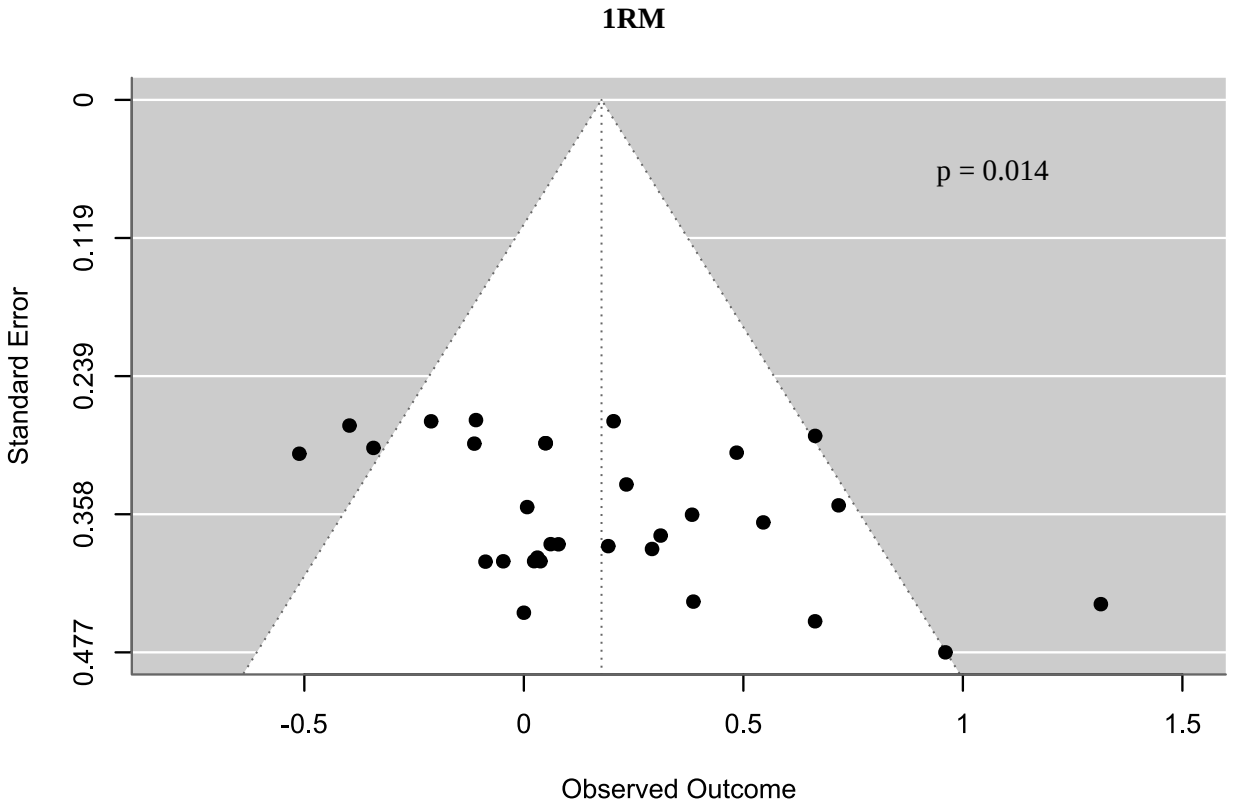


Supplementary Figure 6. Forest plot of the standardized mean differences of the resistance training program between-conditions (hypoxic [H] group vs. normoxic [N] group) on 1-repetition maximum (1RM) sub-analysed by type of routine.

Δ: mean differences between post-pre in H and N or between H-N; n: sample size; Spre: mean baseline standard deviation; Std. MD: standard mean difference; Random: random effect's model; CI; confidence interval; HH: hypobaric hypoxia; NH: normobaric hypoxia; High: severe hypoxia; Moderate: moderate hypoxia; Q: test statistic for the test of heterogeneity; df: degrees of freedom; p; p value; I^2: I^2 test; Z: z value.



Supplementary Figure 7. Funnel plot of the analysed variable.



Supplementary Figure 8. Forest plot of the standardized mean differences of the resistance training program between-conditions (hypoxic [H] group vs. normoxic [N] group) on 1-repetition maximum (1RM) sub-analysed by total weekly training volume per muscle group as a three-level categorical variable.

Δ: mean differences between post-pre in H and N or between H-N; n: sample size; Spre: mean baseline standard deviation; Std. MD: standard mean difference; Random: random effect's model; CI; confidence interval; HH: hypobaric hypoxia; NH: normobaric hypoxia; High: severe hypoxia; Moderate: moderate hypoxia; Q: test statistic for the test of heterogeneity; df: degrees of freedom; p; p value; I^2: I^2 test; Z: z value.