Effects of exercise training on blood pressure: an overview of reviews

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ABSTRACT

BACKGROUND: This overview of reviews aimed to identify, appraise, and synthesize findings from high-quality systematic reviews on the benefits and harms of different exercise training modalities on blood pressure in adults who either are normotensive, pre-hypertensive, or have high blood pressure.

METHODS: This review was reported according to the PRISMA Statement. We searched MEDLINE, EMBASE, Epistemonikos, and PROSPERO to identify systematic reviews of randomized controlled trials (RCTs) in adults diagnosed with high blood pressure, other diseases, or cardiovascular risk factors, that compared exercise training with either active interventions or no exercise. Our major outcomes were blood pressure and adverse events. Pairs of reviewers independently screened the systematic reviews for inclusion, extracted data, and appraised the methodological quality. We assessed the certainty of the evidence by using the GRADE approach.

RESULTS: We included seventeen reviews, who reported on 17 comparisons (290 RCTs; 19 232 adults). Any aerobic training probably resulted in a large reduction in SBP in adults with either type II diabetes, metabolic syndrome, end-stage renal disease, or kidney transplantation at short to long-term follow-up (moderate-certainty evidence). Walking aerobic training probably resulted in a large reduction in DBP at short to long-term follow-up in adults with high blood pressure (moderate-certainty evidence). Combined training probably resulted in a large reduction in DBP in adults who either are normotensive, or have high blood pressure, kidney failure, metabolic syndrome, or end-stage renal disease at short to long-term follow-up (moderate-certainty evidence). The body of evidence for the remaining comparisons was rated as low to very low. Eight reviews provided little to no information on safety data.

DISCUSSION: We found very low to moderate evidence supporting the benefits of exercise training compared with no interventions or placebo for blood pressure in adults with or without comorbidities or risk factors. Scarce safety data were identified. Our certainty in the evidence was downgraded due to methodological limitations, inconsistency, and imprecision. Before drawing more solid conclusions, further well-conducted and well-reported randomized controlled trials are warranted in order to strengthen the evidence base underlying this research question.

Protocol registration: PROSPERO CRD42021247062

Keywords: systematic review, meta-analysis, hypertension, exercise training

INTRODUCTION

Cardiovascular diseases (CVDs) represent the third leading cause of death worldwide, counting for 18 million deaths per year (1). Around 10 million people die each year from high blood pressure (HBP), which represents more than half of the mortality attributed to CVDs (2). The economic burden of HBP is high, and the global medical costs of HBP are estimated at 370 billion dollars per year (3,4).

Different scientific societies recommend exercise training as part of behavioral change interventions for the prevention and management of HBP (5). Recent clinical guidelines have proposed exercise training as an effective non-pharmacological approach for reducing blood pressure (BP) values at clinically significant levels (reductions in systolic blood pressure ranging between 4 to 8 mmHg) (5). Exercise training has proven to be a safe intervention in CVD patients, since it has been related to fewer adverse effects than either pharmacological or surgical treatments (6). However, the evidence for safety data in patients with HBP remains unclear (6).

A recent overview of reviews conducted by researchers from the American College of Sports Medicine (ACSM) concluded that any form of physical activity (PA) reduced BP values in normotensive, pre-hypertensive, and HBP adults (7). The authors summarized data from both exercise training and physical activity into the same analysis, which increased the heterogeneity of their results as evidenced in the analyses. This limitation in the current evidence was further reinforced by incomplete literature searches, as acknowledged recently by European experts in the field (8).

The number of systematic reviews (reviews) on the effects of exercise training for HBP has increased exponentially in recent years. Most of those reviews have serious methodological limitations, report heterogeneous effect estimates, and lack systematic assessments of the quality of the evidence(9–11). Considering this, we propose a systematic overview of high-quality systematic reviews with a transparent approach to grade the quality of the evidence in order to facilitate the translation of research findings into practice.

OBJECTIVES

This overview of reviews aims to identify, appraise, and synthesize findings from high-quality systematic reviews on the benefits and harms of different exercise training modalities on blood pressure in adults who either are normotensive, pre-hypertensive, or have high blood pressure.

METHODS

We registered the review protocol in the International Prospective Register of Systematic Reviews (PROSPERO registration number: CRD42021247062 and Open science framework), and followed both the methodological guidance provided in Chapter V of the Cochrane handbook version 6.2 (12) and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (13,14). For quality purposes, pairs of independent reviewers conducted the following steps: study selection, data extraction, quality appraisal, and assessment of the certainty of the evidence. Disagreements were resolved by consensus or by including a third reviewer if necessary. Additional file 1 provides details on the PRISMA statement.

Eligibility criteria

We used the PICOTS acronym (P - population; I - intervention; C - comparison or control; O- outcome(s), T - Time and S - study design) to guide study selection (15), as follows:

Participants

Adults (≥ 18 years old) with normal, pre-hypertensive, or HBP values, with or without associated risk factors or comorbidities, categorized according to American Heart Association (AHA) criteria (16):

- Normal: Systolic blood pressure (SBP) <120 mm Hg and diastolic blood pressure (DBP) <80 mm Hg.
- Pre-hypertensive: SBP 120–129 mm Hg and DBP <80 mm Hg.
- High blood pressure: SBP 130–139 mm Hg or DBP 80-89 mm Hg.

Interventions

We accepted for inclusion different exercise training modalities, such as dynamic resistance training (DRT), isometric resistance training (IRT), aerobic exercise training (AET), and combined training (CT) (5). Figure 1 presents the definitions of the exercise interventions considered for inclusion.

Figure 1. Definitions of the different exercise training modalities.

Exercise training: Exercise is defined as a planned, structured, repetitive PA aiming to improve or maintain one or more components of physical fitness (i.e., cardiorespiratory fitness and/or muscular fitness) (17). Thus, any PA program which is structured according to parameters and characteristics of Frequency, Intensity, Time, Type, Volume, and Progression) (FITT-VP) was considered as exercise training; otherwise, these programs were discarded.
Dynamic resistance training (DRT): DRT involves an exercise movement using a constant load or a uniform weight regardless of the training program (18).

Isometric resistance training (IRT): IRT is understood as any muscular contraction in which the tension of both the joint and the contractile elements does not vary on the movement range (holding a position or weight without moving against it) (19).
Aerobic training (AET): Cyclic exercises involve a large amount of muscle mass for different time units, where the cardiovascular and respiratory systems predominate (e.g., jogging, swimming, running, cycling, dancing) (18).
Combined training (CT): This training modality represents the systematic integration of both resistance and aerobic exercise within a coherent training plan (20).

We excluded reviews summarizing evidence from PA programs. PA is defined as any movement of the body generated by the skeletal muscles which generate an energy expenditure (18). However, any PA program which is structured according to the parameters and characteristics of FITT-VP would be considered as exercise training; otherwise, these programs were discarded. A threshold of ≥ 50% primary studies reporting on exercise training were accepted for inclusion. We excluded reviews that focused on pregnant women.

Comparators

Standard care (e.g., pharmacological interventions or behavioral change approaches) or any active intervention (e.g., flexibility, yoga, Qigong), waitlist, or no intervention.

Primary outcomes

Blood pressure

SBP, DBP, and mean blood pressure (MBP). BP is defined as the force exerted by the circulating blood through the arteries against the arterial wall (21), and includes two measurements: systolic pressure, which is measured during the heartbeat (maximum pressure moment), and diastolic pressure, which is measured during the rest between two beats (minimum pressure moment). Mean blood pressure (MBP), represents the average blood pressure in the arteries is approximately one-third of the way between the diastolic and systolic pressures (21).

Secondary outcome

Adverse events

The National Institute for Health and Care Excellence (NICE) defines adverse events as any undesirable event experienced by a person while they are having a drug or any other treatment or intervention, regardless of whether the event is suspected to be related to or caused by the drug, treatment or intervention (22).

Time: Both primary and secondary research studies have reported both clinically and statistically significant effects of the different exercise training modalities on SBP, DBP, and MBP values over a 3-weeks follow-up (23). Therefore, we included reviews reporting outcome data at/over 3 weeks post-intervention follow-up.

Study design: We included reviews of randomized controlled trials (RCTs) (15,22). Inclusion was restricted to reviews of high methodological quality , which was appraised by using the Assessment of Multiple Systematic Reviews (AMSTAR) tool (24). In terms of the included trials, we included reviews of both randomized and non-randomized studies as long as the review provides separate information for the RCTs (e.g., subgroup data).

Language: No restrictions were set for language.

Information sources and search strategy

We searched MEDLINE (via Pubmed), EMBASE, and Epistemonikos from inception date to February 02, 2021. No restrictions were applied for the publication date. The search strategy used in MEDLINE is available in the protocol (25); this was tailored to the other databases. Furthermore, one reviewer (AFL-B) inspected the PROSPERO repository for ongoing reviews, the reference lists of the included reviews, as well as the references of clinical guidelines and scientific journals specialized in the field (e.g., Journal of Hypertension).

Study selection process

Two blinded and independent reviewers (AFL-B and EP-B) selected the studies at title, abstract and full-text. These steps were carried out in Rayyan (26).

Data management and extraction

We extracted data from the included reviews into an ad-hoc standardized electronic form created in Google forms (https://docs.google.com/forms/). All reviewers piloted this form in a random sample of two reviews (25). If necessary, we tried to contact the corresponding author of the reviews to clarify data or obtain missing information.

Quality appraisal

Pairs of reviewers independently appraised the methodological quality of the included reviews by using the AMSTAR tool (24). AMSTAR is the most widely used tool for critically appraising reviews of RCTs and contains 11 questions, this information is available in the protocol (25). Each question of AMSTAR is rated as yes (clearly done), no (clearly not done), cannot answer, or not applicable (24). In case any of the reviewers participated as an author in an included review, we acknowledged this and allocated the reviews to another reviewer.

Data synthesis

In line with the methodological literature, we propose a narrative synthesis approach for this study (12). We presented data from each review, sorted by each primary and secondary outcome according to the certainty of the evidence (e.g., high-certainty evidence first, followed by moderate-certainty evidence, etc.), follow-up periods, number of participants, and RCTs. Where possible, we presented effect measures mean difference (MD), standard means difference (SMD), relative risk (RR), and odds ratio (OR) with 95% CIs for both continuous and dichotomized outcome measures. We presented the overall results in 'Summary of findings' tables (12), according to the following subgroups:

- The clinical status of the participants regarding AHA (16) blood pressure values: normal, pre-hypertensive, and high blood pressure.
- Comorbidities (type 2 diabetes mellitus, dialysis chronic kidney disease, non-dialysis chronic kidney disease, coronary heart disease, heart failure, polycystic Ovary syndrome, stroke, overweight, obese, cardiometabolic diseases, peripheral artery disease, heart failure, cardiometabolic risk, cardiac patients, heart disease, transient ischemic attack, metabolic syndrome, intermittent claudication).
- Population under pharmacological antihypertensive treatment.
- Age: ≤ 65 years old and > 65 years old.

Based on evidence from both experimental and observational studies, reductions of 5 mm Hg on SBP and 2 mm Hg on DBP were deemed as clinically important (26–28).

Managing overlapping systematic reviews

We investigated the degree to which the reviews shared the same included studies (overlap). If we found overlap ≥ 50% included studies between two or more reviews, we reported the results from the most recent reviews with the most detailed description. This assessment was based on the primary studies that provided information on the outcomes of interest (29).

Certainty of the evidence: GRADE approach

We followed the GRADE approach (Grading of Recommendations, Assessment, Development, and Evaluation) to assess the certainty of the evidence supporting the effects of each exercise training modality on blood pressure and adverse events (30). According to the GRADE approach, five factors reduce the certainty of the evidence, these are: 1) limitations in study design; 2) inconsistency in results; 3) indirectness of evidence; 4) imprecision; 5) publication bias. Besides, due to the nature of the intervention and that the outcomes were measured objectively (i.e., sphygmomanometer), we decided not to downgrade the certainty of the evidence for blinding of the participants and personnel of the RCT (performance bias). The certainty of the evidence was rated as high, moderate, low, or very low (30). If available, we used GRADE assessments reported in the included reviews and supplied those with our assessment where the reviews that did not provide any GRADE assessment. We followed the guidance provided by Meader et al. (2014) on assessing GRADE in reviews (31).

RESULTS

Study selection

We identified 1851 records from database searching. After the removal of 167 duplicates, we screened 1684 titles and abstracts. We excluded 1488 records at this stage and screened 196 full texts against our selection criteria. One reviewer (AFL-B) retrieved all full-text publications. We excluded 82 reviews and presented the reasons for their exclusion in (Additional file 2). After the quality appraisal, we excluded 78 reviews of either moderate or low quality (Additional file 3). Eighteen out of the remaining 36 reviews are listed as ongoing (Additional file 4). One review (32) was excluded because of overlap. Finally, we included 17 high-quality reviews in the overview. Figure 2 depicts the selection process.

Study characteristics

The 17 reviews included 19.232 adults (ranging from 16 to 84 years old) (33–49). Six (35%) reviews were Cochrane reviews (34,37,41,44,45,47), 29% of the reviews were published in 2019 (5 reviews, 29%) (33,39,40,46,48). Australia was the most common country across the included reviews (4 reviews, 23%) (42,45–47), followed by United Kingdom (3 reviews, 17%) (34,38,40), Brazil (33,35), and China (36,49) (2 reviews, 12%). Other countries like Canada (48), Germany (43), Netherlands (39), Sweden (37), Chile (44), and Taiwan (41) reported one review each (6%). Type II diabetes was the most common comorbidity (5 reviews, 29%) (38,42,43,47,48), followed by moderate or end-stage renal disease, studied in four reviews (23%) (33,35,37,48). The other four reviews included pre-hypertensive and high blood pressure adults (23%) (36,41,45,46). Other reviews (2 reviews, 12%) included normotensive and healthy adults (41,46), adults with cardiovascular risk factors (i.e., overweight and/or obesity) (2 reviews, 12%) (38,44), and adults with coronary artery disease and heart failure (2 reviews, 12%) (34,49). Other review included adults with acute myocardial infarction (1 review, 6 %) (34) and the remaining with intermittent claudication (1 review, 6 %) (39). Three reviews (18%) (37,38,41) reported on participants' physical activity levels or training status; two of those (12%) included sedentary participants (37,38), and the remaining (6%)

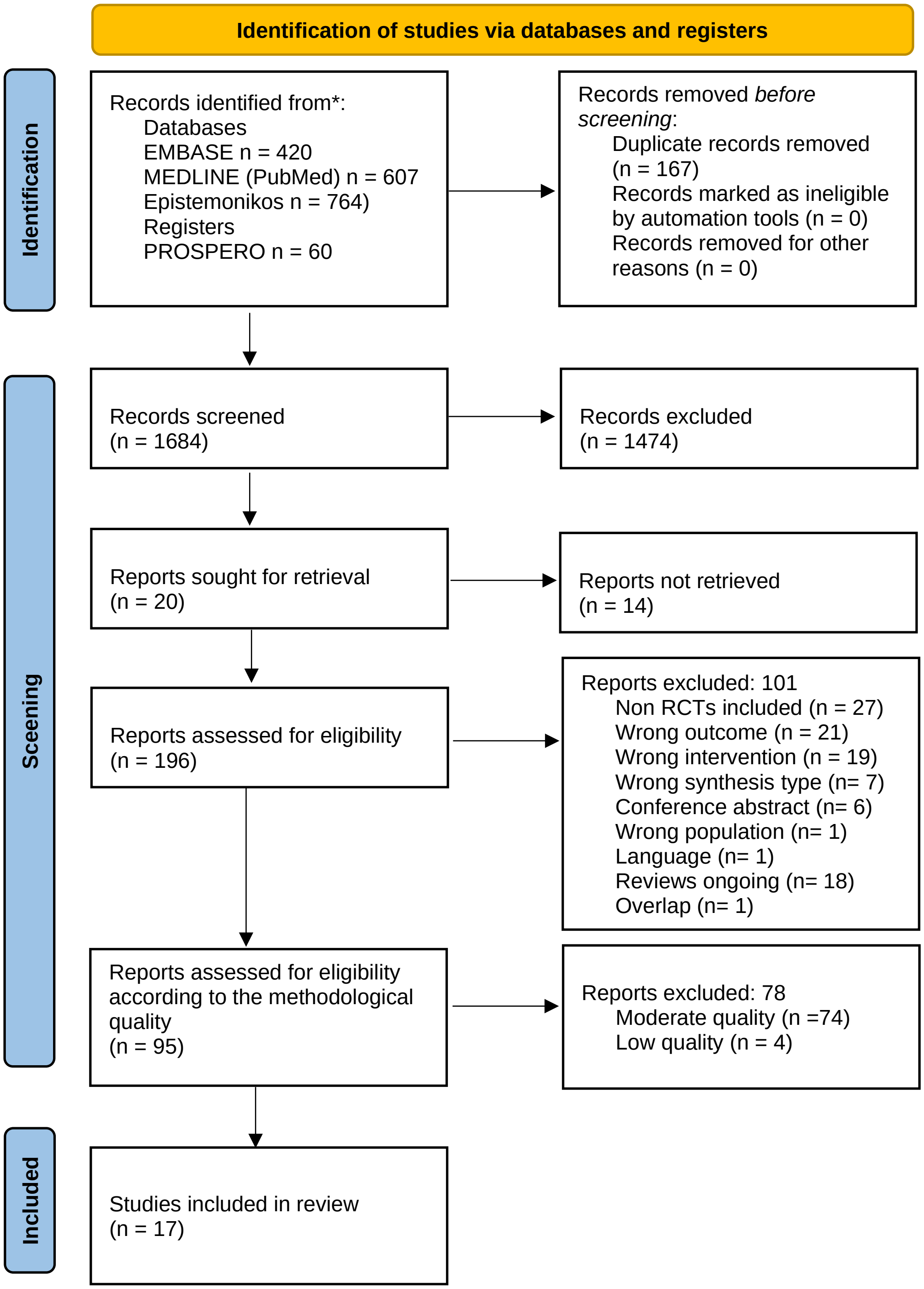


Figure 2. Preferred reporting items for systematic reviews and meta-analyses (PRISMA) flow-chart of the study selection.

included physically inactive adults (41). Moreover, the Cochrane collaboration risk of bias tool version 1 was the most used tool to critically appraise the included studies (14 reviews, 82%) (33–36,38–44,47–49), and the GRADE approach was the most common grading system (6 reviews, 35%) (34–36,38,40,41). Of note, 11 reviews (65%) did not assess the certainty of the evidence (33,37,39,42–49). Table 1 contains further details on the characteristics of the participants.

Table 1. Characteristics of included reviews (n=17)

Review ID, year Country	Number of included trials (participants)	Aim	Intervention and control	Outcomes	Risk of bias and Certainty of evidence
Anderson et al., 2017 (34) United Kingdom (https://doi.org/10.1002/14651858.CD007130) Date search: 2016	10 (2438) Risk factors or comorbidities: Coronary heart disease post-myocardial infarction Revascularization Heart failure	To compare the effect of home-based and supervised center-based cardiac rehabilitation on mortality and morbidity, exercise-capacity, health-related quality of life, and modifiable cardiac risk factors in patients with heart disease.	Int: Aerobic training Con: center-based cardiac rehabilitation **Setting:** Hospital, University, or community setting	SBP, DBP, adverse events	Cochrane RoB 1 GRADE
B Scapini et al., 2019 (33) Brazil (CRD42015020531) Date search: 2018	14 (573) Risk factors or comorbidities: End-stage renal disease in hemodialysis	To assess the effectiveness of different modalities of exercise training on aerobic capacity, arterial blood pressure and hemodialysis efficiency in adults with end-stage renal disease requiring hemodialysis treatment.	Int 1: Dynamic resistance training Int 2: Aerobic training Int 3: Combined training Con: No intervention, Placebo **Setting:** Not reported	SBP, DBP	Cochrane RoB 1 Not assessed
Ferrari et al., 2019 (35) Brazil (CRD42017081338 – https://osf.io/fpj54/) Date search: 2019	12 (408) Risk factors or comorbidities: Patients with end-stage renal disease (ESRD)	To Evaluate the impact of different types of intradialytic training on some parameters important for patients with ESRD, through a systematic review and meta-analysis of randomized clinical trials (RCTs) that primarily evaluated outcomes such as Kt/V (Hemodialysis efficiency (dialyzer clearance of urea), aerobic capacity, and blood pressure (BP), as well as other secondary outcomes.	Int 1: Dynamic resistance training Int 2: Aerobic training Int 3: Combined training Con: Standard care, sham exercises (e.g., stretching) **Setting:** Rehabilitation, home	SBP, DBP, adverse events	Cochrane RoB 1 GRADE
Fu et al., 2020 (36) China	39 (1519) Risk factors or comorbidities:	To assess the comparative effectiveness of different nonpharmacologic interventions for reducing BP in adults with prehypertension to established hypertension and to determine the most efficacious intervention.	Int 1: Dynamic resistance training Int 2: Isometric resistance training Int 3: Aerobic training Int 4: Combined training Con: Standard care, Behavioral change (diet, Reduction in sodium and/or alcohol	SBP, DBP	Cochrane RoB 1 GRADE

Date search: 2019	Prehypertensive High blood pressure		intake), Other active interventions (e.g., flexibility, yoga, Qigong), No intervention **Setting:** Mixed (e.g., clinic and home)		
Heiwe et al., 2011 (37) Sweden (https://doi.org/10.1002/14651858.CD003236) Date search: 2010	11 (419) Risk factors or comorbidities: Moderate kidney failure Kidney transplantation	To assess the effects of regular physical exercise training in adults with CKD and kidney transplant recipients on the following clinically important health outcomes: physical fitness and functioning; cardiovascular dimensions; nutrition; level of physical activity; depression; health-related quality of life; blood lipids; muscle morphology and morphometric systemic inflammation; glucose metabolism; dropout rates; adverse events; and mortality.	Int 1: Dynamic resistance training Int 2: Aerobic training Int 3: Combined training Con: Standard care, Behavioral change (diet, Reduction in sodium and/or alcohol intake), (non-exercise control), usual level of physical activity, usual lifestyle, No exercise training **Setting:** Home, ambulatory	SBP, DBP, adverse events	Jadad scale Not assessed
Herrod et al., 2018 (38) United Kingdom (CRD42017059443) Date search: 2017	50 (3526) Risk factors or comorbidities: Obesity Overweight Type II diabetes	To evaluate the evidence from lifestyle modification RCTs involving participants with a mean age of 65 years or above	Int 1: Dynamic resistance training Int 2: Isometric resistance training Int 3: Aerobic training Int 4: Combined training Con: No intervention **Setting:** Home	SBP, DBP	Cochrane RoB 1 GRADE
Janssen et al., 2019 (39) Netherlands (CRD42017080706) Date search: 2018	7 (333) Risk factors or comorbidities: Intermittent Claudication	To provide a systematic overview of the effectiveness of SET on modifying cardiovascular risk factors in patients with intermittent claudication.	Int: Aerobic training Con: Standard care, Pharmacological interventions, Other active interventions (e.g., flexibility, yoga, Qigong) **Setting:** Home, hospital, community based	SBP, DBP	Cochrane RoB 1 Not assessed
Kite et al., 2019 (40) United Kingdom (CRD42017062576)	4 (158)	To analyze the evidence on the effectiveness of exercise compared to (i) control or usual care, (ii) diet alone, and (iii) exercise combined with diet, as well as the effectiveness of exercise	Int 1: Aerobic training Int 2: Combined training Con: Standard care, Behavioral change (diet, Reduction in sodium and/or alcohol	SBP, DBP, MAP	Cochrane RoB 1 GRADE

Date search: 2017	Risk factors or comorbidities: Polycystic ovary syndrome (PCOS)	combined with diet compared to (i) control or usual care and (ii) diet alone.	intake), No intervention, Pharmacological interventions **Setting:** Not reported		
Lee et al., 2021 (41) Taiwan (https://doi.org/10.1002/14651858.CD008823) Date search: 2020	73 (6473) Risk factors or comorbidities: Normotensive High blood pressure	To determine the effect of walking as a physical activity intervention on blood pressure and heart rate.	Int: Aerobic training Con: No intervention **Setting:** Laboratory, home	SBP, DBP, adverse events	Cochrane RoB 1 GRADE
Ostman et al., 2017 (42) Australia (CRD42017055491) Date search: 2017	16 (364) Risk factors or comorbidities: Type II diabetes Metabolic syndrome	To determine whether high-intensity exercise produced different effect sizes for change in clinical outcomes in MetS compared to vigorous-, moderate- and low-intensity training and sedentary lifestyle. To establish whether the effect on clinical outcomes in MetS varied according to the type of intervention (aerobic versus combined aerobic and resistance training)	Int 1: Aerobic training Int 2: Combined training Con: No intervention **Setting:** Mixed (e.g., clinic and home)	SBP, DBP	Cochrane RoB 1 Not assessed
Qiu et al., 2014 (43) Germany (CRD42014009515) Date search: 2014	12 (509) Risk factors or comorbidities: Type II diabetes	To examine the association of walking with glycemic control, and other cardiovascular risk factors including weight reduction, blood pressure, and lipoprotein profiles among patients with type 2 diabetes. The second aim was to evaluate whether supervised walking would lead to better improvement in glycemic control versus non-supervised walking among patients with type 2 diabetes.	Int: Aerobic training Con: Standard care, No intervention **Setting:** Not reported	SBP, DBP, adverse events	Cochrane RoB 1 Not assessed

Seron et al., 2014 (44) Chile (https://doi.org/10.1002/14651858.CD009387) Date search: 2013	3 (794) Risk factors or comorbidities: Cardiovascular risk factors	To assess the effects of exercise training in people with increased cardiovascular risk but without a concurrent cardiovascular disease on general cardiovascular mortality, incidence of cardiovascular events, and total cardiovascular risk.	Int 1: Aerobic training Int 2: Combined training Con: Standard care, Behavioral change (diet, Reduction in sodium and/or alcohol intake), No intervention, Pharmacological interventions **Setting:** Not reported	SBP, DBP, adverse events	Cochrane RoB 1 Not assessed
Shaw et al., 2006 (45) Australia (https://doi.org/10.1002/14651858.CD003817) Date search: 2005	4 (361) Risk factors or comorbidities: Hypertensive Overweight Obese Non-insulin-dependent type II diabetes	To assess the efficacy of exercise as a means of achieving weight loss in people with overweight and obesity.	Int: Aerobic training Con: Behavioral change (diet, Reduction in sodium and/or alcohol intake), No intervention **Setting:** Clinic, hospital, university campuses, and workplace	SBP, DBP, adverse events	Jadad scale Not assessed
Smart et al., 2019 (46) Australia (CRD42018109167) Date search: 2018	11 (326) Risk factors or comorbidities: Healthy Normotensive Prehypertensive High blood pressure	To examine the efficacy of IRT in managing resting blood pressure. The primary objective was to quantify the change in resting SBP, DBP, and mean arterial pressure (MAP) following more than 3 weeks of IRT. The secondary objective was to explore relationships between baseline characteristics [medication usage, age, sex, BMI, and coronary artery disease (CAD) diagnosis] and the magnitude of changes in resting blood pressure after IRT.	Int: Isometric resistance training Comp: No intervention, Placebo **Setting:** Home, Office	SBP, DBP, MAP	TESTEX scale Not assessed
Thomas et al., 2006 (47) Australia (https://doi.org/10.1002/14651858.CD002968)	5 (150) Risk factors or comorbidities: Non-insulin-dependent type II diabetes	To assess the effects of exercise in type 2 diabetes mellitus.	Int 1: Aerobic training Int 2: Combined training Int 3: Dynamic resistance training Con: No intervention	SBP, DBP, adverse events	Cochrane RoB 1 Not assessed

Date search: 2005			**Setting:** Community		
Thompson et al., 2019 (48) Canada (No reported) Date search: 2017	12 (335) Risk factors or comorbidities: Chronic kidney disease Cardiovascular disease Type II diabetes	To evaluate the evidence for exercise as a strategy to lower blood pressure in people with non-dialysis dependent CKD	Int: Aerobic training Con: No intervention **Setting:** Mixed (center and at home)	SBP, DBP, MAP	Cochrane RoB 1 Not assessed
Xie et al., 2017 (49) China (Not reported) Date search: 2016	8 (376) Risk factors or comorbidities: Chronic heart failure Coronary artery disease	To compare the effects of high-intensity interval training (INTERVAL) and moderate-intensity continuous training (CONTINUOUS) on aerobic capacity in cardiac patients.	Int: Aerobic training – HIIT Con: Aerobic training - MICT **Setting:** Not reported	SBP, DBP	Cochrane RoB 1 Not assessed

BMI: Body mass index; CKD: chronic kidney disease; CFR: cardiorespiratory fitness; Comp: comparator; DBP: diastolic blood pressure; ERSD: end-stage renal disease in hemodialysis; GRADE: grading of recommendations, assessment, development, and evaluation; Int: interventions; IRT: isometric resistance training; MBP: mean blood pressure; Mets: metabolic syndrome; RCTs: randomized controlled trials; RoB: risk of Bias; SBP: systolic blood pressure; SET: supervised exercise therapy

Overlap among RCTs included in the reviews

The included reviews were published between 2006 to 2021 and included 290 RCTs that reported on our outcomes of interest. Among those, 40 RCTs (14%) overlapped across reviews, whereas 250 RCTs (86%) were 'unique' and more recently published (Additional file 5). 197 RCTs (68%) reported the country where they were conducted. All in all, 23% of the RCTs were from North America, 21% from Europe, 11% from Asia, 4% from Oceania, and 3% from South America. See Figure 3.

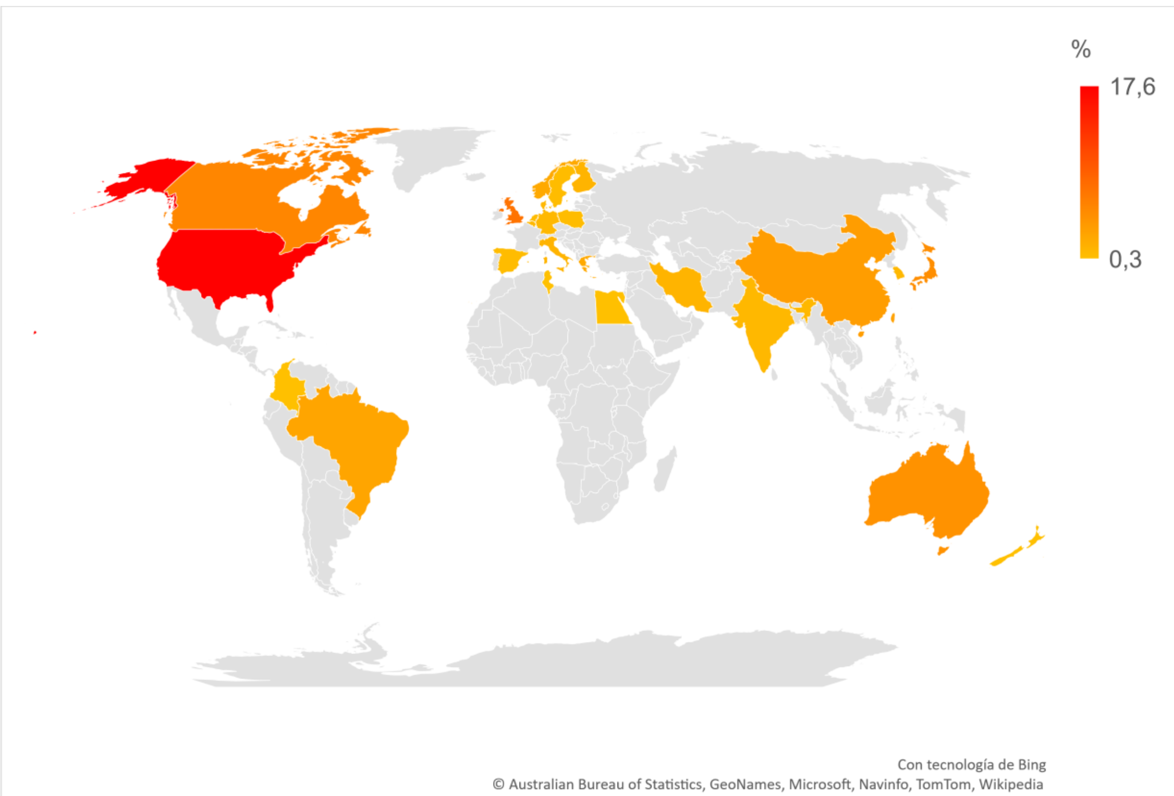


Figure 3. Geographic overview of the randomized controlled trials in the included systematic reviews.

Description of the interventions

The most common exercise training modality investigated for the reviews included was AET (16 reviews , 94%) (33–45,47–49), followed by CT (9 reviews, 53%) (33,35–38,40,42,44,47), DRT (6 reviews, 35%) (33,35–38,47), and IRT (3 reviews, 18) (36,38,46). Twelve reviews (71%) reported the setting in which the intervention took place (34–39,41,42,45–48). Besides, most of the interventions were partially supervised (10 reviews, 58%) (33–35,37,38,40,43,46–48). See Additional file 6.

Aerobic training (16 reviews)

Overall, AET programs had a frequency of 3 to 5 days per week, implemented from 4 to 64 weeks, and each session lasted between 10 to 60 minutes. The volume per week ranged from 90 to 180 minutes, whereas the most common training intensity was 60% to 85% of the maximum heart rate. HIIT interventions were carried out at 80% to 95% of the VO_2 peak.

Dynamic resistance training (6 reviews)

The most common prescription of the DRT programs comprised a frequency of 2, 3, and 4 days per week. The DRT programs were run from 3 to 48 weeks, (8 weeks was the most reported length), and each session lasted around 20-30 minutes. The most common volume was 1 to 3 sets per 6 to 30 repetitions with 6 to 13 exercises per session.

Isometric resistance training (3 reviews)

The most common prescription of the IRT programs comprised a frequency of 3 days per week. The IRT programs were implemented from 4 to 12 weeks, each session had a duration of 12 to 16 minutes. The most common volume was 4 sets per 2 minutes, with 1 to 3 minutes rest between sets. The most common exercises used were manual dynamometry and leg extensions isokinetic dynamometry.

Combined training (9 reviews)

In general, the reviews that evaluated CT reported similar parameters of FITT -VP to those described above for AET and DRT.

Quality appraisal

Overall, few systemic reviews had specific methodological limitations that could introduce bias. The quality appraisal of the included and excluded reviews is presented in Additional file 3. Two reviews (12%) did not report the review protocol (48,49); one review (6%) failed to use applicable for methods to combine the findings of studies (44). Five reviews (30%) did not run comprehensive searches in grey literature resources (33,43,44,48,49). Some reviews (23%) provided no list of excluded studies (36,38,39,43). Additional file 3 presents further details about the quality appraisal.

Results of syntheses

In order to facilitate the use of this review in evidence-informed decision making, we report in the main body of the manuscript the results of the comparisons that are most often studied by international guidelines (16,50) alongside the longest follow-up (i.e., short to long term: 4 to 64 weeks) as recommended by the Cochrane handbook (15):

- Comparison 1: any AET vs control
- Comparison 2: walking AET vs control
- Comparison 3: high-intensity interval training vs moderate-intensity continuous training
- Comparison 4: home-based vs supervised center-based cardiac rehabilitation
- Comparison 5: combined training vs control
- Comparison 6: exercise training (ET) vs control

- Comparison 7: isometric resistance training vs control
- Comparison 8: dynamic resistance training vs control

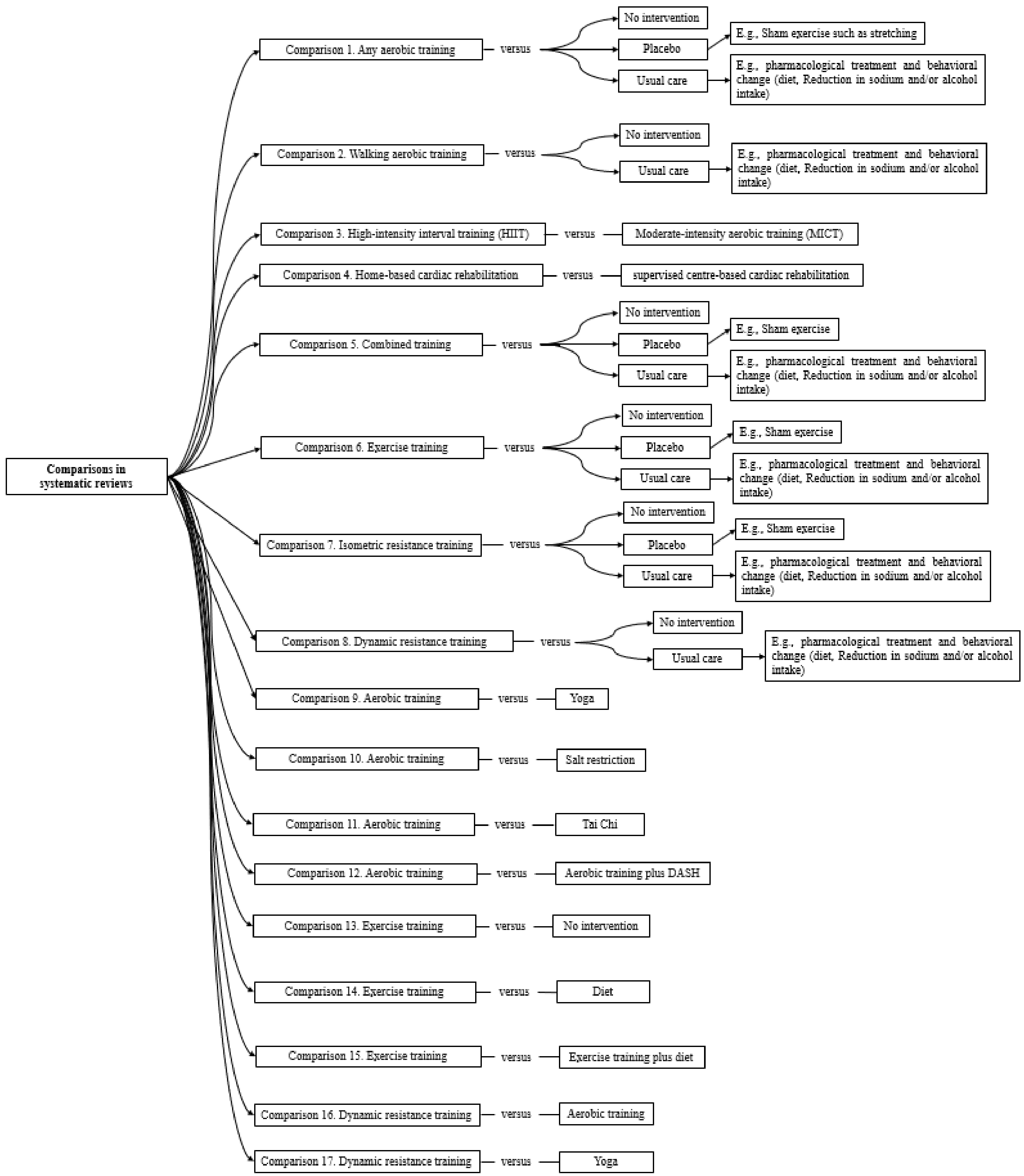
Additional file 7 presents the results for the remaining comparisons and their follow-up periods (i.e., any AET vs control; walking vs control; AET vs yoga; AET vs salt restriction; AET vs Tai Chi; aerobic training vs aerobic training plus Dietary Approaches to Stop Hypertension (DASH); high-intensity interval training vs moderate-intensity aerobic training; home-based vs supervised center-based cardiac rehabilitation; combined training vs control; exercise training vs control; exercise training vs no intervention; exercise training vs diet; exercise training vs diet plus exercise training; isometric resistance training vs control; dynamic resistance training vs control; dynamic resistance training vs aerobic training; dynamic resistance training vs yoga). See Figure 4.

In light of the richness of information reported across reviews, we present effect data and the corresponding assessment of the certainty of the evidence for the following follow-up periods (Tables 2-6 and Additional file 7):

- Short term (up to 16 weeks)
- Short to middle term (12 to 28 weeks)
- Short to long term (4 to 64 weeks)
- Middle term (up to 24-28 weeks)
- Middle to long term (24 to 64 weeks)
- Long term (48 to 64 weeks)

Seventeen (100%) reviews reported on SBP and DBP (33–49); three reviews reported on MBP (18%) (40,46,48). Eight reviews (48%) reported on adverse events related to the exercise training interventions (34,35,37,41,43–45,47); we used a narrative synthesis approach for this outcome due to the incomplete information reported by the reviews. Additional file 8 presents our assessment of the certainty of the evidence for all comparisons and Additional file 9 provides further details about effect estimates.

Figure 4. Comparisons reported in the included reviews.



Primary outcomes: SBP, DBP, and MBP

Aerobic training

Four comparisons reported effect data for AET (i.e., any AET vs control; walking aerobic training vs control; HIIT versus MICT; Home-based versus supervised centre-based cardiac rehabilitation). Results for these comparisons are summarized in Table 2.

Comparison 1: Any aerobic training versus control.

Seven reviews assessed the effects of any aerobic training on SBP and DBP compared with control groups in adults at short to long-term follow-up (33,35–38,42). One review assessed the effects of this intervention on MBP at short-term follow-up (40). The reviews included participants with different diagnoses and risk factors, such as high blood pressure (38), kidney failure (37), type II diabetes, and metabolic syndrome (42). Participants' age ranged from 21 to 71 years (33,35–38,40,42). See Table 1.

Systolic blood pressure: short to long term follow-up

Seven reviews reported data for this follow-up period. In order to provide a more precise analysis of the certainty of the evidence, we decided to report two reviews in a separate analysis (36,38) since these reviews had important methodological strengthens (e.g., narrow confidence intervals and large sample sizes). This approach was followed in the analysis of SBP and DBP, as follows:

Herrod et al., 2018 reported evidence of a clinically relevant difference in SBP between any AET and control in normotensive or high blood pressure adults (24 RCTs; N=1709; MD -5.09 mm Hg, 95% CI -7.22 to -2.97) at 12 to 48 weeks follow-up (38). Similar findings were reported by Fu et al., 2020 on SBP in prehypertensive adults(27 RCTs; N=1029; MD -6.60 mm Hg, 95% CI -8.23 to -4.98) for this follow-up (36). These findings were further confirmed by the same review (36) in the subgroup of adults with high blood pressure (24 RCTs; N=896; MD -6.11 mm Hg, 95% CI -7.82 to -4.45). Moderate quality evidence indicates that any AET probably reduces SBP compared to control in adults with either normotensive, prehypertensive, or with high blood pressure values at short to long-term follow-up (Table 2).

Data from Ostman et al. 2017 (42) suggest that any AET compared to control leads to little effect on SBP in adults with type II diabetes or metabolic syndrome at short to long term follow-up (15 RCTs; N=364; MD -2.54 mm Hg, 95% CI -4.34 to -0.75). Similar evidence was reported by a review on SBP in adults with end-stage renal disease at 8 to 40 weeks follow-up (10 RCTs; N=332; MD -10.07 mm Hg, 95% CI -16.35 to -3.78) (35). No differences between any AET and control were observed for SBP in adults with end-stage renal disease undergoing hemodialysis at 12 to 40 weeks follow-up (8 RCTs; N=204; MD -2.84 mm Hg, 95% CI -11.33 to 5.65) (33). Besides, Heiwe et al. 2011 (37), reported narrative data of no difference between any AET and control on SBP in adults with either moderate kidney failure, dialysis treatment, or kidney transplantation (37).

Diastolic blood pressure: short to long term follow-up

Herrod et al., 2018 found that any AET led to clinically important reductions in DBP compared with control (24 RCTs; N=1709; MD -2.20 mm Hg, 95% CI -3.08 to -1.31) at short to long term follow-up in normotensive or high blood pressure adults (38). These findings were further confirmed by Fu et al., 2020 in the subgroup of prehypertensive (27 RCTs; N=1029; -4.44 mm Hg, 95% CI -5.57 to -3.31) and high blood pressure adults (22 RCTs; N=848; WMD -4.01 mm Hg, 95% CI –5.30 to -2.74), for this follow-up (36). Moderate quality evidence indicates that any AET probably reduces DBP compared to control in adults who either are normotensive or prehypertensive or have high blood pressure at 6 to 64 weeks follow-up (Table 2). Data from Ostman et al., 2017 reported evidence of a clinically relevant reduction in DBP between any AET and control in adults with type II diabetes or metabolic syndrome at short to long-term follow-up (14 RCTs; N=337; MD -2.27 mm Hg, 95% CI -3.47 to -1.06) (42). Besides, no differences between any AET and control in DBP were found in adults with end-stage renal disease for this follow-up (10 RCTs; N=334; MD -2.96 mm Hg, 95% CI -7.71 to 1.78) (35).

These findings were further confirmed by Scapini et al., 2019 on DBP in adults with end-stage renal disease undergoing hemodialysis at 12 to 40 weeks follow-up (8 RCTs; N=204; MD 0.68 mm Hg, 95% CI -4.01 to 5.37) (33). Similarly, Heiwe et al., 2011 observed no difference between groups on DBP in adults with either moderate kidney failure, dialysis treatment, or kidney transplantation at short to long term follow-up (6 RCTs; N=202; MD -0.11 mm Hg, 95% CI -2.88 to 2.66) (37). It is uncertain whether any AET reduces DBP compared to control in adults with either type II diabetes, metabolic syndrome, renal diseases, end-stage renal disease, or kidney transplantation at short to long-term follow-up because the quality of evidence is very low (Table 2).

Mean blood pressure: short term follow-up

Findings from of Kite et al., 2019 (40) provided very low-quality evidence on the effects of any AET compared to control on MBP values in adults with polycystic ovary syndrome up to 16 weeks follow-up (1 RCTs; N=14; MD -6.8 mm Hg, 95% CI -10.6 to -3.0) (Table 2).

Comparison 2: Walking aerobic training versus control.

Two reviews studied the effects of walking aerobic training on SBP and DBP compared with control groups in adults at short to long-term follow-up (41,43). These reviews included adults with different diagnoses and risk factors, such as normotensive and high blood pressure adults (41), and type II diabetes (43). Participants' age ranged from 16 to 84 years (41,43).

Systolic blood pressure: short to long term follow-up

Lee et al., 2021, found that walking AET reduced SBP relative to control in normotensive or high blood pressure adults at short to long-term follow-up (73 RCTs; N=5060; MD -4.11 mm Hg, 95% CI -5.22 to -3.01) (41). In contrast, Qiu et al., 2014 found no evidence of such difference between groups in adults with type II diabetes at 8 to 6 weeks follow-up (11 RCTs; N=497; MD -1.69 mm Hg, 95% CI -5.22 to 1.85) (43). Compared to control, low certainty of evidence suggests that walking AET may reduce SBP in adults who either are normotensive, have high blood pressure, or have type II diabetes at short to long-term follow-up (Table 2).

Diastolic blood pressure: short to long term follow-up

Lee et al., 2021 reported evidence of a difference in DBP between walking AET and control (69 RCTs; N=4711; MD -1.79 mm Hg, 95% CI -2.51 to -1.07) in adults who either are normotensive or have high blood pressure at short to long-term follow-up (41). These findings were further confirmed by Qiu et al., 2014 on DBP in adults with type II diabetes (11 RCTs; N=497; MD -1.97 mm Hg, 95% CI -3.94 to -0.0) (43). Compared to control, low certainty of evidence suggests that walking AET may reduce DBP in adults who either are normotensive, have high blood pressure, or have type II diabetes at short to long-term follow-up (Table 2).

Comparison 3: High-intensity interval training (HIIT) versus moderate-intensity continuous training (MICT).

One review assessed the effects of HIIT compared with MICT on SBP and DBP at short-term follow-up (49) in adults with different diagnoses, such as chronic heart failure or coronary artery disease (participants' mean age 61 years) (49).

Systolic and diastolic blood pressures: short term follow-up

Xie et al., 2017 found lack of evidence of an effect between groups on SBP in adults with chronic heart failure or coronary artery disease at 4 to 12 weeks follow-up (8 RCTs; N=376; MD -0.09 mm Hg, 95% CI -4.82 to 4.65) (49). Similar findings were reported for DBP (8 RCTs; N=376; MD -0.79 mm Hg, 95% CI -3.75 to 2.16) (49). It is uncertain whether HIIT or MICT may reduce SBP and DBP in adults with chronic heart failure or coronary artery disease at short-term follow-up because the quality of evidence is very low (Table 2).

Comparison 4: Home-based versus supervised centre-based cardiac rehabilitation.

One review assessed the effects of home-based cardiac rehabilitation on SBP and DBP compared with supervised centre-based cardiac rehabilitation at short to long-term follow-up (34) in adults with either coronary heart disease, post-myocardial infarction, revascularization, or heart failure. Participants' age ranged 52 to 69 years (34).

Systolic and diastolic blood pressures: short term follow-up

Anderson et al., 2017 (34) found evidence of no difference between home-based cardiac rehabilitation and supervised centre-based cardiac rehabilitation on SBP in adults with either coronary heart disease, post-myocardial infarction, revascularization, or heart failure at 4 to 12 weeks follow-up (10 RCTs; N=1292; MD -0.27 mm Hg, 95% CI -3.13 to 2.60). Similar findings were reported for DBP (9 RCTs; N=1146; MD 0.74 mm Hg, 95% CI -1.04 to 2.53).

Compared to supervised centre-based cardiac rehabilitation, low quality evidence indicates that home-based cardiac rehabilitation may not reduce neither SBP nor DBP in this population at short-term follow-up (Table 2).

Table 2. Summary of findings for the comparison: Aerobic training vs control for systolic, diastolic, and mean blood pressure

Aerobic training vs Control						
Intervention: aerobic training **Comparison:** control **Setting:** mixed **(**Center, home, hospital, community-based, rehabilitation, laboratory, clinic, University)						
Outcomes	Population	Relative effect (95% CI)	**Anticipated absolute effect* (95% CI)**		Nº of Participants (studies)	Certainty of the evidence (GRADE)
			Assumed risk with control	Assumed risk with intervention		
			Systolic blood pressure – short to long term follow-up (6 to 64 weeks)			
Systolic blood pressure (short to long term 12-48 weeks)**	Normotensive High blood pressure	MD -5.09 (-7.22 to -2.97)	Not estimable	Mean SBP (mm Hg) was 5.09 lower (7.22 lower to 2.97 lower)	1709 (24)[a]	
Systolic blood pressure (short to long term 6-64 weeks)**	Prehypertensive	WMD -6.60 (-4.98 to -8.23)	Not estimable	Mean SBP (mm Hg) was 6.60 lower (4.98 lower to 8.23 lower)	1029 (27)[b]	⨁⨁⨁⊝ Moderate[1,2,3]
Systolic blood pressure (short to long term 6-64 weeks)**	High blood pressure	WMD -6.11 (-4.45 to -7.82)	Not estimable	Mean SBP (mm Hg) was 6.11 lower (4.45 lower to 7.82 lower)	896 (24)[b]	
			Systolic blood pressure – short to long term follow-up (4 to 52 weeks)			
Systolic blood pressure (short to long term 8-52 weeks)**	Type II diabetes metabolic syndrome	MD -2.54 (-4.34 to -0.75)	Not estimable	Mean SBP (mm Hg) was 2.54 lower (4.34 lower to 0.75 lower)	364 (15)[c]	
Systolic blood pressure (short to long term 8-40 weeks)**	End-stage renal disease	MD -10.07 (-16.35 to -3.78)	The mean SBP (mm Hg) range was from 132.2 to 179	Mean SBP (mm Hg) was 10.07 lower (16.35 lower to 3.78 lower)	332 (10)[d]	
Systolic blood pressure (Short to long term 12-40 weeks)**	End-stage renal disease on hemodialysis	MD -2.84 (-11.33 to 5.65)	The mean SBP (mm Hg) range was from 131 to 179	Mean SBP (mm Hg) was 2.84 lower (11.33 lower to 5.65 higher)	204 (8)[e]	⨁⨁⊝⊝ Low[1,2,4]
Systolic blood pressure (short to long term 4-52 weeks)**	Moderate kidney failure Dialysis treatment Kidney transplantation	Not estimable	-	-	202 (6)[f]	
			Systolic blood pressure – short to long term follow-up (4 to 64 weeks)			

Systolic blood pressure (short to long term 4 to 64 weeks)***	Normotensive High blood pressure	MD -4.11 (-5.22 to -3.01)	The MD SBP (mm Hg) range was from -8.4 to 7.27	Mean SBP (mm Hg) was 4.11 lower (5.22 lower to 3.01 lower)	5060 (73)[g]	⊕⊕⊖⊖ Low[2,7]
Systolic blood pressure (short to long term 8-36 weeks)***	Type II diabetes	MD -1.69 (-5.22 to 1.85)	Not estimable	Mean SBP (mm Hg) was 1.69 lower (5.22 lower to 1.85 higher)	497 (11)[h]	
			Systolic blood pressure – short term follow-up (4 to 12 weeks)			
Systolic blood pressure (short term 4 to 12 weeks)****	Chronic heart failure Coronary artery disease	MD -0.09 (-4.82 to 4.65)	The mean SBP (mm Hg) range was from -1 to -12	Mean SBP (mm Hg) was 0.09 lower (4.82 lower to 4.65 higher)	376 (8)[i]	⊕⊖⊖⊖ Very Low[2,8,9]
			Systolic blood pressure – short to long term follow-up (12 to 48 weeks)			
Systolic blood pressure (short to long term 12 to 48 weeks)*****	Coronary heart disease Post-myocardial infarction Revascularization Heart failure	MD -0.27 (-3.13 to 2.60)	The MD SBP (mm Hg) range was from -4.3 to 138	Mean SBP (mm Hg) was 0.27 lower (3.13 lower to 2.60 higher)	1292 (10)[j]	⊕⊕⊖⊖ Low[2,8]
			Diastolic blood pressure – short to long term follow-up (6 to 64 weeks)			
Diastolic blood pressure (short to long term 12-48 weeks)**	Normotensive High blood pressure	MD -2.20 (-3.08 to -1.31)	Not estimable	Mean DBP (mm Hg) was 2.20 lower (3.08 lower to 1.31 lower)	1709 (24)[a]	⊕⊕⊖⊖ Moderate[1,2,3]
Diastolic blood pressure (short to long term 6-64 weeks)**	Prehypertensive	WMD -4.44 (-5.57 to -3.31)	Not reported*	Mean DBP (mm Hg) was 4.44 lower (5.57 lower to 3.31 lower)	1029 (27)[b]	
Diastolic blood pressure (short to long term 6-64 weeks)**	High blood pressure	WMD -4.01 (-5.30 to -2.74)	Not reported*	Mean DBP (mm Hg) was 4.01 lower (5.30 lower to 2.74 lower)	848 (22)[b]	
			Diastolic blood pressure – short to long term follow-up (4 to 52 weeks)			
Diastolic blood pressure (short to long term 8-52weeks)**	Type II diabetes metabolic syndrome	MD -2.27 (-3.47 to -1.06)	Not reported*	Mean DBP (mm Hg) was 2.27 lower (3.47 lower to 1.06 lower)	337 (14)[c]	⊕⊖⊖⊖ Very Low[1,2]
Diastolic blood pressure (short to long term 8-40 weeks)**	End-stage renal disease	MD -2.96 (-7.71 to 1.78)	The mean DBP (mm Hg)	Mean DBP (mm Hg) was 2.96 lower (7.71 lower to 1.78 higher)	334 (10)[d]	

			range was from 0.5 to 90.42			
Diastolic blood pressure (Short to long term 12-40 weeks)**	End-stage renal disease on hemodialysis	MD 0.68 (-4.01 to 5.37)	The mean DBP (mm Hg) range was from 131 to 179	Mean DBP (mm Hg) was 0.68 higher (4.01 lower to 5.37 higher)	204 (8)[e]	
Diastolic blood pressure (short to long term 4-48 weeks)**	Moderate kidney failure Dialysis treatment Kidney transplantation	MD -0.11 (-2.88 to 2.66)	The mean DBP (mm Hg) range was from 72.8 to 90.6	Mean DBP (mm Hg) was 0.11 lower (2.88 lower to 2.66 higher)	202 (6)[f]	
			Diastolic blood pressure – short to long term follow-up (4 to 64 weeks)			
Diastolic blood pressure (short long term 4 to 64 weeks)***	Normotensive High blood pressure	MD -1.79 (-2.51 to -1.07)	The MD DBP (mm Hg) range was from -5 to 4.82	Mean DBP (mm Hg) was 1.79 lower (2.51 lower to 1.07 lower)	4711 (69)[g]	⊕⊕⊖⊖ Low[2,7]
Diastolic blood pressure (short to long term 8-36 weeks)***	Type II diabetes	MD -1.97 (-3.94 to -0.0)	Not estimable	Mean DBP (mm Hg) was 1.97 lower (3.94 lower to 0.0 lower)	497 (11)[h]	
			Diastolic blood pressure – short term follow-up (4 to 12 weeks)			
Diastolic blood pressure (short term 4 to 12 weeks)****	Chronic heart failure Coronary artery Disease	MD -0.79 (-3.75 to 2.16)	The mean DBP (mm Hg) range was from 0 to -5	Mean DBP (mm Hg) was 0.79 lower (3.75 lower to 2.16 higher)	376 (8)[i]	⊕⊖⊖⊖ Very Low[2,8,9]
			Diastolic blood pressure – short to long term follow-up (12 to 48 weeks)			
Diastolic blood pressure (short to long term 12 to 48 weeks)*****	Coronary heart disease Post-myocardial infarction Revascularization Heart failure	MD 0.74 (-1.04 to 2.53)	The MD DBP (mm Hg) range was from -3.3 to 87	Mean DBP (mm Hg) was 0.74 higher (1.04 lower to 2.53 higher)	1146 (9)[j]	⊕⊕⊖⊖ Low[2,8]
			Mean blood pressure – short term follow-up (up to 16 weeks)			
Mean blood pressure (short term up to 16 weeks)**	Polycystic ovary syndrome	MD -6.8 (-10.6 to -3.0)	Not estimable	Mean MBP (mm Hg) was 6.8 lower (10.6 lower to 3.0 lower)	14 (1)[k]	⊕⊖⊖⊖ Very Low[5,6]

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). AET: aerobic training; CI: Confidence interval; DBP: diastolic blood pressure; MD: mean difference; RCT: randomized controlled trial; SBP: systolic blood pressure; WMD: weighted mean difference.

** Any aerobic training versus control
*** Walking aerobic training versus control
**** High-intensity interval training (HIIT) versus Moderate-intensity aerobic training (MICT)
***** Home-based cardiac rehabilitation versus supervised centre-based cardiac rehabilitation

[a] Herrod et al., 2018; [b]Fu et al., 2020; [c]Ostman et al., 2017; [d]Ferrari et al., 2019; [e]Scapini et al., 2019; [f]Heiwe et al., 2011, [k]Kite et al., 2019; [g]Qiu et al., 2014; [h]Lee et al., 2021; [i] Xie et al., 2019; [j]Anderson et al., 2017.

[1] Downgraded by two levels due to selection bias (random sequence generations and allocation concealment), detection bias (unblinded outcome assessor), incomplete outcome data (attrition bias), and selective reporting (reporting bias).
[2] Downgraded by one level due to inconsistency (there was statistically significant heterogeneity).
[3] Upgraded by two levels due to very large effect (the effect is rapid and consistent across subjects, no serious problems with precision due to narrow confidence intervals and large sample size).
[4] Upgraded by one level due to very large effect (the effect is rapid and consistent across subjects, no serious problems due to narrow confidence)
[5] Downgraded by two levels due to selection bias (random sequence generations and allocation concealment), detection bias (unblinded outcome assessor), selective reporting (reporting bias), and other bias (contamination).
[6] Downgraded by one level due to small sample size (imprecision).
[7]Downgraded by one level due to selection bias (random sequence generations and allocation concealment), detection bias (unblinded outcome assessor), and incomplete outcome data (attrition bias)
[8] Downgraded by one level due to detection bias (unblinded outcome assessor).
[9] Downgraded by one level due to wide confidence intervals (imprecision).

Comparison 5: Combined training versus Control

Four reviews assessed the effects of combined training compared with control on SBP and DBP in adults at short to long-term follow-up (33,37,38,42). The reviews included participants with different diagnoses and risk factors, such as normotensive adults and high blood pressure (38), kidney failure (37), metabolic syndrome (42), or end-stage renal disease (33). Participants' mean age was 71 years (33,37,38,42). See Table 1.

Systolic blood pressure: short to long term follow-up

Heiwe et al., 2011, reported evidence of a clinically relevant difference in SBP between any AET and control in adults with kidney failure at short to long-term follow-up (4 RCTs; N=186; MD -5.80 mm Hg, 95% CI -10.41 to -1.19) (37). Similar findings were reported by Herrod et al., 2018 on SBP in normotensive or high blood pressure adults for this follow-up (12 RCTs; N=1237; MD -5.86 mm Hg, 95%CI -8.27 to -3.45) (38). These findings were further confirmed by Scapini et al., 2019 in adults with end-stage renal disease at 12 to 40 weeks (7 RCTs; N=292; MD -8.53 mm Hg, 95% CI -13.29 to -3.76) (33), and by Ostman et al., 2017 in metabolic syndrome adults at short to long-term follow-up (3 RCTs; N=652; MD -3.79 mm Hg, 95% CI -6.18 to -1.40) (42). Low certainty of evidence suggests that CT may reduce SBP compared to control in adults who either are normotensive, have high blood pressure, kidney failure, metabolic syndrome, or end-stage renal disease at short to long-term follow-up (Table 3).

Diastolic blood pressure: short to long term follow-up

Heiwe et al., 2011, found that CT led to clinically important differences in DBP compared to control in adults with kidney failure at short to long-term follow-up (4 RCTs; N=229; MD -3.77 mm Hg, 95% CI -5.94 to -1.61) (37). Similar findings were reported by Herrod et al., 2018 in normotensive or high blood pressure adults for this follow-up (12 RCTs; N=1237; MD -3.51 mm Hg, 95%CI -4.43 to -2.59) (38), by Scapini et al., 2019 in adults with end-stage renal disease at 12 to 40 weeks (7 RCTs; N=292; MD -4.57 mm Hg, 95% CI -6.24 to -2.90) (33), and finally by Ostman et al., 2017 in metabolic syndrome adults at short to long-term follow-up (3 RCTs; N=652; MD -0.23 mm Hg, 95% CI -3.53 to -1.55) (42). Moderate quality evidence indicates that CT probably reduces DBP compared to control in adults who either are normotensive, have high blood pressure, kidney failure, metabolic syndrome, or end-stage renal disease at 4 to 52 weeks follow-up (Table 3).

Table 3. Summary of findings for the comparison: Combined training versus control for systolic and diastolic blood pressure

Combined training vs Control						
Intervention: combined training **Comparison:** control **Setting:** mixed (Center, home, hospital, community-based, rehabilitation)						
Outcomes	Population	Relative effect (95% CI)	**Anticipated absolute effect* (95% CI)**		Nº of participants (studies)	Certainty of the evidence (GRADE)
			Assumed risk with control	Assumed risk with intervention		
			Systolic blood pressure – short to long term follow-up (4 to 52 weeks)			
Systolic blood pressure (short to long term12-48 weeks)	Normotensive High blood pressure	MD -5.86 (-8.27 to -3.45)	Not estimable	Mean SBP (mm Hg) was 5.86 lower (8.27 lower to 3.45 lower)	1237 (12)[a]	⊕⊕⊖⊖ Low[1,2]
Systolic blood pressure (short to long term 8-52 weeks)	Metabolic syndrome	MD -3.79 (-6.18 to -1.40)	Not estimable	Mean SBP (mm Hg) was 3.79 lower (6.18 lower to 1.40 lower)	652 (3)[b]	
Systolic blood pressure (short to long term 12 to 40 weeks)	End-stage renal disease and on hemodialysis	MD -8.53 (-13.29 to -3.76)	The mean SBP (mm Hg) range was from 133.7 to 153.1	Mean SBP (mm Hg) was 8.53 lower (13.29 lower to 3.76 lower)	292 (7)[c]	
Systolic blood pressure (short to long term 4-48 weeks)	Moderate kidney failure Dialysis treatment Kidney transplantation	MD -5.80 (-10.41 to -1.19)	The mean SBP (mm Hg) range was from 139.3 to 153.1	Mean SBP (mm Hg) was 5.80 lower (10.4 lower to 1.19 lower)	186 (4)[d]	
			Diastolic blood pressure – short to long term follow-up (4 to 52 weeks)			
Diastolic blood pressure (short to long term12-48 weeks)	Normotensive High blood pressure	MD -3.51 (-4.43 to -2.59)	Not estimable	Mean DBP (mm Hg) was 3.57 lower (4.43 lower to 2.59 lower)	1237 (12)[a]	⊕⊕⊕⊖ Moderate[2]
Diastolic blood pressure (short to long term 8-52 week)	Metabolic syndrome	MD -0.23 (-3.53 to 1.55)	Not estimable	Mean DBP (mm Hg) was 0.23 lower (3.53 lower to 1.55 higher)	652 (3)[b]	
Diastolic blood pressure (short to long term 12 to 40 weeks)	End-stage renal disease and on hemodialysis	MD -4.57 (-6.24 to -2.90)	The mean DBP (mm Hg) range was from 78.4 to 86.0	Mean DBP (mm Hg) was 4.57 lower (13.29 lower to 3.76 lower)	292 (7)[c]	
Diastolic blood pressure (short to long term 4-48 weeks)	Moderate kidney failure Dialysis treatment Kidney transplantation	MD -3.77 (-5.94 to -1.61)	The mean DBP (mm Hg) range was from 76.9 to 81.7	Mean DBP (mm Hg) was 3.77 lower (5.94 lower to 1.61 lower)	229 (4)[d]	

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). CI: Confidence interval; CT: combined training; DBP: diastolic blood pressure; MD: mean difference; RCT: randomized controlled trial; SBP: systolic blood pressure.

[a]Herrod et al., 2018; [b]Ostman et al., 2017; [c]Scapini et al., 2019; [d]Heiwe et al., 2011.

[1] Downgraded by one level due to selection bias (random sequence generations and allocation concealment), detection bias (unblinded outcome assessor), and incomplete outcome data (attrition bias).
[2] Downgraded by one level due to inconsistency (there was statistically significant heterogeneity)

Comparison 6: Exercise training versus Control

Three reviews reported on the effects of exercise training in SBP and DBP compared with control groups at short to long-term follow-up (37,47,48). One review studied the effects of this intervention in MBP at short-term follow-up (48). The reviews included adults with different diagnoses and risk factors, such as moderate kidney failure, kidney transplantation (37), chronic kidney disease, cardiovascular disease, type II diabetes (48), or type II diabetes and non-insulin-dependent adults (47). Participants' age ranged from 52 to 71 years (37,47,48).

Systolic blood pressure: short to long term follow-up

Heiwe et al., 2011 observed evidence of no effect between ET and control on SBP in moderate kidney failure or kidney transplantation adults at short to long-term follow-up (8 RCTs; N=347; MD -5.88 mm Hg, 95% CI -9.48 to 2.28; very low quality of evidence) (37). Similar findings were reported by the same review in SBP when the ET was performed at low intensity (< 60%) (3 RCTs; N=147; MD -0.86 mm Hg, 95% CI -7.82 to 6.10; very low quality of evidence). Different findings were reported by Heiwe et al., 2011 (37), who found that high-intensity ET (≥60%) may reduce SBP compared to control in adults with either moderate kidney failure or kidney transplantation at this follow-up (5 RCTs; N=211; MD -4.60 mm Hg, 95% CI -8.83 to -0.37; low quality of evidence).

Thompson et al., 2019 reported evidence of no difference between ET and control on SBP in adults with either chronic kidney disease, cardiovascular disease, or type II diabetes at short to long-term follow-up (10 RCTs; N=335; MD -4.33 mm Hg, 95% CI -9.04 to 0.38) (48). Similar findings were reported by Thomas et al., 2006 in type II diabetes, non-insulin-dependent adults at 8 to 48 weeks follow-up (4 RCTs; N=127; MD -4.16 mm Hg, 95% CI -

9.46 to -1.14) (47). Overall, low certainty of evidence suggests that ET may reduce SBP compared to control in adults who either have moderate kidney failure, kidney transplantation, chronic kidney disease, cardiovascular disease, or type II diabetes at short to long-term follow-up (Table 4).

Diastolic blood pressure: short to long term follow-up

Heiwe et al., 2011 reported evidence of a clinically important difference in DBP between ET and control in adults who either have moderate kidney failure or underwent kidney transplantation at short to long-term follow-up (10 RCTs; N=419; MD -2.32 mm Hg, 95% CI -4.05 to -0.59). Similar findings were reported by the same review in DBP when the ET was performed with high intensity (≥ 60%) at 8 to 48 weeks follow-up (6 RCTs; N=254; MD -3.98 mm Hg, 95% CI -6.05 to -1.90; low quality of evidence) (37). Furthermore, Thompson et al., 2019 found evidence of no difference between ET and control on DBP in adults with either chronic kidney disease, cardiovascular disease, or type II diabetes for this follow-up (8 RCTs; N=303; MD -1.18 mm Hg, 95% CI -4.76 to 2.40) (48). These findings were further confirmed by Thomas et al., 2006 on DBP in type II diabetes non-insulin-dependent adults at 8 to 48 weeks follow-up (3 RCTs; N=78; MD -0.13 mm Hg, 95% CI -3.70 to 3.45) (47). It is uncertain whether ET reduces DBP compared to control in adults who either have moderate and chronic kidney failure, underwent kidney transplantation, cardiovascular disease, type II diabetes, or type II diabetes non-insulin-dependent at short to long-term follow-up because the certainty of the evidence is very low (Table 4).

Mean blood pressure: short term follow-up

Thompson et al., 2019 (48) found that ET may result in clinically important reductions in MBP compared with control in adults with either chronic kidney disease, cardiovascular disease, or type II diabetes up to 12 weeks follow-up (2 RCTs; N=27; MD -12.11 mm Hg, 95% CI -15.98 to -8.25; low certainty evidence) (Table 4).

Table 4. Summary of findings for the comparison: Exercise training versus control for systolic and diastolic blood pressure

Exercise training versus control						
Intervention: exercise training **Comparison:** control **Setting:** mixed (home, clinic, and community setting)						
Outcomes	Population	Relative effect (95% CI)	**Anticipated absolute effect* (95% CI)**		Nº of participants (studies)	Certainty of the evidence (GRADE)
			Assumed risk with control	Assumed risk with intervention		
			Systolic blood pressure – short to long term follow-up (4 to 52 weeks)			
Systolic blood pressure (short to long term 4-48 weeks)	Moderate kidney failure Dialysis treatment Kidney transplantation	MD -5.88 (-9.48 to -2.28)	The mean SBP (mm Hg) range was from 132.9 to 153.1	Mean SBP (mm Hg) was 5.88 lower (9.48 lower to 2.28 lower)	347 (8)[a]	⊕⊕⊖⊖ Low [1,3]
Systolic blood pressure (short to long term 12-52 weeks)	Chronic kidney disease Cardiovascular disease Type II diabetes	MD -4.33 (-9.04 to 0.38)	Not estimate	Mean SBP (mm Hg) was 4.33 lower (9.04 lower to 0.38 higher)	335 (10[b]	
Systolic blood pressure (short to long term 8-48 weeks)	Non-insulin-dependent type II diabetes	MD -4.16 (-9.46 to 1.14)	Not estimate	Mean SBP (mm Hg) was 4.16 lower (9.46 lower to 1.14 higher)	127 (4)[c]	
			Systolic blood pressure – short to long term follow-up (4 to 48 weeks)			
Systolic blood pressure (short to long term 4-48 weeks)	Moderate kidney failure Dialysis treatment Kidney transplantation	MD -4.60 (-8.83 to -0.37)	The mean SBP (mm Hg) range was from 132.9 to 153.1	Mean SBP (mm Hg) was 4.60 lower (8.33 lower to 0.37 lower)	211 (5)[a#]	⊕⊕⊖⊖ Low[3,4]
			Systolic blood pressure – short to long term follow-up (4 to 48 weeks)			
Systolic blood pressure (short to long term 4-48 weeks)	Moderate kidney failure Dialysis treatment Kidney transplantation	MD -0.86 (-7.82 to 6.10)	The mean SBP (mm Hg) range was from 130.8 to 146	Mean SBP (mm Hg) was 0.86 lower (7.82 lower to 6.10 higher)	147 (3)[a¶]	⊕⊕⊖⊖ Very Low[4,5]
			Diastolic blood pressure – short to long term follow-up (4 to 52 weeks)			
Diastolic blood pressure (short to long term 4-48 weeks)	Moderate kidney failure Dialysis treatment Kidney transplantation	MD -2.32 (-4.05 to -0.59)	The mean DBP (mm Hg) range was from 72.8 to 90.6	Mean DBP (mm Hg) was 2.32 lower (4.05 lower to 0.59 lower)	419 (10)[a]	⊕⊖⊖⊖ Very Low[1,2]
Diastolic blood pressure (short to long term 12-52 weeks)	Chronic kidney disease Cardiovascular disease Diabetes type 2	MD -1.18 (-4.76 to 2.40)	Not estimable	Mean SBP (mm Hg) was 1.18 lower (4.76 lower to 2.40 higher)	303 (8)[b]	

Diastolic blood pressure (short to long term 8-48 weeks)	Non-insulin-dependent type II diabetes	MD -0.13 (-3.70 to 3.45)	Not estimable	Mean DBP (mm Hg) was 0.13 lower (3.70 lower to 3.45 higher)	78 (3)[c]	
			Diastolic blood pressure – short to long term follow-up (4 to 48 weeks)			
Diastolic blood pressure (short to long term 4-48 weeks)	Moderate kidney failure Dialysis treatment Kidney transplantation	MD -3.98 (-6.05 to -1.90)	The mean DBP (mm Hg) range was from 82 to 90.6	Mean DBP (mm Hg) was 3.98 lower (6.05 lower to 1.90 lower)	254 (6)[a#]	⊕⊕⊝⊝ Low[3,4]
			Mean blood pressure – short term follow-up (4 to 16 weeks)			
Mean blood pressure (short term up to 12 weeks)	Chronic kidney disease Cardiovascular disease Diabetes type 2	MD -12.11 (-15.98 to -8.25)	Not estimable	Mean MBP (mm Hg) was 12.11 lower (15.98 lower to 8.25 lower)	27 (2)[b]	⊕⊕⊝⊝ Low[4,5]

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). CI: Confidence interval; DBP: diastolic blood pressure; ET: exercise training; MD: mean difference; RCT: randomized controlled trial; SBP: systolic blood pressure.

[a]Heiwe et al., 2011; [b]Thompson et al., 2019; [c]Thomas et al., 2006.

[a#]Heiwe et al., 2011, high intensity (≥ 60%) ET
[a¶]Heiwe et al., 2011, low intensity (< 60%) ET

[1] Downgraded by one level due to wide confidence intervals (imprecision).
[2]Downgraded by two levels due to selection bias (random sequence generations and allocation concealment), detection bias (unblinded outcome assessor), incomplete outcome data (attrition bias), and selective reporting (reporting bias).
[3] Downgraded by one level due to selection bias (random sequence generations and allocation concealment) and detection bias (unblinded outcome assessor).
[4] Downgraded by one level due to small sample size (imprecision).
[5] Downgraded by one level due to selection bias (random sequence generations and allocation concealment), detection bias (unblinded outcome assessor), incomplete outcome data (attrition bias)

Comparison 7: Isometric resistance training versus control

Three reviews studied the effects of IRT on SBP and DBP compared with control groups (36,38,46); one review reported effect data for this intervention on MBP with the same comparison at short-term follow-up (46). The reviews included adults who either are normotensive, prehypertensive, or have high blood pressure (36,38,46). Participants' age ranged from 18 to 80 years (36,38,46).

Systolic blood pressure: short term follow-up

Smart et al., 2019 observed a clinically important difference in SBP between IRT and control in normotensive, prehypertensive, or high blood pressure adults at 4 to 12 weeks follow-up (12 RCTs; N=326; MD -7.35 mm Hg, 95% CI -8.95 to -5.75) (46). Fu et al., 2020 confirmed these findings in prehypertensive adults (5 RCTs; N=109; WMD -5.77 mm Hg, 95% CI -10.16 to -1.41) and adults with high blood pressure (5 RCTs; N=109; WMD -5.65 mm Hg, 95% CI -9.87 to -1.47) for this follow-up (36). Similar findings were reported by Herrod et al., 2018 on SBP in normotensive or high blood pressure adults at 4 to 10 weeks follow-up (2 RCTs; N=66; MD -9,14 mm Hg, 95% CI -10.76 to -7.51) (38). Notwithstanding, this body of evidence was rated as of very low quality, which suggests that it is uncertain whether IRT reduces SBP compared to control in adults who either are normotensive or prehypertensive or have high blood pressure levels at short-term follow-up (Table 5).

Diastolic blood pressure: short term follow-up

Smart et al., 2019 reported clinically important differences in DBP between IRT and control in normotensive, prehypertensive, or high blood pressure adults at 4 to 12 weeks follow-up (12 RCTs; N=326; MD -3.29 mm Hg, 95% CI -5.12 to -1.46) (46). These findings were further confirmed by

Fu et al. 2020 in prehypertensive adults (5 RCTs; N=109; WMD -4.01 mm Hg, 95% CI -6.93 to -1.07), and adults with high blood pressure (5 RCTs; N=109; WMD -4.00 mm Hg, 95% CI -7.00 to -0.99) for this follow-up (36). Besides, similar findings were reported by Herrod et al., 2018 on DBP in normotensive or high blood pressure adults at short-term follow-up (2 RCTs; N=66; MD -3.01 mm Hg, 95% CI -3.57 to -2.45) (38). Very low quality of evidence suggests that it is uncertain whether IRT reduces DBP compared to control in adults who either are normotensive or prehypertensive, or have high blood pressure levels at short-term follow-up (Table 5).

Mean blood pressure: short term follow-up

Data from Smart et al., 2019 (46) provided very low quality evidence on the effects of IRT on DBP compared to control in adults who either are normotensive or prehypertensive, or have high blood pressure at short-term follow-up (12 RCTs; N=326; MD -4.6 mm Hg, 95% CI -6.18 to -3.09). See Table 5.

Table 5. Summary of findings for the comparison: Isometric resistance training vs control for systolic, diastolic, and mean blood pressure

Isometric resistance training vs control

Intervention: isometric resistance training
Comparison: control
Setting: mixed (home and office)

Outcomes	Population	Relative effect (95% CI)	**Anticipated absolute effect* (95% CI)**		Nº of participants (studies)	Certainty of the evidence (GRADE)
			Assumed risk with control	Assumed risk with intervention		
			Systolic blood pressure – short term follow-up (4 to 12 weeks)			
Systolic blood pressure (short term 4-12 weeks)	Normotensive Prehypertensive High blood pressure	MD -7.35 (-8.95 to -5.75)	The mean SBP (mm Hg) range was from -0.4 to 4.02	Mean SBP (mm Hg) was 7.35 lower (8.95 lower to 5.75 lower	326 (12)[a]	⊕⊖⊖⊖ Very Low[1,2]
Systolic blood pressure (short term 8-12 weeks)	Prehypertensive	WMD -5.77 (-10.16 to -1.41)	Not estimable	Mean SBP (mm Hg) was 5.77 lower (10.16 lower to 1.41 lower)	109 (5)[b]	
	High blood pressure	WMD -5.65 (-9.87 to -1.47)	Not estimable	Mean SBP (mm Hg) was 5.65 lower (9.87 lower to 1.47 lower)	109 (5)[b]	
Systolic blood pressure (short term 4-10 weeks)	Normotensive High blood pressure	MD -9.14 (-10.76 to -7.51)	The mean SBP (mm Hg) range was from -8 to 1	Mean SBP (mm Hg) was 9.14 lower (10.76 lower to 7.51 lower)	66 (2)[c]	
			Diastolic blood pressure – short term follow-up (4 to 12 weeks)			
Diastolic blood pressure (short term 4-12 weeks)	Normotensive Prehypertensive High blood pressure	MD -3.29 (-5.12 to -1.46)	The mean DBP (mm Hg) range was from -0.1 to 4.25	Mean DBP (mm Hg) was 3.29 lower (5.12 lower to 1.46 lower)	326 (12)[a]	⊕⊖⊖⊖ Very Low[1,3]
Diastolic blood pressure (short term 8-10 weeks)	Prehypertensive	WMD -4.01 (-6.93 to -1.07)	Not estimable	Mean DBP (mm Hg) was 4.01 lower (6.93lower to 1.07 lower)	109 (5)[b]	
	High blood pressure	WMD -4.00 (-7.00 to -0.99)	Not estimable	Mean DBP (mm Hg) was 4.00 lower (7.00 lower to 0.99 lower)	3 (61)[b]	
Diastolic blood pressure (short term 4-10 weeks)	Normotensive High blood pressure	MD -3.01 (-3.57 to -2.45)	The mean DBP (mm Hg) range was from -3 to 0	Mean DBP (mm Hg) was 3.01 lower (3.57 lower to 2.45 lower)	66 (2)[c]	
			Mean blood pressure – short term follow-up (4 to 12 weeks)			
Mean blood pressure (short term 4-12 weeks)	Normotensive Prehypertensive High blood pressure	MD -4.6 (-6.18 to -3.09)	The mean MBP (mm Hg) range was from -0.12 to 3.33	Mean MBP (mm Hg) was 4.6 lower (6.18 lower to 3.09 lower)	326 (12)[a]	⊕⊖⊖⊖ Very Low [3,4]

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). CI: Confidence interval; DBP: diastolic blood pressure; MBP: mean blood pressure; MD: mean difference; RCT: randomized controlled trial; SBP: systolic blood pressure; WMD: Weighted mean difference.

[a]Smart et al., 2019; [b]Fu et al., 2020; [c]Herrod et al., 2018.

[1] Downgraded by two levels due to selection bias (random sequence generations and allocation concealment), detection bias (unblinded outcome assessor), and publication bias (Funnel plot asymmetry).
[2] Downgraded by one level due to small sample size (imprecision).
[3] Downgraded by one level due to inconsistency (there was statistically significant heterogeneity).
[4] Downgraded by two levels due to selection bias (allocation concealment), detection bias (unblinded outcome assessor), and publication bias (Funnel plot asymmetry).

Comparison 8: Dynamic Resistance training versus control

One review studied the effects of DRT compared with control on SBP and DBP in adults who either are normotensive or have high blood pressure at short to long-term follow-up. Participants' age ranged from 51 to 70 years (38).

Systolic and diastolic blood pressures: short to long term follow-up

Based on data from Herrod et al., 2018 (38), it is uncertain whether DRT reduces SBP compared to control in adults who either are normotensive or have high blood pressure at short to long-term follow-up (12 RCTs; N=514; MD -5.46 mm Hg, 95% CI -8.61 to -2.31; very low quality evidence). Low quality evidence indicates that DRT may reduce DBP compared to control in adults who either are normotensive or have high blood pressure at 12 to 48 weeks follow-up (12 RCTs; N=514; MD -2.02 mm Hg, 95% CI -3.31 to -0.73) (38). See Table 6.

Table 6. Summary of findings for the comparison: Dynamic resistance training versus control for systolic and diastolic blood pressure.

Dynamic resistance training versus control						
Intervention: dynamic resistance training **Comparison:** control **Setting:** mixed (clinic and home)						
Outcomes	Population	Relative effect (95% CI)	**Anticipated absolute effect* (95% CI)**		Nº of participants (studies)	Certainty of the evidence (GRADE)
			Assumed risk with control	Assumed risk with intervention		
			Systolic blood pressure – short to long term follow-up (12 to 48 weeks)			
Systolic blood pressure (short to long term 12-48 weeks)	Normotensive High blood pressure	MD -5.46 (-8.61 to -2.31)	Not estimable	Mean SBP (mm Hg) was 5.46 lower (8.61 lower to 2.31 lower)	514 (12)[a]	⊕⊖⊖⊖ Very Low [1,2]
			Diastolic blood pressure – short to long term follow-up (12 to 48 weeks)			
Diastolic blood pressure (short to long term 12 to 48 weeks)	Normotensive High blood pressure	MD -2.02 (-3.31 to -0.73)	Not estimable	Mean DBP (mm Hg) was 2.02 lower (3.31 lower to 0.73 lower)	514 (12)[a]	⊕⊕⊖⊖ Low[1]

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). CI: Confidence interval; DBP: diastolic blood pressure; MD: mean difference; RCT: randomized controlled trial; SBP: systolic blood pressure.

[a]Herrod et al., 2018

[1] Downgraded by two levels due to selection bias (random sequence generations and allocation concealment), detection bias (unblinded outcome assessor), incomplete outcome data (attrition bias), and selective reporting (reporting bias)

[2] Downgraded by one level due to inconsistency (there was statistically significant heterogeneity).

Secondary outcome:

Adverse events

Eight reviews mentioned adverse events related to the different exercise training modalities (34,35,37,41,43,45,47); however, only four out of the eight reviews reported specific data on adverse events (34,35,41,43), as follows:

- Lee et al., 2021 show that from 73 included trials, only 21 evaluated adverse events. Of this twenty-one, five reported eight adverse events such as four knee pain, one stress fracture, knee injury, bruised foot, and tripped.
- Anderson et al., 2017 (34): Two RCTs (20%) reported evidence of no difference in revascularization or recurrent myocardial infarction events between home and centre-based cardiac rehabilitation.
- Ferrari et al., 2019 (35): Four episodes of either hypotension or muscle pain occurred in one RCT (8%).
- Qiu et al., 2014 (43): One RCT (8%) reported some cases of mild hypoglycemia.

DISCUSSION

Summary of main results

The body of evidence on the benefits and harms of exercise training for blood pressure outcomes in adults consists of 17 high-quality systematic reviews, which studied different modalities of exercise training (i.e., AET, DRT, IRT, CT, and ET) in heterogeneous populations (e.g., adults with high blood pressure, type II diabetes mellitus, or renal disease). Overall, the included reviews provided data for 17 comparisons; 8 of those are prioritized due to their relevance in clinical practice guidelines and decision-making. The main findings indicate that when compared to control:

- Any aerobic training probably results in a large reduction in SBP and DBP in adults with either type II diabetes, metabolic syndrome, end-stage renal disease, or kidney transplantation at short to long-term follow-up (moderate-certainty evidence),
- Walking aerobic training probably results in a large reduction in either SBP or DBP in adults who either are normotensive, prehypertensive, or have high blood pressure at short to long-term follow-up (moderate-certainty evidence),
- Walking aerobic training probably results in a large reduction in SBP in normotensive adults at short to long-term follow-up (moderate-certainty evidence),
- Walking aerobic training probably results in a large reduction in DBP in adults with high blood pressure at short to long-term follow-up (moderate-certainty evidence),
- Combined training probably results in a large reduction in DBP in adults who either are normotensive, or have high blood pressure, kidney failure, metabolic syndrome, or end-stage renal disease at short to long-term follow-up (moderate-certainty evidence),
- DRT and IRT may result in little to no difference in either SBP or DBP in adults who either are normotensive, prehypertensive, or high blood pressure levels at different follow-up periods (very low to low-certainty evidence).

The remaining comparisons covered different control groups, such as Tai Chi, yoga, or dietary interventions. Like for the main comparisons, our certainty in this evidence varied between low to very low. Eight SRs provided inconclusive evidence about the safety of the exercise interventions

Overall completeness and applicability of evidence

The knowledge base of this overview applies mostly to participants aged 50 to 80 years, with diagnoses like type II diabetes, high blood pressure, renal disease, obesity, coronary disease, acute myocardial infarction, and cardiovascular risk factors (i.e., overweight and/or obesity), as well as either prehypertensive or healthy adults. The included reviews provided incomplete sociodemographic data as well as limited information about key aspects of the exercise training program's implementation, such as rules for starting level and program progression. This last aspect might constrain the applicability of this evidence to clinical practice.

To the best of our knowledge, the current overview represents the most comprehensive and detailed synthesis of secondary research in this field. Our in-depth analysis of the certainty of the evidence, sorted by relevant subgroups and follow-up periods, facilitates a well-detailed understanding on the characteristics of the evidence pertaining each comparison together with the description of the caveats in the evidence.

Certainty of the evidence

Overall, there is a low to very low quality of evidence in this overview, owing mostly to limitations in the risk of bias assessment (e.g., insufficient description of methods for random sequence generation), inconsistency (e.g., statistically significant heterogeneity), and imprecision (e.g., wide confidence intervals and/or small sample size). Despite being assessed as high-quality, the included SRs had some limitations in terms of protocol publication, grey literature searching, publication bias assessment, and conflict of interest disclosure. The RCTs included in the SRs had between low and high risk of bias, mostly due to insufficient description of methods for random sequence generation and allocation concealment, blinding of outcome assessor, incomplete outcome data, and selective reporting

Potential biases in the overview process

This overview of systematic reviews was conducted and reported according to the highest methodological standards (13–15). The comprehensive systematic search, as well as the independent and duplicate conduct of the study selection and data extraction processes, constitute methodological strengths. Moreover, the research team comprised exercise science professionals as well as physiotherapists, and experts in evidence synthesis in the area of exercise in non-communicable diseases. Our well-detailed assessment of the certainty of the evidence facilitates further use of this overview for evidence-informed decision-making purposes. Of note, the limited number of RCTs available for some comparisons as well as the presence of important methodological weaknesses reduces our confidence in these findings. The findings for these comparisons should therefore be interpreted with caution, acknowledging the limitations presented in the summary of findings tables.

Agreements and disagreements with other reviews

Numerous systematic reviews on the effects of exercise for blood pressure outcomes have been published in recent years (51–55), whereas tertiary evidence, an overview of reviews, has been less common in the scientific literature. We identified two tertiary syntheses that partially covered our research question (7,56). Our findings align with those reported by El-Kotob et al., 2020 (56), who based on data from one review, found low to very low evidence in favor of DRT compared to control for changes in SBP and DBP in adults with different comorbidities (e.g., cardiovascular disease, type II diabetes mellitus, and mental health) at various follow-up periods. Besides, the authors of this review deemed exercise as a safe intervention. In 2018, Pescatello et al. reported strong evidence favoring different modalities of PA (i.e., aerobic, dynamic resistance, combined) to reduce blood pressure values in normotensive, prehypertensive, and high blood pressure adults (7). Notwithstanding, direct comparisons regarding the results of these previous overviews (7,56) are not appropriate as our overview included a much larger sample of systematic review and covered a more-detailed assessment of the certainty of the evidence.

Implications for practice

This overview provides the most up-to-date evidence synthesis on the effects of exercise training for blood pressure outcomes in adults with or without comorbidities and cardiovascular risk factors. Our findings might be used by public health authorities in the development of community-wide programs, such as community-based exercise programs (16,50), where political will and stakeholder involvement are essential facilitators. The included reviews provided incomplete information on how the exercise training interventions were implemented, which constrains the transferability of our findings into practice. Besides, we believe that academia should ensure all professionals in charge of exercise prescription be taught on the designing, planning, and prioritizing of exercise training interventions. The detailed subgroup analyses in this overview might inform the tailoring of exercise prescription according to the needs of relevant subgroups (e.g., type II diabetes or end-stage renal disease).

Implications for further research

Findings from this overview highlight the need for further well-conducted RCTs in this research field, whose authors should adhere to international reporting guidance when formulating and publishing these studies, such as the Consensus on Exercise Reporting Template (CERT) tool (57), the SPIRIT checklist (58) and the CONSORT checklist (59). The result from the quality appraisal of the included reviews uncovered important caveats (e.g., no protocol registration and incomplete reporting of the search procedures), these can be tackled by adhering to the PRISMA 2020 statement (13,14). Further reviews should also present the assessment of the certainty of the included evidence to facilitate its use in a decision-making context (60). Another limitation to be addressed by further reviews is the description of the outcome prioritization process and consumer involvement, as none of the included reviews provided such information. Cochrane has published comprehensive guidance in this regard (15).

CONCLUSIONS

We found very low to moderate evidence supporting the benefits of exercise training compared with no interventions or placebo for blood pressure outcomes in adults with different comorbidities or risk factors. Scarce safety data were identified. Our certainty in the evidence was constrained due to methodological limitations, inconsistency, and imprecision. Before drawing more solid conclusions, further well-conducted and well-reported randomized controlled trials are warranted in order to strengthen the evidence base underlying this research question.

OTHER INFORMATION

Abbreviations

AET: Aerobic Training; AMSTAR: the Assessment of Multiple Systematic Reviews; BMI: Body mass index; BP: Blood Pressure; CKD: chronic kidney disease; CFR: cardiorespiratory fitness CT: Combined Training; DBP: Diastolic Blood Pressure; DRT: Dynamic Resistance Training; ERSD: end-stage renal disease in hemodialysis; GRADE: Grading of Recommendations, Assessments, Development and Evaluation; HIIT: High-intensity interval training; IRT: Isometric Resistance Training; MBP: Mean Blood Pressure; MD: Mean difference; Mets: metabolic syndrome; MICT: moderate-intensity continuous training; NICE: National Institute for Health and Care Excellence; OR: odds ratios ORs; PA: Physical activity; PRISMA-P: Preferred Reporting Items for Systematic Review and Meta-Analyses Protocol; PROSPERO: Prospective Register of Systematic Reviews; RCTs: randomized controlled trials; RoB: risk of Bias; SMD: Standardized mean difference; RR: risk ratios, SBP: Systolic Blood Pressure; SET: supervised exercise therapy; WMD: Weighted mean difference.

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Authors' contributions

AFL-B and JFM-E conceptualized the idea for this overview. All authors contributed to performing study selection, data extraction, quality appraisal, and assessment of the certainty of the evidence. AFL-B and JFM-E are the guarantors and drafted the manuscript. All authors read and approved the final manuscript.

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