Exercise training and resting blood pressure: a large-scale pairwise and network meta-analysis of randomised controlled trials

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ABSTRACT

Objective To perform a large-scale pairwise and network meta-analysis on the effects of all relevant exercise training modes on resting blood pressure to establish optimal antihypertensive exercise prescription practices.

Design Systematic review and network meta-analysis.

Data sources PubMed (Medline), the Cochrane library and Web of Science were systematically searched.

Eligibility criteria Randomised controlled trials published between 1990 and February 2023. All relevant work reporting reductions in systolic blood pressure (SBP) and/or diastolic blood pressure (DBP) following an exercise intervention of ≥2 weeks, with an eligible non-intervention control group, were included.

Results 270 randomised controlled trials were ultimately included in the final analysis, with a pooled sample size of 15 827 participants. Pairwise analyses demonstrated significant reductions in resting SBP and DBP following aerobic exercise training (–4.49/–2.53 mm Hg, p<0.001), dynamic resistance training (–4.55/–3.04 mm Hg, p<0.001), combined training (–6.04/–2.54 mm Hg, p<0.001), high-intensity interval training (–4.08/–2.50 mm Hg, p<0.001) and isometric exercise training (–8.24/–4.00 mm Hg, p<0.001). As shown in the network meta-analysis, the rank order of effectiveness based on the surface under the cumulative ranking curve (SUCRA) values for SBP were isometric exercise training (SUCRA: 98.3%), combined training (75.7%), dynamic resistance training (46.1%), aerobic exercise training (40.5%) and high-intensity interval training (39.4%). Secondary network meta-analyses revealed isometric wall squat and running as the most effective submodes for reducing SBP (90.4%) and DBP (91.3%), respectively.

Conclusion Various exercise training modes improve resting blood pressure, particularly isometric exercise. The results of this analysis should inform future exercise guideline recommendations for the prevention and treatment of arterial hypertension.

WHAT IS ALREADY KNOWN?

⇒ The role of exercise training as an effective non-pharmacological antihypertensive intervention is generally well-established.
⇒ Traditional aerobic exercise training remains the primarily recommended exercise approach for the management of high blood pressure.
⇒ Current exercise guidelines for blood pressure control are largely based on older data, requiring an updated analysis with the inclusion of more novel exercise modes, including high-intensity interval training and isometric exercise training.

WHAT ARE THE NEW FINDINGS?

⇒ This large-scale systematic review and network meta-analysis of 270 randomised controlled trials demonstrates the optimal exercise prescription practices in the management of resting blood pressure.
⇒ Aerobic exercise training, dynamic resistance training, combined training, high-intensity interval training and isometric exercise training are all significantly effective in reducing resting systolic and diastolic blood pressure. Overall, isometric exercise training is the most effective mode in reducing both systolic and diastolic blood pressure.
⇒ These findings provide a comprehensive data-driven framework to support the development of new exercise guideline recommendations for the prevention and treatment of arterial hypertension.

INTRODUCTION

Hypertension is a leading modifiable risk factor for morbidity and mortality.[1–3] While differences in diagnostic cut-off points exist in guidelines,[4 5] blood pressure above optimal levels is lineally associated with an escalated risk of cardiovascular disease.[6] With the prevalence of hypertension increasing,[7] particularly in low- and middle-income countries,[8] research into effective antihypertensive interventions remains critical. Medical therapy is an effective means of reducing blood pressure[9]; however, poor adherence,[10–12] adverse side effects[13] and economic expenditure[14] are important limitations. As such, non-pharmacological approaches are favoured.[15 16] Exercise elicits conclusive cardiovascular health benefits and improves long-term survival, with a longitudinal association between physical activity and reduced mortality well documented.[17–20]

Previous large-scale analyses have reported significant systolic and diastolic blood pressure (SBP and DBP) reductions from varying exercise modes.[21–26] Based on previous work, traditional aerobic exercise training (AET) remains the primarily recommended exercise approach for the management of resting blood pressure.[4 5] However, the current exercise guideline recommendations are largely based on older data, with recent investigations demonstrating a growing interest in more novel exercise modes, such as high-intensity interval training (HIIT)[27] and isometric exercise training (IET),[24] as well as a plethora of new data on the role of independent dynamic resistance training (RT)[28] and combined RT and AET.[29 30] As a consequence, the optimal exercise intervention for the management of resting blood pressure is unknown, with existing guidelines probably outdated.

Therefore, this work aimed to provide an updated large-scale systematic review and network meta-analysis (NMA) of randomised controlled trials (RCTs) on the effects of exercise training on resting SBP and DBP. We aimed to perform independent pairwise meta-analyses for each exercise mode with subsequent comparative Bayesian NMAs. We also aimed to perform separate baseline blood pressure-stratified analyses to determine the effects of each exercise mode in those of differing blood pressure classifications.

METHODOLOGY

Search strategy

This review was performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines,[31 32] with PROSPERO registration (CRD42022326565). A comprehensive electronic database search strategy was constructed to identify RCTs reporting the effects of an exercise training intervention on resting blood pressure. The systematic search was performed in PubMed (Medline), the Cochrane library and Web of Science using a combination of relevant medical subject heading (MeSH) terms and text words including exercise, physical activity, blood pressure and hypertension, with the Boolean search terms 'OR' and 'AND' (online supplemental appendix A). No search filters or limits were applied. Separately, the reference lists of previous systematic reviews and meta-analyses were hand searched for additional reports not identified in the initial search. Trials published between 1990 and February 2023 were considered eligible.

Screening and study eligibility

Following the systematic search, two authors (AD and OA) independently screened all papers for eligibility. Studies were initially screened by title and abstract, and subsequently by full text if they met the predetermined inclusion criteria. Any inconsistency and disagreements were discussed by the researchers and a consensus was reached with the opinion of a fourth researcher (JE), if necessary. Following study recruitment, the respective data of all included studies were extracted via Microsoft Excel. A third reviewer (MG) independently assessed and verified all data extraction. Baseline and postintervention mean (SD) SBP and DBP data were initially extracted owing to the common absence of change data being reported in exercise training and blood pressure RCTs. As required for NMAs, we acquired mean change from the baseline and postintervention values. Following the *Cochrane Handbook for Systematic Reviews of Interventions* (Chapter 6),[33] we aimed to calculate SD change from standard errors, 95% CIs, p values or t statistics where available. When studies did not report any such data, SD change was calculated using a correlation coefficient of 0.8 as previously tested and validated in a similar dataset.[22]

Following the participants, interventions, comparators, outcomes PICO) framework, the population included adult humans with no predetermined limitations on health or disease state in representation of the general population, which ensured we did not unnecessarily exclude any potentially valuable data. Considering the intervention, comparator and outcome of this work, trials were determined eligible if they were appropriately randomised, and reported pre- and postintervention SBP and/or DBP in both the exercise and non-intervention control group. To minimise confounding, any considerable dietary, counselling or exercise influence in the non-intervention control group resulted in exclusion. Similarly, studies containing concurrent co-interventions to exercise (such as supplementation or medication changes) were excluded. Only trials published in peer-reviewed journals were considered and thus dissertation theses were not eligible. Studies that might appear eligible but were excluded are available on request from the corresponding author (with the reason for exclusion).

For consistency, the exercise protocol/intensity of each included paper was screened against the Exercise Prescription in Everyday Practice and Rehabilitative Training (EXPERT) tool[34] to be defined and categorised. All protocols were then stratified into one of the following primary exercise mode categories: 'aerobic exercise training' (AET), 'dynamic resistance training' (RT), 'combined training' (CT), 'high-intensity interval training' (HIIT) and 'isometric exercise training' (IET). Each category was then further explored for appropriate subgroups, allowing for the analysis of walking, running and cycling as AET subgroups, sprint interval training (SIT) and aerobic interval training (AIT) as HIIT subgroups, and isometric handgrip (IHG), isometric leg extension (ILE) and isometric wall squat (IWS) as IET subgroups. IET programmes commonly employ protocols of 4×2 min contractions, separated by 1–4 min rest intervals, performed three times a week. IHG is often prescribed at 30% maximum voluntary contraction, while IWS and ILE protocols are typically performed at 95% of the peak heart rate achieved during a laboratory-based maximal incremental isometric exercise test. The IWS may also be prescribed using a self-selected wall squat, with a knee joint angle that would elicit a rate of perceived exertion (RPE) of 3.5–4.5/10 for bout 1; RPE 5–6/10 for bout 2; RPE of 6.5–7.5/10 for bout 3 and RPE of 8–9/10 for bout 4. This review defines HIIT as 'episodic short bouts of high-intensity exercise separated by short periods of recovery at a lower intensity'.[35] As subgroups of HIIT, SIT was defined as an 'all-out' maximal, low-volume protocol, whereas aerobic interval training AIT consisted of 4×4 min protocols of a lower intensity.

For baseline blood pressure stratified analyses, all included studies were categorised as normotension, prehypertension or hypertension based on the baseline SBP and DBP of both the intervention and control group. In accordance with the European Society of Hypertension/European Society of Cardiology (ESC/ESH) guidelines,[5] the SBP and DBP status subgroups were categorised as normotension, prehypertension or hypertension, with values equal to <130/85 mm Hg, 130–139/85–89 mm Hg or >140/90 mm Hg, respectively. Studies in which the intervention and control groups differed in baseline blood pressure categories were excluded from this analysis.

Study quality

Risk of bias and methodological rigour were evaluated using the TESTEX scale.[36] TESTEX is a 15-point (12 item) tool designed for the assessment of exercise training trials. As previously demonstrated in such large-scale reviews,[22] a random 10% sample of trials from each exercise mode was selected for risk of bias assessment. Two reviewers (AD and JE) independently scored all selected articles. Any disputes in quality analyses were resolved by consensus.

Statistical analysis

The pairwise meta-analyses were performed using Comprehensive Meta-Analysis, version 3 (Biostat, Englewood, New Jersey, USA). A pooled analysis was separately performed for each of the primary (AET, RT, CT, HIIT, IET) and secondary (walking, cycling, running, SIT, AIT, IHG, IWS and ILE) exercise mode groups to establish the weighted mean difference (WMD) in SBP and DBP between the exercise group and the non-intervention controls. Parallel pooled analyses were also performed in only those studies free from any cardiovascular or other disease. Each primary exercise mode group was then further dichotomised by categorisation of baseline blood pressure and separately analysed. Meta-regression analyses were performed to ascertain if any study-level moderator variables influenced blood pressure change and explain any of the observed interstudy variance in outcomes. The selected moderators to be run independently were intervention duration (in weeks), training frequency (sessions per week) and training compliance (mean percentage of prescribed sessions attended). Statistical heterogeneity was always tested alongside the pooled analysis and reported as the I^2 statistic. A significance threshold of 40% was applied to the I^2 statistic.[37] Once past this threshold, post hoc tests such as Egger's regression test (1997) was systematically planned to assess the presence of funnel plot asymmetry to account for potential publication bias.[38] The selection of fixed or random effects approaches were dependent on the presence of heterogeneity, with random effects analysis applied when interstudy variability was confirmed through significant heterogeneity. The results of the pooled analysis were considered significant with a p value of <0.05 and a Z-value of >2.

To facilitate the comparison of exercise modes that have not been directly compared in RCT's and enhance the precision of comparative effect estimates (via the inclusion of both direct and indirect data), we performed NMAs. Bayesian NMAs were performed via the MetaInsight tool (version V4.0.2).[39] MetaInsight is an interactive web-based tool powered by Rshiny which uses R packages 'gemtc' and 'BUGSnet' for Bayesian statistical calculations. This analysis runs Markov chain Monte Carlo simulations with four chains and a total of 25 000 iterations (burn-in period of 5000). Convergence of the model was tested via the Gelman-Rubin convergence assessment.[40] Based on pre-established interstudy heterogeneity, random-effects analyses of WMD were selected. Inconsistency between direct and indirect effect size comparisons were assessed via node-splitting models[41] with corresponding Bayesian P values. Residual deviance plots for the NMA with consistency models and unrelated mean effect inconsistency models were produced. For any studies with large residual deviance (>2), further exploration was planned and exclusion in a sensitivity analysis. To assess the moderator effect of baseline SBP and DBP, Bayesian NMA meta-regression analyses were separately performed using WinBUGS version 1.4.[42]

Separate NMAs were run by primary exercise mode categorisation (AET, RT, CT, HIIT and IET), and then via secondary exercise subgroup categorisation (walking, running, cycling, RT, CT, SIT, AIT, IHG, ILE, IWS). As there was no pre-established secondary exercise mode categorisation for RT and CT, these were included in both analyses. Network diagrams were produced to visualise the direct and indirect comparisons across different exercise modes. NMA data are reported as mean effect with 95% credible intervals. Ranking probability analyses were performed, with surface under the cumulative ranking curve (SUCRA) values generated for each exercise mode and submode, and displayed as litmus rank-o-gram SUCRA plots.[43]

Equity, diversity, and inclusion statement

Our study included all identified randomised controlled trials of exercise training for the management of blood pressure, inclusive of all genders, race/ethnicities and socioeconomic levels. Our author team consisted of two women and five men from different disciplines (medical research, sport and exercise science, population health), including three authors considered junior scholars. Our research methods were not altered based on regional, educational or socioeconomic differences.

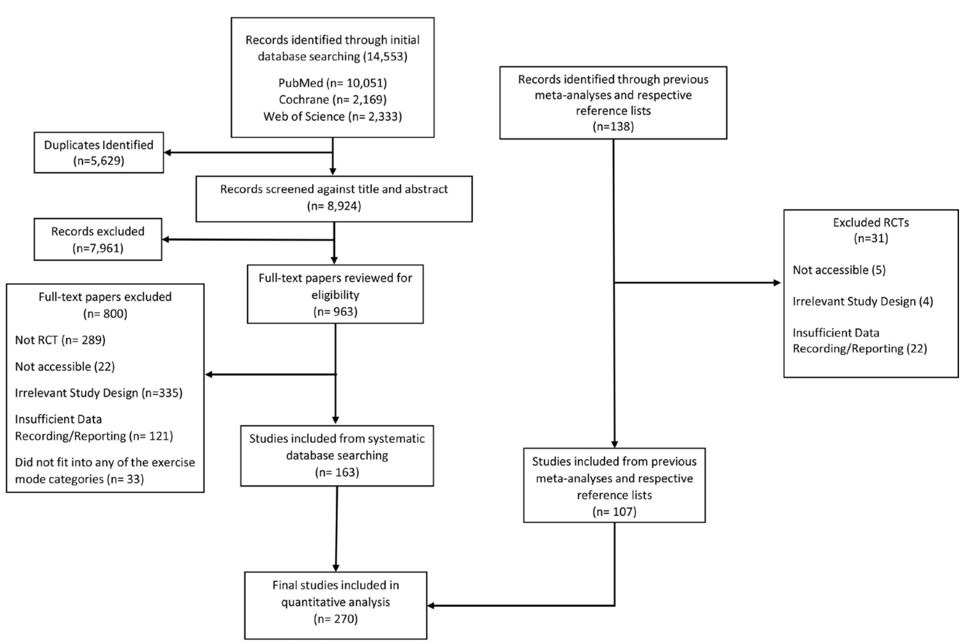

Figure 1 PRISMA systematic review and meta-analysis flow chart. RCT, randomised controlled trial.

Pairwise Analysis, sBP (mmHg) Weighted Mean Difference, 95% CI

Exercise Mode	MD [95%CI]	N. Effect Sizes	I²%	P-Value
Aerobic Exercise Training	4.49 [3.5-5.5]	182	91.5	<0.001
Walking	2.85 [1.6-4.1]	89	77.4	<0.001
Cycling	6.88 [3.9-9.8]	28	92.1	<0.001
Running	6.83 [4.0-9.7]	21	88.4	<0.001
Dynamic Resistance Training	4.55 [3.2-5.9]	57	58.4	<0.001
Combined Training	6.04 [3.2-8.9]	46	92.8	<0.001
High-Intensity Interval Training	4.08 [2.6-5.5]	49	82.4	<0.001
Aerobic Interval Training	1.97 [-1.2-5.2]	13	66.9	0.227
Sprint Interval Training	5.26 [3.9-6.6]	7	0	<0.001
Isometric Exercise Training	8.24 [6.5-10.0]	24	68.8	<0.001
Isometric Handgrip	7.10 [4.7-9.5]	17	68.8	<0.001
Isometric Leg Extension	10.05 [7.3-12.8]	3	0	<0.001
Isometric Wall Squat	10.47 [6.3-14.6]	4	81.0	<0.001

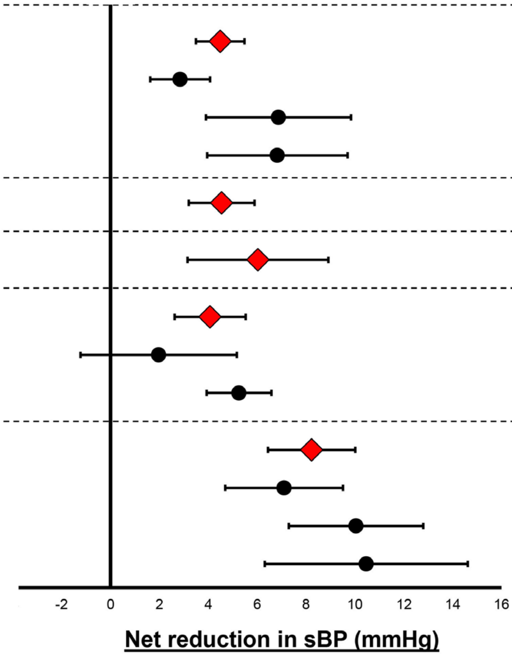

Figure 2 Forest plot depicting overall effects of each primary and secondary exercise mode on systolic blood pressure (SBP).

RESULTS

Figure 1 shows the PRISMA systematic review flow chart. The initial systematic search identified 14553 trials, with an additional 138 trials discovered through screening of previous meta-analyses and their respective reference lists. Following all exclusions, 270 exercise training RCTs were ultimately included, constituting an analysed sample of 15827 (7632 controls) participants. The analysis involved 358 effect sizes, including 182 AET (89 walking, 28 cycling, 21 running and 44 'Other' AET), 57 RT, 46 CT, 49 HIIT (of which 7 are SIT and 13 are AIT) and 24 IET (17 IHG, 4 IWS, 3 ILE).

The full TESTEX risk of bias assessment scoring can be found in online supplemental table S1. The TESTEX assessment demonstrated several consistent limitations throughout the exercise training literature. In particular, most trials failed to monitor control group activity or perform intention-to-treat analysis when appropriate. Study and training characteristics of all 270 trials are presented in online supplemental table S2. For sensitivity and comparative purposes, we also ran parallel primary analyses excluding all diseases (such as type 2 diabetes). Importantly, the inclusion/exclusion of such diseases does not meaningfully influence the overall results, instead often generating wider CIs following the omission of useful data (see online supplemental table S4). Heterogeneity results for each analysis can be found within the respective figures. Sensitivity analysis was performed for the primary outcomes using the in-built Comprehensive Meta-Analysis 'one-study removed' analysis method, which did not significantly influence any of the overall effect sizes.

Pairwise analyses

Figure 2 displays the overall SBP reductions following each exercise mode compared with the control group. There was a significant reduction in SBP following all modes of AET, with an overall reduction of 4.49 mm Hg (95% CI 3.5 to 5.5, Z=8.8, p_{random}<0.001), 2.85 mm Hg for walking, 6.88 mm Hg for cycling and 6.83 mm Hg for running. The post hoc Egger's test was significant for overall AET SBP publication bias (online supplemental figure S1). There were significant reductions in SBP following RT by 4.55 mm Hg (95% CI 3.2 to 5.9, Z=6.6, p_{random}<0.001), and CT by 6.04 mm Hg (95% CI 3.2 to 8.9, Z=4.1, $_{prandom}$<0.001). While there were significant SBP reductions following overall HIIT by 4.08 mm Hg (95% CI 2.6 to 5.5, Z=5.5, p_{random}<0.001) and SIT by 5.26 mm Hg, AIT did not significantly change. All IET modes produced significant reductions in SBP, with an overall reduction of 8.24 mm Hg (95% CI 6.5 to 10.0, Z=9.0, $_{prandom}$<0.001), 7.10 mm Hg for IHG, 10.05 mm Hg ILE and 10.47 mm Hg for IWS.

Figure 3 displays the overall DBP reductions following each exercise mode compared with the control group. There was a significant reduction in DBP following all modes of AET, with an overall reduction of 2.53 mm Hg (95% CI 1.8 to 3.2, Z=7.3, $_{prandom}$<0.001), 1.44 mm Hg for walking, 3.20 mm Hg for cycling and 5.67 mm Hg for running. The post hoc Egger's test was significant for overall AET DBP publication bias (online supplemental figure S2). There were significant reductions in DBP following RT by 3.04 mm Hg (95% CI 2.2 to 3.9, Z=6.9, p_{random}<0.001), and CT by 2.54 mm Hg (95% CI 1.1 to 4.0, Z=3.4, $_{prandom}$=0.001). While there were significant DBP reductions following overall HIIT by 2.50 mm Hg (95% CI 1.2 to 3.8, Z=3.8, p_{random}<0.001) and SIT by 3.29 mm Hg (95% CI 0.1 to 6.5, Z=2.0, p_{random}=0.043), AIT did not significantly change. All IET modes produced significant reductions in DBP, with an overall reduction of 4.0 (95% CI 2.7 to 5.3, Z=6.0, p_{random}<0.001), 3.46 mm Hg for IHG, 4.23 ILE and 5.33 for IWS. The post hoc Egger's test was significant for overall IET DBP publication bias (online supplemental figure S3).

Figure 4 shows the SBP reductions for each exercise mode stratified by baseline blood pressure status. All analyses were statistically significant except the prehypertension group analysis

dBP (mmHg) Weighted Mean Difference, 95% CI

Exercise Mode	MD [95%CI]	N. Effect Sizes	I²%	P-Value
Aerobic Exercise Training	2.53 [1.8-3.2]	176	91.54	<0.001
Walking	1.44 [0.7-2.2]	83	74.12	<0.001
Cycling	3.2 [1.8-4.6]	28	91.39	<0.001
Running	5.67 [3.9-7.5]	21	82.83	<0.001
Resistance Training	3.04 [2.2-3.9]	57	66.61	<0.001
Combined Training	2.54 [1.1-4.0]	45	85.45	0.001
High-Intensity Interval Training	2.50 [1.2-3.8]	47	91.11	<0.001
Aerobic Interval Training	2.60 [-0.5-5.7]	12	83.92	0.105
Sprint Interval Training	3.29 [0.1-6.5]	7	66.62	0.043
Isometric Exercise Training	4.0 [2.7-5.3]	24	63.67	<0.001
Isometric Handgrip	3.46 [1.7-5.2]	17	71.31	<0.001
Isometric Leg Extension	4.23 [1.4-7.0]	3	0.00	<0.001
Isometric Wall Squat	5.33 [3.6-7.0]	4	23.47	<0.001

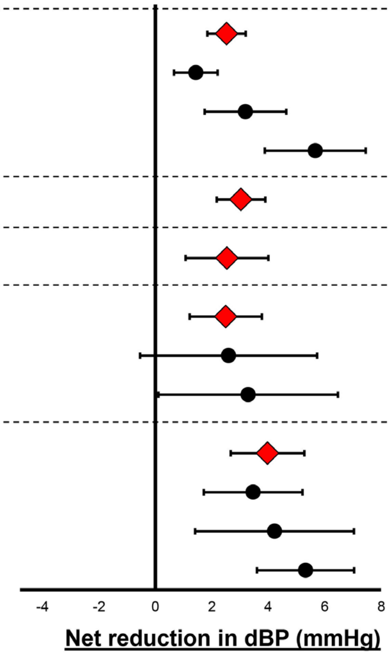

Figure 3 Forest plot depicting overall effects of each primary and secondary exercise mode on diastolic blood pressure (DBP).

for CT and HIIT. While all exercise modes demonstrated statistically significant reductions in SBP in normal blood pressure cohorts, all reductions were substantially larger in those with hypertension. Such baseline category stratified analysis was not feasible in DBP due to limited data.

As shown in online supplemental table S3, there was a significant SBP moderator interaction for AET, with a lower training frequency associated with a greater blood pressure reduction ($B=-1.0596$, $p=0.019$). There was no significant moderator

sBP (mmHg) Weighted Mean Difference, 95% CI, Exercise Category Pairwise Sub-Analysis

Exercise Mode Sub-group	MD [95%CI]	N. Effect Sizes	I²%	P-Value
Aerobic Exercise Training				
Normal Blood Pressure	3.60 [2.5-4.7]	69	69.80	<0.001
Pre-Hypertension	3.91 [2.3-5.6]	36	70.31	<0.001
Hypertension	7.74 [5.8-9.6]	31	92.91	<0.001
Resistance Training				
Normal Blood Pressure	2.86 [1.1-4.6]	32	48.04	<0.001
Pre-Hypertension	5.91 [2.4-9.4]	10	55.85	<0.001
Hypertension	6.32 [3.1-9.5]	9	69.55	<0.001
Combined Training				
Normal Blood Pressure	2.05 [0.6-3.5]	14	11.84	0.006
Pre-Hypertension	1.15 [-1.4-3.7]	10	47.55	0.37
Hypertension	11.14 [4.3-18.0]	14	96.30	0.001
High-Intensity Interval Training				
Normal Blood Pressure	3.92 [1.7-6.1]	25	86.78	<0.001
Pre-Hypertension	2.40 [-1.3-6.1]	8	81.07	0.209
Hypertension	6.59 [3.1-10.1]	7	48.82	<0.001
Isometric Exercise Training				
Normal Blood Pressure	6.65 [4.7-8.6]	7	0	<0.001
Pre-Hypertension	10.93 [9.3-12.6]	6	0	<0.001
Hypertension	9.22 [4.9-13.5]	4	48.36	<0.001

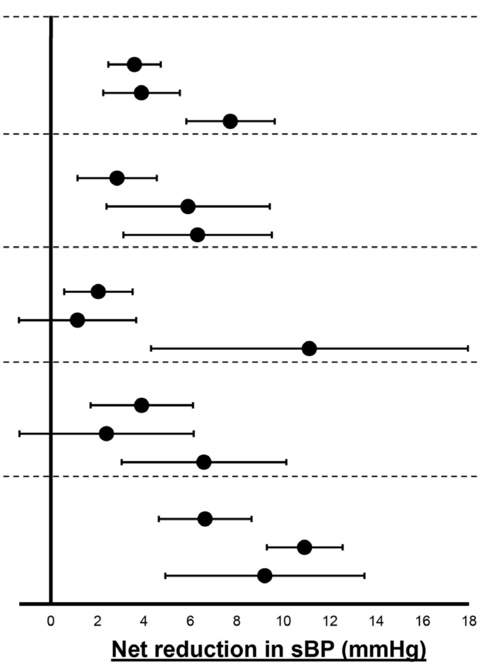

Figure 4 Forest plot depicting overall effects of each primary exercise mode on systolic blood pressure (SBP) stratified via baseline blood pressure category.

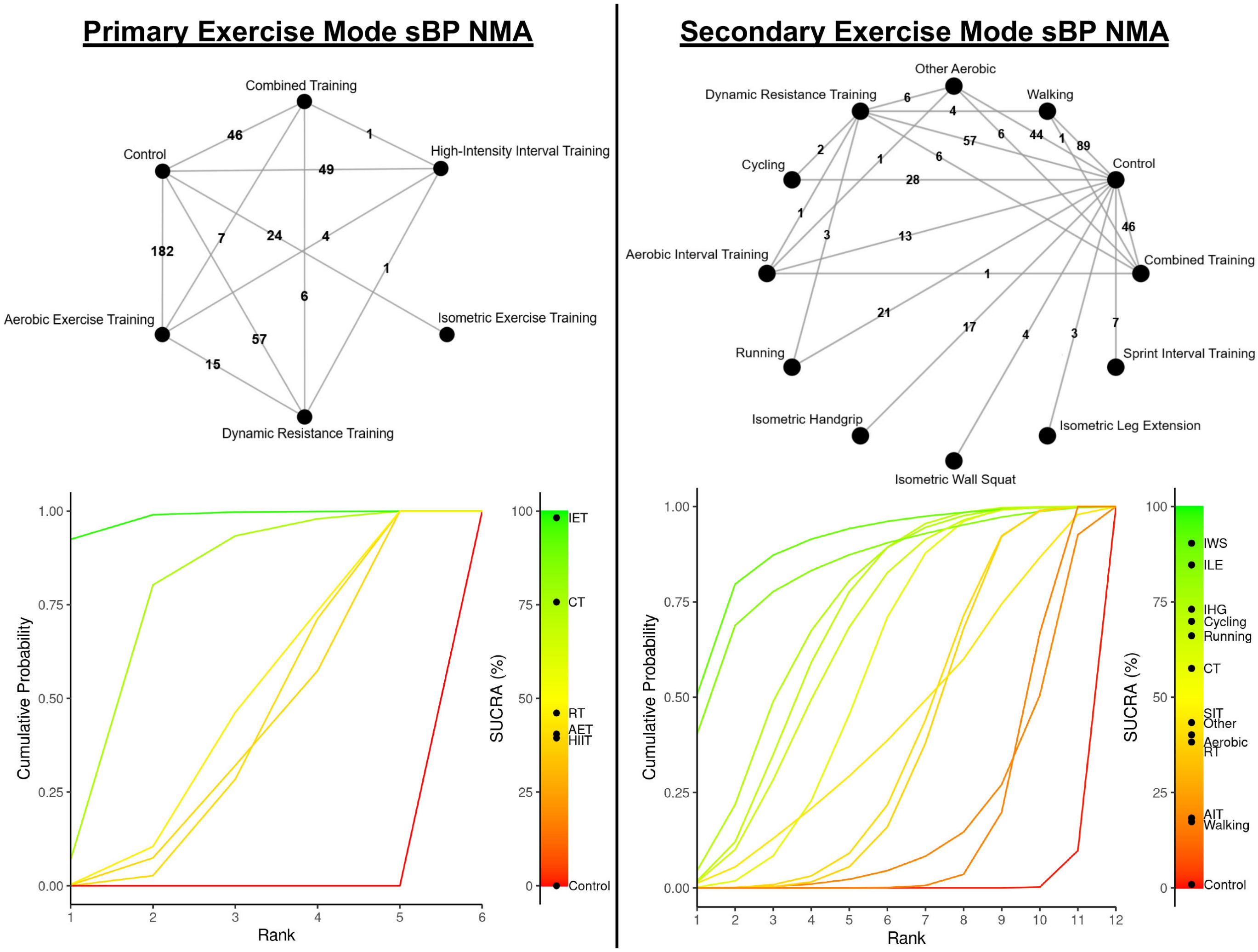

Figure 5 Network diagrams depicting the direct and indirect comparisons for the primary and secondary network meta-analyses and corresponding Bayesian ranking panel plots. AET, aerobic exercise training; AIT, aerobic interval training; CT, combined training; HIIT, high-intensity interval training; IET, isometric exercise training; IHG, isometric handgrip; ILE, isometric leg extension; IWS, isometric wall squat; NMA, network meta-analysis; RT, dynamic resistance training; SBP, systolic blood pressure; SIT, sprint interval training; SUCRA; surface under the cumulative ranking curve.

effect of intervention duration, training frequency or training compliance for any of the other exercise modes.

Network meta-analyses

Figure 5 depicts the network diagrams with corresponding Bayesian ranking panel plots, while tables 1 and 2, online supplemental tables S9 and S10 detail the comparative NMA findings for the primary and secondary exercise SBP and DBP mode analyses, respectively. Advanced analysis results, including the tables of rank probabilities with SUCRA (online supplemental tables S5, S6, S11 and S12), inconsistency tests with node-splitting models (online supplemental tables S7, S8, S13 and S14) and the deviance report plots (online supplemental figures S4, S5, S8 and S9) can be found in the supplementary file. There was no evidence of inconsistency in the primary or secondary NMA.

The primary exercise mode SBP NMA included 305 two-arm studies, 24 multiarm trials and 11 direct comparisons. As seen in table 1 and the Bayesian treatment ranking (figure 5 and Table S5), the order of effectiveness based on SUCRA values were IET (SUCRA: 98.3%), CT (75.7%), RT (46.1%), AET (40.53%)

Table 1 Comparative network meta-analysis for the systolic blood pressure primary exercise modes

	AET	Control	CT	HIIT	IET	RT
AET	**AET**	4.37 (3.45, 5.28)	−1.55 (−3.53, 0.43)	0.1 (−1.84, 2.03)	−3.86 (−6.54,−1.19)	−0.18 (−1.96, 1.6)
Control	−4.37 (−5.28,−3.45)	**Control**	−5.92 (−7.71,−4.11)	−4.27 (−6.02,−2.52)	−8.24 (−10.74,−5.72)	−4.54 (−6.16,−2.93)
CT	1.55 (−0.43, 3.53)	5.92 (4.11, 7.71)	**CT**	1.65 (−0.85, 4.12)	−2.31 (−5.42, 0.77)	1.37 (−1, 3.72)
HIIT	−0.1 (−2.03, 1.84)	4.27 (2.52, 6.02)	−1.65 (−4.12, 0.85)	**HIIT**	−3.95 (−7.03,−0.93)	−0.28 (−2.64, 2.09)
IET	3.86 (1.19, 6.54)	8.24 (5.72, 10.74)	2.31 (−0.77, 5.42)	3.95 (0.93, 7.03)	**IET**	3.68 (0.71, 6.66)
RT	0.18 (−1.6, 1.96)	4.54 (2.93, 6.16)	−1.37 (−3.72, 1)	0.28 (−2.09, 2.64)	−3.68 (−6.66,−0.71)	**RT**

AET, aerobic exercise training; CT, combined training; HIIT, high-intensity interval training; IET, isometric exercise training; RT, dynamic resistance training.

Table 2 Comparative network meta-analysis for the systolic blood pressure secondary exercise modes

	AIT	Control	CT	Cycling	IHG	ILE	IWS	Other aerobic	RT	Running	SIT	Walking
AIT	**AIT**	2.53 (−0.9, 5.99)	−3.39 (−7.22, 0.49)	−4.36 (−8.51,−0.18)	−4.75 (−9.34,−0.18)	−7.32 (−14.99, 0.29)	−8 (−14.74,−1.22)	−2.2 (−6.03, 1.65)	−2.08 (−5.85, 1.7)	−4.07 (−8.4, 0.26)	−2.28 (−8.1, 3.55)	−0.29 (−3.98, 3.39)
Control	−2.53 (−5.99, 0.9)	**Control**	−5.91 (−7.72,−4.1)	−6.88 (−9.22,−4.51)	−7.29 (−10.33,−4.21)	−9.84 (−16.72,−3.03)	−10.52 (−16.3,−4.7)	−4.73 (−6.55,−2.92)	−4.61 (−6.23,−2.98)	−6.61 (−9.21,−3.97)	−4.81 (−9.49,−0.15)	−2.82 (−4.13,−1.5)
CT	3.39 (−0.49, 7.22)	5.91 (4.1, 7.72)	**CT**	−0.97 (−3.9, 1.99)	−1.37 (−4.91, 2.2)	−3.92 (−11.03, 3.13)	−4.6 (−10.66, 1.5)	1.19 (−1.3, 3.65)	1.31 (−1.06, 3.65)	−0.69 (−3.86, 2.51)	1.11 (−3.93, 6.11)	3.1 (0.86, 5.29)
Cycling	4.36 (0.18, 8.51)	6.88 (4.51, 9.22)	0.97 (−1.99, 3.9)	**Cycling**	−0.39 (−4.24, 3.46)	−2.95 (−10.29, 4.28)	−3.65 (−9.92, 2.68)	2.15 (−0.85, 5.12)	2.28 (−0.57, 5.09)	0.28 (−3.26, 3.82)	2.08 (−3.19, 7.29)	4.06 (1.36, 6.74)
IHG	4.75 (0.18, 9.34)	7.29 (4.21, 10.33)	1.37 (−2.2, 4.91)	0.39 (−3.46, 4.24)	**IHG**	−2.57 (−10.09, 4.96)	−3.24 (−9.83, 3.38)	2.56 (−1.04, 6.11)	2.67 (−0.78, 6.15)	0.67 (−3.35, 4.72)	2.49 (−3.15, 8.02)	4.46 (1.13, 7.79)
ILE	7.32 (−0.29, 14.99)	9.84 (3.03, 16.72)	3.92 (−3.13, 11.03)	2.95 (−4.28, 10.29)	2.57 (−4.96, 10.09)	**ILE**	−0.68 (−9.69, 8.3)	5.11 (−1.96, 12.21)	5.21 (−1.77, 12.31)	3.23 (−4.09, 10.58)	5.04 (−3.19, 13.34)	7.01 (0.04, 14.05)
IWS	8 (1.22, 14.74)	10.52 (4.7, 16.3)	4.6 (−1.5, 10.66)	3.65 (−2.68, 9.92)	3.24 (−3.38, 9.83)	0.68 (−8.3, 9.69)	**IWS**	5.79 (−0.33, 11.87)	5.9 (−0.13, 11.96)	3.92 (−2.5, 10.31)	5.71 (−1.71, 13.18)	7.7 (1.69, 13.67)
Other aerobic	2.2 (−1.65, 6.03)	4.73 (2.92, 6.55)	−1.19 (−3.65, 1.3)	−2.15 (−5.12, 0.85)	−2.56 (−6.11, 1.04)	−5.11 (−12.21, 1.96)	−5.79 (−11.87, 0.33)	**Other aerobic**	0.12 (−2.23, 2.48)	−1.87 (−5.05, 1.32)	−0.08 (−5.08, 4.94)	1.91 (−0.32, 4.16)
RT	2.08 (−1.7, 5.85)	4.61 (2.98, 6.23)	−1.31 (−3.65, 1.06)	−2.28 (−5.09, 0.57)	−2.67 (−6.15, 0.78)	−5.21 (−12.31, 1.77)	−5.9 (−11.96, 0.13)	−0.12 (−2.48, 2.23)	**RT**	−2 (−5, 1.03)	−0.19 (−5.16, 4.73)	1.79 (−0.28, 3.84)
Running	4.07 (−0.26, 8.4)	6.61 (3.97, 9.21)	0.69 (−2.51, 3.86)	−0.28 (−3.82, 3.26)	−0.67 (−4.72, 3.35)	−3.23 (−10.58, 4.09)	−3.92 (−10.31, 2.5)	1.87 (−1.32, 5.05)	2 (−1.03, 5)	**Running**	1.79 (−3.6, 7.08)	3.79 (0.83, 6.72)
SIT	2.28 (−3.55, 8.1)	4.81 (0.15, 9.49)	−1.11 (−6.11, 3.93)	−2.08 (−7.29, 3.19)	−2.49 (−8.02, 3.15)	−5.04 (−13.34, 3.19)	−5.71 (−13.18, 1.71)	0.08 (−4.94, 5.08)	0.19 (−4.73, 5.16)	−1.79 (−7.08, 3.6)	**SIT**	1.98 (−2.84, 6.83)
Walking	0.29 (−3.39, 3.98)	2.82 (1.5, 4.13)	−3.1 (−5.29,−0.86)	−4.06 (−6.74,−1.36)	−4.46 (−7.79,−1.13)	−7.01 (−14.05,−0.04)	−7.7 (−13.67,−1.69)	−1.91 (−4.16, 0.32)	−1.79 (−3.84, 0.28)	−3.79 (−6.72,−0.83)	−1.98 (−6.83, 2.84)	**Walking**

AIT, aerobic interval training; CT, combined training; IHG, isometric handgrip; ILE, isometric leg extension; IWS, isometric wall squat; RT, dynamic resistance training; SIT, sSprint interval training.

and HIIT (39.44%). Comparatively, IET was significantly more effective at reducing SBP than AET (WMD: −3.86 mm Hg, 95% CI 1.19 to 6.54), HIIT (WMD: −3.95 mm Hg, 95% CI 0.93 to 7.03) and RT (WMD: −3.68 mm Hg, 95% CI 0.71 to 6.66). There were no other significant differences between primary exercise modes for SBP. In agreement with the pairwise meta-analysis, the NMA meta-regression demonstrated a significant moderator effect of baseline SBP across the exercise modes. Specifically, a single unit increase in mean baseline control group SBP increased the mean intervention change by 0.10 mm Hg (95% CI 0.05 to 0.15). A sensitivity analysis was run excluding a total of three trials with a residual deviance >2 (Figure S10). The effect size of CT was lower in the sensitivity analysis, thereby lowering its place in the Bayesian rankings compared with the primary analysis.

The secondary exercise mode SBP NMA included 282 two-arm studies, 21 multiarm trials and 21 direct comparisons. The order of effectiveness based on SUCRA values were IET IWS (90.4%), ILE (84.7%), IHG (73.1%), cycling (69.9%), running (66.1%), CT (57.6%), SIT (43.3%), other aerobic (40.1%), RT (38.2%), AIT (18.3%) and walking (17.4%). Comparatively, IWS, ILE, IHG, CT, cycling and running were all significantly more effective than walking. IWS, IHG and cycling were also significantly more effective than AIT. There were no other significant SBP differences between secondary exercise modes.

The primary exercise mode DBP NMA included 296 two-arm studies, 24 multiarm trials and 11 direct comparisons. The order of effectiveness based on SUCRA values (Figure S6) were IET (89.0%), RT (67.6%), HIIT (51.5%), CT (46.7%) and AET (45.1%). Comparatively, there were no statistically significant differences between the primary exercise modes for DBP. In agreement with the pairwise meta-analysis, the NMA meta-regression demonstrated a significant moderator effect of baseline DBP across the exercise modes. Specifically, a single unit increase in mean baseline control group DBP increased the mean intervention change by 0.06 mm Hg (95% CI 0.01 to 0.12). A sensitivity analysis was run excluding a total of five trials with a residual deviance>2 (Figure S11). The effect size of CT improved while HIIT decreased in the sensitivity analysis, thereby increasing the place of CT and lowering HIIT in the Bayesian rankings compared with the primary analysis.

The secondary exercise mode DBP NMA included 274 two-arm studies, 21 multiarm trials and 21 direct comparisons. The order of effectiveness based on SUCRA values (Figure S7) were running (91.3%), IWS (86.1%), IHG (57.1%), ILE (56.2%), cycling (54.3%), SIT (54.2%), RT (52.1%), AIT (48.1%), other aerobic (46.9%), CT (38.0%) and walking (14.7%). Comparatively, IWS, RT, running, cycling and other aerobic were all significantly more effective than walking. Running was also significantly more effective than CT, cycling, other aerobic and RT. There were no other significant DBP differences between secondary exercise modes.

DISCUSSION

In this systematic review and NMA, we analysed all relevant RCT data, involving 270 trials and 15 827 participants, to establish optimal exercise prescription practices in the management of resting arterial blood pressure (see figure 6). Pairwise analyses demonstrated a significant reduction in resting SBP and DBP following all exercise modes except AIT. All modes demonstrated substantially larger reductions in hypertensive cohorts than those with normal baseline blood pressure. As shown by the primary NMA, the rank order of effectiveness based on SUCRA values for SBP were IET ranked highest followed by CT, RT, AET and HIIT. IET was also highest ranked in the DBP NMA, followed by RT, HIIT, CT and AET. NMA of the secondary exercise submodes for SBP found IWS to be the most effective, followed by ILE, IHG, cycling, running, CT, SIT, other aerobic, RT, AIT and finally, walking. The DBP secondary NMA found running to be the most effective submode, followed by IWS, IHG, ILE, cycling, SIT, RT, AIT, other aerobic, CT and walking.

To our knowledge, only two previous large-scale meta-analyses of similar proportion have been performed.[21 22] However, the present study is the first to incorporate HIIT as a novel exercise mode, as well as provide advanced submode analyses of walking, cycling, running, SIT, AIT, IHG, ILE and IWS for the purpose of exercise prescription optimisation. Cornelissen *et al*[21] similarly reported IET to be the most effective exercise mode, but largely differed in magnitude for all other mode analyses, which is probably attributable to the substantial number of newer trials included in the present analysis. This is supported by the more recent Naci *et al*[22] NMA, which did not assess DBP, but showed more homogeneous AET, RT and CT SBP changes than in the present work. Given the emphasis placed on the Cornelissen and Smart[21] study in both the ESC/ESH[5] and American College of Cardiology/American Heart Association (ACC/AHA)[4] blood pressure management guidelines, the findings of the present study, combined with that of Naci *et al*,[22] suggest the need for an exercise recommendation guideline update.

A previous meta-review from Hanssen *et al*[44] sought to identify optimal personalised exercise prescription practices in the prevention and treatment of hypertension by indirectly comparing meta-analysis data from varying exercise modes. Differentially, our work applied a more direct approach in statistically comparing all individual RCTs. As such, our differences in findings, particularly for IET, may be in part attributed to the inevitable reliance of Hanssen *et al*[44] on older meta-analysis data to summarise the current effectiveness of IET,[45–47] as well as the inherent limitations of indirect meta-analytic comparisons. In particular, this previous umbrella review showed the inequitable over-representation of AET and RT meta-analysis research, concurrent with the under-representation of IET, CT and HIIT meta-analysis work, resulting in dependence on inadequately powered and dated systematic review and meta-analysis data to draw comparative conclusions.[44] As our analysis sourced the data directly from each RCT, this limiting gap between the dissemination of RCT data and its eventual transfer into published meta-analysis research was not present in our work.

Importantly, this updated analysis now provides large-scale data establishing CT as an effective exercise mode in reducing blood pressure, a mode which was previously considered inconclusive due to insufficient evidence.[21] Naci *et al*[22] previously reported similar SBP changes, but without any DBP data to support, while Hanssen *et al*[44] also provided support for CT but could only make limited comparative inferences on the basis of a single meta-analysis.[48] While the reductions observed from CT ostensibly appear somewhat comparable to those of IET, our novel analysis demonstrates that this magnitude of SBP reduction following CT is predominantly moderated by the greater prevalence of hypertensive populations included within the analysis. Indeed, the magnitude of change is underwhelming in those studies of normal blood pressure and prehypertensive cohorts, and the NMA SBP sensitivity analysis revealed the fragile nature of this body of data. Separately, and conversely to previous reports,[21] RT now appears comparable to AET in reducing resting blood pressure. However, it should be noted that the effectiveness of AET seems dependent on the submode

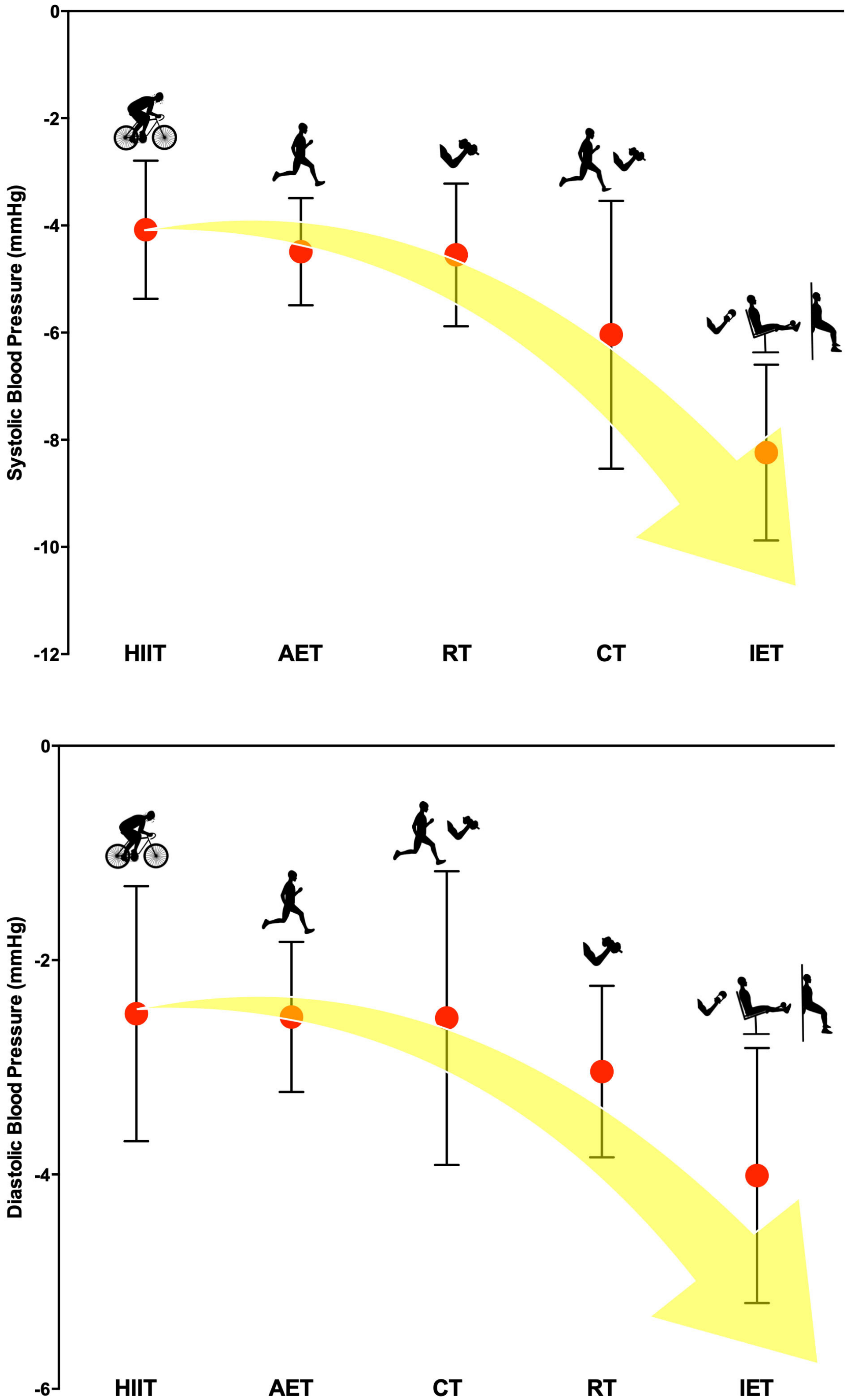

Figure 6 Central illustration. AET, aerobic exercise training; CT, combined training; HIIT, high-intensity interval training; IET, isometric exercise training; RT, dynamic resistance training.

performed, with cycling and running significantly more effective than walking AET. Our meta-regression analyses also reported the tendency for a greater SBP reduction with lower weekly training frequency in AET. Considering the interstudy differences in research protocols, the reason for this finding is unclear, but may provide loose support for the application of AET at a lower (eg, 3 times per week) frequency as opposed to extensive weekly volumes (≥5 times per week).

As a novel intervention, HIIT produced clinically relevant reductions in both SBP and DBP but ranked as the least effective among all primary modes for SBP. Secondary submode analyses (both pairwise and NMA) reveal the overarching SBP reductions to be primarily driven by SIT (low volume, maximal intensity intervals), while AIT (4×4 min intervals) failed to reach statistical significance for either SBP or DBP. This finding, combined with the comparative inferiority of walking against running and cycling AET, appears to highlight the need for higher intensity training to produce the greatest blood pressure reductions.

Similarly to IET, HIIT has recently generated substantial research interest due to its time-efficient and convenient nature, suggesting, although not without some disagreement,[49] the potential for increased adoption and adherence, with both modes having promising future clinical utility.[50–54] However, the outcomes of this analysis support our previous work,[24] which concluded that IET was the superior antihypertensive exercise mode. While IET may still require larger-scale longitudinal RCTs,[51 55] its clinical implementation as the primary recommended exercise mode in managing blood pressure in normotensive, prehypertensive and hypertensive individuals is supported by the present results. Importantly, the previous work of Cornelissen and Smart[21] included only four IET trials in 2013. Since then, a number of IET trials and subsequent meta-analyses over the previous decade have been published,[24 45 56–58] with the present study including 19 RCTs. Subsequently, the confidence interval of this finding has substantially narrowed,[59] providing more accurate SBP and DBP effect sizes of 8.2 and 4.0 mm Hg, respectively, which is comparable to standard-dose antihypertensive monotherapy.[60 61]

Of interest, the NMA findings highlight the IWS as more effective than the traditionally employed IHG. Despite the support of this analysis for IET, a degree of caution when interpreting these findings is advised given the current disparity in the quantity of trials analysed.[56] As seen in figure 5, the NMA included no direct comparative IET data. Previous trials that did not meet the inclusion criteria of this analysis have indeed shown conflicting results regarding the comparative effectiveness of IET against current exercise guidelines,[62 63] which requires consideration when interpreting these findings.

Limitations

Several limitations of this study should be acknowledged. Although only RCTs were included in this analysis, our TESTEX risk of bias assessment demonstrated several limitations consistent across the exercise training literature, including poor control group activity monitoring, missing intention-to-treat analyses and participant and investigator awareness on group allocation. Furthermore, with such a large analysis, we inevitably included trials of varying participant populations, statistical and methodological processes and exercise intervention specifics. As a likely consequence of this interstudy variability, we found significant heterogeneity for the majority of analyses. Additionally, we also found significant publication bias for overall AET SBP and DBP and IET DBP. Some of the more novel exercise modes, such as SIT, AIT, ILE and IWS involved an analysis of comparatively fewer RCTs than that of the more established modes such as AET and RT. As a result, these submodes could not be stratified and analysed by baseline blood pressure status. Finally, the majority of RCTs included in this analysis set a priori minimum attendance thresholds for inclusion in their analysis (eg, >80% of sessions completed). Therefore, our training compliance moderator analysis is, by default, not inclusive of low attendance rates, and these findings should be interpreted only in the context of assessing a compliance moderator effect among those individuals who are already adhering.

Conclusion

Aerobic exercise training, dynamic resistance training, combined training, high-intensity interval training and isometric exercise training are all significantly effective in reducing resting SBP and DBP. Comparatively, isometric exercise training remains the most effective mode. The findings of this analysis should inform future guideline recommendations.

Correction notice This article has been corrected since it published Online First. The article type has been changed to systematic review.

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