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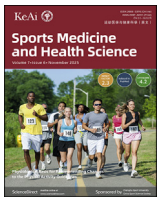

Review Article

The effect of blood flow restricted exercise on measures of health and physical fitness across all populations: An umbrella review and meta-meta-analysis

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ABSTRACT

Purpose: To consolidate and evaluate meta-analyses reporting the effects of blood flow restricted exercise (BFRE) on measures of health and physical fitness across all populations.
Methods: This preregistered umbrella review followed PRISMA guidelines. A comprehensive search of five databases identified meta-analyses evaluating the effects of BFRE interventions (aerobic, resistance, combined) compared to exercising and non-exercising control conditions on measures of health and performance. A multilevel meta-analysis of standardised mean differences (*SMD*s) was conducted to examine the effects of BFRE. Subgroup analyses were conducted for the participant and intervention characteristics. Risk of bias was assessed using the AMSTAR-2.
Results: 47 meta-analyses comprised of 265 unique studies were included. All reviews were rated as low-moderate quality. BFRE had a small effect on hypertrophy ($SMD = 0.39$, $p < 0.001$) and a moderate effect on strength ($SMD = 0.61$, $p < 0.001$) when compared to low load, but not high load resistance training (hypertrophy, $SMD = -0.13$, $p = 0.142$; strength, $SMD = -0.28$, $p < 0.001$). BFRE had small-to-moderate effects on aerobic fitness ($SMD = 0.50$, $p < 0.001$), vascular health ($SMD = 0.45$, $p < 0.001$), blood pressure ($SMD = 0.46$, $p < 0.001$), and muscular power ($SMD = 0.56$, $p < 0.001$). BFRE had no effect on physical function ($SMD = 0.16$, $p = 0.096$), pain ($SMD = 0.00$, $p = 0.996$), and speed ($SMD = 0.22$, $p = 0.213$).
Conclusions: BFRE is a viable option to improve hypertrophy, strength, aerobic fitness, and vascular health across various populations, though its effects on hypertrophy and strength are smaller when compared to traditional high load resistance training. It doesn't appear to offer any additional benefits than other training methods for physical function, pain, or speed, although sub-analyses suggest further research is warranted in select areas of application.

1. Introduction

Blood flow restricted exercise (BFRE), also known as KAATSU training, involves exercising with a cuff or tourniquet placed around the proximal end of an extremity. The cuff is applied at a pressure that allows partial arterial inflow and occludes venous return to the exercising limb.[1,2] Whilst the exact mechanisms which underpin the adaptations associated with BFRE are not fully understood, it has been proposed that the mechanical stress from the cuff occlusion, and the decline in oxygen delivery and metabolite clearance associated, contribute to blood pooling in the capillary beds of the musculature distal to the device, resulting in intramuscular acidosis.[3,4] When BFRE is combined with low-load resistance training (LLRT), it has been shown to increase systemic growth hormone production,[5] fast-twitch muscle fibre recruitment,[6] protein synthesis,[6] intramuscular anabolic and anti-catabolic signalling,[7] and reactive hyperaemia.[8] Additionally, when undertaken in conjunction with aerobic exercise, BFRE has been shown to elicit acute increases in exercising heart rate, blood lactate concentrations, and measures of endothelial function.[3,9] Consequently, chronic BFRE interventions have

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Abbreviations:

1RM	One repetition maximum
ACLR	Anterior cruciate ligament repair
AMSTAR-2	A Measurement Tool to Assess Systematic Reviews
AT	Aerobic training
BALP	Bone-specific alkaline phosphate
BFR	Blood flow restriction
BFRT	Blood flow restricted exercise
BMD	Bone mineral density
CCA	Corrected Covered Area
CI	Confidence interval
CTX	C-terminal telopeptide of type I collagen
HLRT	High load resistance training
LLRT	Low load resistance training
OSF	Open Science Framework
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
QoL:	Quality of Life
RoB	Risk of bias
RT	Resistance training
SMD	Standardized mean difference
$\dot{V}O_{2max}$	Maximal oxygen consumption

been shown to contribute to improvements in a range of health and physical performance outcomes, including cardiovascular health,[10,11] muscular strength,[12–14] hypertrophy,[15–17] pain,[13,18,19] and physical function.[13,20] These improvements have been observed in a range of populations including healthy adults,[21] athletes,[22] older adults,[23] and people with clinical conditions.[24,25]

Typically, high-load resistance training (HLRT) using loads > 70% of one repetition maximum (1RM) has been prescribed to elicit improvements in muscular hypertrophy and strength.[26] However, research has found BFRE undertaken with loads as low as 20% 1RM can increase muscle strength and size.[27] Moreover, several studies have reported that low-intensity aerobic (< 40% of maximal oxygen consumption [$\dot{V}O_{2max}$]) BFRE can facilitate improvements in not only aerobic capacity, but muscular strength and size, which are adaptations not typically associated with aerobic exercise.[4] The ability to induce improvements in performance with less mechanical load has led to the increased use of BRFE in populations with limitations for HLRT.[28] For example, for individuals with joint related conditions (i.e., osteoarthritis, rheumatoid arthritis), BFRE has been shown to improve strength and function, which is particularly relevant if they cannot tolerate HLRT due to joint pain or discomfort. Similarly, BFRE has been shown to offer utility in patients with chronic obstructive pulmonary disease, who may have limited exercise tolerance for HLRT.[29] Conversely, BFRE has been proposed as a low-intensity training intervention for athletes during competitive seasons to enhance muscular strength and size whilst managing training load and recovery.[7] It has also been used successfully to augment improvements aerobic fitness when combined with high intensity interval training, which is highly desirable in elite sporting contexts where the time for physical training needs to be carefully balanced with other sport-related commitments (i.e., skill training).[30] Subsequently, BFRE has become a popular low-intensity exercise modality across a range of populations.

Although numerous studies have demonstrated the effects of BFRE on various measures of health and physical fitness, results are somewhat equivocal, and can vary depending on the population examined. For example, a study undertaken by Takarada et al.,[31] found that BFRE after anterior cruciate ligament repair (ACLR) reduced muscular atrophy by approximately 50% compared to standard practice, whereas another study found no differences between control and intervention groups.[32] Strength and hypertrophic outcomes are also inconsistent across various studies.[16,33–36] For example, some research in young adults has demonstrated BFRE causes smaller improvements in strength compared to HLRT,[37] while research in older adults has shown improvements to be the same.[38] As a consequence of the large volume of primary research on BFRE, numerous systematic reviews and meta-analyses examining BFRE in a range of contexts and populations have been published. However, as the number of systematic reviews increases, it becomes more difficult for researchers, practitioners, and guideline developers to obtain a clear overarching picture of the potential population-specific benefits of BFRE. As such, there is merit in systematically reviewing all of the condition and population specific evidence summaries for the application of BRFE, which will provide a valuable reference to guide practitioners and researchers on the current state of the evidence base for this training approach. The Umbrella Review is an accepted approach to achieve this.[39]

As such, this umbrella review aims to systematically analyse and summarise the findings from published meta-analyses investigating the effects of chronic BFRE interventions on measures of health and physical performance in all populations.

2. Methods

2.1. Protocol and registration

This umbrella review was registered on the open science framework (OSF.IO/K67F2),[40] and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[41]

2.2. Literature search

A systematic literature search was developed with assistance from an Academic Librarian and conducted using the online databases MEDLINE, Scopus, Web of Science, CINAHL and SPORTDiscus, from inception through February 2024. All databases were searched through the following Boolean search syntax using a combination of Medical Subject Headings terms, keywords, and variations of text words associated with BFRE training outcomes for all populations:

("blood flow restrict*" OR "blood flow occlu*" OR "vascular occlu* OR kaatsu* OR "arterial occlu*") AND (perform* OR hypertrophy OR strength OR fitness OR health OR function* OR train OR aerobic OR resistance) AND ("systematic review" OR "meta-analysis" OR "meta analysis").

Two authors (HB and CO) separately conducted electronic searches, which were uploaded to Covidence (Covidence systematic review software, Veritas Health Innovation, Melbourne, Australia) for duplicate removal, screening, and data extraction. The same two authors independently screened all titles and abstracts to identify all potentially relevant studies. The full text of all articles that passed the screening stage were independently assessed by two authors (HB, CO, KG, and JS) to identify their suitability for inclusion. Any discrepancy between authors over screening and inclusion was resolved through discussion with the research team.

2.3. Eligibility criteria

All studies were selected based on a-priori defined inclusion and exclusion criteria using the population, intervention, comparison, outcomes, and study type (PICOS) framework, and were as follows: *Population;* any human populations undertaking a BFRE intervention. *Intervention;* applied BFRE using an external device (i.e., not through hypoxic environments) over an intervention period of at least one week in duration. *Comparator;* any exercise or non-exercise control condition, *Outcome;* report and meta-analyse at least one outcome related to health or physical performance (i.e., hypertrophy, strength, aerobic capacity,

pain, physical function, quality of life). *Study type;* systematic reviews and meta-analysis, or only meta-analysis. No limitations were placed on publication date. All searches were limited to articles published in English language.

2.4. Data extraction

All relevant data from the included reviews were extracted using a custom data extraction template in Covidence and then transferred to an excel spreadsheet (Microsoft Excel Version 16.73) prior to analysis. The data was extracted for the following variables: (a) publication demographics: title, publication date and author/s; (b) study design and population characteristics; (c) BFRE intervention type (i.e., resistance training, aerobic training): duration of intervention and exercise performed; (d) comparator group (i.e., non-active control, control undertaking same intervention without BFR); (e) health/physical performance outcome measure (i.e., hypertrophy, strength, aerobic capacity, pain, physical function, quality of life); and (f) the effect sizes and their respective 95% confidence intervals (*CI*). Data was extracted by one author (HB, CO, KG, or JS), and all data was then cross-checked by a second author for confirmation (JM).

2.5. Evaluation of the methodological quality

Two independent reviewers (CO and JM) assessed the methodological quality of the included meta-analyses using the A Measurement Tool to Assess Systematic Reviews (AMSTAR-2) checklist by completing the grading in a custom excel spreadsheet. Any discrepancies were resolved with input from a third author (HB). This checklist is an accepted measurement tool to assess the quality of systematic reviews and meta-analyses, comprised of 16 items which provide an overall appraisal of the randomised controlled trials and controlled studies included in the meta-analyses.[42] Each item on this checklist was answered with a 'yes' (1 point), a 'partial yes' (0.5 points), or a 'no' (0 points). Based on the summary points score (i.e., maximum 16 points), the meta-analyses were categorised as high quality ($\geq$ 80% of the possible score was achieved), moderate quality (40%–79%), or low quality ($<$ 40%).[43] The initial two authors had an agreement of 88.0%, with 12.0% of all AMSTAR-2 questions being resolved with input from the third author.

2.6. Data synthesis and analysis

Corrected Covered Area (CCA) was calculated using the "ccaR" package in R (version 4.3.1; R Core Team, https://www.r-project.org/) to assess the overlap in the studies that were included across all eligible reviews, and for each outcome measure that was examined by more than one review.[44,45] Using this measure, a CCA of 0% would indicate that every review in our umbrella review consisted of entirely unique RCTs. Conversely, a score of 100% would indicate that every eligible review included the same RCTs. The following cut-offs were used to describe the CCA: 0%–5% = "slight overlap," 6%–10% = "moderate overlap," 11%–15% = "high overlap," and $>$ 15% = "very high overlap".[46] The CCA values in this review have been reported for descriptive purposes, and is not considered in any quantitative synthesis.

In the instance where three or more included reviews examined a single health or performance outcome, they were analysed quantitatively. Where less than three reviews examined a single health of performance outcome, their results were described narratively. Quantitative synthesis was performed with the 'metafor' package in R, with plots produced using the 'ggplot2' package (version 4.3.1; R Core Team, https://www.r-project.org/). A multilevel meta-analysis of standardised mean differences (*SMD*s) between conditions was conducted to examine the effects of BFRE on various health and performance outcomes and control conditions. Effect sizes (*SMD*) were interpreted as trivial ($<$ 0.20), small (0.20–0.49), moderate (0.50–0.79), and large ($\geq$ 0.80).[47] Where studies reported other effect size measures (i.e., mean difference, Hedges' *g*) they were converted to *SMD*s to allow direct comparison between outcomes. Similarly, all *SMD*s are reported in such a way that positive effect sizes favour the BFRE condition, and negative effect sizes favour the control condition. To account for dependency between effect sizes coming from the same review, a multilevel random-effects model (with study identifier included as a random factor) was conducted. The multilevel model was used to estimate the overall effect size and 95% confidence intervals. The heterogeneity between studies was assessed using *Q* and I^2 statistics. I^2 values were interpreted negligible (I^2 = 0%–40%), moderate (I^2 = 30%–60%), substantial (I^2 = 50%–90%), or considerable (I^2 = 75%–100%).[48] For all primary analysis, sigma-squared (σ^2) was also presented to provide an indication of the variance of the true effect sizes across studies.

Publication bias was visualised by funnel plots and examined statistically using Egger's test. Studies with absolute standardized residuals $>$ 2 were considered as outliers and removed from analyses. Where sufficient data was available, sources of heterogeneity were examined by performing subgroup analyses on the following factors: control group comparator (low intensity exercise, high intensity exercise, walking, mixed exercise modalities, usual care), location (lower body, upper body, mixed), population (young adults, older adults, athletes, mixed populations, those with clinical conditions); and in the case where there were a combination of physical tests and self-report measures (i.e., physical function and pain): measurement type (physical test, self-report, combined). When one of the reviews included subgroup analyses that align with the pre-defined subgroup categories mentioned above, only these subgroup analyses were included, and the primary analysis was excluded to ensure dependency of effect sizes. For example, some reviews provided an overall analysis examining the effect of BFRE on hypertrophy compared to all control conditions combined, and two subgroup analyses comparing the effect of BFRE on hypertrophy compared to low intensity and high intensity training, respectively. In this instance, only the primary analysis would be included in our overall analysis of BFRE on hypertrophy. Then, only the subgroup analysis would be included in our subgroup analyses examining whether control group condition influences the effect of BFRE on hypertrophy. All subgroup analyses were performed using the same multilevel meta-analysis of *SMD*s used in the primary analysis, albeit with the relevant factor included as a covariate. The data and code used for analysis are available on Open Science Framework page for this project.[40]

2.7. Levels of evidence

The levels of evidence regarding the effect of BFRE on health and performance outcomes were established for those that underwent quantitative analysis after outliers had been removed, and were classified as reported in line with previous umbrella reviews as follows:[49,50] *convincing* (class I) when number of cases $>$ 1 000, $p < 10^{-6}$, $I^2 < 50\%$, 95% prediction interval excluding the null, no small-study effects, and no excess significance bias; *highly suggestive* (class II) when number of cases $>$ 1 000, $p < 10^{-6}$, largest study with a statistically significant effect, and class I criteria not met; *suggestive* (class III) when number of cases $>$ 1 000, $p < 10^{-3}$, and class I-II criteria not met; *weak* (class IV) when $p <$ 0.05 and class I-III criteria not met; *non-significant* when $p > 0.05$.

3. Results

The systematic search identified a total of 473 relevant articles after the removal of duplicates. A total of 336 articles were excluded after title and abstract screening, and a further 90 articles were excluded after full-text review using the predefined eligibility criteria. Finally, a total of 47 systematic reviews and meta-analyses were eligible and included in this umbrella review. An overview of the article screening and selection process is summarised in the PRISMA flowchart (Fig. 1), and a list of articles excluded at the full text screening stage is provided in Supplementary Digital Content 1.

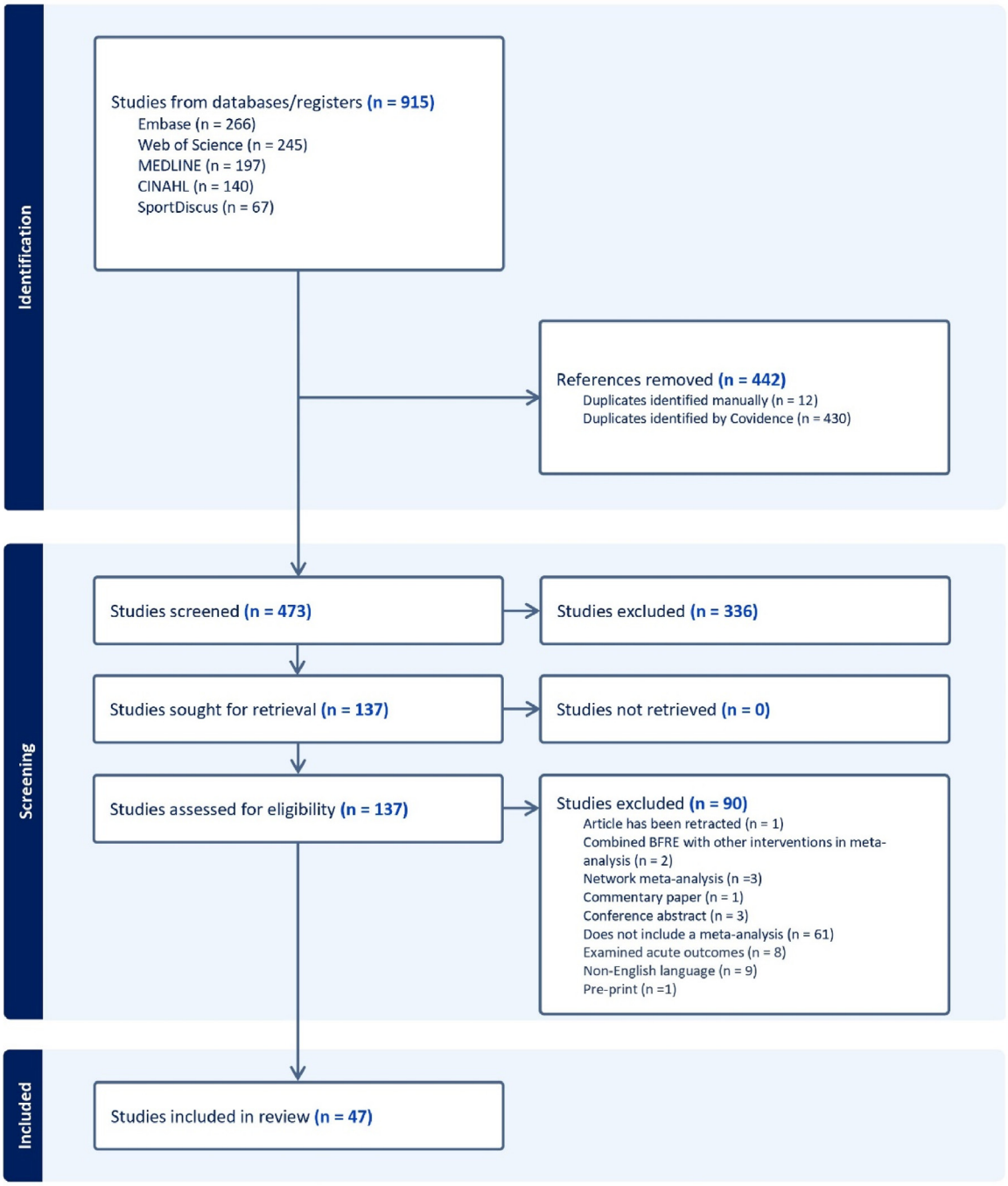

Fig. 1. PRISMA Flowchart. BFRE = blood flow restricted exercise; n = number of studies.

3.1. Characteristics of included reviews

The 47 included meta-analyses were published between 2012 and 2023 and covered a total of 265 unique original studies. The number of included original studies included in each review ranged from three to 53 with an average of 13. Sample sizes of the included reviews ranged from 44 to 1 337 participants with an average of 342. The chronological age of the included participants ranged from 11 to 91 years. Eighteen reviews included healthy adults aged older than 18 years,[14,15,21,33,51–64] nine included healthy older adults,[16,17,34,35,65–69] three included older adults either diagnosed with, or at risk of developing, a chronic illness,[70–72] five focused on healthy and trained athletes of all ages,[11,36,73–75] 11 involved clinical populations (including those diagnosed with a musculoskeletal condition),[13,18–20,76–82] and one included only overweight and obese individuals.[83] The characteristics of the included reviews are summarised in supplementary digital content 2.

3.2. Assessment of the methodological quality

The AMSTAR-2 scores of the included reviews are summarised in supplementary digital content 3. The included articles received scores ranging from 16% to 69%. Five of the included reviews (10.6% of all articles) were rated as low methodological quality, and the remaining 42 (89.4% of all articles) were rated as moderate methodological quality. The area's most commonly misaddressed in the AMSTAR-2 were: (3) explain the selection of study design for inclusion; (7) provide a list of excluded studies and justify the exclusion; (10) report on the sources of funding for the studies included in the review; (12) assess the potential

impact of risk of bias (RoB) in individual studies on the results of the meta-analysis; and (15) carry out an adequate investigation of publication bias and discuss likely impacts on the results of the review.

3.3. Quantitative analysis

3.3.1. Overall Corrected Covered Area

The overall CCA was 2.8%, indicating slight overlap. A heatmap of the CCA can be found in supplementary digital content 4.

3.3.2. Hypertrophy

A total of 17 individual reviews containing 25 primary meta-analyses examined the effect of BFRE on hypertrophy, with a CCA of 5.3% indicating a slight overlap of primary studies (supplementary digital content 7, Fig. 1). Collectively, BFRE had a small effect on hypertrophy (SMD = 0.23, 95%CI = 0.08, 0.37, p = 0.002) (supplementary digital content 5, Fig. 1). There was considerable heterogeneity (QE [df = 24] = 118, p < 0.001; I^2 = 78.8%) and moderate variability between studies (σ^2 = 0.08). Inspection of the funnel plot (supplementary digital content 5, Fig. 2) and results of Egger's test indicated potential publication bias (intercept = 1.9, p < 0.001), and our evaluation of standardised residuals identified two outliers.[16,64] Following the removal of the outliers, the effect of BFRE on hypertrophy became trivial (SMD = 0.18, 95%CI = 0.07, 0.30, p = 0.002) (supplementary digital content 5, Fig. 3) with substantial between-study heterogeneity (QE [df = 22] = 80, p < 0.001; I^2 = 65.9%) and moderate between study variability (σ^2 = 0.03). Inspection of the funnel plot (supplementary digital content 5, Fig. 4) and results of Egger's test indicated potential publication bias remained (intercept = 1.1, p = 0.016).

Hypertrophy subgroup analyses are presented in Table 1. When including the control group condition as a covariate, there was substantial heterogeneity (QE [df = 22] = 50, p < 0.001; I^2 = 65.4%) and moderate between study variability (σ^2 = 0.04). Egger's test indicated potential publication bias (intercept = 2.4, p < 0.001), and evaluation of standardised residuals identified one outlier.[16] After the outlier was removed, there was substantial heterogeneity (QE [df = 21] = 43, p < 0.001; I^2 = 53.2%), small between study variability (σ^2 = 0.02), and potential publication bias remained (intercept = 1.6, p = 0.001). BFRE had a significant effect on hypertrophy when compared to low load RT and walking, but not mixed interventions or usual care. BFRE was significantly less effective when compared to HLRT, and more effective when compared to walking, than when compared to LLRT alone (Table 1).

When including location as a subgroup, there was considerable heterogeneity (QE [df = 22] = 115, p < 0.001; I^2 = 78.8%) and between study variability (σ^2 = 0.06). Egger's test indicated potential publication bias (intercept = 1.9, p < 0.001), and one outlier was identified.[16] After the removal of the outlier, there was still substantial heterogeneity (QE [df = 21] = 81, p < 0.001; I^2 = 67.4%) and moderate between study variability (σ^2 = 0.03), and potential publication bias remained (intercept = 1.3, p = 0.009). BFRE was effective at increasing hypertrophy in the upper and lower body, with no differences between them (Table 1).

When population was included as a subgroup, there was substantial heterogeneity (QE [df = 20] = 88, p < 0.001; I^2 = 62.4%) and between study variability (σ^2 = 0.04). Egger's test indicated potential publication bias (intercept = 1.9, p < 0.001), and three outliers were identified.[13,16,18] After outliers were removed, moderate heterogeneity (QE [df = 17] = 38, p = 0.003; I^2 = 49.4%) and between study variability (σ^2 = 0.02) remained, although the Egger's test was no longer significant (intercept = 0.8, p = 0.157). Young adults experienced greater increases in hypertrophy in response to BFRE than older adults, athletes, mixed cohorts, and clinical populations (Table 1).

Table 1
Hypertrophy subgroup analyses.

Subgroup	n	Individual estimates		Between condition comparison	
		SMD (95% CI)	p	$Difference\ SMD$ (95% CI)	p
Comparison					
Low load RT	11	0.39 (0.23, 0.54)	< 0.001[a]	*Reference*	
High load RT	7	−0.13 (−0.30, 0.05)	0.142	−0.52 (−0.74, −0.29)	< 0.001[a]
Walking	1	1.00 (0.41, 1.59)	0.002[a]	0.61 (0.01, 1.21)	< 0.001[a]
Mixed	5	0.21 (−0.09, 0.50)	0.156	−0.18 (−0.51, 0.15)	0.271
Usual care	2	0.36 (−0.20, 0.92)	0.196	−0.03 -(0.60, 0.54)	0.915
Location					
Lower body	17	0.16 (0.03, 0.30)	0.020[a]	*Reference*	
Upper body	5	0.47 (0.08, 0.87)	0.021[a]	0.31 (−0.10, 0.72)	0.128
Combined	2	0.21 (−0.25, 0.67)	0.347	0.06 (−0.43, 0.53)	0.828
Population					
Young adults	4	0.79 (0.31, 1.26)	0.003[a]	*Reference*	
Older adults	8	0.22 (0.05, 0.38)	0.016[a]	−0.57 (−1.07, −0.06)	0.029[a]
Athletic	2	−0.05 (−0.57, 0.47)	0.847	−0.83 (−1.54, −0.13)	0.023[a]
Mixed	5	0.20 (0.01, 0.39)	0.039[a]	−0.59 (−1.10, −0.08)	0.027[a]
Clinical	3	−0.17 (−0.47, 0.14)	0.268	−0.95 (−1.52, −0.39)	0.003[a]

[a] Denotes $p \leq 0.05$, CI = confidence interval, RT = resistance training, SMD = standardized mean difference.

3.3.3. Strength

A total of 28 individual reviews containing 50 primary meta-analyses examined the effect of BFRE on strength, with a CCA of 5.1% indicating a slight overlap of primary studies (supplementary digital content 7, Fig. 2). Collectively, BFRE had a small effect on strength (SMD = 0.23, 95%CI = 0.10, 0.37, p < 0.001) (supplementary digital content 5, Fig. 5). There was considerable heterogeneity (QE [df = 49] = 526, p < 0.001; I^2 = 81.8%) and high variability between studies (σ^2 = 0.11). Inspection of the funnel plot (supplementary digital content 5, Fig. 6) and results of Egger's test indicated the presence of publication bias (intercept = 1.6, p < 0.001). Evaluation of standardised residuals identified six outliers.[15,16,33,36,58,79] Following the removal of the outliers, the effect of BFRE on strength remained small (SMD = 0.29, 95%CI = 0.18, 0.41, p < 0.001) (supplementary digital content 5, Fig. 7) with substantial between-study heterogeneity (QE [df = 43] = 255, p < 0.001; I^2 = 70.6%) and variability (σ^2 = 0.06). Inspection of the funnel plot (supplementary digital content 5, Fig. 8) and results of Egger's test suggested publication bias was not present (intercept = 0.6, p = 0.265).

The strength subgroup analyses are presented in Table 2. When including the control group condition as a subgroup, there was considerable heterogeneity (QE [df = 49] = 251, p < 0.001; I^2 = 75.2%) and between study variability (σ^2 = 0.08). Egger's test indicated potential publication bias (intercept = 2.5, p < 0.001), and evaluation of standardised residuals identified seven outliers from six reviews.[16,19,36,61,65,71] After the removal of outliers, substantial heterogeneity (QE [df = 43] = 137, p < 0.001; I^2 = 67.6 %) and between study variability (σ^2 = 0.05) was present, and Egger's test suggested publication bias remained (intercept = 1.8, p < 0.001). BFRE was more effective at improving strength than LLRT, mixed interventions, and usual care, but less effective than HLRT (Table 2).

When including location as a subgroup, there was considerable heterogeneity (QE [df = 48] = 558, p < 0.001; I^2 = 86.6%) and high between study variability (σ^2 = 0.17). The results of the Egger's test indicated publication bias (intercept = 1.1, p = 0.018), and eight outliers were identified from six studies.[15,16,36,58,73,79] After the removal of

Table 2
Strength subgroup analyses.

Subgroup	*n*	Individual estimates		Between condition comparison	
		SMD (95% *CI*)	*p*	*Difference SMD* (95% *CI*)	*p*
Comparison					
Low load RT	15	0.61 (0.46, 0.75)	< 0.001[a]	*Reference*	
High load RT	17	−0.28 (−0.41, −0.15)	< 0.001[a]	−0.88 (−1.02, −0.74)	< 0.001[a]
Mixed	9	0.37 (0.10, 0.63)	0.007[a]	−0.24 (−0.54, 0.06)	0.109
Usual care	6	0.87 (0.60, 1.13)	< 0.001[a]	0.26 (−0.02, 0.54)	0.066
Location					
Lower body	33	0.33 (0.17, 0.50)	< 0.001[a]	*Reference*	
Upper body	1	−0.17 (−1.06, 0.72)	0.702	−0.50 (−1.41, 0.40)	0.268
Combined	9	0.01 (−0.24, 0.27)	0.921	−0.32 (−0.62, −0.02)	0.038[a]
Population					
Older adults	10	0.37 (0.12, 0.62)	0.005[a]	*Reference*	
Athletes	5	0.32 (−0.16, 0.80)	0.182	−0.05 (−0.59, 0.49)	0.855
Mixed	18	0.21 (0.03, 0.40)	0.024[a]	−0.15 (−0.46, 0.15)	0.317
Clinical	12	0.33 (0.07, 0.59)	0.016[a]	−0.04 (−0.40, 0.32)	0.821

[a] Denotes $p \leq 0.05$, *CI* = confidence interval, RT = resistance training, *SMD* = standardized mean difference.

outliers there was still considerable heterogeneity (*QE* [*df* = 40] = 339, $p < 0.001$; $I^2 = 81.3\%$) and high between study variability ($\sigma^2 = 0.10$) present. Egger's test suggested publication bias remained present (intercept = 1.1, $p = 0.045$). BFRE was effective at increasing strength of the lower body, but not the upper body (Table 2).

When population was included as a subgroup, there was considerable heterogeneity (*QE* [*df* = 46] = 511, $p < 0.001$; $I^2 = 82.5\%$) and high between study variability ($\sigma^2 = 0.12$). Egger's test indicated publication bias was present (intercept = 1.6, $p < 0.001$), and five outliers were identified.[16,33,36,58,79] After outliers were removed, considerable heterogeneity (*QE* [*df* = 41] = 285, $p < 0.001$; $I^2 = 75.1\%$) and between study variability ($\sigma^2 = 0.08$) remained. Egger's test was non-significant suggesting publication bias was unlikely (intercept = 0.9, $p = 0.085$). All population groups except athletes experienced increases in strength in response to BFRE, with no differences between groups observed (Table 2).

3.3.4. Aerobic fitness

Seven individual reviews containing eight primary meta-analyses examined the effect of BFRE on aerobic fitness, with a CCA of 9.0% indicating a moderate overlap of primary studies (supplementary digital content 7, Fig. 3). Collectively, BFRE had a small effect on aerobic fitness (*SMD* = 0.46, 95%*CI* = 0.18, 0.74, $p = 0.001$) (supplementary digital content 5, Fig. 9). There was substantial heterogeneity (*QE* [*df* = 7] = 29, $p < 0.001$; $I^2 = 60.6\%$) and moderate variability between studies ($\sigma^2 = 0.07$). Inspection of the funnel plot (supplementary digital content 5, Fig. 10) and results of Egger's test did not indicate the presence of publication bias (intercept = 0.3, $p = 0.770$). Evaluation of standardised residuals identified one outlier.[52] Following its removal, the effect of BFRE on aerobic fitness increased to a moderate effect (*SMD* = 0.50, 95% *CI* = 0.27, 0.73, $p < 0.001$) (supplementary digital content 5, Fig. 11) with moderate between-study heterogeneity (*QE* [*df* = 6] = 12, $p = 0.065$; $I^2 = 45.8\%$) and variability ($\sigma^2 = 0.04$). Inspection of the funnel plot (supplementary digital content 5, Fig. 12) and results of Egger's test suggested publication bias was not likely (intercept = 1.5, $p = 0.077$).

The aerobic fitness subgroup analyses are presented in Table 3. When including the control group condition as a subgroup, there was substantial heterogeneity (*QE* [*df* = 7] = 30, $p < 0.001$; $I^2 = 73.0\%$) and high between study variability ($\sigma^2 = 0.16$). The Egger's test did not suggest publication bias (intercept = 0.4, $p = 0.630$), and the evaluation of standardised residuals identified one outlier.[52] After the removal of the outlier, substantial heterogeneity (*QE* [*df* = 6] = 5, $p = 0.037$; $I^2 = 66.5\%$) and between study variability ($\sigma^2 = 0.11$) was present, while the Egger's test remained non-significant (intercept = 1.2, $p = 0.101$). There was no significant difference between control conditions when examining the effect of BFRE on aerobic fitness (Table 3).

When population was included as a subgroup, there was negligible heterogeneity (*QE* [*df* = 6] = 4, $p = 0.650$; $I^2 = 0.0\%$) and between study variability ($\sigma^2 = 0.0$). Egger's test did not indicate publication bias was present (intercept = 1.3, $p = 0.137$) and no outliers were identified. All population groups experienced increases in aerobic fitness in response to BFRE, with athletes observing larger increases than young adults (Table 3).

3.3.5. Physical function

A total of 11 individual reviews containing 18 primary meta-analyses examined the effect of BFRE on physical function, with a CCA of 10.6% indicating a moderate overlap of primary studies (supplementary digital content 7, Fig. 4). Collectively, BFRE had no effect on physical (*SMD* = 0.19, 95%*CI* = −0.02, 0.40, $p = 0.082$) (supplementary digital content 5, Fig. 13). There was moderate heterogeneity between studies (QE [*df* = 17] = 33, $p = 0.012$; $I^2 = 48.8\%$) and moderate variability between studies ($\sigma^2 = 0.08$). Inspection of the funnel plot (supplementary digital content 5, Fig. 14) and results of Egger's test did not indicate the presence of publication bias (intercept = 0.1, $p = 0.914$). Our evaluation of standardised residuals identified one outlier.[70] Following its removal, the effect of BFRE on physical function remained non-significant (*SMD* = 0.16, 95%*CI* = −0.03, 0.36, $p = 0.096$) (supplementary digital content 5, Fig. 14) with moderate between-study heterogeneity (QE [*df* = 16] = 24, $p = 0.094$; $I^2 = 39.7\%$) and between study variability ($\sigma^2 = 0.05$). Inspection of the funnel plot (supplementary digital content 5, Fig. 12) and results of Egger's test suggested publication bias was not present (intercept = 0.1, $p = 0.927$).

The physical function subgroup analyses are presented in Table 4. When including the control group condition as subgroup, there was moderate heterogeneity (*QE* [*df* = 16] = 39, $p = 0.102$; $I^2 = 37.9\%$) and between study variability ($\sigma^2 = 0.05$). Egger's test did not suggest publication bias (intercept = 0.3, $p = 0.785$), and evaluation of standardised residuals identified one outlier.[34] After its removal, negligible

Table 3
Aerobic fitness subgroup analysis.

Subgroup	*n*	Individual estimates		Between condition comparison	
		SMD (95% *CI*)	*p*	*Difference SMD* (95% *CI*)	*p*
Comparison					
Low intensity AT	2	0.76 (−0.15, 1.67)	0.088	*Reference*	
High intensity AT	2	0.22 (−0.77, 1.21)	0.606	−0.54 (−1.47, 0.39)	0.207
Mixed	5	0.57 (0.12, 1.03)	0.022[a]	−0.19 (−1.21, 0.83)	0.670
Population					
Young adults	5	0.32 (0.10, 0.54)	0.013[a]	*Reference*	
Athletes	3	0.92 (0.56, 1.28)	< 0.001[a]	0.60 (0.18, 1.03)	0.013[a]

[a] Denotes $p \leq 0.05$, AT = aerobic training, *CI* = confidence interval, *SMD* = standardized mean difference.

Table 4
Physical function subgroup analysis.

Subgroup	*n*	Individual estimates		Between condition comparison	
		SMD (95% *CI*)	*p*	*Difference SMD* (95% *CI*)	*p*
Comparison					
Low load RT	6	0.06 (−0.23, 0.35)	0.681	*Reference*	
High load RT	6	−0.01 (−0.26, 0.24)	0.939	−0.07 (−0.45, 0.31)	0.716
Mixed	6	0.48 (0.20, 0.76)	0.002[a]	0.42 (0.02, 0.82)	0.040[a]
Usual care	1	0.60 (0.06, 1.14)	0.031[a]	0.55 (−0.07, 1.16)	0.077
Population					
Older adults	6	0.46 (0.20, 0.71)	0.002[a]	*Reference*	
Mixed	2	0.42 (−0.04, 0.88)	0.073	0.04 (−0.57, 0.49)	0.875
Clinical	9	−0.04 (−0.23, 0.15)	0.652	−0.50 (−0.82, −0.17)	0.005[a]
Measurement type					
Physical measure	11	0.28 (0.04, 0.52)	0.026[a]	*Reference*	
Self-reported measure	3	−0.02 (−0.37, 0.33)	0.916	−0.30 (−0.70, 0.11)	0.140
Combined	3	0.07 (−0.32, 0.46)	0.702	−0.21 (−0.66, 0.25)	0.350

[a] Denotes $p \leq 0.05$, *CI* = confidence interval, RT = resistance training, *SMD* = standardized mean difference.

heterogeneity (*QE* [$df = 15$] = 19, $p = 0.214$; $I^2 = 12.7\%$) and between study variability ($\sigma^2 = 0.01$) was present, and the Eggers test remained non-significant (intercept = −0.6, $p = 0.607$). BFRE caused the largest improvements in physical function when compared to mixed interventions (Table 4).

Due to the data presented in the original reviews, all groups included in the primary analysis were also included in the subgroup analyses examining the moderating factors of population and measurement type. As such, the same outlier identified in the overall analysis was excluded from these subgroup analyses. When including population as a subgroup, there was negligible heterogeneity (*QE* [$df = 14$] = 11, $p = 0.684$; $I^2 = 0.0\%$) and between study variability ($\sigma^2 = 0.00$). Older adults observed greater improvements in physical function than clinical populations in response to BFRE. When including the measurement type as a subgroup, there was negligible heterogeneity (*QE* [$df = 14$] = 18, $p = 0.137$; $I^2 = 24.3\%$) and between study variability ($\sigma^2 = 0.03$). BFRE caused significant increases in physical function when measured using physical measures, but not self-report measures. However, there were no between group differences between measurement type.

3.3.6. Pain

A total of eight reviews containing 12 primary meta-analyses examined the effect of BFRE on pain, with a CCA of 26.6% indicating a very high overlap of primary studies (supplementary digital content 7, Fig. 5). Collectively, BFRE had no effect on pain when (*SMD* = 0.02, 95%*CI* = −0.13, 0.17, $p = 0.793$) (supplementary digital content 5, Fig. 17). There was negligible heterogeneity (QE [$df = 11$] = 18, $p = 0.083$; $I^2 = 12.3\%$) and variability between studies ($\sigma^2 = 0.01$). Inspection of the funnel plot (supplementary digital content 5, Fig. 18) and results of Egger's test did not indicate the presence of publication bias (intercept = 0.7, $p = 0.374$). Evaluation of standardised residuals identified one outlier.[13] Following its removal, the effect of BFRE on pain remained non-significant (*SMD* = 0.00, 95%*CI* = −0.16, 0.16, $p = 0.996$) (supplementary digital content 5, Fig. 19) with negligible between-study heterogeneity (QE [$df = 10$] = 14, $p = 0.187$; $I^2 = 21.2\%$) and variability ($\sigma^2 = 0.01$). Inspection of the funnel plot (supplementary digital content 5, Fig. 20) and results of Egger's test suggested publication bias was not present (intercept = −0.2, $p = 0.856$).

The pain subgroup analyses are presented in Table 5. Due to the data presented in the included reviews, all groups included in the primary analysis were also included in the subgroup analyses. As such, the same outlier identified in the overall analysis was excluded from all subgroup analyses. There was only sufficient data to conduct subgroup analysis pertaining to control group comparison. When including control group comparator as a subgroup, there was negligible heterogeneity (*QE* [$df = 7$] = 4, $p = 0.772$; $I^2 = 0.0\%$) and between study variability ($\sigma^2 = 0.00$). BFRE was more effective at reducing pain when compared to HLRT than other intervention types (Table 5).

3.3.7. Speed

A total of four individual reviews containing four primary meta-analyses examined the effect of BFRE on speed, with a CCA of 15.0% indicating a high overlap of primary studies (supplementary digital content 7, Fig. 6). Collectively, BFRE had no effect on speed when compared to equivalent non-BFRE interventions (*SMD* = 0.22, 95%*CI* = −0.13, 0.57, $p = 0.213$) (supplementary digital content 5, Fig. 21). There was negligible heterogeneity (QE [$df = 3$] = 3, $p = 0.364$; $I^2 = 12.0\%$) and variability between studies ($\sigma^2 = 0.02$). Inspection of the funnel plot (supplementary digital content 5, Fig. 22) and results of Egger's test did not indicate the presence of publication bias (intercept = −3.4, $p = 0.158$), and no outliers were identified. There was insufficient data to conduct subgroup analyses for speed outcomes.

3.3.8. Vascular health

A total of three individual reviews containing eight primary meta-analyses examined the effect of BFRE on vascular health, with a CCA of 19.7% indicating a very high overlap of primary studies (supplementary digital content 7, Fig. 7). Collectively, BFRE had a small effect on measures of vascular health (*SMD* = 0.45, 95%*CI* = 0.29, 0.61, $p < 0.001$) (supplementary digital content 5, Fig. 23). There was negligible heterogeneity (QE [$df = 7$] = 10, $p = 0.186$; $I^2 = 0.0\%$) and variability between studies ($\sigma^2 = 0.00$). Inspection of the funnel plot (supplementary digital content 5, Fig. 24) and results of Egger's test did not indicate the presence of publication bias (intercept = −2.3, $p = 0.091$). Evaluation of standardised residuals did not identify any outliers.

The vascular health subgroup analyses are presented in Table 6. Due to the nature of the included studies, all groups included in the primary analysis were also included in the control group comparator subgroup analysis. When including the control group condition as subgroup, there was negligible heterogeneity (*QE* [$df = 6$] = 9, $p = 0.281$; $I^2 = 28.7\%$) and between study variability ($\sigma^2 = 0.03$). There was no difference on the effects of BFRE on physical function between control group conditions.

When including population as a subgroup, there was moderate heterogeneity (*QE* [$df = 6$] = 13, $p = 0.047$; $I^2 = 47.2\%$) and between study variability ($\sigma^2 = 0.06$). There was no significant impact of population on

Table 5
Pain subgroup analysis.

Subgroup	*n*	Individual estimates		Between condition comparison	
		SMD (95% *CI*)	*p*	*Difference SMD* (95% *CI*)	*p*
Comparison					
Low load RT	4	−0.03 (−0.25, 0.20)	0.783	*Reference*	
High load RT	3	0.49 (0.02, 0.96)	0.042[a]	0.42 (0.00, 1.04)	0.049[a]
Mixed	1	0.04 (−0.29, 0.37)	0.784	0.07 (−0.33, 0.47)	0.703
Usual care	3	−0.32 (−0.73, 0.10)	0.113	−0.29 (−0.76, 0.18)	0.189

[a] Denotes $p \leq 0.05$, *CI* = confidence interval, RT = resistance training, *SMD* = standardized mean difference.

Table 6
Vascular health subgroup analyses.

Subgroup	*n*	Individual estimates		Between condition comparison	
		SMD (95% *CI*)	*p*	*Difference SMD* (95% *CI*)	*p*
Comparison					
High load RT	2	0.58 (0.13, 1.02)	0.019[a]	*Reference*	
Mixed	6	0.42 (0.20, 0.64)	0.004[a]	−0.16 (−0.65, 0.34)	0.464
Population					
Older adults	4	0.49 (−0.21, 1.99)	0.139	*Reference*	
Mixed	4	0.36 (−0.21, 0.94)	0.173	−0.13 (1.04, 0.78)	0.743

[a] Denotes $p \leq 0.05$, *CI* = confidence interval, RT = resistance training, *SMD* = standardized mean difference.

the effects of BFRE on physical function. Egger's test suggested potential publication bias (intercept = −3.5, $p = 0.021$), although no outliers were identified through evaluation of standardised residuals. There was no difference on the effect of BFRE on vascular outcomes between older adults and mixed populations (Table 6).

3.3.9. Blood pressure

A total of three individual reviews containing seven primary meta-analyses examined the effect of BFRE on blood pressure, with a CCA of 3.8% indicating a slight overlap of primary studies (supplementary digital content 7, Fig. 8). Collectively, BFRE had a small effect on measures of blood pressure (*SMD* = 0.46, 95%*CI* = 0.20, 0.72, $p < 0.001$) (supplementary digital content 5, Fig. 25). There was negligible heterogeneity (QE [$df = 6$] = 3, $p = 0.783$; $I^2 = 0.0\%$) and variability between studies ($\sigma^2 = 0.00$). Inspection of the funnel plot (supplementary digital content 5, Fig. 26) and results of Egger's test did not indicate the presence of publication bias (intercept = 0.3, $p = 0.700$). No outliers were identified.

The blood pressure subgroup analyses are presented in Table 7. There was only sufficient data to conduct a subgroup analysis on population. Due to the nature of the data presented in the included reviews, all groups included in the primary analysis were also included in the population analysis. When including the population as a subgroup, there was negligible heterogeneity (*QE* [$df = 5$] = 3, $p = 0.755$; $I^2 = 0.0$ %) and between study variability ($\sigma^2 = 0.00$). BFRE improved blood pressure in mixed populations (Table 7).

3.3.10. Power

A total of three individual reviews containing four primary meta-analyses examined the effect of BFRE on power, with a CCA of 16.3% indicating a very high overlap of primary studies (supplementary digital content 7, Fig. 9). Collectively, BFRE had a moderate effect on measures of power compared to HLRT and equivalent non-BFRE interventions (*SMD* = 0.56, 95%*CI* = 0.16, 0.95, $p < 0.001$) (supplementary digital content 5, Fig. 27). There was negligible heterogeneity (QE [$df = 3$] = 4, $p = 0.278$; $I^2 = 23.0\%$) and variability between studies ($\sigma^2 = 0.03$).

Table 7
Blood pressure subgroup analysis.

Subgroup	*n*	Individual estimates		Between condition comparison	
		SMD (95% *CI*)	*p*	*Difference SMD* (95% *CI*)	*p*
Population					
Mixed	5	0.48 (0.13, 0.83)	0.016[a]	*Reference*	
Clinical	2	−0.18 (−2.41, 2.06)	0.846	−0.66 (−2.92, 1.60)	0.489

[a] Denotes $p \leq 0.05$, *CI* = confidence interval, *SMD* = standardized mean difference.

Inspection of the funnel plot (supplementary digital content 5, Fig. 28) and results of Egger's test did not indicate the presence of publication bias (intercept = 1.7, $p = 0.218$). Our evaluation of standardised residuals did not identify any outliers. There was insufficient data to conduct any subgroup analysis for power outcomes.

3.4. Narrative synthesis

3.4.1. Quality of life

Two reviews examined the effect of BFRE on Quality of Life (QoL), with a CCA of 0.0% indicating a slight overlap of primary studies (supplementary digital content 7, Fig. 10). BFRE had no effect on QoL in participants diagnosed with, or at risk of, knee osteoarthritis (*SMD*: 0.15, 95%*CI* = −0.20, 0.60),[78] or in participants undergoing knee surgery when compared to LLRT (*SMD* = 0.14, 95%*CI* = −0.45, 0.73).[18]

3.4.2. Bone metabolism

One review investigated the impact of BFRE on bone metabolism (i.e., bone formation markers (bone-specific alkaline phosphate [BALP]), bone resorption (C-terminal telopeptide of type I collagen [CTX]) and bone mineral density [BMD]).[82] Participants included young adults, the elderly, and patients undergoing musculoskeletal rehabilitation (i.e., ACLR). There was no difference between BFRE and LLRT on BALP (*SMD* = 0.23, 95%*CI* = −0.14, 0.61), although it promoted greater improvements in BMD (*SMD* = 0.90, 95%*CI* = 0.56, 1.24) despite lesser effects on CTX (*SMD* = −0.37, 95%*CI* = −0.73, −0.02). There was no difference between BFRE and HLRT for improving BALP (*SMD* = −0.31, 95%*CI* = -0.79, 0.16), CTX (*SMD* = −0.29, 95%*CI* = −0.65, 0.06), or BMD (*SMD* = −0.18, 95%*CI* = −0.8, 0.44).

3.4.3. Blood lipids and anthropometrics

One review examined the effects of BFRE on blood lipids and anthropometric measures.[83] BFRE significantly improved total cholesterol (*SMD* = 0.69, 95%*CI* = 0.09, 1.3) and high-density lipoprotein cholesterol [HDL-C] (*SMD* = 0.81, 95%*CI* = 0.26, 1.36) compared to equivalent non-BFRE exercise, but no difference in total triglycerides (*SMD* = 0.34, 95%*CI* = −0.21, 0.89) or low-density lipoprotein cholesterol [LDL-C]) (*SMD* = −0.36, 95%*CI* = −0.91, 0.19). Similarly, BFRE demonstrated significant improvements in body mass index (*SMD* = 0.63, 95%*CI* = 0.12, 1.15) compared to equivalent non-BFRE exercise, but not body weight (*SMD* = 0.39, 95%*CI* = −0.13, 0.90) or body fat percentage (*SMD* = 0.44, 95%*CI* = −0.08, 0.96).

3.4.4. Muscle excitation

One review examined the effect of BFRE on chronic measures muscle excitation,[51] reporting a significant large effect compared to LLRT (*SMD* = 0.87, 95%*CI* = 0.38, 1.36). They did not have sufficient data to meta-analyse the effect of BFRE on muscle excitation compared to HLRT.

3.4.5. Balance

Two reviews examined the effect of BFRE on balance, with a CCA of 0.0% indicating a slight overlap of primary studies (supplementary digital content 7, Fig. 11). The first compared BFRE to both non-BFRE, LLRT and walking alone in older adults,[70] with no differences observed between conditions (*SMD* = 0.25, 95%*CI* = −0.40, 0.91). The second compared BFRE to LLRT in middle aged and older adults,[67] with no differences observed between conditions (*SMD* = 0.22, 95%*CI* = −0.08, 0.52).

3.4.6. Heart rate

Two reviews examined the effect of BFRE on resting heart rate, with a CCA of 0.0% indicating a slight overlap of primary studies (supplementary digital content 7, Fig. 12). The first examined the effect of BFRE on heart rate in adults with hypertension, and only compared BFRE to LLRT.[72] They reported a significant large reduction in resting heart rate in response to BFRE (*SMD* = 2.4, 95%*CI* = 0.01, 4.79). The second study

compared the effect of BFRE to LLRT and walking in adults > 18 years,[63] with no difference observed between conditions (*SMD* = −0.03, 95%*CI* = −0.55, 0.49).

3.4.7. Adverse events

One review examined the rate of adverse events (considered as 'exercise induced knee pain') due to BFRE compared to LLRT and HLRT in individuals with knee OA.[20] When compared to both LLRT and HLRT combined, there was no significant difference in adverse events between conditions (relative risk [RR] = 0.45, 95%*CI* = 0.20, 1.01), nor was there any difference when BFRE was compared to LLRT alone (RR = 3.37, 95% *CI* = 0.37, 31.15). However, BFRE resulted in significantly less adverse events than HLRT alone (RR = 0.26, 95%*CI* = 0.09, 0.72).

3.5. Levels of evidence

Of the nine health and performance outcomes that were analysed quantitatively in this umbrella review, only one (aerobic fitness) presented with a convincing level of evidence, while none were classified as highly suggestive. Two outcomes (hypertrophy; strength) presented with a suggestive level of evidence, and three (vascular health; blood pressure; power) a weak level of evidence. The final three (physical function; pain; speed) were classified as non-significant. The full levels of evidence evaluation can be found in supplementary digital content 6.

4. Discussion

This umbrella review is the first to consolidate the effects of BFRE on measures of health and performance across various populations. A total of 47 reviews comprising 265 unique studies were included. Results indicate that BFRE has the potential to promote improvements in muscular hypertrophy, strength, aerobic fitness, vascular health, and power. Improvements observed were similar across all populations, although young adults saw larger improvements in hypertrophy in response to BFRE than all other populations groups. Improvements in outcome measures were similar when BFRE was compared to LLRT, usual care, and mixed interventions, with BRFE less effective when compared to HLRT for improving strength and hypertrophy. BFRE only demonstrated improvements in physical function in older adults, and only improved measures of pain when compared to HLRT. There was no effect of BFRE on speed. These findings support the use of BFRE as a viable method of improving health and performance in a range of populations, particularly when HLRT is not suitable.

4.1. Quality of the included meta-analyses

The methodological quality of the included reviews was low-to-moderate, with ~90% rated as moderate quality according to the AMSTAR 2. As such, it is recommended that users should consider the potential impact of an inadequate rating for each item independently.[42] Most meta-analyses (95.7%) included in this umbrella review did not provide a list of excluded studies with justification for exclusion. Furthermore, very few assessed the risk of publication bias (66.0%), and no studies reported the sources of funding for primary studies included in their respective review. These omissions may be due to word count limits, lack of supplementary databases, or space constraints. Nonetheless, the quality of included reviews underscores the need for future research to prioritise methodological rigor, including detailed review protocols and comprehensive bias assessments to enhance the reliability of BFRE findings. Moreover, when considering the lack of studies exploring publication bias, it is possible that the many previously published meta-analyses examining BFRE have overstated its effectiveness by including outliers in their analysis, which would explain the disparity in effect sizes in the present review and previous meta-analytic literature. Finally, when considering the levels of evidence of the outcomes presented in this review, only aerobic fitness was considered convincing.

4.2. Effect of BFRE on the older adults, chronic disease and clinical populations

Resistance training is widely recognised for its role in improving muscular strength, hypertrophy, functional capacity, and QoL among older adults, individuals with chronic conditions and clinical populations.[84,85] While HLRT is often considered best practice to elicit these outcomes, it may not be viable due to potential contraindications, including cardiovascular risks, joint degeneration, or post-operative recovery. The results of this umbrella review support the use of BFRE to improve strength, hypertrophy, and vascular health in older adults and clinical populations (e.g., osteoarthritis, sarcopenia), and improve functional capacity in older adults, when compared to LLRT alone. This is particularly noteworthy when we consider the association between these outcomes and falls risk, given falls are closely linked to health decline and loss of independence in older adults.[86] Despite the positive effects of BFRE in elderly and clinical populations, results demonstrated HLRT had a greater effect on both strength and hypertrophic outcomes, and as such, HLRT should still be prioritised in settings where it can be implemented safely.

Older adults also saw smaller improvements in hypertrophy in response to BFRE when compared to younger adults. This aligns with prior research indicating that older adults generally observe smaller increases in muscle size than young adults when using the same resistance training program.[87,88] While the exact mechanism for this phenomenon (often described as anabolic resistance) is uncertain, specific reasons have been proposed, including age-related reductions in satellite cell numbers,[89] impairments in the regulation of ribosomal biogenesis,[90] increases in chronic inflammation,[91] and declines in muscle fibre capillarization.[92] Within the context of BFRE, reduced muscle fibre capillarization offers a logical explanation. Type I muscle fibres generally have more capillaries than type II fibres.[92] In young adults, type I fibres have also been shown to have greater propensity for hypertrophy in response to BFRE than what would typically be observed in response to HLRT.[93] As such, it could be that the differences in hypertrophy between younger and older adults observed in the present review is due to older adults experiencing smaller increases in type I fibre size in response to BFRE than their younger counterparts. Recent meta-analytic literature partially supports this suggestion, demonstrating a negative association between age and increases in type I muscle fibre hypertrophy in response to resistance training interventions.[94]

Whilst not quantitatively analysed, one review demonstrated improvements in bone metabolism markers in response to BFRE, including a small effect on BALP, and a large effect on BMD, when compared to LLRT alone.[82] This may suggest that BFRE could support bone health, and could offer a method of rehabilitative exercise in people with conditions such as osteoporosis.

4.3. Effect of BFRE in healthy and athletic populations

BFRE has become increasingly common among healthy and athletic populations given its ability to promote physiological adaptations (i.e., improved strength and hypertrophy) at lower training intensities. This offers a favourable exercise modality in situations where reducing mechanical tension, joint stress, or training load may be required (i.e., during post-injury rehabilitation or during a competitive season).[73] The present results indicate BFRE can improve strength and hypertrophy in healthy and athletic populations when compared to LLRT, supporting this notion. Moreover, BFRE within an aerobic training context was shown to elicit significant improvements in aerobic fitness when compared to the same exercise intervention without the application of BFR. Aerobic BFRE has been proposed to decrease stroke volume and increase heart rate due to reductions in arterial blood flow and increased venous pooling in the exercising limb. This is thought to increase mechanical stress on the heart, driving cardiovascular adaptions, but also enhance metabolite accumulation within the working limb, driving

peripheral muscular adaptations.[3] While the mechanism of action cannot be elucidated from this review, these results suggest that the addition of BFR to aerobic exercise may augment desirable aerobic adaptations in healthy and athletic populations.

Interestingly, BFRE provided greater benefits for the aerobic fitness of athletic populations than healthy untrained or recreationally trained young adults. Although the exact reason for this finding is uncertain, there are possible explanations. Firstly, BFRE has been shown to cause increases in the resting diameter of arteries,[95] something that is not commonly observed under normal exercising conditions. This could result in reductions in microvascular resistance, increases in peripheral blood flow, and improved oxygen delivery to working muscle.[96] Secondly, it has also been demsontrated to improve intracellular buffering capacity to a greater extent than normal aerobic training.[97] These adaptations may be more relevant to athletic populations who already have well-developed aerobic systems, and may therefore receive greater benefits from novel interventions that promote improvements in aerobic fitness and performance via means that are not obtained to a great extent via traditional training methods. Comparatively the typical control intervention would elicit greater change in untrained individuals that have not already exhausted the capacity for aerobic adaptation, such that the addition of BRFE stimuli may lead to relatively less additive benefit.

Interestingly, BFRE was also shown to have a positive effect on muscular power in comparison to similar interventions without BFR in healthy individuals and athletes. It has been hypothesised that the increased recruitment of high threshold motor units associated with BFRE may facilitate neuromuscular adaptations that contribute to greater power output.[74] However, it is important to note that only three reviews examined the influence of BFRE on power output,[36,62,74] none of which conducted subgroup analysis with consideration for the type of exercise BFRE was compared to. As such, it is plausible that BFRE would only augment improvements in power when the exercise intervention it is combined with is insufficient to maximise motor unit recruitment. Similarly, it may not offer any benefits when combined with high-load or maximal velocity exercises that are often prescribed to optimise jump height.[98]

4.4. Safety of BFRE

Only one meta-analysis in the present review reported on the safety of BFRE, which was specific to individuals with knee OA and whereby exercise induced knee pain was its outcome of interest.[20] There was no difference in the safety of BFRE compared to LLRT alone, however BFRE resulted in significantly less adverse events than HLRT alone. This finding may be explained by the fact that exercise intensity (which increases with greater relative loads) has been shown to increase the risk of musculoskeletal injury during resistance exercise.[99] As BFRE is almost exclusively combined with LLRT, it likely poses lower risk of musculoskeletal pain or injury than HLRT. While this may imply that BFRE offers a safer alternative to HLRT, it is important to note that these data were in a very specific context and are unlikely to apply to all situations. Indeed, other safety concerns have been raised.

BFRE has been shown to cause heightened central (i.e., heart rate and blood pressure) and peripheral (i.e., arterial compliance and endothelial function) cardiovascular responses in comparison to non-occluded exercise,[100] suggesting it may be contraindicated for certain populations, including those with peripheral vascular or artery disease, hypertension, venous thromboembolism, sickle cell disease, clotting disorders, peripheral neuropathy, and a prior history of stroke, amongst others.[101] Despite their being some research indicating that BFRE is safe in individuals with hypertension,[72] intermittent claudication,[102] and who have previously had a stroke,[103] these studies have been in small samples that may not generalise to larger populations. Moreover, the safety profile of BFRE in other potentially contraindicated populations has not been explored. As such, the safety of BFRE in many clinical populations is unknown.

4.5. Strengths and methodological limitations

This umbrella review synthesises the highest level of evidence regarding the effects of BFRE training on health and performance outcomes in various populations, providing insight for future researchers, practitioners, and clinicians implementing BFRE exercise. A key strength is the use of a rigorous eligibility criteria that ensured that only the most relevant and reliable evidence was sourced to base valid conclusions from. However, his review only included articles published in English, resulting in some non-English articles being excluded. Similarly, while the search processes permitted comprehensive coverage of potentially eligible studies, the impact of excluding grey literature is also unknown. Another limitation is the poor methodological quality of most reviews, as highlighted by the low-to-moderate AMSTAR scores. This raises concerns about potential biases and lack of transparency in the systematic reviews and meta-analyses included. There was also high heterogeneity present in most of the overall analyses conducted. This likely reflects the considerable variation in methods, populations, and interventions, of the studies within the included reviews. As such, the overall results should be interpreted with caution, and the subgroup analyses may provide a clearer picture of BFRE on health and performance outcomes. Furthermore, while the overlap among the reviews included in this study were reported, it was not accounted for in our quantitative synthesis, which could conceivably inflate the precision of the pooled estimates reported. Finally, it is important to note that while health outcomes were a key focus of this work, very few meta-analyses examined health related factors, and only measures of cardiovascular health, metabolic health, balance, pain, and bone metabolism were reported on. As such, further research examining the effects of BFRE on other aspects of health is warranted (i.e., mental health, cognitive health, etc). Similarly, the search strategy applied the broad search term “health” to capture health related reviews that met the inclusion criteria. However, if a condition specific meta-analysis did not contain the word health in the title, abstract, or keywords, it would not have been captured. The authors consider this a low probability due to trialling multiple search strategies that included specific condition types, but it is possible that some health-related meta-analyses were not included as a result.

4.6. Practical applications and recommendations for future research

The current body of research provides evidence supporting the use of BFRE in all populations to improve muscle hypertrophy and strength. This may be particularly beneficial in older populations, and in those with musculoskeletal conditions where traditional HLRT may not be safe. Positively, BFRE has also been shown to improve vascular health and functional capacity in these same populations, which may enhance health and quality of life. When considering its applications to younger adults and athletes, it is likely that BFRE is best reserved for situations where high external loads are not desirable as it appears less effective than HLRT for these outcomes. BFRE also appears to offer an effective way to augment improvements in aerobic fitness and performance when combined with aerobic training. Practitioners working with athletes should consider the addition of BFRE into a training regime to achieve unique adaptations that may not be obtained via traditional aerobic exercise.

The current review identified a large body of meta-analytic research in areas pertaining to strength and hypertrophy across a range of populations, and aerobic fitness in younger adults and athletes. However, there appears to be a lack of research examining the effect of BFRE on the aerobic fitness of older adults, which is an area that warrants attention. Similarly, there was a paucity of reviews examining the effect of BFRE on non-cardiovascular measures of health. The safety profile of BFRE in clinical populations also remains largely unknown. As such, future original and meta-analytic research should focus on these unexplored areas to provide a greater understanding of where BFRE is best applied in practice. Furthermore, very few of the included reviews assessed the risk

of publication bias or considered the quality of the included studies in their analysis. This is noteworthy, as it could conceivably inflate the reported effects of BFRE. Future reviews should consider conducting sensitivity analysis whereby both outliers and low-quality studies are removed to determine their influence on the overall effect. Similarly, future primary studies should look to adhere to checklists, such as the Standards Method for Assessment of Resistance Training in Longitudinal Designs,[104] to ensure repeatable and robust reporting.

5. Conclusion

The findings of this umbrella review highlight the broad applicability of BFRE across various populations, including healthy adults, athletes, elderly individuals, clinical populations, or those undergoing musculoskeletal rehabilitation. Evidence supports the efficacy of BFRE as a training intervention that can enhance various measures of health and performance, though its effects are often comparable, or less pronounced, than those achieved by HLRT alone. However, BFRE offers valuable stimulus to elicit favourable adaptations in populations where high-load training is not feasible or recommended due to injury, chronic disease, or other health considerations. Many of the included meta-analyses were of moderate-to-low quality, and thus, it is recommended that more rigorous randomised controlled trials and subsequently meta-analyses are undertaken to strengthen the evidence base and efficacy towards BFRE.

CRediT authorship contribution statement

Cooper Oborn: Writing – review & editing, Writing – original draft, Supervision, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Maximillian J. Nelson:** Writing – review & editing, Visualization, Supervision, Project administration, Methodology, Conceptualization. **Kade Davison:** Writing – review & editing, Visualization, Supervision, Project administration, Methodology, Conceptualization. **James Murray:** Writing – review & editing, Visualization, Validation, Resources, Methodology, Investigation, Data curation. **Kent Green:** Writing – review & editing, Visualization, Validation, Methodology, Investigation, Data curation. **Jawaria Shahid:** Writing – review & editing, Visualization, Validation, Methodology, Data curation. **Hunter Bennett:** Writing – review & editing, Visualization, Validation, Supervision, Resources, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization.

Declaration of competing interest

The authors have no direct or indirect competing interests to declare.

Protocol registration

This umbrella review was registered on the open science framework (OSF.IO/K67F2)[40] on the July 9, 2024 and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).

Data availability statement

The data and code used for the analyses on this study are available on the Open Science Framework page for this project (https://osf.io/b5wv3/).

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.smhs.2025.02.011.

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