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The Influence of Concurrent Exercise Training on Baseline Blood Pressure: A Meta-Analysis

Lauren M. Lamberti
University of Connecticut - Storrs, lauren.lamberti@uconn.edu

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Lauren M. Lamberti

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A Meta-Analysis

Presented by:

Lauren M. Lamberti

Major Advisor Linda S. Pescatello
Linda S. Pescatello, PhD, FACSM

Associate Advisor
Blair T. Johnson, PhD

Associate Advisor
Paulo V. Farinatti, PhD

University of Connecticut

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Chapter 1. Introduction

1.1 Background and Significance

Cardiovascular disease (CVD) is the leading cause of death in the United States (U.S.) and a major public health concern (2, 4, 13, 15, 22, 33, 36). CVD contributes the highest health care costs of any disease category, approximately $320 billion dollars in direct ($195.6 billion) and indirect ($124.5 billion) healthcare expenses (2, 4, 13, 15, 22, 33, 36). Nearly half (49%) of all American adults have at least one risk factor for CVD (2, 13, 15, 33). Of these risk factors, hypertension is the most prevalent, costly, but modifiable (2, 4, 13, 15, 22, 33, 36).

Hypertension, defined as blood pressure (BP) levels >140 mmHg systolic and/or >90 mmHg diastolic BP, affects one in three (80 million) adults in the U.S. (2, 4, 13, 15, 22, 33). Hypertension is the most costly CVD risk factor, contributing to nearly 40% ($46.4 billion) of all CVD-related healthcare expenses (2). Compared with other CVD risk factors, hypertension is the leading cause of death for women and second leading cause of death in men in the U.S.; only smoking contributes more deaths in men (2, 13, 33). Furthermore, it is estimated that 69% of people who experience a first heart attack, 77% of first-time stroke patients, and 74% of people with chronic heart failure have hypertension (2, 4, 13, 33). In fact, people with hypertension are three to four times more likely to die from CVD and expected to live on average 5 years less than people without hypertension matched for age and sex (13, 22, 33). Overall, hypertension shortens overall life expectancy, percentage of life living CVD free, and increases the percentage of life with CVD (13, 22, 33).

Therefore, by effectively lowering BP in individuals with hypertension, these risks can be mitigated. Since 2010, the incidence of hypertension has gradually decreased from 29.9% to 26.9%, surpassing goals set by Healthy People 2020 (1). Unfortunately, this trend has plateaued, underscoring the need for cost-effective, sustainable lifestyle intervention strategies

to prevent, treat and control hypertension, one of which includes participation in regular exercise (3, 4, 10, 12, 13, 19, 30, 31, 36).

1.2 The Role of Exercise as Antihypertensive Therapy

Exercise has been recommended for its many health benefits, including lower BP. The global accessibility, low cost and few adverse side effects of exercise make it an advantageous option for use as antihypertensive therapy (14). Several meta-analyses (8, 9, 24, 26, 27, 37) and systematic reviews (17) have investigated the BP response to aerobic exercise (7, 8, 24, 27, 37) and resistance training (9, 17, 26). Whelton et al. performed a meta-analysis of 38 randomized control trials investigating the BP response to aerobic exercise training in a sample ranging from 21-79 years in age, and with overweight (25.4 $kg \cdot m^{-2}$) and prehypertension [(Systolic BP (SBP)/Diastolic BP (DBP)) 126.5 mmHg/77.0 mmHg] (38). The authors reported significant reductions in both SBP (-3.8 mmHg) and DBP (-2.6 mmHg), and these reductions were greatest in samples with hypertension (-4.9 mmHg/-3.7 mmHg) versus normal BP (-4.0 mmHg/-2.3 mmHg), following a dose-response relationship (38). Three other meta-analyses have replicated these findings regarding the antihypertensive effects of aerobic exercise (21, 25, 27) culminating in an average BP response of 5-7 mmHg following aerobic exercise among samples with hypertension.

Fewer studies and meta-analyses exist that have examined the BP response following resistance training. Cornelissen et al. performed a meta-analysis that included 28 resistance training trials (8). On average the sample was overweight (26.1 $kg \cdot m^{-2}$) with prehypertension (125.6 mmHg/74.7 mmHg) (8). Overall, BP was reduced by -3.5 mmHg SBP and -3.2 mmHg DBP in response to RT. In 2013, the same authors replicated their previous findings.(8). A meta-analysis by Kelley et al. further substantiates these findings, reporting BP reductions of -3.0 mmHg SBP and -3.0 mmHg DBP in response to resistance training, and it was speculated that these reductions would be greater in samples with hypertension (26). Last, Gordon et al. performed a systematic review of 20 aerobic exercise and resistance training studies, of which 10

reported BP outcomes. The authors reported that 30% (k=3) reported significant BP reductions following resistance training and that there is evidence that these reductions would be maximized in samples with hypertension (17). Overall, the current literature suggests that resistance training elicits BP reductions ~3 mmHg, a lesser magnitude than aerobic exercise training and potential benefits may be maximized if performed among adults with hypertension.

The American College of Sports Medicine (ACSM) (36), among other health organizations (3, 4, 10, 12, 19, 30, 31), currently recommends primarily aerobic exercise to lower BP because it elicits BP reductions of 5-7 mmHg, and resistance exercise as an adjunct modality because it lowers BP by 2-3 mmHg among adults with hypertension. Reductions in BP as modest as 5 mmHg reduces the risk of heart disease by 8% and stroke by 14%, substantiating the clinical importance of exercise as antihypertensive lifestyle therapy (4, 19). Accordingly, the current ACSM exercise prescription (ExR_x) for adults with hypertension recommends 30 minutes of moderate intensity (40-60% VO_{2max}) aerobic exercise on most days (≥5 days·week^{-1}) of the week supplemented by resistance training 2-3 days per week to lower BP (36).

1.3 What is Concurrent Exercise?

Although the BP response to aerobic exercise and resistance training has been more extensively examined, it is not well understood how the combined effects of aerobic exercise and resistance training, termed *concurrent exercise training*, may influence resting BP among adults with hypertension. Concurrent exercise training refers to an ExR_x that includes both aerobic and resistance training components performed in close proximity to each other; on the same day either performing aerobic *before* or *after* resistance training, simultaneously in a circuit training format, or on separate days otherwise known as "combined training" (11, 23, 29). Nonetheless, researchers often do not disclose the proximity of the aerobic exercise and resistance training components of the concurrent exercise training program nor the order in which they are applied. Participation in concurrent training programs allows for simultaneous improvement in cardiorespiratory fitness, muscle strength and endurance, and the cardiometabolic profile (16, 28,

29, 34). However, there are no formal recommendations for the use of concurrent exercise training as antihypertensive therapy.

1.4 Concurrent Exercise Training as Antihypertensive Therapy

To date, four meta-analyses have investigated the BP response to concurrent exercise training (5, 8, 18, 35), with mixed results. More specifically, Chudyk et al. performed a meta-analysis of 10 "combined" exercise training trials in patients with type 2 diabetes mellitus (T2DM) and prehypertension [mean (range)= 134 mmHg (129-138 mmHg)] that performed a "combined" exercise training program 2-5 sessions per week at an aerobic intensity of 35-85% heart rate maximum, for 8-24 months (5). The resistance training components varied widely among the included trials but the authors did not provide summary statistics of the concurrent exercise training intervention. (5). Overall, there was a significant reduction in SBP of ~4 mmHg (5). The authors did not report DBP values (5). Similar BP reductions were reported by Hayashino et al. who performed a meta-analysis of 14 trials in a similar population of middle-aged (~56.7 years) participants with T2DM (~6.1 years since diagnosis) (18). It should be noted that only five of the trials included samples with hypertension (~36%) (18). Hayashino et al. reported BP reductions following "combined" exercise that were of the same magnitude as those reported by previously by Chudyk et al. (-3.2 mmHg/-1.9 mmHg) in similar populations (i.e., T2DM) (5, 18).

In contrast, Cornelissen et al. conducted a meta-analysis of 14 concurrent exercise training trials in samples without chronic disease and found significant DBP [-2.2 mmHg (-3.9, -0.48)] reductions but not SBP (p>0.05) (8). Of interest, the authors reported that the BP reductions following concurrent exercise training did not differ from either aerobic (-3.5 mmHg/-2.5 mmHg) or resistance (-1.8 mmHg/-3.2 mmHg) exercise training alone (ps>0.05) (8). Pattyn et al. performed a meta-analysis of two trials to assess cardiovascular risk factors in subjects with the metabolic syndrome and reported no significant BP reductions following concurrent exercise training (35). Overall, the investigative teams of these meta-analyses found BP responses to concurrent exercise training ranging from 0 to 4 mmHg among a variety of patient populations that

did not include adults with hypertension *per se*; rather they included those with T2DM (5, 18), the metabolic syndrome (35), and healthy adults without CVD or other chronic conditions (8). Therefore, it is unclear whether the results from these meta-analyses are generalizable to populations with hypertension, and whether concurrent exercise training is efficacious antihypertensive therapy.

1.3 State of the Meta-Analytic Literature Examining Exercise and BP

Meta-analyses are often the foundation for scientific statements and clinical guidelines. As such, efforts have been made to improve the quality of meta-analytic procedures and reporting standards in documents such as Assessment of Multiple Systematic Reviews or AMSTAR and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses or PRISMA guidelines (32).

Johnson et al. investigated the methodological quality of published meta-analyses that examined the BP response to exercise (20). Overall, 33 meta-analyses were included, of which none satisfied all methodological study quality items using an augmented version of the Assessment of Multiple Systematic Reviews ($AMSTAR_{ExBP}$) with an average score of 56.0± 21.4% of items satisfied (20). The majority of the meta-analyses failed to disclose details of the search strategy, methods for trial selection, and data extraction (20). Furthermore, few trials assessed study quality of individual trials, incorporated study quality in moderator analyses or discussed in the context of major findings (20).

Similar deficiencies were observed in previous concurrent exercise training meta-analyses, satisfying an average of 70.3% quality items on the $AMSTAR_{ExBP}$ (20). Of these, 75% (k=3) failed to disclose search strategy methods, 75% failed to assess methodological study quality within the framework of their meta-analysis, and 50% (k=2) failed to fully disclose the average FIT of the concurrent exercise training intervention (6, 8, 18, 20, 35). Furthermore, only two of these meta-analyses included BP as a primary outcome (8, 18) and the lack of moderator analyses also resulted in an inability to profile individuals who may benefit the most from the

antihypertensive effects of concurrent exercise training. These departures from contemporary methodology and reporting standards may contribute to our lack of understanding of the antihypertensive effects of concurrent exercise training and potential sample and FITT features that may modulate the BP response. Additional evidence is warranted to better evaluate the potential of concurrent exercise training to lower BP and for whom concurrent exercise training is most effective.

1.4 Specific Aims and Hypotheses

Therefore, the purpose of our meta-analysis was to determine the efficacy of concurrent exercise training as antihypertensive therapy adhering to high quality, contemporary methodological standards. In addition, we sought to examine important potential moderators of the BP response to concurrent exercise training in an attempt to profile the individuals who would benefit the most for concurrent exercise training as antihypertensive therapy. The primary aims of this study are;

Specific Aim 1*:* To perform a high quality meta-analysis, adhering to contemporary methodological standards, of the existing concurrent exercise literature to determine the efficacy of concurrent exercise as antihypertensive therapy.

Hypothesis 1: Concurrent exercise training interventions will result in significant BP reductions compared to non-exercise control or comparison conditions.

Alternate Hypothesis 1: Concurrent exercise training interventions will not result in significant BP reductions compared to non-exercise control or comparison conditions.

***Specific Aim 2*:** To examine potential moderators that may modulate the BP response to concurrent exercise training.

Hypothesis 2: Study characteristics (e.g., randomization, study design), clinical characteristics (e.g., age, weight, sex), features of the concurrent exercise intervention (e.g., frequency, intensity, time, length of session, volume of exercise), study quality, and their interactions, will

explain a significant proportion of the variability in the BP response to concurrent exercise training.

Alternate Hypothesis 2: Study characteristics (e.g., randomization, study design), clinical characteristics (e.g., age, weight, sex), features of the concurrent exercise intervention (e.g., frequency, intensity, time, and type), study quality, and their interactions, will not explain a significant proportion of the variability in the BP response to concurrent exercise training.

1.5 Significance

Hypertension is the leading risk factor for CVD and a major public health concern affecting 80 million American adults (2, 13, 33). Individuals with hypertension are at disproportionate risk of developing CVD and are three to four times more likely to die from CVD than those without hypertension (13, 33). Since 2010, the incidence of hypertension has gradually decreased from 29.9% to 26.9%, surpassing national health goals set by Healthy People 2020 (1, 13). Unfortunately, this trend has reached an impasse underscoring the need for cost-effective sustainable lifestyle intervention strategies to prevent, treat and control hypertension (13, 33). In addition, hypertension contributes to over $47.5 billion in annual healthcare expenses, costs that, without intervention are expected to triple by the year 2030 (2, 13). Therefore, there is a critical need for cost-effective, sustainable lifestyle intervention strategies to lower BP (13).

The results from our project would initiate a comprehensive investigation of the available concurrent exercise training literature, promoting the expansion of the existing exercise guidelines to include concurrent exercise training as antihypertensive therapy. In addition, by identifying the optimal dose of concurrent exercise training and population characteristics for who might benefit most from concurrent exercise, clinicians can better personalize exercise regimens to lower BP, possibly enhance exercise adherence, and in turn reduce the burden of CVD in society.

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Chapter 2
The Influence of Concurrent Exercise Training on Blood Pressure: A Meta-Analysis

Address for Correspondence:

Lauren Lamberti, BS, MLS (ASCP)^{CM}

Department of Kinesiology

College of Agriculture, Health, and Natural Resources

University of Connecticut

Gampel Pavilion Room 206

2095 Hillside Rd, U-1110

Storrs, CT 06269-1110

Phone: (847)-337-3763

Email: Lauren.Lamberti@uconn.edu

2.1 ABSTRACT

Aerobic training, and to a lesser degree resistance training, are recommended to lower blood pressure (BP) among adults with hypertension. Yet, the combined influence of these exercise modalities, termed *concurrent exercise training*, on resting BP is unclear. **Purpose**: To perform a meta-analysis to determine the efficacy of concurrent training as antihypertensive therapy. **Methods**: Electronic databases were searched for trials that included: adults (>19yr); controlled concurrent training interventions; and BP measured pre- and post-intervention. Study quality was assessed with a modified Downs and Black checklist. Analyses incorporated random-effects assumptions. **Results**: 68 trials yielded 76 interventions. Subjects (n=4110) were middle-aged (55.8±14.4yr) and overweight (28.0±3.6kg·m^{-2}) with prehypertension (systolic BP [SBP]/diastolic BP [DBP] 134.6±10.9/80.7±7.5mmHg). Concurrent training was performed at moderate intensity (aerobic=55% maximal oxygen consumption; resistance=60% one-repetition maximum), 2.9±0.7d·wk^{-1} for 58.3.2±20.1min·session^{-1} for 19.7±17.8wk. Studies were of fair quality, satisfying 60.7%±9.4% of quality items. Overall, concurrent training reduced SBP (d_+=-0.32; -3.2mmHg) and DBP (d_+=-0.35; -2.5mmHg) versus control (ps<0.01). BP reductions followed a dose response pattern with the largest reductions among samples with hypertension (-5.9/-5.6mmHg, k=11, p=0.00) than prehypertension (-2.9/-3.6 mmHg) and normal BP (+2.9/-1.5mmHg). Greater BP reductions were observed when: BP was a primary outcome (SBP only, -8.4mmHg, k=5) versus not (-3.4mmHg, k=7); and trials of higher (-3.6/-4.8mmHg; k=5) than lower (-1.9/-2.3mmHg; k=13) quality (p=0.01). **Conclusions:** Concurrent training lowered BP ~3mmHg. However, the greatest BP reductions occurred among samples with hypertension (~6mmHg), when BP was a primary outcome (~8mmHg), and among higher quality trials (4-5mmHg). Concurrent training appears to be efficacious antihypertensive therapy; but due to the fair quality of this literature, randomized controlled concurrent training trials with BP as the primary outcome among samples with hypertension are warranted.

Key Words: Endurance Training, Hypertension, Resistance Training, Systematic Review

2.2 INTRODUCTION

Hypertension is the most common, costly, and preventable cardiovascular disease (CVD) risk factor, affecting one in three (80 million) American adults (30). Adults with hypertension are at disproportionate risk for developing CVD, as they are three to four times more likely to die from CVD than those without hypertension (12, 30). Since 2010, the incidence of hypertension has gradually decreased from 29.9% to 26.9%, surpassing the goal set by Healthy People 2020 (12). Unfortunately, this trend has reached a plateau underscoring the need for cost-effective, sustainable lifestyle intervention strategies to prevent, treat, and control hypertension, one of which includes regular exercise (3, 5, 11, 22, 35).

Aerobic exercise training lowers blood pressure (BP) 5-7 mmHg, while resistance training lowers BP 2-3 mmHg among adults with hypertension (35). A reduction in BP as modest as 5 mmHg reduces the risk of heart disease by 8% and stroke by 14%, substantiating the clinical importance of exercise as antihypertensive lifestyle therapy (5). Accordingly, the American College of Sports Medicine (ACSM) recommends 30 minutes of moderate intensity aerobic exercise on most days of the week supplemented by resistance training 2-3 days per week among adults with hypertension (33).

Although the ACSM recommends aerobic exercise supplemented by resistance training as antihypertensive lifestyle therapy, it is not well understood how the combined effects of aerobic exercise and resistance training, termed *concurrent exercise training*, influence resting BP among adults with hypertension. Concurrent exercise training is defined as AE and RT performed in close proximity to each other (i.e., in a single session or on separate days) (9, 15, 31, 39). Nonetheless, researchers often do not disclose the proximity of the aerobic exercise and resistance training components of the concurrent exercise training program nor the order in which they are applied. As a result, the working definition of concurrent exercise training remains loosely characterized, which may contribute to the mixed state of this literature (6, 8, 18, 32).

To date, four meta-analyses have examined the BP response to concurrent exercise training (6, 8, 18, 32), reporting SBP and DBP reductions ranging from 0 to 4 mmHg (6, 8, 18, 32). The studies included in these meta-analyses examined a variety of patient populations including those with type 2 diabetes mellitus (6, 18), the metabolic syndrome (32), and healthy adults without cardiovascular disease or other chronic conditions (4); and surprisingly they did not include adults with hypertension *per se.* Furthermore, only two of these meta-analyses examined BP as a primary outcome (8, 18); moderator analyses were rarely performed in an attempt to explain heterogeneity in the BP response; and whether the proximity or the order that the aerobic exercise and resistance training components were applied was not examined to determine if they influenced the BP response (6, 8, 18, 32).

Therefore, the purpose of our meta-analysis was to determine the efficacy of concurrent exercise training as antihypertensive therapy adhering to high quality, contemporary methodological standards. In addition, we sought to examine important potential moderators of the BP response to concurrent exercise training in an attempt to profile the individuals who would benefit the most for concurrent exercise training as antihypertensive therapy.

2.3 Methods

This meta-analysis was conducted consistent with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) standards (29).

Search Strategy and Selection Criteria

Aided by a medical librarian, multiple electronic databases (PubMed, CINAHL, Web of Science, SportDiscus, and Scopus) were systematically searched from their inception until January 31, 2015. Qualifying exercise trials included: adult populations (>19 years old); a non-exercise control comparison group; BP (systolic and/or diastolic) reported pre- and post-intervention for the concurrent exercise training and control conditions; and the features of the concurrent exercise training intervention, i.e., the Frequency, Intensity, Time, and Type principle or *FITT*. Cross-sectional studies, epidemiological study designs, weight loss trials,

pharmacologic interventions, or populations with disease other than CVD were excluded [See Appendix 5.1). Potential reports were screened (LL, HM, AB) first by title, then title and abstract, and last full-text review. A modified PRISMA flow diagram detailing the systematic search process is presented in Figure 1. The systematic search terms are available in Appendix 5.2.

Data Extraction: Coding and Reliability

Two independent coders extracted all data using a uniform coding form (Appendix 5.3). Coded variables broadly covered study characteristics, experimental design, study quality, sample clinical characteristics, and the *FITT* of the concurrent exercise training intervention. Coder reliability was high across all dimensions with a mean Cohen's κ=0.83 and Pearson's correlation r=0.87 (4, 19). Coding disagreements were resolved through discussion with a third independent party (HVM, LSP). Study quality was assessed with a modified version of the Downs and Black checklist gauged as percentage of total items satisfied (7, 10). Details of the modified version of the Downs and Black checklist are available in Appendix 5.4.

Effect Size Calculations

The standardized mean difference effect size (d) was used to quantify the effectiveness of concurrent exercise training as antihypertensive therapy; defined as the difference in mean BP values between the concurrent training and control groups divided by the pooled pretest standard deviation, correcting for small sample size bias and baseline differences (1, 4, 19). Due to potential confounding of the "active content" control group on the comparison between concurrent exercise training versus control groups (14), within-group effect sizes were also independently calculated for the concurrent exercise training and control groups; defined as the difference between the mean BP values post- minus pre-intervention divided by the pre-intervention standard deviation (1, 4, 19, 23). Negative d values indicated greater BP reductions relative to baseline or to the control group. Multiple effect sizes were calculated to represent each group for trials that included ≥1 concurrent exercise training interventions (e.g., high versus low intensity concurrent exercise training) (1, 4, 19). Sensitivity analyses were performed

to confirm dependence did not influence the effect sizes calculated for the included trials (1, 4, 19). Equivalent BP change in mmHg is provided as a supplement to the observed *d* for clinical interpretation.

The homogeneity statistic (*Q*) was calculated to estimate whether the degree of similarity in the observed effect sizes in our sample was significant (4, 19, 21). The *Q* statistic was further converted into a standardized measure of homogeneity as the I^2 statistic and corresponding confidence interval (95%CI) reported from 0-100%, to gauge the amount of heterogeneity in the included sample (4, 19, 21). As the value I^2 approaches 100%, homogeneity is less likely and heterogeneity is more likely (i.e., the variability in the effect size is due to more than sampling error alone) (4, 19, 21). A *CI* for I^2 that does not include 0% indicates that the hypothesis of homogeneity is rejected, and an inference of heterogeneity is justified (4, 19, 21).

Publication Bias

We assessed potential publication bias graphically using funnel plots, plotting the standardized mean effect size contrasted to the inverse standard error, while observing for asymmetry and the presence of outliers (2, 4, 13, 20). Suspected asymmetry in the funnel plots was confirmed with Begg and Eggers test for asymmetry and revealed evidence of potential publication bias amongst the included trials (2, 13). Two effect sizes from the same study, one for SBP and one for DBP, were determined to be outliers (i.e., more than three standard deviations larger than the mean, given that the effect size is negative); to reduce their influence on results, they were windsorized to be the same magnitude as the next smallest SBP and DBP effect sizes (16). Funnel plots for the within-group effect size distributions for SBP and DBP appear in Figure 2 without windsorization.

Moderator Analyses

In the presence of significant heterogeneity, moderator analyses were used to explain variability in *d*s for SBP and DBP, using weighted regression models with maximum likelihood estimation; the weights were the inverse random-effects variance for each *d* (4, 19, 24). All

interaction terms were generated with bivariate moderators and tested for significance (4, 19). The moving constant technique was applied to estimate the magnitude of weighted mean effect sizes ($\hat{d}_+$) and their *CIs* at different levels of interest for individual moderators in the model while statistically controlling the influence of other moderators (24). Windsorized within group effect sizes (post- to pre- intervention) for the concurrent exercise training and non-exercise control or comparison groups separately were used in moderator analyses (16). Analyses were performed in Stata version 13 (College Station, TX) with macros for meta-analysis that incorporated random-effects assumptions (4, 19, 28, 37). Statistics are presented as mean ± standard deviation unless otherwise noted. Significance was set at $p< 0.05$.

2.4 Results

Sample Characteristics

In total, 68 trials and 76 interventions qualified for analysis. Of the included trials, 33% (k=25) of included trials used an "active content" control comparison (14), while the remaining trials (67%, k=51) used a non-exercise control group (14). Furthermore, 45 trials reported samples being "healthy", while the remaining trials (k=31) reported populations with chronic diseases and health conditions including: type 2 diabetes (k=13); CVD (k=3); the metabolic syndrome (k=3); chronic kidney disease (k=3); or a combination of chronic diseases and health conditions (k=9). Sample baseline characteristics did not differ between the concurrent exercise training intervention and control comparison groups (p>0.05) (Table 1). Overall, the included trials satisfying 60.7 ± 9.4% of the total items on the modified Downs and Black methodological quality checklist (7, 10, 25), indicating the overall our sample of trials was of fair quality.

Features of the Concurrent Exercise Training Interventions

Briefly, the average concurrent exercise training intervention was performed 2.9±0.7 days·week^{-1} at moderate intensity (aerobic exercise 55% maximal oxygen consumption; resistance training 60% one-repetition maximum), 58.3±20.1 minutes·session^{-1}, for 19.7±17.8 weeks (Table 2). A majority of the concurrent exercise training trials interventions failed to report

the order and proximity of aerobic exercise and resistance training components of the concurrent exercise training intervention (57.9%, *k*=44). Of those that disclosed these details, 7.9% (*k*=6) of the trials performed AE and RT on separate days (i.e., "combined training"); while the remainder of the trials performed both modalities on the same day either performing: a circuit training format (6.6%, *k*=5); aerobic exercise first (15.8%, *k*=12); or resistance training first (11.8%, *k*=9). The majority of the concurrent exercise training interventions were supervised (64.5%, *k*=49) versus unsupervised (2.6%, *k*=2). Seven trials (9.2%) incorporated a combination of both supervised and unsupervised exercise sessions, while 18 trials (23.4%) failed to report the level of supervision of the concurrent training intervention. Summary characteristics of included trials appear in more detail in Appendix 5.6.

The Antihypertensive Effects of Concurrent Exercise Training

On average, concurrent exercise training lowered BP compared to control 3.2 mmHg for SBP [d_+= -0.32; 95 % *CI* (-0.44, -0.20); I^2= 68.6 (60.3, 75.2)] and 2.5 mmHg for DBP [d_+= -0.35; 95%CI (-0.47, -0.22); I^2= 65.7 (55.8, 73.4)].

Regarding the within group comparisons, concurrent exercise training lowered SBP 3.6 mmHg [d_+= -0.36; 95 % *CI* (-0.44, -0.27); I^2= 57.0 (44.4, 66.7)] and DBP 3.9 mmHg [d_+= -0.39; 95 % *CI* (-0.49, -0.29); I^2= 70.1 (61.8, 76.6)]. The non-exercise control and/or comparison group lowered SBP 1.1 mmHg [d_+= -0.11; 95 % *CI* (-0.18, -0.22); I^2= 43.3 (25.3, 57.0)] but DBP was not different (p>0.05). The distributions of effect sizes displayed significant heterogeneity indicated by the I^2 statistic.

Moderator Analysis of the BP Response to Concurrent Exercise Training

Tables 3 and 4 further detail the multiple moderator models for SBP and DBP, respectively. SBP was reduced to the greatest extent among samples with hypertension (-5.9 mmHg, *k*=11, *p*=0.01) compared to prehypertension (-2.9 mmHg, *k*=6, *p*=0.01) or normal BP (+2.9 mmHg, *k*=3, *p*=0.01). Furthermore, greater SBP reductions were observed among samples with hypertension when BP was examined as a primary study outcome (-8.4 mmHg,

k=5, *p*=0.01) versus those that did not examine BP as a primary outcome (-3.4 mmHg, *k*=7, *p*=0.01). We also observed greater SBP reductions in trials of higher study methodological quality (-3.6 mmHg, *k*=5, *p*=0.01) than trials of lower study methodological quality (-1.9 mmHg, *k*=13, *p*=0.002).

We observed greater DBP reductions in samples with hypertension (-5.6 mmHg, *k*=1, *p*=0.01) than prehypertension (-3.6 mmHg, *k*=51, *p*=0.01) or normal DBP (-1.5 mmHg, *k*=15, *p*=0.01). Greater DBP reductions were also observed among studies of higher methodological quality (-4.8 mmHg, *k*=5, *p*=0.01) versus lower methodological quality (-2.3 mmHg, *k*=13, *p*=0.013). Greater SBP reductions were found among the "active content" control comparison groups (-1.9 mmHg, *k*=25, *p*=0.01) than the non-exercise or wait-list control groups (0.0 mmHg, *k*=51, *p*=0.955). There were no significant interactions observed for DBP (*p*>0.05) (Tables 3 and 4).

2.5 Discussion

The present meta-analysis investigated the efficacy of concurrent exercise training as antihypertensive therapy. We found that concurrent exercise training on average reduced BP by ~ 3 mmHg compared to control, and these reductions were greatest among samples with hypertension (-5.9/-5.6 mmHg) compared to prehypertension (-2.9/-3.6 mmHg) or normal BP (+2.9/-1.5 mmHg). In addition, greater BP reductions were observed when: BP was a primary study outcome (for SBP only, -8.4, *k*=5) versus studies in which it was not (-3.4mmHg, *k*=7); and trials of higher (-3.6/-4.8 mmHg; *k*=5) than lower (-1.9/-2.3 mmHg; *k*=13) methodological quality (*p*=0.01). Concurrent exercise training appears to result in BP reductions of a magnitude comparable to aerobic exercise training for adults with hypertension, notably among studies adhering to higher methodological quality contemporary standards that measured BP as the primary study outcome. Nonetheless, the order and proximity which aerobic and resistance training should be performed to optimize the resultant BP reductions remains unclear.

Exercise is recommended as initial antihypertensive lifestyle therapy for its many health benefits with few adverse effects, negligible cost, and broad accessibility to the general population (14). The ACSM recommends 30 minutes of moderate intensity aerobic exercise on most days of the week supplemented by resistance training 2-3 days per week to lower BP 5-7 mmHg among adults with hypertension (35). However, these recommendations do not provide specific guidance regarding the frequency, intensity, and time (FIT) of concurrent exercise training (36). Our finding that the magnitude of the BP reductions resulting from concurrent exercise training is comparable to that achieved with aerobic training exercise suggest that the ACSM exercise recommendations for hypertension should be expanded to include the specifics of the FIT of the concurrent exercise training regimen (8, 26)(Supplemental ref 51,54,60).

Our meta-analysis adds other novel information to the literature, namely we are the first to demonstrate that concurrent exercise training elicits BP reductions in dose-response fashion such that the greatest BP reductions were found among samples with hypertension (~6 mmHg) followed by samples with prehypertension (~3-4 mmHg), whereas those found among samples with normal BP were negligible. This finding is consistent with previous meta-analyses that investigated the independent effects of aerobic exercise (8, 27, 38) and resistance training (17) that reported the greatest BP reductions occur in samples with the highest resting BP. Unfortunately, nearly 90% (SBP k=11; DBP k=1) of the concurrent exercise training trials in our meta-analysis did not include samples with hypertension but rather ~80% (SBP k=61; DBP k=51) included those with prehypertension and ~4% (SBP k=3; DBP k=15) those with normal BP, calling into question the generalizability of this literature to adults with hypertension.

Second, our meta-analysis is the first to examine methodological study quality as a moderator of the BP response to concurrent exercise training. We found greater BP reductions in studies of higher methodological quality (~4-5 mmHg) than lower methodological quality (~2 mmHg). Despite the importance of assessing study methodological quality to identify potential sources of sample bias, only one (18) of the four (6, 8, 18, 32) previous meta-analysis determined

the methodological quality of the qualifying trials; and found some evidence of publication bias, although they did not specifically examine methodological study quality as a moderator of the BP response to the concurrent exercise training. Furthermore, the instrument used what to assess methodological study quality in these meta-analyses did not use the most comprehensive tools available to assess quality for health outcome (29).

The 'fair to moderate' quality of this literature leaves open the possibility that biases exist that may inhibit or limit the ability to make definitive conclusions about the antihypertensive effects of concurrent exercise training. One potential source of bias in this literature is that only 14% (k=11) of trials examined BP as a primary outcome, and those that did found BP reductions that were over twice the magnitude than of those trials that did not examine BP as a primary outcome (~8 mmHg versus 3 mmHg, respectively). If the purpose of the investigation was to measure the effectiveness of concurrent exercise training as antihypertensive therapy and BP was not the primary outcome, the potential exists that the intervention was not appropriately designed in terms of the FIT principle of exercise prescription to optimize the BP lowering effects of the intervention, generating unwanted heterogeneity in the findings, possibly masking important moderator patterns, and underestimating the antihypertensive effects of concurrent exercise training (14, 25). In fact, trials that examined BP as a primary outcome tended to incorporate exercise programs that were higher in intensity and volume when compared to those trials that did not examine BP as a primary outcome. When BP is the primary outcome, unwanted heterogeneity may be minimized that more easily allows for identification of significant moderator patterns; and as we found for the first time, BP was reduced in dose response fashion following concurrent exercise training with the greatest reductions seen in the samples with hypertension.

Furthermore, we found that 30% of our sample incorporated "active content" (k=23) versus "non-exercise" control groups (69.7%, k=53). The active content groups included activities such as education sessions or pamphlets, chronic disease management, and stretching or relaxation routines. Surprisingly, we found that the active content comparison groups experienced

significant SBP reductions of -1.1 mmHg, while BP was not different pre- to post intervention among the "non-exercise" control groups [+0.0 mmHg, 95%CI (-0.09, 0.10)]. Ekkekakis et al. suggested that while the use of "active content" control groups are done with the best of intentions, their inclusion is paradoxical because they may act as interventions in and of themselves, may not be appropriate for the desired comparisons being made, and their use may underestimate the effectiveness of the intervention (14). Stretching and relaxation routines have been shown to favorably impact BP (14, 34). Indeed, when compared to the active content comparison groups, concurrent exercise training elicited BP reductions of ~1.0 mmHg, while concurrent exercise training elicited reductions of ~4.5 mmHg when compared to the non-exercise control groups. This observation, as well as our finding regarding BP as a primary outcome, illustrate the importance of study design features that must be carefully attend to so that more definitive conclusions can be made about the antihypertensive effects of concurrent exercise training.

We found several other noteworthy gaps in this literature. Our meta-analysis is the first to examine the FIT (or sample characteristics) as moderators of the BP response to concurrent exercise training. In our sample, no FIT characteristics emerged as moderators of the BP response to concurrent exercise training in our meta-analysis. Unfortunately this finding may be the result of the majority of included trials not fully disclosing the FIT characteristics of the concurrent exercise training interventions (86.8%, k=66). To our knowledge, only Okamoto et al. has directly investigated the role of modality order in a sample of young (19.0±0.2 yr), healthy adults with normal BP (113.5±3.4 mmHg) and found that when aerobic exercise was performed before resistance training (-2.4 mmHg/-2.0 mmHg) or aerobic exercise was performed after resistance training (-3.4 mmHg/-5.2 mmHg), the resultant BP reductions were not different (SDC 5 ref 40) (p>0.05).

Even though there is strong evidence for aerobic exercise training as antihypertensive therapy, there is a paucity of evidence directly comparing the BP response among aerobic,

resistance, and concurrent exercise training. Hayashino et al. performed a meta-analysis of 42 trials, of which 14 were concurrent exercise training trials (18). Overall, the sample included middle-aged adults (~58 yr) with type 2 diabetes mellitus and ~36% had hypertension. The authors reported BP reductions following aerobic of -1.66 mmHg/-2.3 mmHg, resistance of -2.8 mmHg/-2.3 mmHg, and concurrent exercise training of -3.2 mmHg/-1.9 mmHg) that were not different among modality groups (p=0.96) (18). Similarly, Cornelissen et al. found in a sample of 93 trials (14 concurrent exercise training) BP reductions following aerobic of -3.5 mmHg/-2.5 mmHg, resistance of-1.8 mmHg/-3.2 mmHg, and concurrent exercise training of-2.2 mmHg), and once again, the BP reductions were not different among modality groups (p>0.05) (8). Although our findings are promising, the limitations in this literature do not allow more formal FIT recommendations to be made regarding the use of concurrent exercise training as antihypertensive therapy.

Our meta-analysis had several strengths. The trial selection process was comprehensive, and absent of publication year restrictions, language filters, and restrictions on grey/unpublished literature, yielding the largest meta-analysis of concurrent exercise training trials conducted to date (i.e., k=76 versus previous meta-analyses k=2-12) (6, 8, 18, 32). Also, we performed *a priori* moderator analyses that, until now, have not been done. Consequently, our meta-analysis adhered to high-quality, contemporary methodological meta-analytic reporting standards (25), satisfying 94% of items on the Assessment of Multiple Systematic Reviews or AMSTAR scale (25).

In summary, our findings indicate that concurrent exercise training is effective antihypertensive therapy lowering BP ~6 mmHg among samples with hypertension. In addition, BP reductions were greater among trials that examined BP as a primary outcome and those adhering to higher methodological study quality. To our knowledge, we are the first to demonstrate that the antihypertensive effect of concurrent training follows a dose-response relationship with the greatest BP reductions occurring in those with the highest resting BP. Our

finding that the magnitude of the BP reductions resulting from concurrent exercise training is comparable to that achieved with aerobic training exercise among those with hypertension suggest that the ACSM exercise recommendations for hypertension be expanded to include the specifics of the FIT of concurrent exercise training regimen. Our results, albeit positive, warrant additional studies that investigate BP as a primary outcome, include samples with hypertension, use appropriate non-exercise control comparison groups, and manipulate the FIT (including the order and proximity of aerobic exercise and resistance training components) of the concurrent exercise training regimen to further clarify the optimal FIT exercise prescription to optimize the BP lowering effects of concurrent exercise training among adults with hypertension.

Acknowledgements
None

Conflicts of Interest
None

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2.7.1 Figure 1. PRISMA Diagram of the Trial Selection Process

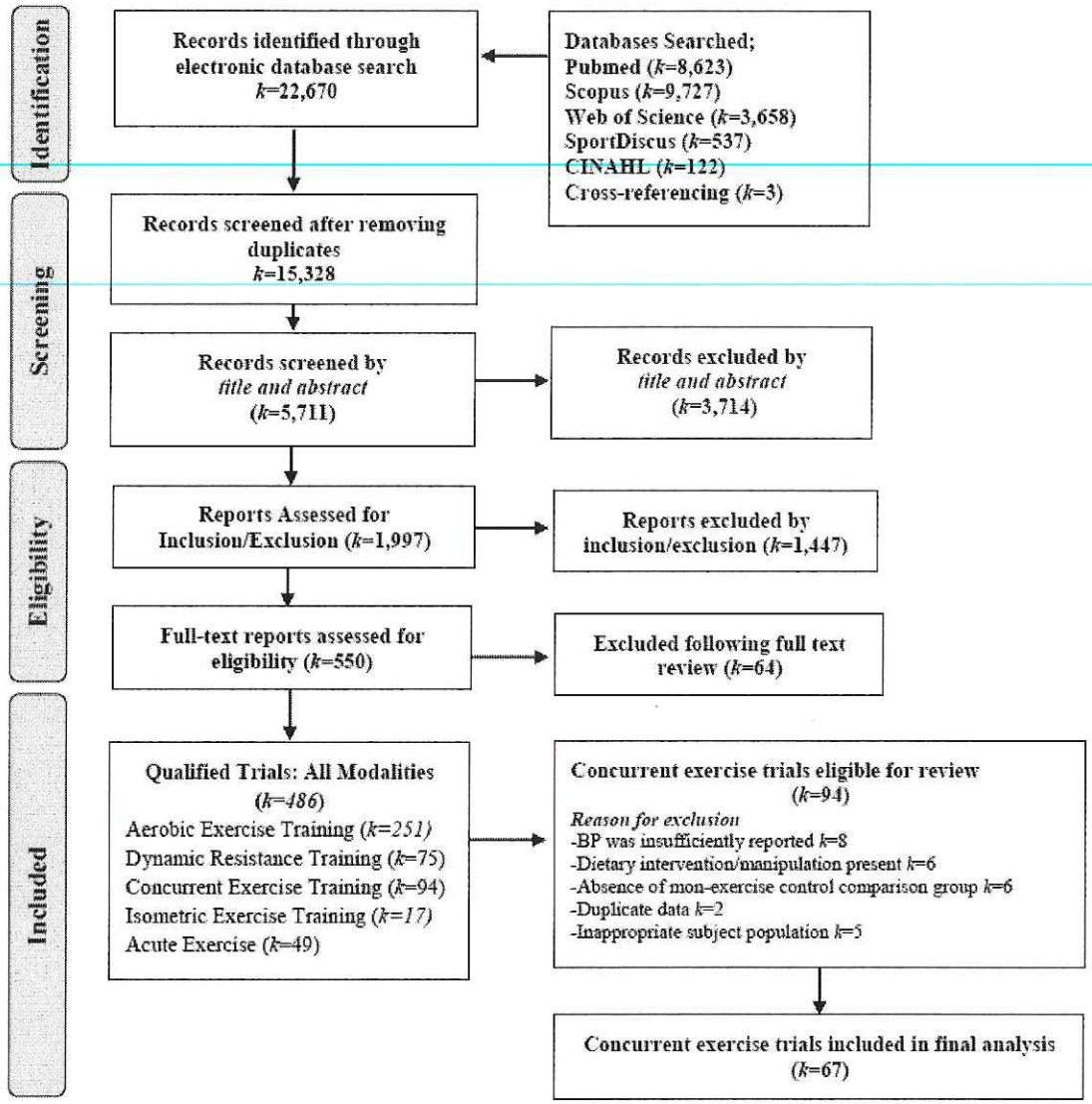
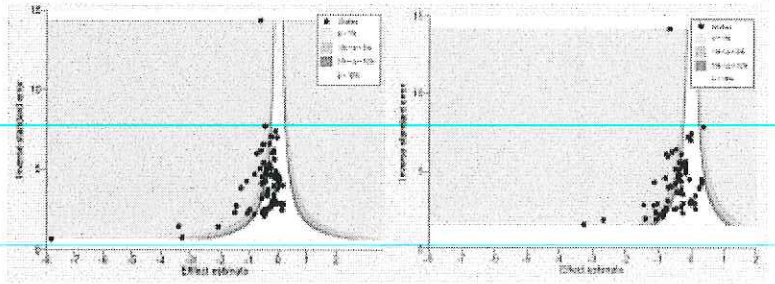


Figure 1.1 Flow Chart Detailing the Systematic Search of Potential Reports (*k*) and Selection Process of Included Concurrent Exercise Training Trials.

2.7.2 Figure 2. Funnel Plot of the Within-Group Effect Size Distribution for SBP and DBP

Figure 2. Mean Standardized Effect of Concurrent Exercise Training on Systolic (left) and Diastolic (right) Blood Pressure



Note: Contour enhanced funnel plots of the mean standardized effect of concurrent exercise training on systolic (presented left) and diastolic (presented right) on blood pressure. Data are presented as the standardized mean difference plotted on the horizontal and the inverse standard error on the vertical. Negative effect sizes indicate a favorable blood pressure response to concurrent exercise training. Data has not undergone windsorization.

2.7.3 Table 1. Pre-Training Sample Characteristics for Concurrent Exercise Training and Non-Exercise Control or Comparison Group

Table 1. Pre-Training Sample Characteristics for Concurrent Exercise Training and Non-Exercise Control or Comparison Group

		Total Sample (n=4,110)	
Characteristic	k	Control (n=1,965)	Concurrent (n=2,144)
Age (years)	76	55.9±14.5	55.8±14.4
Women in Sample (%)	68	54.8±34.3	54.5±34.0
Body Mass Index (kg·m^{-2})	58	27.9±3.6	28.0±3.6
Physical Activity Status (% Sedentary)	35	95.3±18.3	98.1±9.2
Pre-Systolic BP (mmHg)	75	135.1±10.7	134.6±10.9
Pre-Diastolic BP (mmHg)	68	80.6±10.3	80.7±7.5
Pre-HR (bpm)	30	69.8±5.7	70.8±6.9

Note: All statistics are presented as mean ± standard deviation unless otherwise noted. Abbr. k=number of observations. BP=blood pressure. HR=heart rate. bpm=beats per minute. There are no differences in baseline statistics between the groups $p>0.05$.

2.7.4 Table 2. Features of the Concurrent Exercise Training Program

Table 2. Features of the Concurrent Exercise Training Program

Characteristic	*k*	Mean±SD	Range
Length (wks)	76	19.7±17.8	3-144
Frequency (d·wk^{-1})	66	2.9±0.73	1-5
Average Intensity (MET)	76	4.4±1.2	2-8
Average Session Length (min·session^{-1})	56	58.3±20.1	20-120
Attrition (%)	76	7.9±12.9	0-56
Aerobic Exercise Component			
Time Spent in Aerobic Exercise (min·session^{-1})	42	35.1±15.3	15-80
Resistance Exercise Component			
Time Spent in Resistance Exercise (min·session^{-1})	31	32.3±18.7	10-75
Number of exercises·session^{-1}	44	8.01±2.2	3-13
Number of sets·exercise^{-1}	49	3.1±3.5	1-27
Number of reps·set^{-1}	51	11.8±2.9	8-20

Note: Abbr. *k*= number of observations. SD=standard deviation. Wk(s)=week(s). d=days MET=metabolic equivalent. min=minute. reps=repetitions. All statistics are presented as mean ± standard deviation unless otherwise stated.

2.7.5 Table 3. Multiple Moderator Analysis of the Systolic Blood Pressure Response to Concurrent Exercise Training

Table 3. Multiple Moderator Analysis of the Systolic Blood Pressure Response to Concurrent Exercise Training

Study Dimension/Level	*k*	d_+(95% CI)	β_+	*p*	Raw Difference (mmHg)
Resting Pre-Concurrent Exercise Training Systolic BP			-0.747	0.001	
Normal BP=115±10 mmHg	3	0.29 (0.07,0.52)			2.9
Prehypertension= 135±10 mmHg	61	-0.29 (-0.39, -0.19)			-2.9
Hypertension= 145±10 mmHg	11	-0.59 (-0.71, -0.47)			-5.9
Methodological Study Quality			-0.245	0.01	
Lower Quality= 50%±10%	13	-0.19 (-0.32, -0.07)			-1.9
Median Quality= 60%±10%	58	-0.28 (-0.38, -0.17)			-2.8
Higher Quality= 70%±10%	5	-0.36 (-0.46, -0.25)			-3.6
Resting Pre-Concurrent Exercise Training Systolic BP x Study Outcome			0.537	0.001	
Primary Outcome					
Normal BP=115±10 mmHg*	0				
Prehypertension= 135±10 mmHg	71	-0.34 (-0.51, -0.17)			-3.4
Hypertension= 145±10 mmHg	5	-0.84 (-1.0, -0.64)			-8.4
Not Primary Outcome					
Normal=115±10 mmHg	3	-0.08 (-0.24, 0.07)			-0.8
Prehypertension= 135±10 mmHg	66	-0.25 (-0.32, -0.18)			-2.5
Hypertension= 145±10 mmHg	7	-0.34 (-0.44, -0.24)			-3.4

Note: Effect sizes (*d*) are modeled using fixed-effect slopes and a random-effects constant; moderator dimensions are entered simultaneously. Predicted estimates (95%CI) of the standardized mean difference within the concurrent exercise intervention. Negative values imply the control comparison group reduced blood pressure pre- to post intervention. This model statistically controls for study quality assessed using the Downs and Black checklist; whether blood pressure was a primary outcome; and whether the concurrent exercise intervention was performed on the same day or different days.
Abbr. *k*= number of observations. BP= blood pressure. CI= confidence interval.
* insufficient cases to provide estimates.

2.7.6 Table 4. Multiple Moderator Analysis of the Diastolic Blood Pressure Response to Concurrent Exercise Training

Table D. Multiple Moderator Analysis of the Diastolic Blood Pressure Response to Concurrent Exercise Training

Study Dimension/Level	*k*	d_+(95% CI)	β_+	*p*	Raw Difference (mmHg)
Baseline Diastolic BP			-0.445	0.001	
Normal BP=75±7 mmHg	15	-0.21 (-0.36, -0.06)			-1.5
Prehypertension= 85±7 mmHg	51	-0.49 (-0.64, -0.33)			-3.6
Hypertension= 95±7 mmHg	1	-0.77 (-0.99, -0.54)			-5.6
Study Quality					
Lower Quality= 50%±10%	13	-0.23 (-0.41, -0.05)			-2.3
Median Quality= 60%±10%	58	-0.36 (-0.50, -0.21)			-3.6
Higher Quality= 70%±10%	5	-0.48 (-0.63, -0.33)			-4.8

Note: Effect sizes (*d*) are modeled using fixed-effect slopes and a random-effects constant; moderator dimensions are entered simultaneously. Predicted estimates (95%CI) of the standardized mean difference within the concurrent exercise intervention. Negative values imply the control comparison group reduced blood pressure pre- to post intervention. This model statistically controls for study quality assessed using the Downs and Black checklist; whether blood pressure was a primary outcome; and whether the concurrent exercise intervention was performed on the same day or different days.
Abbr. *k*= number of observations. BP= blood pressure. CI= confidence interval.

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Chapter 3. Methods

We investigated the effect of concurrent exercise training on BP and to what extent sample risk characteristics (e.g., age, body mass index, baseline BP), features of the exercise intervention (e.g., frequency, intensity, length of exercise session), and/or study methodology (e.g., intervention supervision, methodological study quality) modulate the BP response to concurrent exercise training. The following chapter outlines the procedures used to conduct this meta-analysis including: the systematic search strategy, data extraction and coding, effect size calculations, publication bias, test for homogeneity, meta-regression, and multiple moderator analyses. The details of this meta-analysis are reported consistent with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) standards (18).

3.1 Search Selection Criteria

Inclusion Criteria

Studies considered for inclusion investigated the BP response to concurrent exercise training interventions or related outcomes, such as CVD or metabolic risk. Relevant trials were identified by *a priori* criteria: a) adult populations (>19 years old); b) a non-exercise control comparison group; c) provided sufficient BP statistics to calculate an effect size for the concurrent exercise and the control comparison group; and d) reported all aspects of the concurrent training FITT (e.g., *Frequency, Intensity, Time* and *Type*). Furthermore, qualifying concurrent training trials included both an aerobic (e.g., walking, running, cycling, swimming) and resistance training (e.g., free weights, machine weights, therabands) component performed within the same exercise session or on separate days (e.g., combined exercise training).

Exclusion Criteria

Trials were excluded if they involved populations with chronic disease or conditions unrelated to CVD, which included: a) cancer patients or survivors; b) fibromyalgia; c) Alzheimer's disease or cognitive impairments, learning disabilities; d) substance abusers; e) debilitating stoke; f) people involved in weight loss drugs/therapy/modification; g) epilepsy; and

h) communicable or infectious diseases including but not limited to influenza, septicemia, pneumonia, human immunodeficiency virus or AIDS, and meningitis. In addition, trials were excluded if environmental stressors were manipulated in the intervention (e.g., temperature, dehydration, altitude, compression gear). Epidemiological, retrospective, or cross-sectional study designed were also excluded from the sample (Appendix 5.1).

3.2 Systematic Search and Screening of Potential Reports

With the assistance of a medical librarian at the University of Connecticut, a Boolean electronic database search was performed to locate relevant concurrent exercise training trials. The following databases were searched for qualifying trials for inclusion in this meta-analysis: PubMed, CINAHL, Web of Science, SportDiscus, and Scopus. Trials were located using medical subject headings (MeSH) and keywords related to BP, hypertension, exercise, physical activity and study design. Search terms were designed to yield the greatest number of potential reports. There were no language or restrictions on grey or unpublished literature. Full search terms and MESH headings appear in Appendix 5.2.

Reports from each independent electronic database search were compiled into a single triage database, after removing duplicates. Reports were screened with duplication of effort for inclusion/exclusion by *title* and *abstract* by three independent reviewers (LML, HVM, AB). A compiled list of qualifying trials by *title* and *abstract* was further screened by *full text review* for final inclusion. Approximately 10% of all trials located were assessed by two of more reviewers to ensure consistent screening. A flow diagram of the trial selection process appears in Section 2.7.1.

3.2 Coding, Coder Reliability, and Data Extraction

Data Extraction

Relevant information was extracted using a previously developed uniform coding sheet (Appendix 5.3), by a panel of experts and pilot tested. Information that was extracted included; demographics (e.g., age, gender, ethnicity, socioeconomic status), features of study design

(e.g., randomization procedures, intervention length, type of control comparison group), study methodology (e.g., study quality, BP measurement techniques), CVD risk characteristics (e.g., age, body mass index, body fat percent, disease status, medication status, resting BP), and features of the concurrent exercise intervention (e.g., frequency, intensity, minutes per session of exercise). Sample characteristics were coded for both the concurrent exercise and non-exercise control comparison group. These characteristics represent *a priori* moderators that have been previously been documented to influence the BP response to exercise interventions. Relative change values from baseline were calculated and incorporated in analyses for all sample characteristics when data was reported. The complete coding form appears in Appendix 5.3.

The Exercise Prescription (ExR_x) of the Concurrent Exercise Intervention

The FITT (e.g., *Frequency, Intensity, Time* and *Type*) of concurrent training program were extracted for both the aerobic and resistance training components of the concurrent exercise intervention. Exercise intensity was extracted in the metric reported in each trial (e.g., heart rate maximum (%HR_{max}), heart rate reserve (%HRR), maximal oxygen consumption (%VO_{2max})), and then converted to a standardized measure of intensity, metabolic equivalent units (METS). An average intensity for the concurrent exercise intervention was calculated. In addition, volume of concurrent exercise was calculated for the aerobic, resistance and the total concurrent exercise intervention ($MET \cdot min \cdot week^{-1}$).

Methodological Quality of Included Trials

Study quality was assessed using a modified version of the Downs and Black methodological checklist (4, 5), which contains 26 items assessing different methodological aspects of the intervention including: a) reporting (e.g., did the author's fully disclose the main outcome, population characteristics, and intervention characteristics); b) external validity (e.g., were the subjects representative of the population from which they were recruited; c) internal validity-bias (e.g., was there adequate blinding and randomization of for the given intervention;

d) internal validity-confounding (e.g., was there adjustment for potential confounds in analyses); and e) power (e.g., the intervention was sufficiently powered to detect the outcome in question) (5). The Downs and Black tool has been validated to assess quality in health outcome research (5) and is widely used (15). Several items were added to the checklist to capture important potential specific biases related to concurrent exercise intervention studies and BP (Appendix 5.4) to yield a total of 33 items.

Coder Reliability

A random sample of the qualified concurrent exercise trials (*k*=71*)*, approximately 51% (*k=36)* were double coded by an independent reviewer (LL, AB) to ensure that extracted data was consistent and replicable. Coder reliability was calculated for all continuous and categorical variables using Pearson's correlation and Cohen's κ coefficient, respectively (3, 9, 17). Coder reliability was high across all dimensions, with a mean Cohen's κ= 0.83 (range= 0.60-1.0) and Pearson's correlation of r= 0.87 (range= 0.75-1.0). Coder and data extraction disagreements were resolved through discussion with an impartial third reviewer (HVM, LSP) at weekly lab research meetings (3, 9, 17).

3.3 Statistical Analyses

Effect Size Calculations

The primary outcome of our meta-analysis was the magnitude and direction of the BP change (± mmHg) pre- to post-training. The standardized mean difference effect size (*d*) was used to quantify the effectiveness of concurrent exercise as antihypertensive therapy, defined as the difference in mean BP values between concurrent exercise and control groups divided by the pooled pretest standard deviation, correcting for small sample size bias and baseline differences (1, 3, 9, 17). Repeated measure effects were calculated for the independent concurrent exercise group and control group, defined as the difference between the mean BP values post minus pre-intervention (1, 3, 9, 13, 17), divided by the pre-intervention standard deviation. A reduction in BP, or negative effect size (*d*) indicated a favorable response to the

concurrent exercise intervention and a positive *d* indicated the reverse. Many of included trials (22%) incorporated an "active content" control comparison group (i.e., education session, stress management, relaxation) (7). Due to potential confounds associated with "active content" control comparison groups, multiple moderator analyses for the concurrent exercise and control comparison group analyses were conducted independently (7).

Multiple effect sizes were calculated to represent each group for trials that included ≥1 concurrent exercise intervention (e.g., high versus low intensity concurrent exercise) (1, 3, 9, 10, 17). Sensitivity analyses were performed to confirm dependence did not influence the effect sizes calculated for the included trials (1, 3, 9, 17). Equivalent BP change in mmHg (unstandardized mean difference) is provided as a supplement to the observed d_+ for clinical interpretation. Two effect sizes from the same study, one for SBP and one for DBP were outliers (i.e., more than 3 standard deviations larger than the mean). To reduce their influence on results, these were windsorized to be the same magnitude as the next smaller SBP and DBP effect sizes.

Weighted mean effect sizes were calculated following both fixed- and random-effects assumptions. Fixed-effects models assume a single population effect size (3, 9). Random-effects models assume variability in the effect sizes between included trials (3, 9) and, under heterogeneity provide wider confidence intervals; therefore, they represent a more conservative approach to estimate the mean effects of concurrent exercise training on BP (3, 9).

3.4 Publication Bias

Prior to further analysis, funnel plots were assessed for the presence of publication bias in the included sample (2, 3, 6, 9). Funnel plots act as a graphical representation of the variability in the observed effect sizes for the included trials plotted in contrast to the inverse standard error of the effect size observing for asymmetry (2, 3, 6, 9). If there was evidence of potential publication bias, it was tested for significance with Begg and Eggers test for publication bias (2, 6). In a heterogeneous sample, it may be more difficult to detect publication bias (12).

Funnel plots for SBP and DBP are presented for the within and between group effect size distributions (Appendix 5.5).

3.5 Heterogeneity and Moderator Analyses

We tested both the between- and within-group effect sizes for the presence of heterogeneity using Hedge's test for homogeneity, first by calculating the *Q* statistic (3, 9-11). The *Q* statistic evaluates whether the variation in effect sizes is greater than that expected by sampling error alone. If significant, the hypothesis of homogeneity is rejected and an inference of significant heterogeneity is justified. *Q* was further converted into the I^2 statistic (3, 9-11), which gauges, on a scale from 0 to 100%, the degree of heterogeneity in the sample (3, 9-11). As I^2 increases, homogeneity is less likely and heterogeneity is more likely. A confidence interval (*CI*) for I^2 that does not include zero indicates that the hypothesis of homogeneity is rejected, and an inference of heterogeneity is merited (3, 9-11).

In the presence of heterogeneity, we examined a set of *a priori* moderators expected to influence BP and/or the response to exercise (e.g., baseline BP, age, body mass index, exercise intensity) using weighted regression models with maximum likelihood estimation of the random-effects weights, the inverse of the variance for each d_+ *(3, 9, 14)*. Moderators were tested in bivariate analyses for significance and then incorporated into multiple moderator models (3, 9, 14). Interaction terms were generated with moderators and tested for significance (3, 9, 14). The moving constant technique was used to estimate the magnitude of weighted mean effect sizes (d_+) and their *CIs* at different levels of interest for individual moderators in the model while statistically controlling for the influence of other moderators (14). Windzorized within group effect sizes (pre- to post-intervention) for the independent concurrent exercise training and non-exercise control or comparison group were used in moderator analyses (8).

Study quality was assessed in bivariate as well as incorporated into multiple moderator models. Interactions with study quality were tested to determine whether the effects of *a priori* moderators depended on study quality (16). In our sample, higher quality was defined as scores

one standard deviation above the median quality score or within the 90th percentile (≥26 or 70% of items satisfied) and lower quality was defined as scores one standard deviation below the median or within the 10th percentile (≤14 or 50% of items satisfied).

3.6 Statistical Computing

All statistical analyses were performed using the most updated version of Stata 13 (College Station, Texas) (17, 19) using macros for meta-analysis including; meanes, confunnel, metaf, metareg, metatrim, metan (17, 19). Significance for all analyses was set at $p<0.05$.

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Chapter 4. Discussion

The present thesis reports a meta-analysis that investigated the efficacy of concurrent exercise training as antihypertensive therapy and examined potential moderators of the BP response to concurrent exercise training. This chapter serves as the concluding statement of the findings. First, the findings will be put in the context of the specific aims and hypotheses. This will be followed by a discussion of the implications of our findings on the current ExR_x guidelines for adults with hypertension. Finally, potential directions for future research will be discussed.

4.1 Specific Aims and Hypothesis

The results from this thesis and meta-analysis support our initial specific aims and hypotheses outlined in chapter 1. Below find a reiteration of our major findings in the context of our specific aims and hypotheses.

Specific Aim 1: To perform a high quality meta-analysis, adhering to contemporary methodological standards to determine the efficacy of concurrent exercise as antihypertensive therapy.

Hypothesis 1: Concurrent exercise training interventions will result in significant BP reductions compared to non-exercise control or comparison conditions. We observed that concurrent exercise training on average reduced BP by ~ 3 mmHg compared to control. Of note, the greatest BP reductions were observed among samples with hypertension (-5.9/-5.6 mmHg) than prehypertension (-2.9/-3.6 mmHg) or normal BP (+2.9/-1.5 mmHg). Concurrent exercise training appears to result in BP reductions of a magnitude comparable to aerobic exercise training for adults with hypertension.

Specific Aim 2: To examine potential moderators that may modulate the BP response to concurrent exercise training.

Hypothesis 2: Study characteristics (e.g., randomization, study design), clinical characteristics (e.g., age, weight, sex), features of the concurrent exercise intervention (e.g., frequency,

intensity, time, length of session, volume of exercise), study quality, and their interactions-, will explain a significant proportion of the variability in the BP response to concurrent exercise training. We observed that methodological study quality, baseline BP and BP as a primary outcome emerged as significant moderators of the BP response to concurrent exercise training. Greater BP reductions were observed when: BP was a primary study outcome (for SBP only, -8.4, *k*=5) versus studies in which it was not (-3.4mmHg, *k*=7); and trials of higher (-3.6/-4.8 mmHg; *k*=5) than lower (-1.9/-2.3 mmHg; *k*=13) methodological quality (*p*=0.01). Last, we observed that the greatest BP reductions were observed among samples with the highest baseline BP; samples with hypertension (-5.9/-5.6 mmHg) than prehypertension (-2.9/-3.6 mmHg) or normal BP (+2.9/-1.5 mmHg).

4.2 Additional Findings

Furthermore, we found that 30% of our sample incorporated "active content" (*k*=23) versus "non-exercise" control groups (69.7%, *k*=53). The active content groups included activities such as education sessions or pamphlets, chronic disease management, and stretching or relaxation routines. We found that the active content comparison groups experienced significant SBP reductions of -1.1 mmHg, while BP was not different pre- to post intervention among the "non-exercise" control groups [+0.0 mmHg, 95%CI (-0.09, 0.10)]. When compared to the active content comparison groups, concurrent exercise training elicited BP reductions of ~1.0 mmHg, while concurrent exercise training elicited reductions of ~4.5 mmHg when compared to the non-exercise control groups.

4.3 Implications for the ExR_x among Adults with Hypertension

Exercise is recommended as initial antihypertensive lifestyle therapy for its effectiveness to lower BP, numerous health benefits with few adverse effects, negligible cost, and broad accessibility to the general population (3). The ACSM recommends 30 minutes of moderate intensity (40-60% VO_{2max}) aerobic exercise on most days of the week (≥5 days·week^{-1}) supplemented by resistance training 2-3 days per week to lower BP 5-7 mmHg among adults

with hypertension (15). However, these recommendations do not provide specific guidance regarding the frequency, intensity, and time (FIT) of concurrent exercise training (16). Our finding that the magnitude of the BP reductions resulting from concurrent exercise training is comparable to that achieved with aerobic training exercise suggest that the ACSM exercise recommendations for hypertension should be expanded to include the specifics of the FIT of the concurrent exercise training regimen (2, 8, 19-22). The addition of concurrent exercise training recommendations would provide additional options for health professionals and physicians to personalize exercise prescription to prevent, manage and control BP.

Based on the synthesis of the concurrent exercise training literature presented in this meta-analysis, the following concurrent exercise training ExR_x guidelines are suggested as an expansion of the existing guidelines to lower BP among adults with hypertension.

***F*requency**: Concurrent exercise training reduced baseline BP with the greatest reductions among adults with hypertension (~6mmHg). These reductions were observed among concurrent exercise training regimens performed 1-5 days per week. Accordingly, concurrent exercise training should be performed most days per week to achieve benefits. These recommendations are similar to that of the ACSM ExR_x for aerobic training in isolation (13).

***I*ntensity**: Moderate (aerobic exercise 40-60% VO_{2max}; resistance training 60-80% 1-repetition maximum; or 4-6 METS) intensity concurrent training appears sufficient to elicit BP reductions of ~6 mmHg among adults with hypertension. A gradual progression to vigorous intensity exercise may be efficacious in those who are able. These recommendations are similar to that of the ACSM ExR_x for aerobic and resistance training in isolation.

***T*ime**: BP reductions of ~6 mmHg were conferred when 20-50 min·session^{-1} of aerobic exercise and 15-50 min·session^{-1} of resistance training including 6-8 exercises, 3-6 sets of 10-12 repetitions targeting major muscle groups of the upper and lower body were performed. Weekly training sessions should total ≥150 min·week^{-1}. Training session length and time spent in each exercise modality may vary based on how aerobic and resistance training components are

combined. These recommendations align with the established ExR_x for aerobic and resistance training performed alone in healthy adults (13).

***T*ype**: Concurrent exercise training must include both aerobic and resistance training components, performed on the same day or different days. It appears that the BP benefits in response to concurrent exercise training are independent of whether aerobic exercise is performed *before* or *after* resistance training (11). There should be an emphasis on performing aerobic activities such as walking, jogging, swimming, running, and cycling. Resistance training should involve machine, free weights or circuit-style training targeting major muscle groups of the upper and lower body.

***V*olume**: Samples that performed concurrent exercise training ~3 days·week^{-1}, at a moderate intensity (aerobic exercise 40-60% VO_{2max}; resistance training 60-80% 1-repetition maximum; or 4-6 METS) totaled an average of ≥500-1000 MET·min·week^{-1}. This volume of exercise is consistent with the ACSM recommendations for healthy adults (13). This 'dose' of exercise conferred the greatest benefit in samples with hypertension.

***P*rogression**: Overall, the FITT-VP principle of the ExR_x for healthy adults is applicable for those with hypertension. Modifications may need to be made to the ExR_x under circumstances such as; a) improvement or worsening of BP control; b) development of comorbidies; c) changes to medication use; d) injury or physical disability. In general, special considerations for concurrent exercise training should follow the established ACSM guidelines for aerobic and resistance training (13). As with aerobic and resistance training performed in isolation, the progression of concurrent exercise training should be gradual, and tailored to individual ability and tolerance (13).

4.4 Additions to the Concurrent Exercise Training Literature

Our meta-analysis adds novel information to the literature, namely we are the first to demonstrate that concurrent exercise training elicits BP reductions according to the law of initial values (e.g., dose-response relationship) such that the greatest BP reductions were found among

samples with hypertension (~6 mmHg) followed by samples with prehypertension (~3-4 mmHg), whereas those found among samples with normal BP were negligible. This finding is consistent with previous meta-analyses that investigated the independent effects of aerobic exercise (2, 9, 23) and resistance training (4) that reported the greatest BP reductions occur in samples with the highest resting BP. Unfortunately, nearly 90% (SBP *k*=11; DBP *k*=1) of the concurrent exercise training trials in our meta-analysis did not include samples with hypertension but rather ~80% (SBP *k*=61; DBP *k*=51) included those with prehypertension and ~4% (SBP *k*=3; DBP *k*=15) those with normal BP, calling into question the generalizability of this literature to adults with hypertension.

Second, our meta-analysis is the first to examine methodological study quality as a moderator of the BP response to concurrent exercise training. We found greater BP reductions in studies of higher methodological quality (~4-5 mmHg) than lower methodological quality (~2 mmHg) when assessing study quality as a sum score converted into a percent score. Previous reviews that critically assess the use of study quality in meta-analyses, suggest that sum scores (alone or as a calculated percentage) may not fully describe quality strengths or weaknesses in a body of literature. In our meta-analysis, we were able to better pinpoint these important quality deficiencies (e.g., sources of bias) by examining individual study quality items and subscales (e.g., power, internal validity, external validity, reporting) on the Downs and Black checklist. Furthermore, despite the importance of assessing study methodological quality to identify potential sources of sample bias, only one (5) of the four (1, 2, 5, 12) previous meta-analysis determined the methodological quality of the qualifying trials; and found some evidence of publication bias, although they did not specifically examine methodological study quality as a moderator of the BP response to the concurrent exercise training. The instrument used what to assess methodological study quality in these meta-analyses was not the most comprehensive tool available to assess quality for health outcome research (10).

The 'fair to moderate' quality of this literature leaves open the possibility that biases exist which may confound or limit the ability to make definitive conclusions about the antihypertensive effects of concurrent exercise training (7). One potential source of bias in this literature is that only 14% (k=11) of trials examined BP as a primary outcome, and those that did found BP reductions that were over twice the magnitude than those trials that did not examine BP as a primary outcome (~8 mmHg versus 3 mmHg, respectively). If the purpose of the investigation was to measure the effectiveness of concurrent exercise training as antihypertensive therapy and BP was not the primary outcome, the potential exists that the exercise intervention was not designed to optimize the BP lowering effects of the intervention, generating unwanted heterogeneity in the findings, possibly masking important moderator patterns, and underestimating the antihypertensive effects of concurrent exercise training (3, 6). In fact, included trials that focused on BP tended to incorporate exercise regimes that were of higher intensity and volume, maximizing BP reductions following exercise. In contrast, when BP is the primary outcome, unwanted heterogeneity is minimized which more easily allows for identification of significant moderator patterns; and as we found for the first time, BP was reduced in dose response fashion following concurrent exercise training with the greatest reductions seen in the samples with hypertension.

Pescatello et al. conducted a review that offers a discussion of additional study design features that may contribute to the discrepancies (or sources of heterogeneity) in the concurrent exercise training literature (14). First and foremost, because the majority of our included trials did not examine BP as a primary outcome, it is unclear whether concurrent exercise training trials were able to detect BP effects following an exercise intervention (14). More specifically, it has been well established that BP reductions following exercise are greatest among samples with hypertension, followed by prehypertension and then normal BP (i.e., law of initial values). In our sample, only 30.2% of trials (k=23) included subjects with hypertension and tended to be in trials where BP was considered the primary outcome. To achieve the most accurate depiction of the

antihypertensive effects of concurrent exercise training, it would be advantageous to examine samples with hypertension, and to date, primary level trials have been rarely conducted in this population. In contrast, examining samples with normal BP underestimates the true antihypertensive effect of concurrent exercise training and limits the generalizability of results to samples with hypertension (14). Furthermore, only 21.1% (*k*=16) reported power analyses for the primary study outcome which begs the question; were concurrent exercise training trials adequately powered to detect BP effects regardless of other potentially interfering study design features (14)?

Secondly, it is unclear how BP was being assessed amongst our included sample and how these methods may have contributed to the BP response to concurrent exercise training. In our sample, the BP measurement methods used were not significant moderators of the BP response to concurrent exercise. In addition, BP measurement methods were not different among trials that investigated BP as a primary outcome and those trials that did not. However, important BP measurement technique variables were underreported, some of which included; a) body position during measurement (46%, *k*=35); a) manual or automated measurement techniques (53.9%, *k*=41) b) use of a previously validated BP procedure (55.3%, *k*=42) (17, 18); and c) conditions of the setting where the measurement was taken (67.1%, *k*=51). The poor reporting of these variables prevents definitive conclusions about how BP measurement methodology may have influenced our results.

Lastly, we found that 30% of our sample incorporated "active content" (*k*=23) versus "non-exercise" control groups (69.7%, *k*=53). The active content groups included activities such as education sessions or pamphlets, chronic disease management, and stretching or relaxation routines. Surprisingly, we found that the active content comparison groups experienced significant SBP reductions of -1.1 mmHg, while BP was not different pre- to post intervention among the "non-exercise" control groups [+0.0 mmHg, 95%CI (-0.09, 0.10)]. Ekkekakis et al. suggested that while the use of "active content" control groups are done with the best of

intentions, but their inclusion is paradoxical because they may act as interventions in and of themselves, may not be appropriate for the desired comparisons being made, and their use may underestimate the effectiveness of the intervention (3). Stretching and relaxation routines have been shown to favorably impact BP (3, 14). Indeed, when compared to the active content comparison groups, concurrent exercise training elicited BP reductions of ~1.0 mmHg, while concurrent exercise training elicited reductions of ~4.5 mmHg when compared to the non-exercise control groups. These observations, as well as our finding regarding BP as a primary outcome, illustrate the importance of study design features that must be carefully attend to so that more definitive conclusions can be made about the antihypertensive effects of concurrent exercise training.

4.5 Limitations

We found several other noteworthy gaps in this literature. No previous meta-analysis until ours has examined the FIT (or sample characteristics) as moderators of the BP response to concurrent exercise training. Unfortunately, no FIT characteristics emerged as moderators of the BP response to concurrent exercise training in our meta-analysis. This finding may be the result of the majority of included trials did not fully disclose the FIT characteristics of the concurrent exercise training interventions (86.8%, k=66) that included the order and proximity by which the aerobic and resistance training exercise modalities were applied. To our knowledge, only Okamoto et al. has purposely investigated the role of modality order in a sample of young (19.0±0.2 yr), healthy adults with normal BP (113.5±3.4 mmHg) and found that when aerobic exercise was performed before resistance training (-2.4 mmHg/-2.0 mmHg) or aerobic exercise was performed after resistance training (-3.4 mmHg/-5.2 mmHg), the resultant BP reductions were not different (p>0.05) (11). No trial to date has examined the role of modality proximity on the BP response following concurrent exercise training (i.e., same day versus different days)

Even though there is strong evidence for concurrent exercise training as antihypertensive therapy, there is a paucity of evidence comparing the BP response following aerobic, resistance,

and concurrent exercise training within the same primary-level trial or review/meta-analysis. Hayashino et al. performed a meta-analysis of 42 trials, of which 14 were concurrent exercise training trials (5). Overall, the sample included middle-aged adults (~58 yr) with type 2 diabetes mellitus and ~36% had hypertension. The authors reported BP reductions following aerobic of -1.66 mmHg/-2.3 mmHg, resistance of -2.8 mmHg/-2.3 mmHg, and concurrent exercise training of -3.2 mmHg/-1.9 mmHg that were not different among modality groups (p=0.96) (5). Similarly Cornelissen et al. found in a sample of 93 trials (14 concurrent exercise training) BP reductions following aerobic of -3.5 mmHg/-2.5 mmHg, resistance of-1.8 mmHg/-3.2 mmHg, and concurrent exercise training of-2.2 mmHg, and once again the BP reductions were not different among modality groups (p>0.05) (2). Although our findings are promising, there are significant limitations in this literature. Additional research is warranted examining the antihypertensive effects of concurrent training and how to optimally prescribe concurrent exercise training to populations that stand to benefit most.

4.6 Strengths

Our meta-analysis had several strengths. The trial selection process was comprehensive, and absent of publication year restrictions, language filters, and restrictions on grey/unpublished literature, yielding the largest meta-analysis of concurrent exercise training trials conducted to date (i.e., k=76 versus previous meta-analyses k=2-12) (1, 2, 5, 12). Also, we performed *a priori* moderator analyses, which until now have not been done. Consequently, our meta-analysis adhered to high-quality, contemporary methodological meta-analytic reporting standards (6), satisfying 94% of items on the Assessment of Multiple Systematic Reviews or AMSTAR scale (6).

4.7 Conclusions

In summary, our findings indicate that concurrent exercise training is effective antihypertensive therapy lowering BP ~6 mmHg among samples with hypertension. In addition, BP reductions were greater among trials that examined BP as a primary outcome and those adhering to higher methodological study quality. To our knowledge, we are the first to

demonstrate that the antihypertensive effect of concurrent training follows a dose-response relationship with the greatest BP reductions occurring in those with the highest resting BP. Our finding that the magnitude of the BP reductions resulting from concurrent exercise training is comparable to that achieved with aerobic training exercise among those with hypertension suggest that the ACSM ExR_x for hypertension be expanded to include the specifics of the FIT of concurrent exercise training regimen. Our findings suggest the following FITT-VP for the use of concurrent exercise training as antihypertensive therapy.

***F*requency**: Concurrent exercise should be performed most days·week^{-1}

***I*ntensity**: Moderate (aerobic exercise 40-60% VO_{2max}; resistance training 60-80% 1-repetition maximum; or 4-6 METS). Progression to vigorous intensity exercise may be warranted.

***T*ime**: Weekly training sessions should total ≥150 min·week^{-1} including ~20-50 min·session^{-1} of aerobic exercise and 15-50 min·session^{-1} including 6-8 exercises, 3-6 sets of 10-12 repetitions of resistance training targeting major muscle groups of the upper and lower body.

***T*ype**: Aerobic exercise can be performed *before, after,* or *interchanged (circuit training)* with resistance exercise. There should be an emphasis on performing aerobic activities such as walking, jogging, swimming, running, and cycling. Resistance training should involve machine and/or free weights. Exercise performed should target major muscle groups of the upper and lower body.

***V*olume**: A moderate 'dose' of concurrent exercise training totaling ≥500-1000 MET·min·week^{-1}.

***P*rogression**: In general, special considerations for concurrent exercise training should follow the established ACSM guidelines for aerobic and resistance training performed in isolation. The progression of concurrent exercise training should be gradual, and tailored to individual ability and tolerance.

Our results, albeit positive, warrant additional studies that investigate BP as a primary outcome, include samples with hypertension, use appropriate non-exercise control comparison groups, and manipulate the FIT (including the order and proximity of aerobic exercise and

resistance training components) of the concurrent exercise training regimen to further clarify the optimal FIT ExR_x to optimize the BP lowering effects of concurrent exercise training among adults with hypertension.

4.8 References

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Chapter 5. Appendices

5.1 Inclusion/Exclusion Criteria

Study ID: _____
Coder: _____

Blood Pressure Meta-Analysis Selection Criteria

Inclusion Criteria **Trials MUST match all of these criteria:**		Exclusion Criteria **Studies CANNOT include any of the following:**	
Pre- AND Post-Exercise Blood Pressure Measurements (OR enough data to calculate an effect size, i.e., baseline & change value)	☐	Cancer Survivors	☐
A non-exercise control and/or comparison group	☐	Fibromyalgia	☐
Exercise involves all of the **FITT characteristics** **(Note: ALL FITT criteria must be satisfied) :**		Alzheimer's disease	
Frequency	☐	Pregnant Women	
Intensity *(if missing intensity- OK, assign MET value later)*	☐	People on Weight-Loss Drugs or Diet Therapy or Diet Modification	☐
Time	☐	Dehydration Studies	☐
Type	☐	Epileptics	☐
Adults (age 19+)	☐	Influenza, flu, pneumonia	☐
		Septicemia	☐
		HIV/AIDs	☐
		Meningitis	☐
		Substance Abusers	☐
		Alcoholics	☐
		Cross-Section Studies	
		Epidemiologic Studies	☐
		Position statements	☐
		Clinical guidelines/ recommendations	☐
		Animal studies (i.e., SHR)	☐

5.2 Search Strategy and Subject MESH Terms

PubMed

Dates: 06/18/2013-present

("mean arterial" OR "blood pressure"[mesh] OR "blood pressure" OR "blood pressures" OR "arterial pressure" OR "arterial pressures" OR hypertension OR hypotension OR normotension OR hypertensive OR antihypertensive OR hypotensive OR normotensive OR "systolic pressure" OR "diastolic pressure" OR "pulse pressure" OR "venous pressure" OR "pressure monitor" OR hypotension OR "pre hypertension" OR "bp response" OR "bp decrease" OR "bp reduction" OR "bp monitor" OR "bp monitors" OR "bp measurement") AND ("exercise"[majr] OR exercise[ti] OR exercises[ti] OR exercising[ti] OR postexercise[ti] OR running[mesh] OR running[ti] OR bicycling[mesh] OR bicycling OR bicycle* OR cycling[ti] OR treadmill* OR ergometer* OR "weight lifting" OR "weight training" OR "resistance training" OR "strength training" OR "endurance training" OR "speed training" OR "circuit training" OR "training duration" OR "training frequency" OR "training intensity" OR "aerobic endurance" OR "aerobic training" OR "interval training" OR "combination training" OR "combined training" OR plyometric* OR "HIIT" OR walking[mesh] OR walking[ti] OR swimming) AND ("randomized controlled trial"[pt] OR "controlled clinical trial"[pt] OR "random allocation" [mh] OR "clinical trial"[pt] OR "clinical trial"[tw] OR "latin square"[tw] OR random*[tw] OR "research design" [mh:noexp] OR "comparative study"[publication type] OR "evaluation studies"[publication type] OR "prospective studies" [mh] OR "cross-over studies" [mh] OR control[tw] OR controlled[tw]) NOT ("DASH"[tiab] OR cancer OR neoplasms OR review[pt] OR fibromyalgia OR alzheimers OR alzheimer OR pregnant OR pregnancy OR "obesity/drug therapy"[mesh] OR pharmacol*[ti] OR drug[ti] OR pharmacist*[ti] OR "diet therapy"[mesh] OR "diet therapy"[subheading] OR "nutritional intervention" OR "dietary intervention" OR "nutritional counseling" OR "dietary counseling" OR caffeine OR "eating change" OR "activities of daily living" OR "dehydration" OR "dehydrate" OR "dehydrated" OR "dietary salt" OR sodium OR epilepsy OR influenza OR flu OR pneumonia OR septicemia OR arthritis OR hiv OR "Acquired Immunodeficiency Syndrome" OR meningitis OR "substance abuse" OR alcoholism OR "drug abuse" OR "Cross-Sectional Studies"[MeSH Terms] OR "Case Reports"[pt] OR Comment[pt] OR Editorial[pt] OR Letter[pt] OR Review[pt] OR "case control"[ti] OR "case report"[ti] OR "case study"[ti] OR "case series"[ti] OR "Case-Control Studies"[Mesh] OR "Follow-Up Studies"[Mesh] OR "observational study"[ti] OR "prospective cohort"[ti] OR "cohort studies" [Mesh:NoExp] OR "cohort study"[ti] OR "Longitudinal Studies" [Mesh:NoExp] OR "Follow-Up Studies"[mesh] OR "Retrospective Studies"[mesh] OR "non-randomized"[ti] OR "follow up study"[ti] OR rat[ti] OR rats[ti] OR mice[ti] OR mouse[ti] OR dog[ti] OR dogs[ti] OR cats[ti] OR "epidemiology"[Subheading])

Scopus

Exclude: Document Type: Review, Letter, Note, Editorial
Dates: 1960-present

Line 1 (in article, title, abstract, keywords): ({mean arterial} OR {blood pressure} OR {blood pressures} OR {arterial pressure} OR {arterial pressures} OR hypertension OR hypotension OR normotension OR hypertensive OR hypotensive OR normotensive OR {systolic pressure} OR {diastolic pressure} OR {pulse pressure} OR {venous pressure} OR {pressure monitor} OR hypotension OR {pre hypertension} OR {bp response} OR {bp decrease} OR {bp reduction} OR {bp monitor} OR {bp monitors} OR {bp measurement})

AND

Line 2 (in article, title, abstract, keywords): (bicycling OR bicycle* OR treadmill* OR ergometer* OR {weight lifting} OR {weight training} OR {resistance training} OR {strength training} OR {endurance training} OR {speed training} OR {circuit training} OR {training duration} OR {training frequency} OR {training intensity} OR {aerobic endurance} OR {aerobic training} OR {interval training} OR {combination training} OR {combined training} OR plyometric* OR HIIT OR swimming)

OR

Line 3 (in article title): (exercise OR exercises OR exercising OR postexercise OR running OR cycling OR walking)

AND

Line 4 (in article, title, abstract, keywords): ({clinical trial} OR {latin square} OR random* OR {comparative study} OR {evaluation study} OR {evaluative study} OR {prospective study} OR {cross-over study} OR control OR controlled)

NOT

Line 5 (in article, title, abstract, keywords): (DASH OR cancer OR neoplasms OR fibromyalgia OR alzheimer* OR pregnant OR pregnancy OR {nutritional intervention} OR {diet therapy} OR {dietary intervention} OR {nutritional counseling} OR {dietary counseling} OR caffeine OR {eating change} OR {activities of daily living} OR dehydration OR dehydrate OR dehydrated OR {dietary salt} OR sodium OR epilepsy OR influenza OR flu OR pneumonia OR septicemia OR arthritis OR hiv OR {Acquired Immunodeficiency Syndrome} OR meningitis OR {substance abuse} OR alcoholism OR {drug abuse})

OR

Line 6 (in article title): (review OR pharmacol* OR drug OR pharmacist* OR {cross-sectional} OR {case report} OR comment OR commentary OR editorial OR letter OR {case control} OR {case study} OR {case series} OR {follow-up study} OR {observational study} OR {prospective cohort} OR {cohort study} OR {longitudinal study} OR {retrospective study} OR {non-randomized} OR rat OR rats OR mice OR mouse OR dog OR dogs OR cats OR {epidemiology})

Web of Science (also known as Web of Knowledge)
Dates: 1974 – present
Limiters: Document Types: Article, Proceedings Paper

Due to database limitations, excluded terms (NOTs) were only searched in the article titles. This was done using RefWorks.

Line 1 (in topic): ("mean arterial" OR "blood pressure" OR "blood pressures" OR "arterial pressure" OR "arterial pressures" OR hypertension OR hypotension OR normotension OR hypertensive OR hypotensive OR normotensive OR "systolic pressure" OR "diastolic pressure" OR "pulse pressure" OR "venous pressure" OR "pressure monitor" OR hypotension OR "pre hypertension" OR "bp response" OR "bp decrease" OR "bp reduction" OR "bp monitor" OR "bp monitors" OR "bp measurement")

AND

Line 2 (in topic): (bicycling OR bicycle* OR treadmill* OR ergometer* OR "weight lifting" OR "weight training" OR "resistance training" OR "strength training" OR "endurance training" OR "speed training" OR "circuit training" OR "training duration" OR "training frequency" OR "training intensity" OR "aerobic endurance" OR "aerobic training" OR "interval training" OR "combination training" OR "combined training" OR plyometric* OR HIIT OR swimming)

OR

Line 3 (in article title): (exercise OR exercises OR exercising OR postexercise OR running OR cycling OR walking)

AND

Line 4 (in topic): ("clinical trial" OR "latin square" OR random* OR "comparative study" OR "evaluation study" OR "evaluative study" OR "prospective study" OR "cross-over study" OR control OR controlled)

NOT

Line 5 (in title): (DASH OR cancer OR neoplasms OR fibromyalgia OR alzheimer* OR pregnant OR pregnancy OR "nutritional intervention" OR "diet therapy" OR "dietary intervention" OR "nutritional counseling" OR "dietary counseling" OR caffeine OR "eating change" OR "activities of daily living" OR dehydration OR dehydrate OR dehydrated OR "dietary salt" OR sodium OR epilepsy OR influenza OR flu OR pneumonia OR septicemia OR arthritis OR hiv OR "Acquired Immunodeficiency Syndrome" OR meningitis OR "substance abuse" OR alcoholism OR "drug abuse" OR review OR pharmacol* OR drug OR pharmacist* OR "cross-sectional" OR "case report" OR comment OR commentary OR editorial OR letter OR "case control" OR "case study" OR "case series" OR "follow-up study" OR "observational study" OR "prospective cohort" OR "cohort study" OR "longitudinal study" OR "retrospective study" OR "non-randomized" OR rat OR rats OR mice OR mouse OR dog OR dogs OR cats OR "epidemiology")

SportDiscus
Dates: 1975-present
Limiters: Publication Type: Journal Articles; Peer Reviewed; Academic Journals

Line 1: ("mean arterial" OR "blood pressure" OR "blood pressures" OR "arterial pressure" OR "arterial pressures" OR hypertension OR hypotension OR normotension OR hypertensive OR hypotensive OR normotensive OR "systolic pressure" OR "diastolic pressure" OR "pulse

pressure" OR "venous pressure" OR "pressure monitor" OR hypotension OR "pre hypertension" OR "bp response" OR "bp decrease" OR "bp reduction" OR "bp monitor" OR "bp monitors" OR "bp measurement")

AND

Line 2: (bicycling OR bicycle* OR treadmill* OR ergometer* OR "weight lifting" OR "weight training" OR "resistance training" OR "strength training" OR "endurance training" OR "speed training" OR "circuit training" OR "training duration" OR "training frequency" OR "training intensity" OR "aerobic endurance" OR "aerobic training" OR "interval training" OR "combination training" OR "combined training" OR plyometric* OR HIIT OR swimming)

OR

Line 3 (in article title): (exercise OR exercises OR exercising OR postexercise OR running OR cycling OR walking)

AND

Line 4: ("clinical trial" OR "latin square" OR random* OR "comparative study" OR "evaluation study" OR "evaluative study" OR "prospective study" OR "cross-over study" OR control OR controlled)

NOT

Line 5 (in title): (DASH OR cancer OR neoplasms OR fibromyalgia OR alzheimer* OR pregnant OR pregnancy OR "nutritional intervention" OR "diet therapy" OR "dietary intervention" OR "nutritional counseling" OR "dietary counseling" OR caffeine OR "eating change" OR "activities of daily living" OR dehydration OR dehydrate OR dehydrated OR "dietary salt" OR sodium OR epilepsy OR influenza OR flu OR pneumonia OR septicemia OR arthritis OR hiv OR "Acquired Immunodeficiency Syndrome" OR meningitis OR "substance abuse" OR alcoholism OR "drug abuse" OR review OR pharmacol* OR drug OR pharmacist* OR "cross-sectional" OR "case report" OR comment OR commentary OR editorial OR letter OR "case control" OR "case study" OR "case series" OR "follow-up study" OR "observational study" OR "prospective cohort" OR "cohort study" OR "longitudinal study" OR "retrospective study" OR "non-randomized" OR rat OR rats OR mice OR mouse OR dog OR dogs OR cats OR "epidemiology")

CINAHL
Dates: 1981-present
Limiters: Research Article; Human; Exclude MEDLINE records; Age Groups: All Adult

Line 1: ("mean arterial" OR "blood pressure" OR "blood pressures" OR "arterial pressure" OR "arterial pressures" OR hypertension OR hypotension OR normotension OR hypertensive OR hypotensive OR normotensive OR "systolic pressure" OR "diastolic pressure" OR "pulse pressure" OR "venous pressure" OR "pressure monitor" OR hypotension OR "pre hypertension" OR "bp response" OR "bp decrease" OR "bp reduction" OR "bp monitor" OR "bp monitors" OR "bp measurement")

AND

Line 2: (bicycling OR bicycle* OR treadmill* OR ergometer* OR "weight lifting" OR "weight training" OR "resistance training" OR "strength training" OR "endurance training" OR "speed training" OR "circuit training" OR "training duration" OR "training frequency" OR "training intensity" OR "aerobic endurance" OR "aerobic training" OR "interval training" OR "combination training" OR "combined training" OR plyometric* OR HIIT OR swimming)

OR

Line 3 (in article title): (exercise OR exercises OR exercising OR postexercise OR running OR cycling OR walking)

AND

Line 4: ("clinical trial" OR "latin square" OR random* OR "comparative study" OR "evaluation study" OR "evaluative study" OR "prospective study" OR "cross-over study" OR control OR controlled)

NOT

Line 5 (in title): (DASH OR cancer OR neoplasms OR fibromyalgia OR alzheimer* OR pregnant OR pregnancy OR "nutritional intervention" OR "diet therapy" OR "dietary intervention" OR "nutritional counseling" OR "dietary counseling" OR caffeine OR "eating change" OR "activities of daily living" OR dehydration OR dehydrate OR dehydrated OR "dietary salt" OR sodium OR epilepsy OR influenza OR flu OR pneumonia OR septicemia OR arthritis OR hiv OR "Acquired Immunodeficiency Syndrome" OR meningitis OR "substance abuse" OR alcoholism OR "drug abuse" OR review OR pharmacol* OR drug OR pharmacist* OR "cross-sectional" OR "case report" OR comment OR commentary OR editorial OR letter OR "case control" OR "case study" OR "case series" OR "follow-up study" OR "observational study" OR "prospective cohort" OR "cohort study" OR "longitudinal study" OR "retrospective study" OR "non-randomized" OR rat OR rats OR mice OR mouse OR dog OR dogs OR cats OR "epidemiology")

5.3 SPIRE Data Extraction and Coding Form

CODER_____ **Coder** (TaShauna = 1, Hayley = 2, Lauren = 3, Other = 4)

Study Information
ID _____ **Study ID** (first 3 letters of 1st author's last name & number to denote) _____
(example: Pescatello= PES001*)* *(Author last name, year)*

PUB_YR _____ **Publication year** (*consider this missing if unpublished)*
DATA _____ **Estimated year of data collection** (*earliest date for data collection or manuscript submission/publication; if unpublished and date unknown, use year manuscript was acquired; for dissertation or thesis, use year)*

LANG_____ **Language of publication**
1=English 3=Japanese 2=Spanish 4=Other, specify:
_____
SOURCE_____ **Publication Type**:
1=journal 2=book 3=thesis/dissertation 4=conference paper 5= unpublished document

SCORE _____ **Impact Score of the Journal** *(use ISI Web of Knowledge journal citation reports)*

JOURNAL NAME _____
PUBMED NAME/ ABBR. _____

FUNDING SOURCE_____ 1= Gov'nt (i.e., CDC, NIH, etc) 2= Academic/University 3= Private 4= Other
For all, *specify source/grant:* _____

BP_OUTCOME_____ 1= Primary 2= Secondary 3= part of CVD risk factors 4= unclear/not disclosed in outcome(s)

NOTE_STUDY_____ **Notes on intervention within study relevant to coding (*note here if multi-arms*)**
1= AE vs CON 2= AE vs RT vs CON 3= AE vs CE vs CON 4= AE vs RT vs CE vs CON
5=RT vs CE vs CON

Sample Characteristics *(proportion: 0.0- 1.0)* ***Note: IF ethnicity is reported, ETH_EST will be == 0***

ETH _____ **Ethnicity reported?** 1 = yes; 0 = no
PROP_WH _____ Proportion White; if whole number available: _____
PROP_BLK _____ Proportion Black; if whole number: _____
PROP_HISP _____ Proportion Latino/Hispanic; if whole number: _____
PROP_CARIB _____ Proportion Caribbean; if whole number: _____
PROP_ASIAN _____ Proportion Asian; if whole number: _____
PROP_MIX _____ Proportion Mixed/other; if whole number: _____

ETH_EST _____ Assumed ethnicity (0= n/a, 1= White, 2= Asian, 3= Black, 4= Unreported, 5= Hispanic/Latino)

EDU _____ **Education reported?** 1 = yes; 0 = no
SES _____ **SES reported?** 1 = yes; 0 = no

NUM_FemCON _____ **# of Females in Sample; Proportion (*#females/total sample*):**_____
NUM_FemEX1 _____ **# of Females in Sample; Proportion (*#females/total sample*):**_____

NUM_FemEX2 _____ **# of Females in Sample; Proportion (#*females/total sample*):**_____
NUM_FemEX3 _____ **# of Females in Sample; Proportion (#*females/total sample*):**_____

REGION_____ **Location of sample** (*if unreported, use location of first author as estimate of study location)*

1=American city: _____
2=other U.S. general region (*city not specified)*: _____
3=Canada (city: _____)
4=Europe (city: _____)
5=South or Central America, Mexico, Caribbean (city: _____)
6=Africa (city: _____)
7=Asia (city: _____)
8=Australia (city: _____)

US_ZIP _____ **Zip Code (US Only)**

POP _____ **Population** 0=not reported
1=school or college 3= clinical/hospital (e.g., cardiac rehab, outpatient clinic, etc.)
_____
2=community (senior center, flyers, etc.) _____

NOTE_RECRUIT **Notes on recruitment/ sample location**
_____

Risk Characteristics- *report values of* ***sample baseline data****; located within text (methods) or in table (results)*
KEEP DATA SEPARATE FOR CONTROL & INTERVENTION GROUPS; NOTE IF DATA ARE COLLAPSED

TOTAL_POP _____ **Reported as total sample?** (1=yes, 0=no)

Characteristic	CONTROL (total sample *n*=____)	EXS #1 (total sample *n*=____)	EXS #1 (total sample *n*=____)
Mean age (years)	AGE	AGE	AGE
SD for age (years)	AGE_SD	AGE_SD	AGE_SD
Mean height (cm)	HT	HT	HT
SD of height (cm)	HT_SD	HT_SD	HT_SD
Mean Pre-weight (kg) **SD pre-weight**	WT preWT_SD	WT preWT_SD	WT preWT_SD
Mean Post-weight (kg) **SD post-weight**	WT postWT_SD	WT postWT_SD	WT postWT_SD
Mean pre-waist circumference (cm) **SD of preWC**	preWC preWC_SD	preWC preWC_SD	preWC preWC_SD
Mean post-waist circumference (cm) **SD of postWC**	postWC postWC_SD	postWC postWC_SD	postWC postWC_SD
Mean preWaist-to-Hip Ratio **SD of preWaist-to-Hip Ratio**	preWHR preWHR_SD	preWHR preWHR_SD	preWHR preWHR_SD
Mean postWaist-to-Hip Ratio **SD of postWaist-to-Hip Ratio**	postWHR postWHR_SD	postWHR postWHR_SD	postWHR postWHR_SD
preBody Mass Index (BMI, kg•m^{-2}) *(can calculate w/ NHLBI)* **SD of preBMI**	preBMI preBMI_SD	preBMI preBMI_SD	preBMI preBMI_SD
postBMI (kg•m^{-2}) *(can calculate w/ NHLBI)* **SD of postBMI**	postBMI postBMI_SD	postBMI postBMI_SD	postBMI postBMI_SD

Characteristic	CONTROL (total sample *n*=____)	EXS #1 (total sample *n*=____)	EXS #1 (total sample *n*=____)
Mean preBody Fat % (BF%) **SD of preBF%**	preBF preBF_SD	preBF preBF_SD	preBF preBF_SD
Mean postBF% **SD of postBF%**	postBF postBF_SD	postBF postBF_SD	postBF postBF_SD
Mean preFat Mass (kg, FM) **SD of preFM**	preFM preFM_SD	preFM preFM_SD	preFM preFM_SD
Mean postFat Mass (kg, FM) **SD of postFM**	postFM postFM_SD	postFM postFM_SD	postFM postFM_SD
Mean preFat-Free Mass (kg, FFM) **SD of preFFM**	preFFM preFFM_SD	preFFM preFFM_SD	preFFM preFFM_SD
Mean preFat-Free Mass (kg, FFM) **SD of postFFM**	postFFM postFFM_SD	postFFM postFFM_SD	postFFM postFFM_SD
Method of Body Fat % Assessment 1= Skinfold thickness 2= Hydrostatic weighing 3= Bioelectrical impedance 4= Air displacement plethysmography 5= DEXA 6= Other, specify:_____	BF_ASS	BF_ASS	BF_ASS
Orientation BP *(i.e., separate occasion)* *(0= not provided, 1=yes)*			
Initial SBP (mmHg)	INITIAL_SBP	INITIAL_SBP	INITIAL_SBP
Initial_SD (mmHg)	INITIAL_SD	INITIAL_SD	INITIAL_SD
Initial DBP (mmHg)	INITIAL_DBP	INITIAL_DBP	INITIAL_DBP
Initial_SD (mm Hg)	INITIAL_SD	INITIAL_SD	INITIAL_SD
Known disease(s)/chronic condition(s) 0= Healthy 3= CVD(s), including: CAD, PAD, congestive HF, MI 4= Stroke 5= Diabetes 6= Metabolic Syndrome (MetS) 7= Arthritis 8= Other, specify:_____ 9= Multiple, specify #s:_____	DISEASE	DISEASE	DISEASE
If disease: report prop. & number *(if "healthy" denote 0= n/a; if missing = ".")*	PROP_DISEASE NumberDisease	PROP_DISEASE NumberDisease	PROP_DISEASE NumberDisease
If congestive HF, report classification (*RE: NYHA criteria*) 0= NA 1= Class I 2= Class II 3= Class III 4= Class IV 5= multiply, specify_____	CHF	CHF	CHF
If MetS: report grouping system 0= NA 1= specify: _____	MET_SYN	MET_SYN	MET_SYN

Characteristic	CONTROL (total sample *n*=____)	EXS #1 (total sample *n*=____)	EXS #1 (total sample *n*=____)
Proportion of sample that is sedentary (≤ 2d/ wk of regular physical activity)	PROP_SED NumberSED	PROP_SED NumberSED	PROP_SED NumberSED
Medication use (0=no, 1= yes)	MED	MED	MED
If yes, report prop & number; *if no meds, use 0=NA (if missing =".")*	PROP_USE NumberMED	PROP_USE NumberMED	PROP_USE NumberMED
Medication Type (*if no meds == 0)* 1= β Blockers 2= Nitrates 3= Calcium Channel Blockers 4= Angiotension Converting Enzyme (ACE) Inhibitors 5= Diuretics 6= Vasodilators 7= NSAIDs 8= Aspirin 9= Other, specify: _____ 10= Multiple, specify: _____	MED_TYPE	MED_TYPE	MED_TYPE
BP Medication use *(1= yes, 0=no) If unreported == "."*	BPMedUse	BPMedUse	BPMedUse
If yes, report prop. & number *(if "no"=0, NA) *** if missing denote == " "*	BPMedProp BPMedNumber	BPMedProp BPMedNumber	BPMedProp BPMedNumber
If taking meds, is BP controlled? yes= 1, SBP & DBP ≤140 & ≤90 mmHg; **no= 0,** SBP OR DBP >140 >90 mmHg *(*if no BP use == NA)*	BPControl	BPControl	BPControl
LIFESTYLE VARIABLES			
Oral Contraceptive (0=no, 1= yes) OR **Hormone replacement therapy**	OC_USE HRT_USE	OC_USE HRT_USE	OC_USE HRT_USE
Reported regular EtOH consumption	PROP_ETOH NumberETOH	PROP_ETOH NumberETOH	PROP_ETOH NumberETOH
Smokers/smokers ≤6 mo.(0=no,1=yes)	SMOKE	SMOKE	SMOKE
If yes, report smoker prop. & number	PROP_SMOKE NumberSMOKE	PROP_SMOKE NumberSMOKE	PROP_SMOKE NumberSMOKE

NOTE_RISK **Notes on risk characteristics relevant to coding**

_____

Methods & Design

CON_GRP _____ **Type of control group used**

1= random assignment of individuals to conditions including a non-exercise control group
2= random assignment of individuals to conditions including a non-exercise control session
3= random assignment of individuals to conditions including a control group of stretching or yoga
4= other, specify:

_____

Experiment/ Intervention Conditions

EXPERIMENT_____ **INTERVENTIONS/EXPERIMENTAL CONDITION(S)**

Independent groups: 1= non-exercise control/comparison + 1 interventions

2= non-exercise control/ comparison + 2 interventions
3= non- exercise control/ comparison + 3 interventions

Non-Independent groups:

4= non-exs. control/comparison + 1 intervention 6= non-exs control/comparison + 3 interventions

5= non-exs. control/comparison + 2 interventions 7= non-exs. control/comparison + >3 interventions

EXP_SETTING_____ **Setting of Intervention(s)**

1= hospital
2= clinic
specify:_____
3= academic research laboratory
specify:_____
4= fitness center, gym
5= Other,
6= multiple,

PERSP _____ **theory-based ExRx:** 0= None 1= Psychological 2= Other,
specify:_____

BEHAV_TECH_____ **Behavioral technique/ Monitoring system used?** (0= none; 1= yes) **If yes, specify:**
_____
_____
_____

Examples: positive reinforcement/contingency management, exercise & lifestyle information/lectures; PA or diet logs, etc.

INTER_LVL_____ **Level of intervention *or supervision* used in the study**

1=primarily one-on-one (e.g., personal training)
2=small group processes (supervisor & group members)
3= supervised session(s)
4= unsupervised session(s)
5= multiply, specify #'s:-
_____

NOTE_EXP & METHODS **Notes related to study design & delivery of intervention:**
_____

Training Intervention Characteristics (SUBGROUP_AE: _____)

TRAINING CHARACTERISTICS	*List interventions from LOWEST intensity to HIGHEST intensity*			
	CONTROL	**EXERCISE #1**	**EXERCISE #2**	**EXERCISE #3**
PART_BEG *# participants @ start*				
PART_END *# participants @ end (completed)*				
PART_LOST *# of drop outs*				
ADHERENCE (report %) *If reported as # of sessions completed, use==* ($\frac{completed\ sessions}{total\ sessions}$ x 100)				
AE_INTENSITY (0= control/ non-exercise comparison) **if range, use average of range*				
AE_UNIT 1= HRreserve, 2=VO2max, 3=VO2peak, 4=HRmax, 5= Other				
RT_INTENSITY (0= control/ non-exercise comparison) **if range, use average of range*				
RT_UNIT 1=1RM, 2= MV, 3= 5RM, 4= 10RM, 5=Other				
EX_PROGRESS If intensity was increased during intervention, report here # of increments *(0= none; 1=AE; 2=RT, 3= both)*				
INTENSITY_AE1				
INTENSITY_AE2				
INTENSITY_AE3				
INTENSITY_AE4				
INTENSITY_RT1				
INTENSITY_RT2				
INTENSITY_RT3				
INTENSITY_RT4				
Were MET values estimated or reported? 0=AE and RT were both estimated 1=AE was reported 2=RT was reported 3=AE and RT were both reported				
MET_AE value (see sheet) (*include code*)				
MET_RT value (see sheet) (*include code*)				
AVG_MET *use mean value of AE & RT*				
Was order of exercise during a session disclosed? 0=not reported 1= Aerobic was performed first				

TRAINING CHARACTERISTICS	*List interventions from LOWEST intensity to HIGHEST intensity*			
	CONTROL	**EXERCISE #1**	**EXERCISE #2**	**EXERCISE #3**
2= Resistance was performed first 3= AE and RT were performed on separate days				
For AE component only				
AE_HIIT *was high intensity interval training used?* *(1=yes; 0= no)*				
HIIT_WORK *if yes, report "work" intensity*				
WORK_MET *if yes, report MET for intensity*				
WORK_TIME *if yes, report "work" duration (s)*				
HIIT_REST *if yes, report "work" intensity*				
REST_MET *if yes, report MET for intensity*				
REST_TIME *if yes, report "rest" duration (s)*				
EX_TYPE (Aerobic) 0= non-exs. control 4= walk/ jog combination 1= walking 5= cycle ergometer 2= jogging 6= Other: _____ 3= running 7= Multiple (#'s): _____				
EX_TYPE (Resistance) 0=non-exercise control 1=Dynamic RT (free weights) 2=Dynamic RT (machines) 3=Isometric or static RT 4=Isometric Hand Grip RT 5=RT bands (elastic bands, therabands, etc.) 6. Other, specify_____ 7. Multiple_____				
For RT components of CE only				
RT_PROTOCOL 0= control (non-exercise comparison) 1= Traditional protocol 2= Progressive 3= Circuit protocol 4= Traditional + Split (upper vs. lower body) protocol 5= Other *specify*:_____				
MUSCLE_GRP Targeted muscle group/ grouping 0= control (non-exercise comparison) 1= Lower body 2= Upper body 3= Upper and lower body (i.e., full body)				
MUSCLE_GRP Targeted muscle group/ grouping 0= control (non-exercise comparison) 1= Lower body 2= Upper body 3= Upper and lower body (i.e., full body)				
UPPER_RT # of upper body exercises in intervention				

TRAINING CHARACTERISTICS	*List interventions from LOWEST intensity to HIGHEST intensity*			
	CONTROL	**EXERCISE #1**	**EXERCISE #2**	**EXERCISE #3**
LOWER_RT **(include core exercises with lower body)** # of lower body exercises in intervention				
TOTAL_RT total # of exercises in session (*in database =V118 +V119)*				
PERCENT_LOWER *(database calculation=* $\frac{\#\ lower\ body\ exercises}{total\ \#\ exercises}$ x100)				
RT_SETS # of sets for *each exercise*				
RT_REPS # of reps for *each set* of exercises				
TOTAL_SETS *database calculation=*$(RT\_SETS) * (TOTAL\_RT)$				
Volume_RT (for intervention) *DB calculation:* =$\#\ of\ exercises * \frac{sets}{exercise} * \frac{reps}{set}\ per\ session)$*(wks)				
VOLUME_LOAD RT (for intervention) *DB calculation* =$\#\ of\ exercises * \%1RM * \frac{sets}{exercises} * \frac{reps}{set}\ per\ session)$*(wks)				
EX_LENGTH intervention length (weeks) 0= acute				
FREQ_EX Frequency (sessions/wk) 0=acute				
MIN_WK Weekly dose= *(d/wk)*(min/wk)* (0=acute)				
EX_TIME_AE Duration (min/ session)				
EX_ TIME_RT Duration (min/ session)				
EX_TIME_TOTAL (min/session)				
VOLUME_SESSION (*calculate in database*) == *(AVG_MET intensity)*(TOTAL min/session)*				
VOLUME_WK (*calculate in database*) = (MET-*intensity)*(TOTAL min/session)*(days/week)*				
preVO$_2$ (either peak or max) 0= acute				
preVO2_unit 1= L/min, 2= ml/kg/min, 3= other unit				
postVO$_2$ (either peak or max) 0= acute				
postVO2_unit 1= L/min, 2= ml/kg/min, 3= other unit				
ChangeVO2_raw *absolute change (post-pre)*				
ChangeVO2_percnt *relative change (%, post-pre)*				
PreLOWER_ST *Baseline lower body strength Use leg press or squat; if other, specify:* _____				
PostLOWER_ST *post-lower body strength*				
LOWER_unit				

TRAINING CHARACTERISTICS	*List interventions from LOWEST intensity to HIGHEST intensity*			
	CONTROL	**EXERCISE #1**	**EXERCISE #2**	**EXERCISE #3**
ChangeLOW_raw *absolute change (post-pre)*				
ChangeLOW_percnt *relative change (%, post-pre)*				
PreUPPER_ST *Baseline upper body strength Use chest or bench, if other, specify:* _____				
PostUPPER_ST *Post-upper body strength Use chest or bench, if other, specify:* _____				
UPPER_unit				
ChangeUP_raw *absolute change (post-pre)*				
ChangeUP_percnt *relative change (%, post-pre)*				
INTER_TIME (HRS) (***acute:*** time b/w sessions) ***** use minimum time; convert days to hours *****				

Blood Pressure Assessment & Outcome Table

BLOOD PRESSURE ASSESSMENT	*List intervention from LOWEST intensity to HIGHEST intensity*			
	CONTROL	EXERCISE #1	EXERCISE #2	EXERCISE #3
BP_SETTING (BP assessment site) 0=unreported 1= physician office, clinic, other clinical setting 2= laboratory (research, same as intervention setting) 3= home (i.e., with BP monitor system) 4= laboratory & during ambulating hours (i.e. with ABP) 5= other, *specify location:*_____				
BP_ASSESS (BP Measurement tool) 1= Manual, random zero- sphygmomanometer 2= Manual, mercury sphygmomanometer 3= Ambulatory (ABP), hrs monitored: _____ 4= Automated 5= multiple, specify #s_____ **choose tool used to measure **primary outcome***				
BP_POSITION (BP Measurement Position) 1= Seated 2= Standing 3= Supine 4= ambulatory (i.e., with ABP monitor) 5= multiple (i.e., if laboratory & ABP data are *both outcomes*) **choose position of **primary outcome***				
[a]BP_STANDARD (BP Methodology) ***Did BP assessment follow the gold standard procedure?*** (see Pickering et al. 2005 AHA Statement) 0= *no, methods unreported; 1=yes; 2= no, other method(s) described*				
PreAE_BPlab baseline pre-BP assessment (min) *if missing = "."*				
PostAE_BPlab Time of post-BP assessment **following** last AE session (min) *if missing = "."*				

NOTE_Methods **Notes relevant to BP Assessment**_____

BPdata_GRAPH _____ Flag is BP data is reported on graph vs. text *(1= graph, 0= no, text or table)*

BP_STATUS: *0= Normal (SBP/DBP <120/80) 1= preHTN (120-139/80-89) 2= HTN (SBP>140 OR DBP>90)* **CONTROL:**_____ **EX1:**_____ **EX2:**_____ **EX3:**_____

BLOOD PRESSURE OUTCOMES (mmHg)		*List intervention from LOWEST intensity to HIGHEST intensity*			
		CONTROL	EXERCISE #1	EXERCISE #2	EXERCISE #3
SBPpre_LAB	Pre-intervention SBP				
SBPpre_SD	Pre-SBP SD (or SEM)				
SBPpost_LAB	Post- intervention SBP				
SBPpost_SD	Post-SBP SD (or SEM)				
SBPchange_LAB	Post-Pre (raw, mmHg)				
SBPchange_LAB (SD)	Post-Pre SD (raw)				
SBPpercnt_LAB	Post-Pre (relative, %)				
SBPpercnt_LAB (SD)	Post-Pre SD (relative)				
DBPpre_LAB	Pre-intervention DBP				
DBPpre_SD	Pre-DBP SD (or SEM)				
DBPpost_LAB	Post- intervention DBP				
DBPpost_SD	Post-DBP SD (or SEM)				
DBPchange_LAB	Post-Pre (raw, mmHg)				
DBPchange_LAB (SD)	Post-Pre SD (raw)				
DBPpercnt_LAB	Post-Pre (relative, %)				
DBPpercnt_LAB (SD)	Post-Pre SD (relative)				
Was MAP reported or calculated? 0=Calculated 1=Reported					
MAPpre_LAB	Pre-intervention MAP				
MAPpre_SD	Pre-MAP SD (or SEM)				
MAPpost_LAB	Post- intervention MAP				
MAPpost_SD	Post-MAP SD (or SEM)				
MAPchange_LAB	Post-Pre (raw, mmHg)				
MAPchange_LAB (SD)	Post-Pre SD (raw)				

BLOOD PRESSURE OUTCOMES (mmHg)		*List intervention from LOWEST intensity to HIGHEST intensity*			
		CONTROL	EXERCISE #1	EXERCISE #2	EXERCISE #3
MAPpercnt_LAB	Post-Pre (relative, %)				
MAPpercnt_LAB (SD)	Post-Pre SD (relative)				
Was Pulse Pressure reported or calculated? 0=Calculated 1=Reported					
PPpre_LAB	Pre-intervention PP				
PPpre_SD	Pre-PP SD (or SEM)				
PPpost_LAB	Post- intervention PP				
PPpost_SD	Post-PP SD (or SEM)				
PPchange_LAB	Post-Pre (raw, mmHg)				
PPchange_LAB (SD)	Post-Pre SD (raw)				
PPpercnt_LAB	Post-Pre (relative, %)				
PPpercnt_LAB (SD)	Post-Pre SD (relative)				
HRpre_LAB	Pre-intervention HR				
HRpre_SD	Pre-HRSD (or SEM)				
HRpost_LAB	Post- intervention HR				
HRpost_SD	Post-HRSD (or SEM)				
HRchange_LAB	Post-Pre (raw, BPM)				
HRchange_LAB (SD)	Post-Pre SD (raw)				
HRpercnt_LAB	Post-Pre (relative, %)				
HRpercnt_LAB (SD)	Post-Pre SD (relative)				

Mechanism(s) Investigated_____ MECH *(see SOP for detailed explanations)*
0= None reported
1= Vascular (i.e., vasoconstrictors, vasodilators, eNOS, nitric oxide, etc.)
2= Baroreceptor, baroreflex
3= Sympathetic NS (beta receptor, beta-adrenergic receptor, beta-adrenoceptor, nor-epi/ epinephrine, catecholamine, etc.)
4= Renal (RAS, RAAS, ACE, etc.)
5= Haemodynamic (Stroke volume, cardiac output, HR, total peripheral resistance, etc.)
6= Other, specify:_____
7= If multiple, specify #s:_____

Were Other Measures of Peripheral Resistance Measured?
0=No
1=Yes

Specify_____

5.4 Downs and Black Methodological Study Quality Checklist

Modified Methodological Quality checklist developed by Downs & Black, 1998

Reviewer's initials _____
First Author _____ *Journal:* _____ *Year published*_____

Reporting		Yes	No	U/D	*Partially*
1.	Is the hypothesis/aim/objective of the study clearly described?	1	0	0	
2A.	Are the main outcomes to be measured clearly described in the Introduction or Methods section?	1	0	0	
2B.	Is BP a primary outcome?	1	0	0	
3.	Are the characteristics of the study population included in the study clearly described?	1	0	0	
4.	Are the interventions under study clearly described?	2	0	0	1
5.	Are the distributions of principal confounders in each group of study participants to be compared clearly described?	1	0	0	
6.	Are the main findings of the study clearly described?	1	0	0	
7.	Does the study provide estimates of the random variability (e.g., standard error, standard deviation, confidence intervals, interquartile range) in the data for the main outcomes?	1	0	0	
8A.	Have all important adverse events/negative outcomes that may be a consequence of the intervention been reported?	1	0	0	
8B.	Were the screening criteria for study eligibility specified?	1	0	0	
9.	Have the characteristics of study participants lost to follow up been described?	1	0	0	
10.	Have actual probability values been reported (e.g., 0.035 rather than <0.05) for the main outcomes except where the probability value is less than 0.001?	1	0	0	

Total reporting score:_____/13

External validity		Yes	No	U/D	*Partially*
11.	Were the study participants asked to participate representative of the entire population from which they were recruited?	1	0	0	
12.	Were study participants who agreed to participate representative of the entire population from which they were recruited?	1	0	0	
13.	Were the staff, places, and facilities where the study participants received the intervention representative of the intervention the majority of subjects receive?	1	0	0	

Total external validity score:_____/3

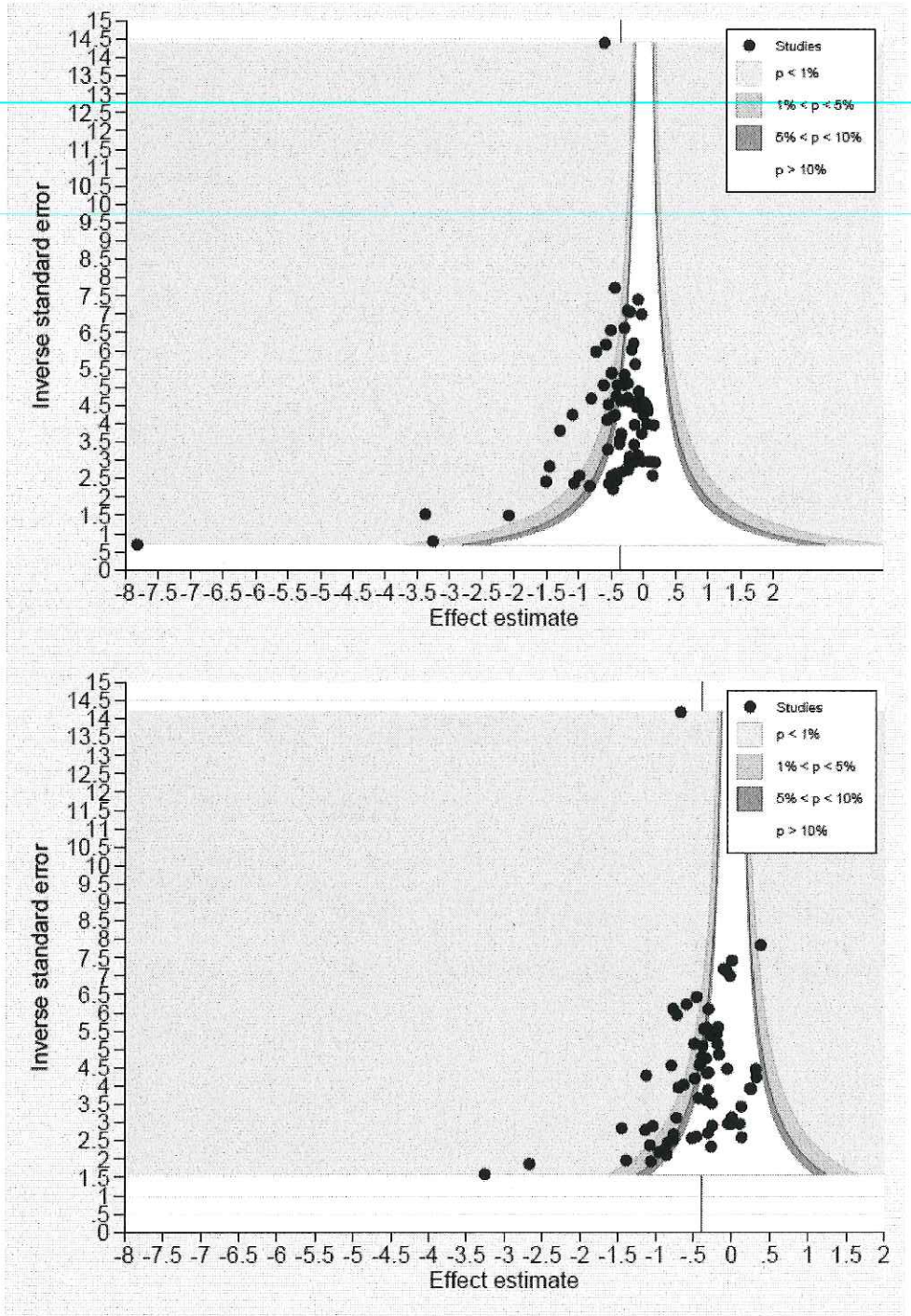
Internal validity – bias		Yes	No	U/D	*Partially*
14.	Was an attempt made to blind study participants to the	1	0	0	

	intervention they received?				
15.	Was an attempt made to blind those measuring the main outcomes of the intervention?	1	0	0	
16.	If any of the results of the study were based on "data dredging," was this made clear?	1	0	0	
17.	In trials and cohort studies, do the analyses adjust for different lengths of follow-up of study participants, or in case-control studies, is the time period between the intervention and outcome the same for cases and controls?	1	0	0	
18.	Were the statistical tests used to assess the main outcomes appropriate?	1	0	0	
19.	Was compliance with the intervention reliable?	1	0	0	
20.	Were the main outcome measures used accurate (valid and reliable)?	2	0	0	1
		Total bias score:_____ /8			
Internal validity – confounding		Yes	No	U/D	*Partially*
21.	Were the study participants in the different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited from the same population?	1	0	0	
22.	Were study participants in the different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited over the same period of time?	1	0	0	
23.	Were study participants randomized to intervention groups?	2	0	0	1
24.	Was the randomized intervention assignment concealed from both study participants and intervention staff until recruitment was complete and irrecoverable?	1	0	0	
25.	Was there adequate adjustment for confounding in the analyses from which the main findings were drawn?	1	0	0	
26.	Were losses of study participants to follow-up taken into account?	1	0	0	
		Total confounding score:_____ /7			
Power		es, ≥2 outcome	Yes, 1 outcome		No
27.	Did the study mention having conducted a power analysis to determine the sample size needed to detect a significant difference in effect size for one or more outcome measures?	2	1		0
		Total power score:_____ /2			
	****Total quality score: _____ /33***				

*Note. *sum of all domain scores*

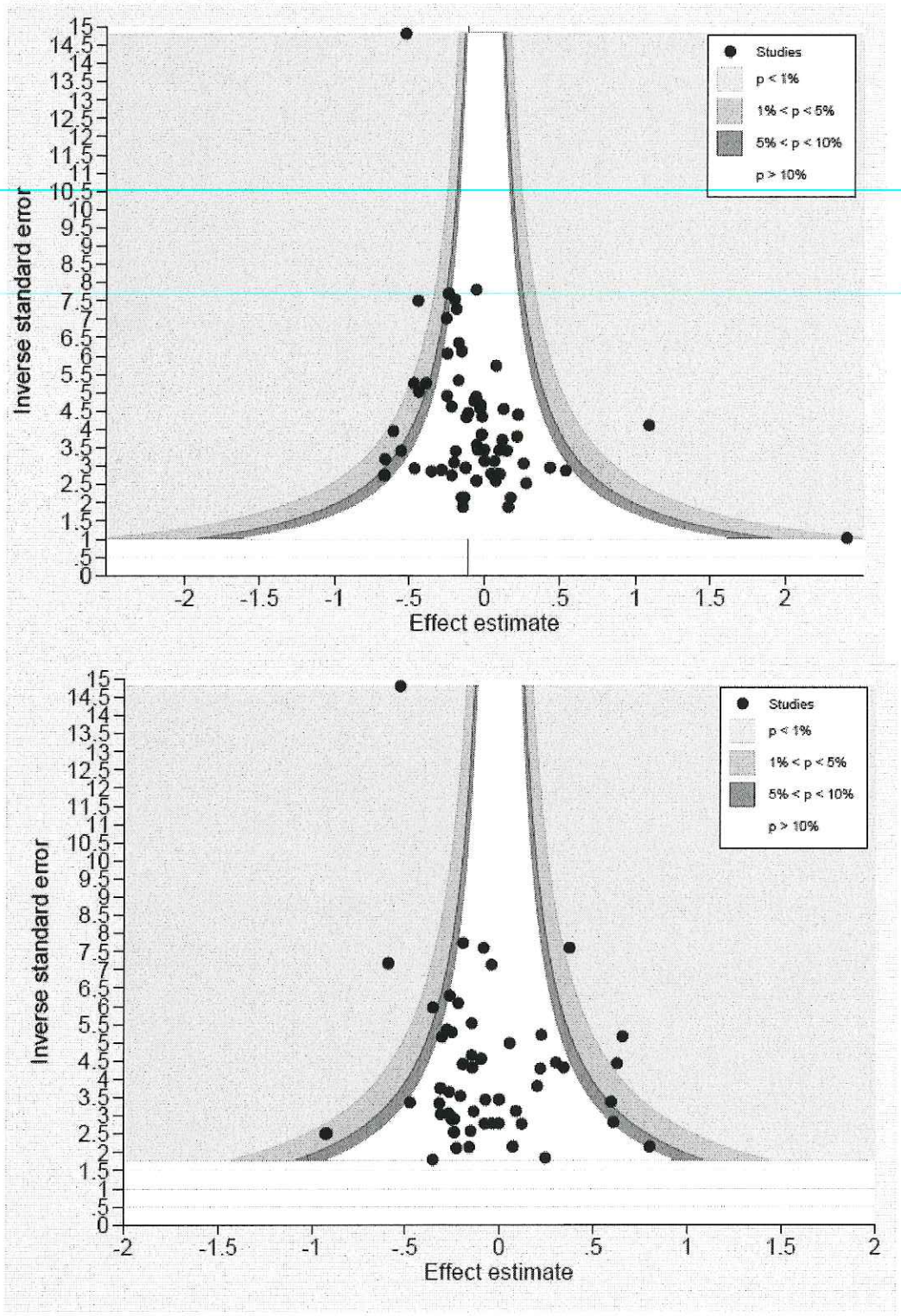
5.5 Additional Funnel Plots: Effect Size Distributions for Systolic BP and Diastolic BP Within-Group and Between-Group Comparisons

Distribution of Effect Sizes (d_+) of the BP Response to Concurrent Exercise Training (within-group) for Systolic (top) and Diastolic (bottom) BP. The red line denotes the average BP response to concurrent exercise training. Negative effect sizes indicate a reduction in BP.



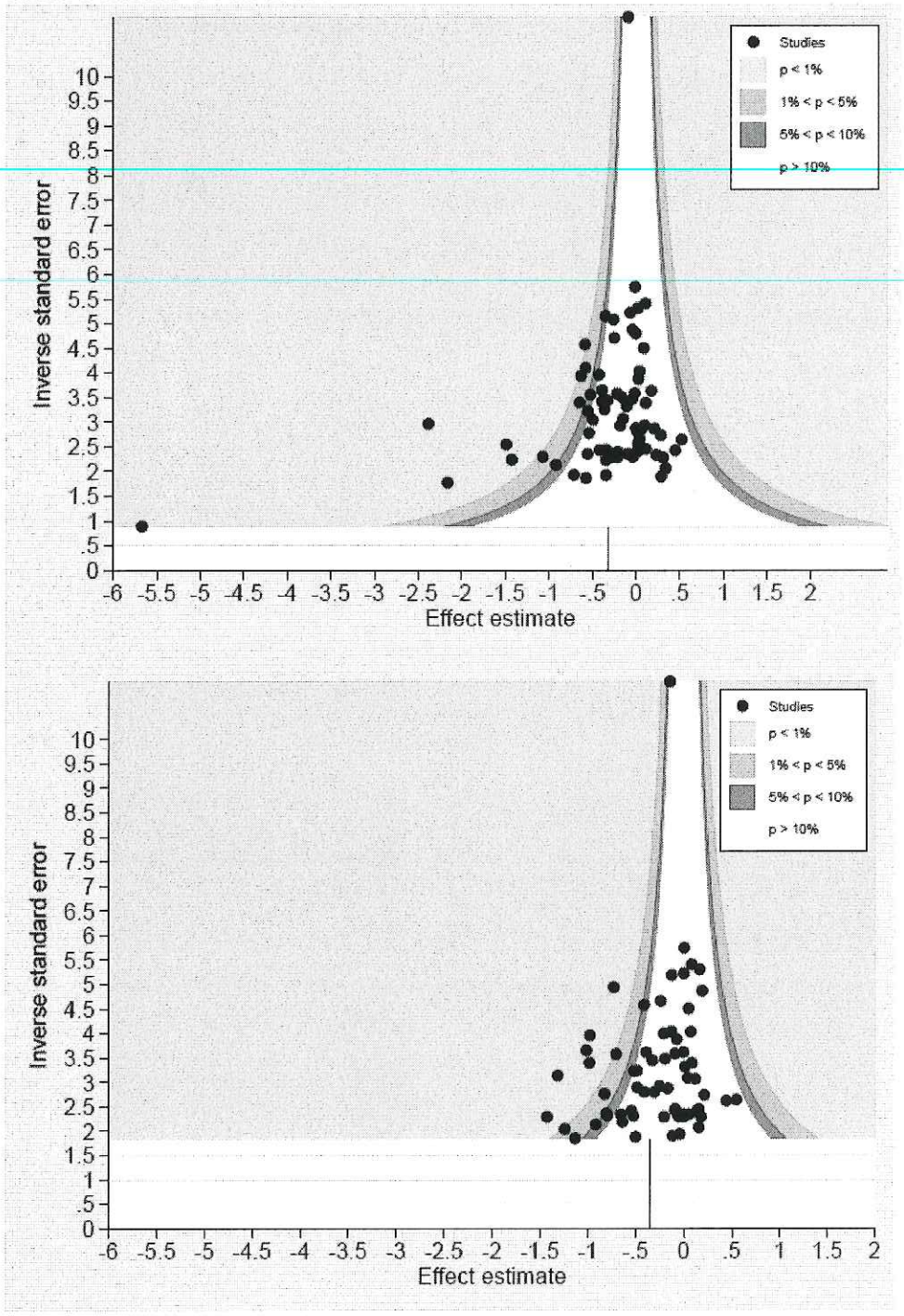
Distribution of Effect Sizes (d_+) of the BP Response to the Non-Exercise Control Comparison Group (within-group) for Systolic (top) and diastolic (bottom) BP. The red

line denotes the average BP response to non-exercise control. Negative effect sizes indicate a reduction in BP.



Distribution of Effect Sizes (d_+) of the BP Response to Concurrent Exercise Training versus Non-Exercise Control Comparison Group (between-group) for Systolic (top) and

Diastolic (bottom) BP. The red line denotes the average BP response to concurrent exercise training over and above the non-exercise control condition. Negative effect sizes indicate a reduction in BP.



5.6 Summary Table of Included Concurrent Exercise Training Trials

Appendix 5.6. Summary Study Characteristics of Included Concurrent Exercise Training Trials (k=76)

	Baseline Sample Characteristics			Features of the Concurrent Training Intervention and Control Comparison Condition			BP Change pre- to post- for CE, CON, and CE vs CON (mmHg)[a]		Methodological Measures		
First Author, Year	N Sample (W)	Resting SBP/DBP (mmHg)	BP and Health Status (% sample)	Length (wks)	Aerobic Exercise	Resistance Exercise	SBP	DBP	Reported Study Outcome	Random?	Study Quality (items satisfied out of 33 *100)
Abdelaal et al. 2014 (2)	N=39(21) CE=20(11) Con=19(10)	CE 145.5±1.91/94.0±0.86[b] Con 145.0±2.94/94.0±1.63[b]	T2DM (100) T2DM (100)	12 12	F: 3 d·wk^{-1} I: Moderate T: NR T: Circuit training Order: NR Con Received regular drug therapy	F: 3 d·wk^{-1} I: Moderate T: NR T: Circuit training	CE -3.1* CE vs Con -1.6* Con +2.2	CE +0.9* CE vs Con -1.8* Con +3.4	BP, Obesity Indices	Yes	58
Bateman et al. 2011 (3)	N=25(12) CE=25(12)	CE 118.0±14.6/77.9±8.36 CON 118.0±14.6/77.9±8.36	MetS (100) MetS (100)	32 32	F: 12 miles·wk^{-1} I: 65-80% VO_{2max} T: 12 miles per week T: walking or jogging Order: NR Con Non-exercise control session, crossover design trial	F: 3 d·wk^{-1} I: 65-80% VO_{2max} T: 3 sets, 8-12 reps T: free weights or machines	CE -2.5	CE -4.1	MetS criteria, CVD risk factors	Yes	82
Bouchonville et al. 2013 (4)	N=107(67) CE=26(16) Con=27(18)	CE 131.2±11.7/70.9±8.3 Con 133.3±18.6/71.5±10.7	CVD (30) CVD (27)	52 52	F: 3 d·wk^{-1} I: 65-75% HR_{max} T: 90 min·ses^{-1}, 30 min·ses^{-1} aerobic exercise T: Treadmill, stationary cycling, stair stepping Order: Performed on the same day, Specific order NR Con Educational information about healthy diet habits, monthly visits	F: 3 d·wk^{-1} I: 65-85% 1RM T: 90 min·ses^{-1}, 30 min·ses^{-1} resistance training, 1-2 sets of 8-12 reps T: weight machines	CE -0.1 CE vs Con +1.7 Con -2.4	CE -3.3 CE vs Con -3.9 Con +0.1	Insulin Sensitivity Index (ISI)	Yes	64
Bunchen et al. 2013 (5)	N=32(17) CE=18(9) Con=14(8)	CE 132.2±13.0/85.0±9.0 Con 127.2±19.0/85.3±10.0	Healthy (100) Healthy (100)	10 10	F: 3 d·wk^{-1} I: CPET threshold T: 30 min·ses^{-1} T: walking, running Order: RT before AE on the same day Con Non-exercise control	F: 3 d·wk^{-1} I: 50% 1RM T: 2 sets of 12 reps T: resistance exercise for upper and lower limbs	CE +1.6 CE vs Con +0.0 Con +1.5	CE -3.1 CE vs Con -3.1 Con +0.0	Quality of Life	Yes	39

Chang Ho-Ha et al. 2012 (16)	N=16(16) CE=7(7) Con=9(9)	CE 113.7±11.22/76.4±6.1	Healthy (100)	12	F: 3 d·wk^{-1} I: 60-80% HRR T: 60 min·ses^{-1} T: Treadmill running	F: 3 d·wk^{-1} I: 10-15RM T: 30 min·ses^{-1}, 3 sets of 10-15 T: Resistance exercises	CE -5.4* CE vs Con -7.1* Con +1.7	CE -10.8* CE vs Con -11.3* Con +0.1	Body Comp and MetS Factors	Yes	58
					Order: RT before AE, on the same day						
		Con 114.3±11.2/69.1±5.4	Healthy (100)	12	Con Non-exercise control						
Cortez-Cooper et al. 2008 (5)	N=37(27) CE=12(9) Con=12(8)	CE 118.0±3.0/ 68.0±2.0[$]	Healthy (100)	13	F: 2 d·wk^{-1} I: 60-75%HRR T: 30-45 min·ses^{-1} T: walking, cycle ergometer	F: 2 d·wk^{-1} I: 70%1-RM T: 30-45min·ses^{-1} T: 10 exercises, 1 set of 8-12 reps, weight machines	CE -1.0 CE vs Con +1.1 Con -2.0	CE 0.0 CE vs Con -0.1 Con +0.1	Central arterial compliance	Yes	67
					Order: AE and RT performed on separate days						
		Con 122.0±4.0/87.0±3.0[$]	Healthy (100)	13	Con F: 3 d·wk^{-1} I: NR T: 30-40 min·ses^{-1} T: mild stretching for major muscle groups						
do Rego et al. 2011 (67)	N=41(41) CE=26(26) Con=15(15)	CE 135.4±17.0/74.6±9.1	Healthy (100)	18	F: 2 d·wk^{-1} I: Weak to moderate T: 35 min·ses^{-1} T: "aerobic endurance exercise"	F: 2 d·wk^{-1} I: Weak to moderate T: 35 min·ses^{-1} T: "muscle strengthening exercise"	CE -5.5* CE vs Con -5.0 Con -0.1	CE -1.7* CE vs Con +0.0 Con -2.0	BP	Yes	55
					Order: RT before AE, performed on the same day						
		Con 138.8±23.6/77.5±5.8	Healthy (100)	18	Con Non-exercise control						
Dobrosielski et al. 2012 (7)	N=140(59) CE=70(29) Con=70(30)	CE 126.9±1.6/71.1±1.1[&]	T2DM (100)	26	F: 3 d·wk^{-1} I: 60-90% HR_{max} T: 45 min·ses^{-1} T: Treadmill, stationary bike, or stair stepper	F: 3 d·wk^{-1} I: 50% 1RM T: 2 sets, 7 exercises, 10-15 reps T: weight machines	CE +0.0 CE vs Con +0.0 Con -1.9	CE +0.0 CE vs Con +1.6 Con -0.1	BP	Yes	67
					Order: AE and RT performed on the same day, order NR						
		Con 126.7±1.6/72.4±1.1[&]	T2DM (100)	26	Con Monthly visits, BP monitoring, Education information on dietary guidelines, Education information on exercise guidelines, Subjects were asked to not change diet or exercise						

Dos Santos et al. 2014 (8)	N=60(60) ERT=20(20) CRT=20(20) Con= 20(20)	ERT 162.7±7.8/90.2±4.3 CRT 167.6±4.3/91.3±3.6	HTN, Healthy (100)	16	ERT and CRT F: 3 d·wk^{-1} I: 65-75% HR_{max} T: 20 min·ses^{-1} T: Treadmill	CRT F: 3 d·wk^{-1} I: 70-90% 1RM T: 3 sets of 10 reps T: traditional concentric training with free weights and machines CE-ERT F: 3 d·wk^{-1} I: 100-110% 1RM T: 50-60 min·ses^{-1} T: Eccentric training with free weights and machines	ERT -33.8* ERT vs Con -29.4* CRT -26.7* CRT vs Con -37.0* Con +1.9	ERT -11.9* ERT vs Con -13.7* CRT -12.1* CRT vs Con -13.9* Con +1.9	Acute and Chronic CV Response	Yes	69
					Order: AE before RT, performed on the sameday						
		Con 160.7±9.1/89.9±4.8	HTN, Healthy (100)	16	Con Non-exercise control						
Dunstan et al. 1998 (9)	N=21(8) CE=11(3) Con=10(5)	CE 126.0±3.0/73.0±2.0[5]	T2DM (100)	8	F: 3 d·wk^{-1} I: 3.0 MET T: 30 seconds aerobic bout, followed by resistance training for 60 min·ses^{-1} T: Cycling as part of circuit training	F: 3 d·wk^{-1} I: 50-55% 1RM T: 10-15 reps in 30 seconds followed by aerobic bout for 60 min·ses^{-1} T: Weight machines as part of circuit training	CE +0.1 CE vs Con +3.1 Con -2.2	CE +0.0 CE vs Con +0.0 Con +0.0	Glycemic Control	Yes	55
					Order: AE and RT performed together, circuit training, on the same day						
		Con 130.0±4.0/72.0±2.0[5]	T2DM (100)	8	Con BP and glucose monitoring, instructed to not change diet, meetings fortnightly						
Ehsani et al. 2003 (10)	N=46 (NR) CE=22(NR) Con=24(NR)	CE 145.3±21.0/76.8±11.0	CVD, Frailty (100)	36	F: 2.61 d·wk^{-1} I: 70-75% HR_{max} T: 69.4 min·ses^{-1} T: HIIT, walking, cycle, rowing	F: 2.61 d·wk^{-1} I: 70-75% HR_{max} T: 69.4 min·ses^{-1} T: "muscle strengthening"	CE -1.2 CE vs Con +1.1 Con -2.1	CE -0.1 CE vs Con +0.1 Con -1.5	Cardiac Output	Yes	57
					Order: AE before RT, performed on the same day						
		Con 147.4±20.0/78.7±12.0	CVD, Frailty (100)	36	Con 3 d·wk^{-1} home exercise program of stretching, yoga, relaxation, 1 d·wk^{-1} sessions were supervised						
Faulkner et al. 2013 (11)	N=60(31) CE=30(16) Con=30(15)	CE 140.0±14.3/81.9±8.1	CVD (87)	8	F: 2 d·wk^{-1} I: 50-85%HR_{max} T: 30 min·ses^{-1} aerobic, 90 min·ses^{-1} T: cycle ergometer	F: 2 d·wk^{-1} I: 15 Borg RPE scale T: 30 min·ses^{-1} resistance, 60 min·ses^{-1} T: "resistance exercises"	CE -5.2* CE vs Con -2.1 Con -3.1	CE -4.6* CE vs Con -3.5 Con -1.2	Vascular risk	Yes	73
					Order: NR						
		Con 137.9±12.0/80.4±8.0	CVD (60)	8	Con Disease management, educational pamphlets						

Figueroa et al. 2011 (12)	N=24(24) CE=12(12) Con=12(12)	CE 124.0±2.9/74.0±2.0[a] Con 120.0±4.0/74.0±1.0[a]	Healthy (100) Healthy (100)	12 12	F: 3 d·wk^{-1} I: 60%HR_{max} T: 20 min·ses^{-1} aerobic, 40 min·ses^{-1} T: walking Con Non-exercise control	F: 3 d·wk^{-1} I: 60%1RM T: 20 min·ses^{-1} resistance, 40 min·ses^{-1} T: weight machines Order: AE before RT, performed on the same day	CE -10.7* CE vs Con -10.7* Con +0.0	CE -10.7* CE vs Con -8.1 Con -2.9	Arterial stiffness, BP, muscle strength	Yes	69
Gram et al. 2013 (14)	N=67(NR) CE=32(NR) Con=35(NR)	CE 135.0±14.0/86.0±10.0 Con 132.0±17.0/85.0±11.0	Healthy (100) Healthy (100)	12 12	F: 3 d·wk^{-1} I: 70%VO_{2max} T: 20 min·ses^{-1} T: row, cycle ergometer Con Health education	F: 3 d·wk^{-1} I: 60%1RM T: 20 min·ses^{-1}, 12 exercises T: free weights Order: AE and RT performed on the same day, order NR	CE -1.3 CE vs Con +0.0 Con -1.7	CE -1.8 CE vs Con +0.0 Con -2.3	Aerobic capacity, muscle strength	Yes	14
Guimaraes et al. 2010 (15)	N=43(30) CONT=16(12) INT=16(9) Con=11(9)	CONT 136.0±10.0/89.0±9.0 INT 134.0±11.0/90.0±8.0 Con 134.0±13.0/89.0±11.0	Healthy (100) Healthy (100)	16 16	CONT F: 3 d·wk^{-1} I: 60% HRR T: 40 min·ses^{-1} aerobic, 60 min·ses^{-1} T: "treadmill" INT F: 3 d·wk^{-1} I: 50-80% HRR T: 40 min·ses^{-1} aerobic, 60 min·ses^{-1} T: "treadmill" Con Non-exercise control	CONT F: 3 d·wk^{-1} I: submaximal T: 40 min·ses^{-1} aerobic, 60 min·ses^{-1} T: "resistance exercise" INT F: 3 d·wk^{-1} I: submaximal T: 40 min·ses^{-1} aerobic, 60 min·ses^{-1} T: "resistance exercise" Order: AE before RT, performed on the same day	CONT CE -3.2 CONT vs Con -0.4 INT CE -5.0 INT vs Con -2.2 Con -2.8	CONT CE -3.0 CONT vs Con -0.1 INT CE -4.6 INT vs Con -2.1 Con -2.5	BP and arterial stiffness	Yes	70
Ho et al. 2012 (17)	N=46 (NR) CE=25(NR) Con=21(NR)	CE 117.7±3.3/66.4±1.5[a] Con 120.1±1.7/65.4±1.9[a]	Healthy (100) Healthy (100)	12 12	F: 5 d·wk^{-1} I: Moderate T: 15 min·ses^{-1} aerobic, 30 min·ses^{-1} T: walking Con Non-exercise control	F: 5 d·wk^{-1} I: Moderate T: 15 min·ses^{-1} resistance, 30 min·ses^{-1} T: free weights, machines Order: AE and RT performed on the same day, specific order NR	CE -3.5 CE vs Con +2.0 Con -5.5	CE -4.3 CE vs Con -1.7 Con -2.6	BP, Arterial Stiffness	Yes	22

Hordern et al. 2008 (18)	N=132(NR) CE=68(NR) Con=64(NR)	CE 137.1±18.1/79.8±8.5	T2DM (100)	4	F: 4 d·wk^{-1} I: 12-13 Borg RPE T: 60 min·ses^{-1} T: walk, jog, cycle, step, row	F: 4 d·wk^{-1} I: 12-13 Borg RPE T: 60 min·ses^{-1} T: weight machines, free weights, resistance bands	CE -4.5* CE vs Con +0.0 Con -4.4*	CE +3.8 CE vs Con +0.0 Con +3.7	Blood glucose	Yes	58
					Order: AE and RT were performed on the same day, specific order NR						
		Con 129.2±15.3/76.9±9.0	T2DM (100)	4	Con Disease management						
Hsu et al. 2014 (19)	N=120(120) CE=60(60) Con=60(60)	CE 134.4±21.2/73.6±12.9	Healthy (100)	12	F: 3 d·wk^{-1} I: 60-80% HR_{max} T: 20 min·ses^{-1} aerobic, 60 min·ses^{-1} T: walking, jog, run, cycle	F: 3 d·wk^{-1} I: 60-80% 1RM T: 20 min·ses^{-1} resistance, 60 min·ses^{-1} T: weight machines	CE -2.5 CE vs Con -1.9 Con -0.1	CE -1.0 CE vs Con -2.6 Con +1.6	Body comp	Yes	45
					Order: NR						
		Con 136.4±24.7/75.4±14.6	Healthy (100)	12	Con Non-exercise control						
Jorge et al. 2011 (20)	N=48(31) CE=12(8) Con=12(8)	CE 132.5±15.8/86.3±9.2	T2DM (100)	12	F: 3 d·wk^{-1} I: lactate threshold T: 60 30 min·ses^{-1} T: cycling	F: 3 d·wk^{-1} I: lactate threshold T: 60 30 min·ses^{-1} T: 7 exercise circuit targeting large muscle groups	CE -2.2 CE vs Con +4.5 Con -6.6	CE -7.6* CE vs Con +1.6 Con -9.2*	Metabolic control, inflammatory markers, adipocytokines, muscle signaling	Yes	69
					Order: AE and RT performed on the same day, specific order NR						
		Con 135.8±16.2/85.0±6.7	T2DM (100)	12	Con Light stretching exercises designed not to elicit exercise benefits						
Kadoglou et al. 2007 (21)	N=60(35) CE=30(17) Con=30(18)	CE 137.7±15.7/83.3±8.9	T2DM (100)	24	F: 4 d·wk^{-1} I: 50-75% VO_{2peak} T: 30-45 min·ses^{-1} T: walk, jogging, cycle	F: 4 d·wk^{-1} I: NR T: 30-45 min·ses^{-1} T: Calisthenics	CE -12.9* CE vs Con -2.4* Con +10.9*	CE -7.9* CE vs Con -10.1* Con +2.2*	Inflammation	Yes	61
					Order: AE and RT performed on the same day, specific order NR						
		Con 144.2±17.0/81.0±8.2	T2DM (100)	24	Con Non-exercise control						
Kawano et al. 2006 (22)	N=39(0) CE=11()) Con=16(0)	CE 115.0±2.0/68.0±2.0[&]	Healthy (100)	16	F: 3 d·wk^{-1} I: 60% HR_{max} T: 30 min·ses^{-1} T: cycling	F: 3 d·wk^{-1} I: 80% 1RM T: 45 min·ses^{-1} T: free weights, machines	CE +1.4 CE vs Con +0.0 Con +1.2	CE -8.3* CE vs Con -1.4 Con +5.9*	Carotid Arterial Compliance	Yes	55
					Order: RT before AT, performed on the same day						
		Con 118.0±2.0/68.0±2.0[&]	Healthy (100)	16	Con Instructed to not change normal activity level						

Kawasaki et al. 2011 (23)	N=57(35) CE=35(24) Con=22(11)	CE 136.6±3.2/81.0±1.6[a] Con 133.9±2.3/77.8±1.5[a]	Healthy (100) Healthy (100)	24 24	F: 2 d·wk^{-1} I: 50% VO_{2peak} T: 60 min·ses^{-1} aerobic T: cycle ergometer, swimming Order: AE and RT performed on the same day, specific order NR Con Non-exercise control	F: 2 d·wk^{-1} I: 50% VO_{2peak} T: 10 min·ses^{-1} resistance T: "land-based muscle strengthening"	CE -5.0* CE vs Con -3.9 Con +0.1	CE -3.6* CE vs Con -7.0 Con +0.1	BP, Lipids, Glucose, and Balance	Yes	48
Kolbe-Alexander et al. 2006 (24)	N=81 (NR) CE1=32 (NR) CE2=27(NR) Con=22 (NR)	CE1 148.0±13.0/90.0±10.0 CE2 143.1±14.0/92.0±10.0 Con 147.0±13.0/91.0±10.0	CE1: T2DM, Arthritis (43) CE2: T2DM, Arthritis (33) T2DM, Arthritis (81)	20 20	CE1 F: 2 d·wk^{-1} I: Low T: 45-50 min·ses^{-1} T: Marching, hand clapping, clicking CE2 F: 2 d·wk^{-1} I: Low T: 45-50 min·ses^{-1} T: Marching, hand clapping, clicking Order: CE1: AE and RT performed on the same day, specific order NR CE2: NR Con Non-exercise control	CE1 F: 2 d·wk^{-1} I: Low T: 45-50 min·ses^{-1}, 2 sets of 10-15 reps T: Water bottles filled with sand acted as weights CE2 F: 2 d·wk^{-1} I: Low T: 45-50 min·ses^{-1}, 2 sets of 10-15 reps T: Water bottles filled with sand acted as weights	CE1 -3.0 CE1 vs Con -5.3 CE2 -4.3* CE2 vs Con -6.5* Con +2.2	CE1 -2.0 CE1 vs Con +0.0 CE2 -3.9 CE2 vs Con -2.0 Con -1.9	Quality of Life Measures	Yes	39
Kouidi et al. 2013 (25)	N=23(6) CE=11(3) Con=12(3)	CE 129.5±7.2/78.5±6.0 Con 128.6±7.4/77.4±4.6	Renal Transplant (100) Renal Transplant (100)	24 24	F: 4 d·wk^{-1} I: 50-75% VO_{2peak} T: 30-40 min·ses^{-1} T: cycling, jogging, step aerobics, calisthenics, dancing Order: AE and RT performed on the same day, specific order NR Con Non-exercise control	F: 4 d·wk^{-1} I: 70-80% 1RM T: 10-30 min·ses^{-1}, 1-3 sets of 1-12 reps T: weight stations	CE +0.0 CE vs Con -5.6 Con +5.3	CE -0.1 CE vs Con -6.5 Con +6.0	Autonomic function	Yes	58
Kraemer et al. 2001 (26)	N=15(15) CE=9(9) Con=6(6)	CE 122.8±7.8/80.9±7.1 Con 120.3±12.8/79.0±5.5	Healthy (100) Healthy (100)	12 12	F: 3 d·wk^{-1} I: 80-90% HR_{max} T: 20 min·ses^{-1} T: Step aerobics Order: AE before RT, performed on the same day Con Non-exercise control	F: 3 d·wk^{-1} I: 80-90% HR_{max}, 1RM T: 2-5 sets of 10 reps T: free weights	CE -4.2 CE vs Con -5.8 Con +1.6	CE -8.5 CE vs Con -5.0 Con -3.5	Women's health profile to resistance training	Yes	67

Laterza et al. 2007 (27)	N=42(10) HTN=11(NR) NBP=12(0)	HTN 145.0±2.0/94.0±64.0[a] NBP 117.0±2.0/78.0±1.0[a]	Untreated HTN (47.8%)	16	CE (HTN and NBP) F: 3 d·wk^{-1} I: anaerobic threshold T: 40 min·ses^{-1} aerobic T: cycle ergometer Order: RT before AE, performed on the same day	CE (HTN and NBP) F: 3 d·wk^{-1} I: NR T: 60 min·ses^{-1} T: calisthenics	HTN CE -20.1* NBP CE -1.4 CE vs Con -16.0*	HTN CE -13.9* NBP CE 0.0 CE vs Con -9.0*	Bareoreflex sensitivity	Yes	69
		Con 145.0±4.0/94.0±2.0[a]	Non-treated HTN (100%)	16	Con Instructed to avoid regular exercise for study duration		Con +1.0 CE vs Con -2.0	Con +1.0 CE vs Con +1.0			
Lubans et al. 2013 (31)	N=44(44) CE=22(22) Con=22(22)	CE 138.3±11.5/82.7±11.8	Healthy (100)	8	F: 2 d·wk^{-1} I: 12-16 borg rating of perceived exertion T: 55-75 min·ses^{-1} T: walking, jogging in place Order: NR	F: 2 d·wk^{-1} I: 13-16 borg rating of perceived exertion T: 55-75 min·ses^{-1}, 2 sets of 10-15 reps, 1 exercises T: body weight, resistance bands	CE -0.1 CE vs Con -0.1 Con +0.0	CE -0.1 CE vs Con -1.6 Con +0.1	Efficacy of RT program using behavioral model	Yes	64
		Con 136.1±12.9/79.1±8.4	Healthy (100)	8	Con Provided pedometer, and education session about physical activity						
Loimaala et al. 2003 (30)	N=49 (0) CE=24(0) Con=25(0)	CE 142.0±17.0/NR	T2DM (100)	52	F: 2 d·wk^{-1} I: 65-75% VO_{2max} T: at least 30 min·ses^{-1} T: walking Order: NR	F: 2 d·wk^{-1} I: 70-80% MVC T: at least 30 min·ses^{-1} T: "strength training"	CE -2.3 CE vs Con -1.6	NR	Baroreflex Sensitivity	Yes	55
		Con 145.0±14.0/NR	T2DM (100)		Con Non-exercise control		Con -0.1				
Loimaala et al. 2009 (28)	N=48 (0) CE=24(0) Con=24(0)	CE 144.0±17.0/NR	T2DM (100)	144	F: 2 d·wk^{-1} I: 65-75% VO_{2max} T: 30 min·ses^{-1} T: walking, jogging Order: AE and RT were performed on separate days	F: 2 d·wk^{-1} I: 70-80% MVC T: 30 min·ses^{-1}, 3 sets of 18-10 reps T: muscle strengthening for large muscle groups	CE -0.1 CE vs Con +0.0	NR	Myocardial diastolic tissue velocity	Yes	45
		Con 146.0±15/NR	T2DM (100)	144	Con Non-exercise control		Con +0.0				
Loimaala et al. 2009 (29)	N=50(0) CE=24(0) Con=24(0)	CE 142.0±2.8/NR	T2DM (100)	288	F: 4 d·wk^{-1} I: 65-75% VO_{2max} T: 30 min·ses^{-1} T: walking, jogging Order: AE and RT performed on separate days	F: 4 d·wk^{-1} I: 60% MVC T: 30 min·ses^{-1} T: free weights and machines	CE -2.1 CE vs Con -1.4	NR	CVD risk factors, pulse wave velocity (PWV)	Yes	45
		Con 145.0±2.8/NR	T2DM (100)	288	Con Non-exercise control		Con -0.1				

Lucio-Mazini-Filho et al. 2013 (13)	N=54(54) CE=33(33) Con=21(21)	CE 145.3±14.3/95.8±8.6	Healthy (100)	16	F: 3 d·wk^{-1} I: moderate T: 25 min·ses^{-1} aerobic T: walking	F: 3 d·wk^{-1} I: moderate, Omni scale 3-5 T: 15 min·ses^{-1} resistance T: resistance bands	CE -8.2* CE vs Con +0.0 Con -8.0*	CE -11.2* CE vs Con -9.8 Con -1.4	BP, Body Mass Index, Metabolic Parameters	Yes	58
		Con 147.8±12.2/92.1±7.5	Healthy (100)	16	Order: AE before RT, performed on the same day Con Non-exercise control						
Luk et al. 2011 (32)	N=64(16) CE=32(8) Con=32(8)	CE 144.0±15.0/80.0±7.0	CVD, T2DM (100)	8	F: 3 d·wk^{-1} I: 80% HR_{max} T: 60 min·ses^{-1} T: walking, jogging, cycling, rowing, arm ergometery	F: 3 d·wk^{-1} I: 80% HR_{max} T: 60 min·ses^{-1} T: dumbbell weight training	CE -8.1* CE vs Con -4.2 Con -3.9*	CE -4.9* CE vs Con -2.1 Con -2.8	Brachial flow mediated dilation	Yes	67
		Con 145.0±20.0/84.0±8.0	CVD, T2DM (100)	8	Order: AE and RT performed on the same day, specific order NR Con Non-exercise control						
Malin et al. 2013 (33)	N=16(11) CE=8(5) Con=8(6)	CE 136.8±2.4/NR	Impaired glucose tolerance (100)	12	F: 3 d·wk^{-1} I: 70% HR_{max} T: 45 min·ses^{-1} T: cycling	F: 2 d·wk^{-1} I: 70% 1RM T: 2 sets of 12 reps, 6 exercises T: whole body resistance exercises	CE -8.8* CE vs Con -5.6* Con +2.4*	NR	CVD risk factors	Yes	58
		Con 126.1±134.5	Impaired glucose tolerance (100)	12	Order: NR Con Non-exercise control						
McGavock et al. 2004 (34)	N=18(18) CE=11(11) Con=7(7)	CE 133.0±15.0/76.0±9.0	T2DM (100)	10	F: 3 d·wk^{-1} I: 70% HRR T: 30-55 min·ses^{-1} T: cycle ergometer	F: 3 d·wk^{-1} I: 65-70% 1RM T: 3 sets of 10-15 reps T: weight machines	CE +1.8 CE vs Con +3.4 Con -1.5	CE +0.0 CE vs Con +1.8 Con -1.6	LV filling dynamics, arterial compliance	Yes	48
		Con 139.0±17.0/74.0±11.0	T2DM (100)	10	Order: AE and RT performed on the same day Con Non-exercise control						
McMurdo et al. 1992 (35)	N=77(NR) CE=44(NR) Con=43(NR)	CE 143.1±18.0/88.6±11.7	Healthy (100)	32	F: 3 d·wk^{-1} I: low T: 45 min·ses^{-1} T: endurance exercise to music	F: 3 d·wk^{-1} I: low T: 45 min·ses^{-1} T: muscle strengthening	CE -1.6 CE vs Con +0.1 Con -2.5	CE -3.0 CE vs Con +0.1 Con -3.5*	Flexibility and strength	Yes	61
		Con 136.8±15.4/87.4±10.6	Healthy (100)	32	Order: AE and RT performed on the same day, specific order NR Con Health education classes on a regular schedule						

Miura et al. 2008 (36)	N=98 (98) 1Day=29(29) 2Day=25(25) Con=23(23)	CE-1 Day 126.2±14.0/73.8±7.8 CE-2 Day 123.3±13.7/73.0±9.2	Healthy (100)	12	1Day F: 1 d·wk^{-1} I: 70-75% HR_{max} T: 40 min·ses^{-1} T: Circuit training 2Day F: 2 d·wk^{-1} I: 70-75% HR_{max} T: 40 min·ses^{-1} T: Circuit training Order: AE and RT were performed on the same day, circuit training	1Day F: 1 d·wk^{-1} I: 70-75% HR_{max} T: 40 min·ses^{-1} T: Circuit training, bands and light dumbbells 2Day F: 2 d·wk^{-1} I: 70-75% HR_{max} T: 40 min·ses^{-1} T: Circuit training, bands and light dumbbells	1 Day CE -2.4 CE1 vs Con -2.2 2 Day CE -3.2 CE2 vs Con -3.3 Con +0.0	1 Day CE -1.9 CE1 vs Con -0.1 2 Day CE -4.2 CE2 vs Con -3.3 Con -0.1	Arterial stiffness	Yes	58
		Con 122.9±13.7/71.7±9.1	Healthy (100)	12	Con Non-exercise control						
Nishijima et al. 2007 (37)	N=531(327) CE=281(166) Con=280(161)	CE 139.3±16.4/82.3±9.7	T2DM, Arthritis (30.2%)	24	F: 2-4 d·wk^{-1} I: 40-70% HR_{max} T: 20-40 min·ses^{-1} aerobic, 60-90 min·ses^{-1} T: cycle ergometer Order: AE and RT performed on the same day, specific order NR	F: 2-4 d·wk^{-1} I: mild to moderate, RPE T: 60-90 min·ses^{-1}, 2 sets of 20 reps, 4 exercises T: machine weights	CE -6.1* CE vs Con -0.1 Con -5.2*	CE -6.7* CE vs Con -1.4 Con -5.3*	BP, LDL cholesterol, hemoglobin A1C	Yes	76
		Con 141.3±17.6/83.3±10.6	T2DM, Arthritis (27.5%)	24	Con Adhere to lifestyle guidelines, not reported						
Ohkubo et al. 2001 (38)	N=65(32) CE=32(16) Con=33(16)	CE 143.0±2.1/78.7±2.4[a]	Healthy (100)	25	F: 2 d·wk^{-1} I: 25-60% HRR T: 10-25 min·ses^{-1} T: cycle ergometer Order: AE and RT performed on the same day, specific order NR	F: 2 d·wk^{-1} I: 25-60%HRR T: 3 exercises, 1 set x 20 reps T: therabands	CE -11.0* CE vs Con -6.3* Con -4.6*	CE -2.7 CE vs Con -1.3 Con -1.5	Home BP Measurements	Yes	65
		Con 144.1±2.5/81.4±2.1[a]	Healthy (100)	25	Con Education classes unrelated to physical activity						
Okada et al. 2010 (39)	N=38(17) CE=21(11) Con=17(6)	CE 129.0±21.6/74.6±11.6	T2DM (100)	8	F: 3-5 d·wk^{-1} I: training heart rate calculated T: 30 min·ses^{-1} aerobic, 75 min·ses^{-1} T: cycle ergometer, aerobic dance Order: NR	F: 3-5 d·wk^{-1} I: training heart rate calculated T: 20 min·ses^{-1} aerobic, 75 min·ses^{-1} T: "resistance exercise"	CE +0.1 CE vs Con -1.5 Con +2.1	CE +3.2 CE vs Con +1.2 Con +2.0	Incidence of CVD, vascular function	Yes	61
		Con 126.6±16.8/73.8±11.8	T2DM (100)	8	Con Received same disease management and dietary information as CE group						

Okamoto et al. 2007 (40)	N=33(22) BRT=11(7) ART=11(7) Con=11(8)	BRT 113.6±3.4/62.5±2.2[a] ART 113.5±4.3/64.5±1.9[a]	NBP, Healthy (100)	8	BRT F: 2 d·wk^{-1} I: 60% HR_{max} T: 20 min·ses^{-1} T: running ART F: 2 d·wk^{-1} I: 60% HR_{max} T: 20 min·ses^{-1} T: running Order: BRT: AE before RT, performed on the same day ART: RT before AE, performed on the same day	BRT F: 2 d·wk^{-1} I: 80% 1RM T: 5 sets of 8-10 reps, 7 exercises T: weight machines ART F: 2 d·wk^{-1} I: 80% 1RM T: 5 sets of 8-10 reps, 7 exercises T: weight machines	BRT CE -2.0 BRT vs Con -0.1 ART CE -2.2 ART vs Con -0.1 Con +1.1	BRT CE -2.5 BRT vs Con +0.0 ART CE -7.6 ART vs Con -5.2 Con +1.1	Vascular function pulse wave velocity	Yes	65
		Con 113.9±3.2/63.3±2.1[a]	NBP, Healthy (100)	8	Con Non-exercise control					
Oliviera et al. 2012 (66)	N=22(14) CE=10(6) Con=12(8)	CE 132.5±15.8/86.2±9.1	T2DM (100)	12	F: 3 d·wk^{-1} I: lactate threshold T: 60 min·ses^{-1} T: cycling Order: AE and RT performed on the same day, specific order NR	F: 3 d·wk^{-1} I: 50% 1RM T: 60 min·ses^{-1} T: machine weights	CE -4.3 CE vs Con +2.3 Con -6.6	CE -8.7* CE vs Con +0.1 Con -9.3*	Stress markers, metabolic control	Yes	61
		Con 135.8±16.2/85.0±6.7	T2DM (100)	12	Con Glycemic control monitoring, disease management, stretching classes					
Opdenacker et al. 2007 (41)	N=180(90) CE1=60(30) CE2=60(30) Con=60(30)	CE1 144.8±2.3/86.6±1.3[a] CE2 148.6±2.3/87.9±1.3[a]	Healthy (100)	24	CE1 F: 2.5 d·wk^{-1} I: 75% HRR, moderate to vigorous T: 60-90 min·ses^{-1} T: cycle ergometer, walk, cycle, step, swim CE2 F: home-based I: at increased heart rate T: NR T: cycle ergometer, walk, cycle, step, swim Order: CE1: AE and RT performed on the same day, specific order NR CE2: AE and RT performed on the same day, specific order NR	CE1 F: 2.5 d·wk^{-1} I: moderate, 10RM T: 60-90 min·ses^{-1} T: resistance bands CE2 F: home-based I: increased heart rate T: NR T: "resistance exercise"	CE1 -3.0* CE1 vs Con -0.1 CE2 -5.9* CE2 vs Con -3.5 Con -2.3	CE1 -5.9* CE1 vs Con +0.0 CE2 -7.2* CE2 vs Con -1.3 Con -5.9*	CVD risk factors	Yes	55
		Con 143.1±2.2/84.5±1.2[a]	Healthy (100)		Con Non-exercise control					

					CE1 F: 2 d·wk^{-1} I: 60-85% HR_{max} T: 50-60 min·ses^{-1} T: "aerobic exercise"		CE1 F: 2 d·wk^{-1} I: 60-85% 10RM T: 50-60 min·ses^{-1} T: "resistance exercise"		CE1 -3.7		CE1 -10.4*				
		CE1 130.1±8.8/87.2±5.5 CE2 130.1±11.6/86.1±7.5			CE2 F: 4 d·wk^{-1} I: 60-85% HR_{max} T: 50-60 min·ses^{-1} T: "aerobic exercise"		CE2 F: 4 d·wk^{-1} I: 60-85% 10RM T: 50-60 min·ses^{-1} T: "resistance exercise"		CE1 vs Con -3.1 CE2 +0.0		CE1 vs Con -7.6 CE2 -3.3		Hemodyna mic parameters	Yes	45
Opperman et al. 2012 (1)	N=41(0) CE1=16(0) CE2=16(0) Con=9(0)		Healthy (100)	12	Order: CE1: AE and RT performed on the same day, specific order NR CE2: AE and RT performed on the same day, specific order NR Con Non-exercise control				CE2 vs Con +0.0 Con -0.1		CE2 vs Con -0.1 Con -2.4				
		Con 135.8±15.5/87.2±8.3	Healthy (100)	12											
Pantelic et al. 2013 (42)	N=60(0) CE=30(0) Con=30(0)	CE 130.3±16.6/80.6±9.6 Con 132.0±13.0/83.3±8.0	CVD (100) CVD (100)	3 3	F: 7 d·wk^{-1} I: 55-70% HR_{max} T: 45-60 min·ses^{-1} T: cycle Order: AE and RT performed on the same day, specific order NR Con Usual drug therapy		F: 7 d·wk^{-1} I: calisthenics T: 45-60 min·ses^{-1} T: calisthenics		CE -4.0* CE vs Con +0.0 Con -4.3*		CE -3.8 CE vs Con -0.3 Con -3.0		Cardio respiratory fitness	Yes	58
Petraki et al. 2008 (43)	N=43(11) CE=22(7) Con=21(4)	CE 137.2±18.7/82.9±8.3 Con 135.7±16.1/83.6±7.9	CKD (100) CKD (100)	28 28	F: 3 d·wk^{-1} I: 13 Borg RPE scale T: 30-60 min·ses^{-1} T: cycle Order: AE and RT performed on the same day, specific order NR Con Non-exercise control		F: 3 d·wk^{-1} I: theraband MET T: 30-60 min·ses^{-1} T: resistance bands		CE -4.8* CE vs Con -3.6 Con -1.2		CE -6.3* CE vs Con -4.9 Con -1.4		Baroreflex sensitivity	Yes	58
Puggard et al. 2000 (44)	N=38(38) CE=22(22) Con=14(14)	CE 161.0 (130-197)/84.0(62-113)[%] Con 153(114-190)/77(61-92)[%]	Healthy (100) Healthy (100)	32 32	F: 1-7 d·wk^{-1} I: 69% VO_{2max} T: NR T: walking Order: AE and RT performed on the same day, specific order NR Con Non-exercise control		F: 1-7 d·wk^{-1} I: 69% MVC T: NR T: "resistance exercise"		CE -0.1 CE vs Con -1.8 Con +0.1		CE -4.8 CE vs Con -4.8 Con +0.0		Maximal oxygen uptake, muscle strength, walking speed	Yes	39
Riess et al. 2011 (45)	N=31(17) CE=16(8) Con=15(9)	CE 130.4±12.2/76.0±7.4 Con 137.3±18.0/76.6±8.9	CKD (100) CKD (100)	12 12	F: 2 d·wk^{-1} I: 85% HR_{max} T: 30-60 min·ses^{-1} T: walking, cycle Order: NR Con Non-exercise control		F: 2 d·wk^{-1} I: 61% 1RM T: 30-60 min·ses^{-1} T: weight machines		CE -1.5 CE vs Con +0.0 Con -1.9		CE +1.3 CE vs Con +0.4 Con -3.2		Exercise capacity, muscle strength, quality of life, body composition , CVD risk	Yes	58

Seo et al. 2010 (46)	N=15(15) CE=8(8) Con=7(7)	CE 126.5±14.4/86.5±11.7	Healthy (100)	12	F: 3 d·wk^{-1} I: 70% HRR T: 60 min·ses^{-1} T: walking, aerobics	F: 3 d·wk^{-1} I: 60% 1RM T: 60 min·ses^{-1}, 3 sets of 8 reps, 8 exercises T: machine weights	CE -4.8 CE vs Con -3.4 Con -1.3	CE -2.7 CE vs Con +0.0 Con -2.3	Growth Hormone	Yes	55
		Con 132.0±13.8/87.3±10.0	Healthy (100)	12	Order: AE and RT performed on the same day, specific order NR Con Flexibility exercise program, 3 d·wk^{-1}						
Seo et al. 2011 (47)	N=20(20) CE=10(10) Con=10(10)	CE 121.2±8.0/72.8±10.7	Healthy (100)	12	F: 3 d·wk^{-1} I: 65% HRR T: 30 min·ses^{-1} aerobic, 60 min·ses^{-1} T: running	F: 3 d·wk^{-1} I: 65%HRR T: 30 min·ses^{-1} resistance, 60 min·ses^{-1}, 3 sets of 10 reps T: resistance exercise	CE -2.4 CE vs Con -3.4 Con +1.0	CE -5.2 CE vs Con -6.4 Con +1.2	Visfatin	Yes	61
		Con 119.9±9.8/72.8±10.7	Healthy (100)	12	Order: RT before AE, performed on the same day Con Non-exercise control						
Shaw et al. 2010 (48)	N=25(0) CE=13(0) Con=12(0)	CE 131.54±9.28/NR	Healthy (100)	16	F: 3 d·wk^{-1} I: 60-75%HR$_{max}$ T: 22 min·ses^{-1} aerobic, 60 min·ses^{-1} T: treadmill, cycle ergometer, stepping	F: 3 d·wk^{-1} I: 60-75% 1RM T: 22 min·ses^{-1} resistance, 60 min·ses^{-1} T: machine weights	CE -9.9* CE vs Con -1.4* Con +4.4	NR	Framingham Heart Risk Scores	Yes	52
		Con 122.0±5.72/NR	Healthy (100)	16	Order: AE and RT performed on the same day, specific order NR Con Non-exercise control						
Shin et al. 2009 (49)	N=60 (60) CE=30(30) Con=30(30)	CE 140.0±16.5/88.2±13.5	Healthy (100)	8	F: 2 d·wk^{-1} I: 40-50% HR$_{max}$ to 60-65% HR$_{max}$ T:30-50 min T: Rhythmic movements for increasing cardiopulmonary endurance	F: 2 d·wk^{-1} I: 40-50% HR$_{max}$ to 60-65% HR$_{max}$ T: 30-50 min T: Rhythmic movements for strengthening muscles	CE -4.4 CE vs Con -3.9 Con -0.1	CE -6.9* CE vs Con -13.2* Con +6.2	Physical fitness, depression, self efficacy	Yes	65
		Con 139.8±19.4/138.7±19.0	Healthy (100)	8	Order: AE and RT performed on the same day, circuit training Con Wait-list non-exercise control						
Sigal et al. 2007 (50)	N=251 (91) CE= 64 (24) Con=63 (22)	CE 131.0±22.0/79.0±13.0	T2DM (100)	26	F: 3 d·wk^{-1} I: 60-75%HR$_{max}$ T: 15-45 min·ses^{-1} T: treadmill, cycle ergometer	F: 3 d·wk^{-1} I: 7-9RM T: 3 sets x 7 reps T: weight machines	CE -0.1 CE vs Con +1.1 Con -2.0	CE +0.0 CE vs Con +0.1 Con -0.1	Glycemic Control	Yes	76
		Con 133±20.0/80.0±12.0	T2DM (100)	26	Order: NR Con Dietary recommendations as part of disease management for T2DM						

Sillanpaa et al. 2009 (women) (51)	N=30(30) CE=18(18) Con=12(12)	CE 125.0±17.0/75.0±8.0 Con 130.0±18.0/76.0±9.0	Healthy Healthy	21 21	F: 2-3 d·wk^{-1} I: anaerobic threshold T: 30-90 min·ses^{-1} aerobic, 60-90 min·ses^{-1} T: cycle ergometer Order: AE and RT performed on separate days Con Non-exercise control	F: 2-3 d·wk^{-1} I: 40-80% 1RM T: 2-3 sets, 8-15 reps T: weight machines	CE +0.1 CE vs Con +5.2 Con -4.7*	CE +2.3 CE vs Con +5.5 Con -3.1	Body composition, fitness, and metabolic health	Yes	58
Sillanpaa et al. 2009 (men) (52)	N=63(0) CE=15(0) Con=15(0)	CE See graph (SD NR) Con	Healthy (100) Healthy (100)	21 21	F: 4 d·wk^{-1} I: anaerobic threshold T: 60-90 min·ses^{-1} T: cycle ergometer Order: AE and RT performed on separate days Con Non-exercise control	F: 4 d·wk^{-1} I: 40-80% 1RM T: 3-4 sets, 6-20 reps T: free weights	CE -3.8 CE vs Con +2.8 Con -6.6*	CE -2.8 CE vs Con +2.2 Con -4.7	Metabolic risk factors	Yes	58
Silva et al. 2002 (53)	N=24(6) CE=12(3) Con=12(3)	CE 136.0±33.0/NR Con 154.0±36.0/NR	CVD (100) CVD (100)	12 12	F: 3 d·wk^{-1} I: 60-80%HR$_{max}$ T: 30-60 min·ses^{-1} T: walking Order: NR Con Non-exercise control	F: 3 d·wk^{-1} I: 60-80%HR$_{max}$ T: 30-60 min·ses^{-1} T: calisthenics, body weight exercise	CE -0.1 CE vs Con -3.4 Con +2.6	NR	Physical capacity in heart failure	Yes	55
Sousa et al. 2013 (54)	N=59(0) CE1=20(0) CE2=19(0) Con=20(0)	CE1 148.5±15.1/82.8±9.6 CE2 149.4±25.1/80.4±7.6 Con 136.8±15.9/81.4±8.8	Healthy (100) Healthy (100)	32 32	CE1 F: 3 d·wk^{-1} I: 12-13 borg scale T: 30 min·ses^{-1} T: walking, jog, dance CE2 F: 3 d·wk^{-1} I: moderate T: 30 min·ses^{-1} T: walking, jog dance Order: CE1: AE and RT performed on separate days CE2: RT before AE, performed on the same day Con Non-exercise control	CE1 F: 3 d·wk^{-1} I: 70% 1RM T: NR T: weight machines CE2 F: 3 d·wk^{-1} I: low T: 10 min·ses^{-1} T: body weight exercise	CE1 -15.1* CE1 vs Con -14.9* CE2 -5.8* CE2 vs Con -5.4 Con +0.0	CE1 -11.4* CE1 vs Con -8.3* CE2 -7.2* CE2 vs Con -4.1 Con -3.1	BP, body fat	Yes	67
Spina et al. 2004 (55)	N=36(19) CE=22(11) Con=14(8)	CE 134.0±18.0 Con 143.0±21.0	Healthy (100) Healthy (100)	156 156	F: 3.0 d·wk^{-1} I: 82% HR$_{max}$ T: 69.4 min·ses^{-1} T: walk, cycle, row Order: AE and RT performed on separate days Con Relaxation, yoga stretching performed 3 d·wk^{-1}	F: 3.0 d·wk^{-1} I: 82% HR$_{max}$ T: 69.4 min·ses^{-1}, 1-6 sets of10-12 reps T: weight machines	CE +0.1 CE vs Con +0.1 Con +0.0	CE -3.1 CE vs Con -2.5 Con -0.1	Cardiac Output	Yes	61

Stensvold et al. 2010 (56)	N=43(17) CE=11(NR) Con=10(NR)	CE 148.6±14.0/89.0±7.1	MetS (100)	12	F: 3 d·wk^{-1} I: 70-95% HR_{max} T: 43 min·ses^{-1} T: walk, jog	F: 3 d·wk^{-1} I: 40-50% 1RM T: 40 min·ses^{-1} T: resistance exercise	CE -2.3 CE vs Con -2.8	CE +0.1 CE vs Con +1.8	Metabolic syndrome criteria	Yes	76
		Con 141.5±12.3/90.1±7.1	MetS (100)	12	Order: AE and RT performed on separate days Con Non-exercise control		Con +0.0	Con -0.1			
Stewart et al. 2005 (57)	N=104(53) CE=51(26) Con=53(27)	CE 140.3(138.2,142.4)/76.8(74.8,78.9)[a]	Healthy (100)	24	F: 3 d·wk^{-1} I: 60-90% HR_{max} T: 45 min·ses^{-1} T: walk; cycle ergometer, stepper	F: 3 d·wk^{-1} I: 50% 1RM T: 2 sets for 10-15 reps, 7 exercises T: weight machines	CE -5.1* CE vs Con -2.6	CE -7.7* CE vs Con -7.3*	BP	Yes	69
		Con 141.7(139.7,143.8)/76.4(73.9,78.9)[a]	Healthy (100)	24	Order: AE before RT, performed on the same day Con Subjects were given recommendations for hypertension from the AHA, and National Institute on Aging		Con -2.5	Con +0.0			
Taylor-Piliae et al. 2010 (58)	N=95(69) CE=39(28) Con=56(41)	CE NR	T2DM, Arthritis, CVD (89.7)	24	F: at least 3 d·wk^{-1} I: Vigorous T: 15-20 min·ses^{-1} T: walking	F: at least 3 d·wk^{-1} I: Light T: 15-20 min·ses^{-1} T: calisthenics	CE -1.9 CE vs Con +0.0	NR	Cognitive and physical functioning	Yes	45
		Con NR	T2DM, Arthritis, CVD (80.3)	24	Order: AE and RT performed on the same day, specific order NR Con Educational classes on health and aging, 1 d·wk^{-1}, 90 min·ses^{-1}		Con -1.9				
Thomas et al. 2004 (59)	N=34(NR) CE=21(NR) Con=14(NR)	CE 126.0±14.4/NR	Healthy (100)	12	F: 3 d·wk^{-1} I: 4-6 MET T: 30 min·ses^{-1} aerobic, 60 min·ses^{-1} T: walk	F: 3 d·wk^{-1} I: 4-6 MET T: 30 min·ses^{-1} resistance, 60 min·ses^{-1} T: weight machines	CE +0.0 CE vs Con +0.0	NR	Strength, flexibility, cardiorespiratory fitness	Yes	58
		Con 131.0±18.9/NR	Healthy (100)	12	Order: RT before AE, performed on the same day Con Non-exercise control		Con +0.0				
Tseng et al. 2013 (60)	N=20(0) CE=10(0) Con=10(0)	CE 130.2±2.5/82.8±1.7[b]	Healthy (100)	12	F: 5 d·wk^{-1} I: 55-65% HR_{max} T: 60 min·ses^{-1} T: walking	F: 5 d·wk^{-1} I: 55-75% 1RM T: 60 min·ses^{-1} T: machine weights	CE -8.3 CE vs Con -9.2	CE -9.5* CE vs Con -9.2	HDL cholesterol	Yes	67
		Con 126.0±1.3/81.7±1.6[b]	Healthy (100)	12	Order: AE and RT performed on separate days Con Non-exercise control		Con +0.1	Con +0.0			

Van Vilsteren et al. 2004 (68)	N=103(31) CE=60(19) Con=43(13)	CE 145.0±23.2/81.0±14.2	CKD dialysis dependent (100)	12	F: 2-3 d·wk^{-1} I: Borg RPE, moderate T: 20-30 min·ses^{-1} T: cycle ergometer	F: 5 d·wk^{-1} I: Borg RPE, moderate T: 20-30 min·ses^{-1} T: calisthenics	CE -2.1 CE vs Con +0.0 Con -1.7	CE -0.1 CE vs Con +1.9 Con -2.6	Behavior change, physical fitness and quality of life	Yes	65
					Order: AE and RT performed on the same day, specific order NR						
		Con 150.0±23.0/83.0±15.0	CKD dialysis dependent (100)	12	Con Disease Management, Dialysis						
Vianna et al. 2011 (61)	N=70 (46) CE=35(36) Con=35(20)	CE 142.3±18.3/81.4±6.0	Healthy (100)	12	F: 2 d·wk^{-1} I: 55-65% HR_{max} T: 60 min·ses^{-1} T: walking, hydrogymnastics	F: 1 d·wk^{-1} I: 55-65% HR_{max} T: 60 min·ses^{-1} T: muscle strengthening exercises	CE -5.0* CE vs Con -5.8* Con +0.1	CE -3.3 CE vs Con -9.8* Con +6.5*	BP	Yes	67
					Order: AE and RT performed on the same day, specific order NR						
		Con 141.1±17.9/82.3±7.7	Healthy (100)	12	Con Monthly phone calls to subjects with study updates						
Viecili et al. 2008 (63)	N=88(54) CE=48(33) Con=40(21)	CE 144.0±20.0/88.0±15.0	T2DM, hypercholesterolemia (29)	12	F: 3 d·wk^{-1} I: 70% VO_{2max} T: 90 min·ses^{-1} T: walking	F: 3 d·wk^{-1} I: 40% MVC T: 90 min·ses^{-1} T: "muscle strengthening exercise"	CE -7.4* CE vs Con -5.9* Con -1.5	CE -4.6* CE vs Con -2.4 Con -2.2	Exercise Frequency	Yes	58
					Order: RT before AE, performed on the same day						
		Con 140.0±13.0/87.0±9.0	T2DM, hypercholesterolemia (30)	12	Con BP monitoring						
Vincente-Campos et al. 2012 (62)	N=43(25) CE=22(12) Con=21(13)	CE 135.2±4.4/81.1±6.8	Healthy (100)	28	F: 2-3 d·wk^{-1} I: 55% HR_{max} T: 50 min·ses^{-1} aerobic, T: "aerobic activity"	F: 2-3 d·wk^{-1} I: 65% HR_{max} T: 50 min·ses^{-1} T: "strengthening exercise"	CE -5.7* CE vs Con -5.5 Con +0.0	CE -3.0 CE vs Con -5.2 Con +2.2	Cerebral vasoreactivity	Yes	58
					Order: AE and RT performed on the same day, circuit training						
		Con 135.7±5.5/81.2±4.2	Healthy (100)	28	Con Non-exercise control						
Wescott et al. 2011 (64)	N=52(48) CE=18(NR) Con=(NR)	CE 124.3±16.8/68.6±6.4	Healthy (100)	36	F: 2-3 d·wk^{-1} I: moderate T: 25 min·ses^{-1} aerobic, 60 min·ses^{-1} T: cycle ergometer	F: 2-3 d·wk^{-1} I: moderate T: 25 min·ses^{-1} resistance, 60 min·ses^{-1} T: machine weights	CE -1.4 CE vs Con -4.2 Con +2.8	CE +2.5 CE vs Con -5.4 Con +8.0	Lean weight, BP	Yes	39
					Order: AE and RT performed on the same day, specific order NR						
		Con 117.1±9.5/68.0±6.8	Healthy (100)	36	Con Non-exercise control						

Wood et al. 2001 (65)	N=36(19) CE=9(5) Con=6(3)	CE 128.7±13.8/76.6±8.3	Healthy (100)	12	F: 3 d·wk^{-1} I: 65% HRR T: 30 min·ses^{-1} aerobic, 55 min·ses^{-1} T: walk, cycle Order: AE and RT performed on the same day, specific order NR	F: 3 d·wk^{-1} I: 75% 5RM T: 25 min·ses^{-1} resistance, 55 min·ses^{-1}, 1 set of 10 reps, 8 exercises T: weight machines	CE +1.4 CE vs Con +2.9 Con -1.4	CE +1.3 CE vs Con -1.1 Con +2.4	Battery of tests for physical fitness in older adults	Yes	58
		Con 133.5±22.4/78.3±6.9	Healthy (100)	12	Con Non-exercise control						

Note: Abbr. AE= aerobic exercise. ART=after resistance training. BP= blood pressure. BRT= before resistance training. CE=concurrent exercise. CI=confidence interval. CKD= chronic kidney disease. Comp=composition. Con=control or comparison group. CONT=continuous. CV=cardiovascular. CVD=cardiovascular disease. CRT= concentric resistance training. DBP= diastolic blood pressure. ERT=eccentric resistance training. FITT= frequency, intensity, time and type of exercise. HR_{max}= maximum heart rate. HRR=heart rate reserve. HDL=high-density lipoprotein cholesterol. HTN=hypertension (>140/>90 mmHg). INT= interval training. *k*=number of observations. MET=metabolic equivalents. MetS=metabolic syndrome. MVC=maximal voluntary contraction. N=number of participants. NBP=normal blood pressure (<120/<80 mmHg) NR=not reported. PreHTN=prehypertension (120-139/80-89 mmHg). SBP=systolic blood pressure. T2DM= type 2 diabetes mellitus. VO_{2max}=maximal oxygen consumption. RM=repetition maximum. RPE=rating of perceived exertion. RT= resistance training. W=number of women. Wks=weeks. Data are presented as mean ± standard deviation unless otherwise specified. Study quality was assessed using a modified version of the Downs and Black Methodological checklist. A score of total items satisfied out 33 is given and converted into a percent score, taking the total score divided by the total possible score (33) multiplied by 100.

*Significant changes in blood pressure were observed pre- to post intervention ($p<0.05$)

[&]data are presented as mean ± standard error

[‡]data are presented as mean (95% confidence interval). An interval which does not contain zero indicates a significant reduction in blood pressure.

[%]data are presented as mean (range)

[^]data are presented as within-group effect sizes (CE and Con) and between group effect sizes (CE vs Con) for the individual studies, converted into the raw BP changes in mmHg