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

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What is already known?

- The role of exercise training as an effective non-pharmacological anti-hypertensive intervention is generally well-established.
- Traditional aerobic exercise training remains the primarily recommended exercise approach for the management of 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 evidences 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. Importantly, 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 in the prevention and treatment of arterial hypertension.

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 anti-hypertensive 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 systolic blood pressure (sBP) and/or diastolic (dBP) reductions following an exercise intervention ≥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/-2.53mmHg, P<0.001), dynamic resistance training (-4.55/-3.04mmHg, P<0.001), combined training (-6.04/-2.54mmHg, P<0.001), high intensity interval training (-4.08/-2.50mmHg, P<0.001) and isometric exercise training (-8.24/-4.00mmHg, P<0.001). As evidenced 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 sub-modes 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.

Introduction

Hypertension is a leading modifiable risk factor for morbidity and mortality [1–3]. Whilst differences in diagnostic cut-offs 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 anti-hypertensive 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 likely 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 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" (supplementary file, 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 was extracted via Microsoft Excel. A third reviewer (MG) independently assessed and verified all data extraction. Baseline and post-intervention mean and standard deviation (SD) sBP and dBP data were initially extracted due 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 post-intervention values. Following the Cochrane Handbook for Systematic Reviews of Interventions (Chapter 6) [33], we aimed to calculate SD change from standard errors, 95% confidence intervals, 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 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 post intervention 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 exclusion reason).

For consistency, the exercise protocol/intensity of each included paper was screened against the 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 sub-groups, allowing for the analysis of Walking, Running and Cycling as AET sub-groups, Sprint Interval Training (SIT) and Aerobic Interval Training (AIT) as HIIT sub-groups, and Isometric Handgrip (IHG), Isometric Leg Extension (ILE) and Isometric Wall Squat (IWS) as IET sub-groups. IET programmes commonly employ protocols of 4 x 2-minute contractions, separated by 1–4-minute rest intervals, performed 3x per week. IHG is often prescribed at 30% maximum voluntary contraction, while IWS and ILE protocols are typically performed at 95% peak heart rate. This review defines HIIT as 'episodic short bouts of high intensity exercise separated by short periods of recovery at a lower intensity' [35]. As sub-groups of HIIT, sprint interval training (SIT) was defined as an 'all-out' maximal, low-volume protocol, whereas aerobic interval training (AIT) consisted of 4 x 4-minute protocols of a lower intensity.

For baseline blood pressure stratified analyses, all included studies were categorised as normotension (NTN), pre-hypertension (pre-HTN) or hypertension (HTN) based on the baseline sBP and dBP of both the intervention and control group. In accordance with the ESC/ESH guidelines [5], the sBP and dBP status sub-groups were categorised as NTN, pre-HTN or HTN with values equal to <130/85mmHg, 130-139/85-89mmHg or >140/90mmHg 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 was 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 via consensus.

Statistical analysis

The pairwise meta-analyses were performed using Comprehensive Meta-Analysis (Comprehensive Meta-Analysis Version 3, Biostat, Englewood, NJ, 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 dichotomized by baseline blood pressure categorisation 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 inter-study 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 dependant on the presence of heterogeneity, with random effects analysis applied when interstudy variability is confirmed through significant heterogeneity. The results of the pooled analysis was 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 utilises R packages 'gemtc' and 'BUGSnet' for Bayesian statistical calculations. This analysis runs Markov chain Monte Carlo (MCMC) simulations with 4 chains and a total of 25,000 iterations (burn-in period of 5,000). Convergence of the model was tested via the Gelman-Rubin convergence assessment [40]. Based on pre-established inter-study 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 (UME) inconsistency models were produced. Any studies with large residual deviance (>2) were planned for further exploration 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 sub-group categorisation (Walking, Running, Cycling, RT, CT, SIT, AIT, IHG, ILE, IWS). As there were 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 is 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 sub-mode, 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.

Results

Figure 1 details the PRISMA systematic review flowchart. The initial systematic search identified 14,553 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 15,827 (7632 controls) participants. The analysis involved 358 effect sizes, of which included 182 AET (89 walking, 28 cycling, 21 running and 44 'Other' AET), 57 RT, 46 CT, 49 HIIT (7 SIT and 13 AIT) and 24 IET (17 IHG, 4 IWS, 3 ILE).

The full TESTEX risk of bias assessment scoring can be found in 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 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 confidence intervals following the omission of useful data (see 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 CMA '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 to the control group. There was a significant reduction in sBP following all modes of AET, with an overall reduction of 4.49mmHg (95% CI = 3.5-5.5, Z= 8.8, P_{random}<0.001), 2.85mmHg for walking, 6.88mmHg for cycling and 6.83mmHg for running. The post-hoc Egger's test was significant for overall AET sBP publication bias (Figure S1). There were significant reductions in sBP following RT by 4.55mmHg (95% CI = 3.2-5.9, Z= 6.6, P_{random}<0.001), and CT by 6.04mmHg (95% CI = 3.2-8.9, Z= 4.1, P_{random}<0.001). While there were significant sBP reductions following overall HIIT by 4.08mmHg (95% CI = 2.6-5.5, Z= 5.5, P_{random}<0.001) and SIT by 5.26mmHg, AIT did not significantly change. All IET modes produced significant reductions in sBP, with an overall reduction of 8.24mmHg (95% CI =

6.5-10.0, Z= 9.0, P_{random}<0.001), 7.10mmHg for IHG, 10.05mmHg ILE and 10.47mmHg for IWS.

Figure 3 displays the overall dBP reductions following each exercise mode compared to the control group. There was a significant reduction in dBP following all modes of AET, with an overall reduction of 2.53mmHg (95% CI = 1.8-3.2, Z= 7.3, P_{random}<0.001), 1.44mmHg for walking, 3.20mmHg for cycling and 5.67mmHg for running. The post-hoc Egger's test was significant for overall AET dBP publication bias (Figure S2). There were significant reductions in dBP following RT by 3.04mmHg (95% CI = 2.2-3.9, Z= 6.9, P_{random}<0.001), and CT by 2.54mmHg (95% CI = 1.1-4.0, Z= 3.4, P_{random}=0.001). While there were significant dBP reductions following overall HIIT by 2.50mmHg (95% CI = 1.2-3.8, Z= 3.8, P_{random}<0.001) and SIT by 3.29mmHg (95% CI = 0.1-6.5, 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 = 2.7-5.3, Z= 6.0, P_{random}<0.001), 3.46mmHg for IHG, 4.23 ILE and 5.33 for IWS. The post-hoc Egger's test was significant for overall IET dBP publication bias (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 pre-hypertension group analysis 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 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 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, 2, 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 (Tables S5, S6, S11 and S12), inconsistency tests with node-splitting models (Tables S7, S8, S13 and S14) and the deviance report plots (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 multi-arm 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%) and HIIT (39.44%). Comparatively, IET was significantly more effective at reducing sBP than AET (WMD: -3.86mmHg, 95% CI= 1.19-6.54), HIIT (WMD: -3.95mmHg, 95%CI= 0.93-7.03) and RT (WMD: -3.68mmHg, 95% CI= 0.71-6.66). 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 0.10mmHg (95% CI= 0.05-0.15). A sensitivity analysis was run excluding a total of 3 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 from the primary analysis.

The secondary exercise mode sBP NMA included 282 two-arm studies, 21 multi-arm 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 multi-arm 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 0.06mmHg (95% CI= 0.01-0.12). A sensitivity analysis was run excluding a total of 5 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 from the primary analysis.

The secondary exercise mode dBP NMA included 274 two-arm studies, 21 multi-arm 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. 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 evidenced 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 sub-modes for sBP found IWS as the most effective, followed by ILE, IHG, Cycling, Running, CT, SIT, Other Aerobic, RT, AIT and finally, Walking. The dBP secondary NMA found running as the most effective sub-mode, 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 sub-mode 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 likely 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 evidenced more homogenous AET, RT and CT sBP changes to the present work. Given the emphasis placed on the Cornelissen & Smart [21] study in both the ESC/ESH [5] and 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 that of IET, may be in part attributed to Hanssen et al's [44] inevitable reliance 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 evidenced the inequitable overrepresentation of AET and RT meta-analysis research, concurrent to the underrepresentation of IET, CT and HIIT meta-analysis work, resulting in the 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 that 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 pre-hypertensive cohorts, and the NMA sBP sensitivity analysis revealed the fragile nature of this body of data. Separately, and converse to previous reports [21], RT now appears comparable to that of AET in reducing resting blood pressure. However, it should be noted that the effectiveness of AET seems dependent on the sub-mode performed, with cycling and running significantly more effective than that of walking AET. Our meta-regression analyses also reported the tendency for a greater sBP reduction with lower weekly training frequency in AET. Considering the inter-study differences in research protocols, the reason for this finding is unclear, but may provide loose support for the application of AET at a lower (e.g. 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 amongst all primary modes for sBP. Secondary sub-mode analyses (both pairwise and NMA) reveal the overarching sBP reductions to be primarily driven by SIT (low volume, maximal intensity intervals), while AIT (4 x 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

necessity of higher intensity training in producing the greatest BP reductions. Similar to IET, HIIT has recently generated substantial research interest due to its time-efficient and convenient nature, postulating, albeit not without confliction [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 conclude IET as the superior anti-hypertensive 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, pre-hypertensive and hypertensive individuals is supported by the present results. Importantly, the previous work of Cornelissen & Smart [21] included only 4 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 4.0mmHg respectively, which is comparable to standard dose anti-hypertensive 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

There are several limitations that should be acknowledged regarding the present results. 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 inter-study 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 sub-modes could not be stratified and analysed by baseline BP status. Finally, the majority of RCTs included in this analysis set a-priori minimum attendance thresholds for inclusion in their analysis (e.g. >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 amongst those that 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.

Declarations

Ethics approval and consent to participate: Not applicable.

Contributorship: JE and JO'D contributed to the conception and design of the study. JE and JO'D contributed to the development of the search strategy. JE and JO'D conducted the systematic review. JE, AD, MG and OA completed the acquisition of data. JE, NC and JO'D performed the data analysis. JE and JO'D were the principal writers of the manuscript. All authors contributed to the drafting and revision of the final article. All authors approved the final submitted version of the manuscript.

Consent for publication: Not applicable.

Availability of data and materials: Data may be available on request to the corresponding author.

Competing interests: All authors declare that they have no conflicts of interest relevant to the content of this review.

References

1   Lim SS, Vos T, Flaxman AD, *et al.* A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990-2010: A systematic analysis for the Global Burden of Disease Study 2010. *The Lancet* 2012;**380**:2224–60. doi:10.1016/S0140-6736(12)61766-8

2   Abbafati C, Abbas KM, Abbasi-Kangevari M, *et al.* Global burden of 87 risk factors in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. *The Lancet* 2020;**396**:1223–49. doi:10.1016/S0140-6736(20)30752-2/ATTACHMENT/A38D7E68-5900-4997-AA22-E0B9885F4B45/MMC2B.PDF

3   Yusuf S, Joseph P, Rangarajan S, *et al.* Modifiable risk factors, cardiovascular disease, and mortality in 155 722 individuals from 21 high-income, middle-income, and low-income countries (PURE): a prospective cohort study. *Lancet* 2020;**395**:795–808. doi:10.1016/S0140-6736(19)32008-2

4   Whelton PK, Carey RM, Aronow WS, *et al.* 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task F. In: *Journal of the American Society of Hypertension*. Elsevier 2018. 579.e1-579.e73. doi:10.1016/j.jash.2018.06.010

5   Williams B, Mancia G, Spiering W, *et al.* 2018 ESC/ESH Guidelines for themanagement of arterial hypertension. Eur Heart J. 2018;**39**:3021–104. doi:10.1093/eurheartj/ehy339

6   Bundy JD, Li C, Stuchlik P, *et al.* Systolic blood pressure reduction and risk of cardiovascular disease and mortality a systematic review and network meta-analysis. *JAMA Cardiol* 2017;**2**:775–81. doi:10.1001/jamacardio.2017.1421

7   Mills KT, Stefanescu A, He J. The global epidemiology of hypertension. *Nat Rev Nephrol* 2020;**16**:223. doi:10.1038/S41581-019-0244-2

8   Zhou B, Carrillo-Larco RM, Danaei G, *et al.* Worldwide trends in hypertension prevalence and progress in treatment and control from 1990 to 2019: a pooled analysis of 1201 population-representative studies with 104 million participants. *The Lancet* 2021;**398**:957–80. doi:10.1016/S0140-6736(21)01330-1/ATTACHMENT/F57BA96E-DFA3-4B0C-9FD5-188725B928ED/MMC1.PDF

9   Adler A, Agodoa L, Algra A, *et al.* Pharmacological blood pressure lowering for primary and secondary prevention of cardiovascular disease across different levels of blood pressure: an individual participant-level data meta-analysis. *The Lancet* 2021;**397**:1625–36. doi:10.1016/S0140-6736(21)00590-0/ATTACHMENT/5AC3AA1C-33CE-4399-954E-A4FC00AC2CED/MMC1.PDF

10   Vrijens B, Vincze G, Kristanto P, *et al.* Adherence to prescribed antihypertensive drug treatments: Longitudinal study of electronically compiled dosing histories. *BMJ* 2008;**336**:1114–7. doi:10.1136/bmj.39553.670231.25

11   Choudhry NK, Kronish IM, Vongpatanasin W, *et al.* Medication Adherence and Blood Pressure Control: A Scientific Statement From the American Heart Association. *Hypertension* 2022;**79**:E1–14. doi:10.1161/HYP.0000000000000203

12   Burnier M, Egan BM. Adherence in Hypertension. *Circ Res* 2019;**124**:1124–40. doi:10.1161/CIRCRESAHA.118.313220

13   Cohen JS. Adverse Drug Effects, Compliance, and Initial Doses of Antihypertensive Drugs Recommended by the Joint National Committee vs the Physicians' Desk Reference. *Arch Intern Med* 2001;**161**:880–5. doi:10.1001/ARCHINTE.161.6.880

14   Wang G, Grosse SD, Schooley MW. Conducting Research on the Economics of Hypertension to Improve Cardiovascular Health. Am J Prev Med. 2017;**53**:S115–7. doi:10.1016/j.amepre.2017.08.005

15   Cernota M, Kroeber ES, Demeke T, *et al.* Non-pharmacological interventions to achieve blood pressure control in African patients: a systematic review. *BMJ Open* 2022;**12**:e048079. doi:10.1136/BMJOPEN-2020-048079

16   Valenzuela PL, Carrera-Bastos P, Gálvez BG, *et al.* Lifestyle interventions for the prevention and treatment of hypertension. *Nature Reviews Cardiology 2020 18:4* 2020;**18**:251–75. doi:10.1038/s41569-020-00437-9

17   Lear SA, Hu W, Rangarajan S, *et al.* The effect of physical activity on mortality and cardiovascular disease in 130 000 people from 17 high-income, middle-income, and low-income countries: the PURE study. *The Lancet* 2017;**390**:2643–54. doi:10.1016/S0140-6736(17)31634-3

18   Leitzmann MF, Park Y, Blair A, *et al.* Physical Activity Recommendations and Decreased Risk of Mortality. *Arch Intern Med* 2007;**167**:2453–60. doi:10.1001/ARCHINTE.167.22.2453

19   Wang Y, Nie J, Ferrari G, *et al.* Association of Physical Activity Intensity With Mortality: A National Cohort Study of 403 681 US Adults. *JAMA Intern Med* 2021;**181**:203–11. doi:10.1001/JAMAINTERNMED.2020.6331

20   Blond K, Brinkløv CF, Ried-Larsen M, *et al.* Association of high amounts of physical activity with mortality risk: a systematic review and meta-analysis. *Br J Sports Med* 2020;**54**:1195–201. doi:10.1136/BJSPORTS-2018-100393

21   Cornelissen VA, Smart NA. Exercise training for blood pressure: a systematic review and meta-analysis. J Am Heart Assoc. 2013;**2**. doi:10.1161/JAHA.112.004473

22   Naci H, Salcher-Konrad M, Dias S, *et al.* How does exercise treatment compare with antihypertensive medications? A network meta-analysis of 391 randomised controlled trials assessing exercise and medication effects on systolic blood pressure. Br J Sports Med. 2019;**53**:859–69. doi:10.1136/bjsports-2018-099921

23 Whelton SP, Chin A, Xin X, *et al.* Effect of aerobic exercise on blood pressure: A meta-analysis of randomized, controlled trials. *Ann Intern Med* 2002;**136**:493–503. doi:10.7326/0003-4819-136-7-200204020-00006

24 Edwards J, de Caux A, Donaldson J, *et al.* Isometric exercise versus high-intensity interval training for the management of blood pressure: a systematic review and meta-analysis. *Br J Sports Med* 2022;**56**:506–14. doi:10.1136/bjsports-2021-104642

25 Cornelissen VA, Fagard RH, Coeckelberghs E, *et al.* Impact of Resistance Training on Blood Pressure and Other Cardiovascular Risk Factors. *Hypertension* 2011;**58**:950–8. doi:10.1161/HYPERTENSIONAHA.111.177071

26 Lee LL, Mulvaney CA, Wong YKY, *et al.* Walking for hypertension. *Cochrane Database of Systematic Reviews* 2021;**2021**. doi:10.1002/14651858.CD008823.PUB2/MEDIA/CDSR/CD008823/IMAGE_N/NCD 008823-CMP-008.02.SVG

27 Costa EC, Hay JL, Kehler DS, *et al.* Effects of High-Intensity Interval Training Versus Moderate-Intensity Continuous Training On Blood Pressure in Adults with Pre- to Established Hypertension: A Systematic Review and Meta-Analysis of Randomized Trials. Sports Medicine. 2018;**48**:2127–42. doi:10.1007/s40279-018-0944-y

28 Ashton RE, Tew GA, Aning JJ, *et al.* Effects of short-term, medium-term and long-term resistance exercise training on cardiometabolic health outcomes in adults: systematic review with meta-analysis. *Br J Sports Med* 2020;**54**:341–8. doi:10.1136/BJSPORTS-2017-098970

29 Xi H, He Y, Niu Y, *et al.* Effect of combined aerobic and resistance exercise on blood pressure in postmenopausal women: A systematic review and meta-analysis of randomized controlled trials. *Exp Gerontol* 2021;**155**. doi:10.1016/J.EXGER.2021.111560

30 Schroeder EC, Franke WD, Sharp RL, *et al.* Comparative effectiveness of aerobic, resistance, and combined training on cardiovascular disease risk factors: A randomized controlled trial. *PLoS One* 2019;**14**. doi:10.1371/JOURNAL.PONE.0210292

31 Page MJ, McKenzie JE, Bossuyt PM, *et al.* The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 2021;**372**. doi:10.1136/BMJ.N71

32 Hutton B, Salanti G, Caldwell DM, *et al.* The PRISMA Extension Statement for Reporting of Systematic Reviews Incorporating Network Meta-analyses of Health Care Interventions: Checklist and Explanations. *https://doi.org/107326/M14-2385* 2015;**162**:777–84. doi:10.7326/M14-2385

33 Higgins JPT, Li T, Deeks JJ. Choosing effect measures and computing estimates of effect. *Cochrane Handbook for Systematic Reviews of Interventions* 2019;:143–76. doi:10.1002/9781119536604.CH6

34 Hansen D, Dendale P, Coninx K, *et al.* The European Association of Preventive Cardiology Exercise Prescription in Everyday Practice and Rehabilitative Training (EXPERT) tool: A digital training and decision support system for optimized exercise

prescription in cardiovascular disease. Concept, definitions and construction methodology. *Eur J Prev Cardiol* 2017;**24**:1017–31. doi:10.1177/2047487317702042

35   Campbell WW, Kraus WE, Powell KE, *et al.* High-Intensity Interval Training for Cardiometabolic Disease Prevention. *Med Sci Sports Exerc* 2019;**51**:1220. doi:10.1249/MSS.0000000000001934

36   Smart NA, Waldron M, Ismail H, *et al.* Validation of a new tool for the assessment of study quality and reporting in exercise training studies: TESTEX. *Int J Evid Based Healthc* 2015;**13**:9–18. doi:10.1097/XEB.0000000000000020

37   Huedo-Medina TB, Sánchez-Meca J, Marín-Martínez F, *et al.* Assessing heterogeneity in meta-analysis: Q statistic or I 2 Index? *Psychol Methods* 2006;**11**:193–206. doi:10.1037/1082-989X.11.2.193

38   Egger M, Smith GD, Schneider M, *et al.* Bias in meta-analysis detected by a simple, graphical test. *BMJ* 1997;**315**:629–34. doi:10.1136/BMJ.315.7109.629

39   Owen RK, Bradbury N, Xin Y, *et al.* MetaInsight: An interactive web-based tool for analyzing, interrogating, and visualizing network meta-analyses using R-shiny and netmeta. *Res Synth Methods* 2019;**10**:569. doi:10.1002/JRSM.1373

40   Brooks SP, Gelman A. General Methods for Monitoring Convergence of Iterative Simulations.

41   Dias S, Welton NJ, Sutton AJ, *et al.* Evidence synthesis for decision making 4: inconsistency in networks of evidence based on randomized controlled trials. *Med Decis Making* 2013;**33**:641–56. doi:10.1177/0272989X12455847

42   Lunn DJ, Thomas A, Best N, *et al.* WinBUGS - A Bayesian modelling framework: Concepts, structure, and extensibility. *Stat Comput* 2000;**10**:325–37. doi:10.1023/A:1008929526011/METRICS

43   Nevill CR, Cooper NJ, Sutton AJ. A multifaceted graphical display, including treatment ranking, was developed to aid interpretation of network meta-analysis. *J Clin Epidemiol* Published Online First: 2 March 2023. doi:10.1016/J.JCLINEPI.2023.02.016

44   Hanssen H, Boardman H, Deiseroth A, *et al.* Personalized exercise prescription in the prevention and treatment of arterial hypertension: a Consensus Document from the European Association of Preventive Cardiology (EAPC) and the ESC Council on Hypertension. *Eur J Prev Cardiol* Published Online First: 24 March 2021. doi:10.1093/eurjpc/zwaa141

45   Carlson DJ, Dieberg G, Hess NC, *et al.* Isometric exercise training for blood pressure management: a systematic review and meta-analysis. *Mayo Clin Proc* 2014;**89**:327-334. doi:10.1016/j.mayocp.2013.10.030

46   Kelley GA, Kelley KS. Isometric handgrip exercise and resting blood pressure: a meta-analysis of randomized controlled trials. *J Hypertens* 2010;**28**:411–8. doi:10.1097/HJH.0B013E3283357D16

47   Corso LML, Macdonald H v., Johnson BT, *et al.* Is Concurrent Training Efficacious Antihypertensive Therapy? A Meta-analysis. *Med Sci Sports Exerc* 2016;**48**:2398–406. doi:10.1249/MSS.0000000000001056

48   Goessler K, Polito M, Cornelissen VA. Effect of exercise training on the renin–angiotensin–aldosterone system in healthy individuals: a systematic review and meta-analysis. *Hypertension Research 2016 39:3* 2015;**39**:119–26. doi:10.1038/hr.2015.100

49   Ekkekakis P, Biddle SJH. Extraordinary claims in the literature on high-intensity interval training (HIIT): IV. Is HIIT associated with higher long-term exercise adherence? *Psychol Sport Exerc* 2023;**64**:102295. doi:10.1016/J.PSYCHSPORT.2022.102295

50   Batacan RB, Duncan MJ, Dalbo VJ, *et al.* Effects of high-intensity interval training on cardiometabolic health: A systematic review and meta-analysis of intervention studies. Br J Sports Med. 2017;**51**:494–503. doi:10.1136/bjsports-2015-095841

51   Millar PJ, McGowan CL, Cornelissen VA, *et al.* Evidence for the role of isometric exercise training in reducing blood pressure: Potential mechanisms and future directions. Sports Medicine. 2014;**44**:345–56. doi:10.1007/s40279-013-0118-x

52   Stensvold D, Viken H, Steinshamn SL, *et al.* Effect of exercise training for five years on all cause mortality in older adults—the Generation 100 study: randomised controlled trial. *BMJ* 2020;**371**. doi:10.1136/BMJ.M3485

53   Edwards JJ, Taylor KA, Cottam C, *et al.* Ambulatory blood pressure adaptations to high-intensity interval training: a randomized controlled study. *J Hypertens* 2021;**39**:341–8. doi:10.1097/HJH.0000000000002630

54   MacInnis MJ, Gibala MJ. Physiological adaptations to interval training and the role of exercise intensity. *J Physiol* 2017;**595**:2915–30. doi:10.1113/JP273196

55   O'Driscoll J, Edwards J, Coleman D, *et al.* One year of isometric exercise training for blood pressure management in men: a prospective randomized controlled study. *J Hypertens* 2022.

56   Edwards JJ, Wiles J, O'Driscoll J. Mechanisms for blood pressure reduction following isometric exercise training: a systematic review and meta-analysis. *J Hypertens* 2022;**Publish Ah**.

57   Inder JD, Carlson DJ, Dieberg G, *et al.* Isometric exercise training for blood pressure management: A systematic review and meta-analysis to optimize benefit. *Hypertension Research* 2016;**39**:89–94. doi:10.1038/hr.2015.111

58   López-Valenciano A, Ruiz-Pérez I, Ayala F, *et al.* Updated systematic review and meta-analysis on the role of isometric resistance training for resting blood pressure management in adults. J Hypertens. 2019;**37**:1320–33. doi:10.1097/HJH.0000000000002022

59   Sánchez-Meca J, Marín-Martínez F. Confidence intervals for the overall effect size in random-effects meta-analysis. *Psychol Methods* 2008;**13**:31–48. doi:10.1037/1082-989X.13.1.31

60   Law MR, Morris JK, Wald NJ. Use of blood pressure lowering drugs in the prevention of cardiovascular disease: Meta-analysis of 147 randomised trials in the context of expectations from prospective epidemiological studies. *BMJ (Online)* 2009;**338**:1245. doi:10.1136/bmj.b1665

61   Paz MA, De-La-Sierra A, Sáez M, *et al.* Treatment efficacy of anti-hypertensive drugs in monotherapy or combination: ATOM systematic review and meta-analysis of randomized clinical trials according to PRISMA statement. Medicine (United States). 2016;**95**. doi:10.1097/MD.0000000000004071

62   Pagonas N, Vlatsas S, Bauer F, *et al.* Aerobic versus isometric handgrip exercise in hypertension: a randomized controlled trial. *J Hypertens* 2017;**35**:2199–206. doi:10.1097/HJH.0000000000001445

63   Goessler KF, Buys R, VanderTrappen D, *et al.* A randomized controlled trial comparing home-based isometric handgrip exercise versus endurance training for blood pressure management. *Journal of the American Society of Hypertension* 2018;**12**:285–93. doi:10.1016/J.JASH.2018.01.007

Figure Legend

Figure 1: PRISMA systematic review and meta-analysis flowchart.

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

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

Figure 4: Forest plot depicting overall effects of each primary exercise mode on systolic blood pressure 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.

Figure 6: Central Illustration.

Table 1. Comparative Network Meta-Analysis for the sBP 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

Note: Aerobic Exercise Training (AET), Dynamic Resistance Training (RT), Combined Training (CT), High-intensity Interval Training (HIIT) and Isometric Exercise Training (IET).

Table 2. Comparative Network Meta-Analysis for the sBP 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**

Note: Aerobic Interval Training (AIT), Dynamic Resistance Training (RT), Combined Training (CT), Sprint Interval Training (SIT), Isometric Handgrip (IHG), Isometric Leg Extension (ILE) and Isometric Wall Squat (IWS).