Title

Effects of exercise training on metabolic syndrome risk factors in post-menopausal women – a systematic review and meta-analysis of randomised controlled trials

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Abstract

Background & Aims: Alterations in the hormonal profiles as women transition to the menopause predisposes individuals to the metabolic syndrome (MetS). In post-menopausal women, this can be exacerbated by sedentary behaviour and physical inactivity. Physical activity can convey many health benefits including improvement in MetS risk factors. However, it remains to be elucidated how differing exercise intensities and its mode of delivery can ameliorate MetS risk factors and resultant progression amongst post-menopausal women. The purpose of this systematic review and meta-analysis was to investigate the effects and efficacy of exercise training on MetS risk factors in post-menopausal women.

Methods: Database searches using PubMed, Scopus, Web of Science and the Cochrane Central Register of Controlled Trials were conducted from inception to December 2021 for randomised controlled studies (RCTs) investigating exercise training (>8 weeks) in at least one of the MetS risk factors in post-menopausal women. Utilising the random-effects model, appropriate standardised mean differences (SMD) or mean differences (MD) with 95% confidence interval (CI) for each MetS risk factor were used to calculate the overall effect size between the exercise and control groups. Sub-group analyses were performed for exercise intensity, modality, and duration for each risk factor. Meta-regression was performed for categorical (health status) and continuous (body mass index) covariates.

Results: 39 RCTs (40 studies) involving 2,132 participants were identified as eligible. Overall, the meta-analysis shows that exercise training significantly improved all MetS risk factors: waist circumference (WC) [MD: -2.61 cm; 95% CI: -3.39 to -1.86 cm; $p < 0.001$; 21 studies]; triglycerides (TG) [SMD: -0.40 mmol/L; 95% CI: -0.71 to -0.09 mmol/L; $p = 0.01$; 25 studies]; high-density lipoprotein (HDL) [SMD: 0.84 mmol/L; (95% CI: 0.41 to 1.27 mmol/L; $p < 0.001$; 26 studies]; fasting glucose (BG) [SMD: -0.38 mmol/L (95% CI: -0.60 to -0.16 mmol/L; $p < 0.001$; 20 studies]; systolic blood pressure (SBP) [MD: -5.95 mmHg (95% CI: -7.98 to -3.92 mmHg; $p < 0.001$; 23 studies]; and diastolic blood pressure (DBP) [MD: -4.14 mmHg (95% CI: -6.19 to -2.08 mmHg; $p < 0.001$; 23 studies]. Furthermore, sub-group analyses identified that

moderate intensity and combined exercise training significantly improved MetS risk factors ($p < 0.05$) except for HDL, with combined exercise being the most effective. Long duration (≥12 weeks) training also significantly improved MetS risk factors except for TG. Meta-regression revealed no moderating effects on any MetS risk variables.

Conclusion: This study reinforces the importance of regular physical activity as a non-pharmacological tool in the reduction of MetS risk in post-menopausal women, with significant metabolic improvements seen in interventions spanning 8 – 10 weeks. Moderate intensity and combined training significantly benefitted abdominal obesity, dyslipidaemia, dysglycaemia and hypertension in post-menopausal women. Improvements in at least one MetS risk were also seen with other exercise modalities and intensities.

Keywords: Cardiometabolic health, Aging, Women's health, Exercise Interventions

1. Introduction

Metabolic syndrome (MetS) is defined by a cluster of risk factors of metabolic origin that is linked to elevated risk of cardiovascular disease (CVD)[1]. These risk factors are increased waist circumference (WC), elevated blood pressure (BP), blood glucose (BG) and triglyceride (TG) levels, and diminished high-density lipoprotein cholesterol (HDL) levels[2]. In individuals with MetS, the risk of CVD events such as stroke and myocardial infarction is twice as high compared to those without MetS[3]. The prevalence of MetS is strongly associated with age[4], and this risk is exacerbated in women following the menopausal transition[5].

The menopausal transition is a significant phase that every woman will experience, commonly occurring between the ages of 45 – 55 years depending on sociodemographic, genetic and lifestyle factors[6,7]. Menopause signifies the permanent cessation of menstrual cycles, identified as twelve months after the last menstrual period[8]. Changes in hormonal milieu during the menopausal transition are associated with weight gain, dysregulated lipid profiles and increased blood glucose levels[9,10]. Furthermore, post-menopausal oestrogen deficiency accentuates metabolic dysfunction, via adipose tissue redistribution resulting in

increased abdominal adiposity[11]. Metabolic disturbances associated with the menopause phase including hypertension, abnormalities in blood lipid and glucose profiles and increased visceral adipose tissue (VAT) accumulation can impede normal endothelial function and accelerate vascular ageing, contributing to increased cardiovascular risk[12,13]. Albeit an inevitable part of a woman's life, the cumulative effects of ageing and menopause can affect quality of life, therefore highlighting the need for concern within this population.

Unhealthy lifestyle habits such as physical inactivity and sedentary behaviour are contributors to increased MetS prevalence in post-menopausal women[14–16]. Recommendations of regular physical activity in this cohort are ubiquitous across literature. Regular exercise training has been shown to elicit reductions in independent cardiometabolic risk factors in post-menopausal women through improvements in: blood pressure[17–20], inflammatory markers[21–25], endothelial function[26–28], body composition[18,29–31], insulin resistance[18,32,33], HDL[34] and cardiorespiratory fitness[35,36]. However, there is limited robust research examining the efficacy of exercise intensity and modality on combined risk factors focused on MetS progression within predisposed post-menopausal women.

Although physical activity is advised and considered as a non-pharmacological alternative to improve cardiometabolic health, the exercise dosage and the mode of delivery in ameliorating MetS risk factors and resultant progression within this cohort still remains unclear. Therefore, the purpose of this study is to systematically review and meta-analyse randomised controlled trials assessing the effect of exercise training on the individual MetS risk factors in post-menopausal women. The study aims to assess the magnitude of effectiveness of exercise training on each risk factor of MetS and to determine which exercise intensity, modality and duration have the most beneficial impact on MetS risk factors in post-menopausal women.

2. Materials and methods

2.1. Registration

This review was registered at PROSPERO (registration number CRD42021283944). This systematic review and meta-analysis was performed in accordance to the Preferred Reporting

Items for Systematic Reviews and Meta-analyses (PRISMA) statement guidelines and the Cochrane Handbook of Systematic Reviews of Interventions[37].

2.2. Eligibility criteria

The following pre-defined criteria were employed to the study inclusion: 1) randomised-controlled trials (RCT); 2) studies explicitly including women who are post-menopausal (defined by at least one year of amenorrhea and/or follicle stimulating hormone (FSH) levels ≥30 IU/L); 3) peer-reviewed, full-text studies with training program lasting at least 8 weeks, in a pre-post design; 4) studies analysed and reporting the effects of exercise training in at least one variable of MetS (BG, HDL, TG, systolic BP (SBP), diastolic BP (DBP), and/or WC; 5) blood measurements had to be performed in a fasted state categorised as >8 hours without food or after an overnight fast; 6) studies containing an exercise-only arm if the study is a multicomponent treatment. If studies included men or pre-/peri-menopausal women, outcome variables of post-menopausal women had to be analysed separately. Papers were excluded if: 1) post-menopausal status was not predefined in the inclusion criteria; 2) women had cancer or non-alcoholic fatty disease (NAFLD); 3) not published in peer-reviewed journals; 4) not written in the English language; 5) conducted in animals; 6) addressing interventions applying novel exercise technologies (e.g., whole-body vibration, exergaming etc.); 7) not of RCT design, review articles, literature reviews, study protocol, abstracts or conference papers.

2.3. Search strategy

All literature investigating the effect of exercise training on risk factors of MetS in post-menopausal women were searched and obtained utilising PubMed, Scopus, web of science and the Cochrane Central Register of Controlled Trials from inception to December 2021. The search strategy included various combinations of the keywords and MeSH terms: postmenopausal, exercise training, metabolic syndrome. Boolean search terms (AND, OR) were utilised. A detailed search strategy is presented in Supplementary Materials. These searches were limited to RCTs and human studies. Papers accepted were in English language only. To increase generalisability of results, papers were accepted regardless of the

participants' health status (except cancer or NAFLD). In addition, reference lists of all relevant systematic reviews and meta-analysis were searched manually to locate additional relevant studies.

Database results were imported into Covidence systematic review software (Veritas Health Innovation, Australia). Abstracts and titles were independently reviewed by two reviewers (A.T and R.C). Papers were initially classified as 'yes', 'no' or 'maybe', of which those classified as 'yes' or 'maybe' proceeded to full-text screening. Full-text papers were then classified as 'yes' or 'no' with subsequent final papers classified as 'yes'. Any disagreements were resolved by reaching a consensus.

2.4. Risk of bias and quality assessment

The revised Cochrane Risk of Bias tool (RoB 2) was independently used by two authors (A.T and R.C) to assess risk of bias[38]. The following aspects were evaluated for the quality of the studies: 1) bias arising from the randomisation process; 2) bias due to deviations from the intended interventions; 3) bias due to missing outcome data; 4) bias in the measurement of the outcome; 5) bias in the selection of the reported result. The details of the RoB2 assessment are provided in Supplementary Materials Table S1. The overall risk of bias for each study was determined as low risk, some concerns, or high risk. Any disagreements were examined by all authors before reaching a consensus. Sensitivity analyses were conducted by omitting each individual study and evaluating the effect on standardised mean differences (SMD) or mean differences (MD), and heterogeneity.

2.5. Data extraction

Extraction of data from included studies were performed by a single author (A.T) into an electronic spreadsheet (Excel 2016, Microsoft Corporation USA) according to the following study characteristics: (A) first author; (B) year of publication; (C) study design; (D) characteristics of the participants including health status, mean age, baseline body mass index (BMI) and sample size; (E) exercise training characteristics including exercise modality, duration and frequency; (F) pre- and post-intervention measurements of MetS outcome

variables (BG, HDL, TG, SBP, DBP and/or WC) and corresponding measurements of MetS outcome variables (BG, HDL, TG, SBP, DBP and/or WC) in the non-exercise control group. If studies had multi-interventions arms, only data of exercise and control (non-exercise) arms were included. All data extracted were checked for accuracy by a second author (R.C).

Following data extraction, BG, HDL, TG, SBP and DBP were converted to SI units (BG, HDL and TG: mmol/L). For each of the six outcomes of interest, mean change scores were calculated from pre- and post-intervention mean and standard deviation (SD) values in both the exercise and control arms for the meta-analyses. In studies reporting 95% confidence intervals, interquartile range (IQR) or standard error (SE), these were converted to a standard deviation [39]. Additionally, WebPlotDigitizer Version 4.2 (Ankit Rohatgi, USA) was used for the extraction of data from graphs and figures when required. One study was excluded as no response was received when the corresponding author was contacted due to insufficient data [40].

2.6. Data synthesis and analysis

Data synthesis and analysis were performed by one author (A.T), statistical analyses were completed utilising JASP (JASP Software version 0.16.4, JASP, Amsterdam, Netherlands) and Review Manager software (RevMan Version 5.4, Cochrane Collaboration, Oxford, UK). Using the random-effects model, SMD or MD with 95% confidence (CI) were calculated. Heterogeneity was assessed utilising the I^2 statistic, with >50% indicating large heterogeneity. To establish the magnitude of the effects of exercise training vs control on all MetS risk factors, effect sizes were calculated in accordance with Cochrane guidelines using the following: 0.2 – 0.49, 0.5 – 0.79 and ≥ 0.8 for small, moderate and large effects respectively[41]. Six separate pooled meta-analyses were conducted for each of the MetS risk factors. Sub-group analyses of exercise intensity were performed for all MetS risk factors in accordance with Table 1. Studies that included a combination of intensities used for exercise training were denoted as light-moderate, light-vigorous, and moderate-vigorous. Similarly, exercise modality (continuous, resistance, combined or interval) and intervention duration (short term: <12

weeks; long term: ≥12 weeks; very long term: ≥6 months) were included. Meta-regressions were also performed to determine the potential effect of participant characteristics on all MetS risk factors: continuous covariate (BMI) and categorical covariate (health status). Publication bias of included studies for all MetS risk variables were assessed using visual interpretation of funnel plots. Egger's regression test of $p < 0.05$ was used as a secondary determinant to confirm significant publication bias[42].

	Very light	**Light**	**Moderate**	**Vigorous**	**Very vigorous**
Oxygen uptake (VO_2max) (mL/kg/min)	< 20	20 – 39	40 – 59	60 – 84	≥ 85
Heart rate reserve (HRR%)	< 20	20 – 39	40 – 59	60 – 84	≥ 85
Maximum heart rate (%)	< 50	50 – 63	64 – 76	77 – 93	≥ 94
Metabolic Equivalent of Task (METs) (MET Unit)		< 3	3 – 6	> 6	
RPE (Borg scale unit)	≤ 10	10 – 12	13 – 14	15 – 16	17 - 18
1-RM (%)		≤ 50	60 – 70	> 70	> 100

Table 1. Criteria for exercise intensity classification in accordance to The American College of Sports Medicine guidelines[43]. METs: Metabolic Equivalents; RPE: Rate of Perceived Exertion; RM: Resistance Maximum.

3. Results

3.1. Study selection

A total of 5,452 papers were initially identified from database searches. After removal of 888 duplicates, title and abstract screening excluded 4,413 studies. 151 papers were sought for retrieval for full-text versions, of which 7 were removed due to no full-text available. Of the remaining 144 full-text papers retrieved, 105 were excluded (28 had no MetS variables analysed, 16 had inappropriate study design, 12 had duplicated data, 15 reported inadequate outcomes, 2 did not analyse post-menopausal women separately, 2 were non-English language, 28 did not predefine post-menopause status in their inclusion criteria and 2 did not

state that blood measurements were taken in a fasted state/following an overnight fast). 39 final papers were identified to be eligible for inclusion in the review and meta-analysis[18,21,22,24,26,28,29,32,36,44–73]. 1 paper[21] conducted multiple studies of the same intervention in two different cohorts of interest each, a total of 40 separate studies were included in the analysis. The PRISMA diagram of the selection process is detailed in Figure 1.

3.2. Study characteristics

Characteristics of the exercise interventions and participants are described in Table 2. The mean ± SD age and BMI of the participants in the studies ranged from 52.9 ± 1.9 years[45] to 76.0 ± 5.0 years[65], and 22.2 ± 2.0 kg/m^2[59] to 34.0 ± 1.3 kg/m^2[72], respectively. All participants were post-menopausal (defined by at least one year of amenorrhea and/or follicle stimulating hormone (FSH) levels ≥30 IU/L). Many of the studies were performed in overweight or obese individuals with no additional MetS risk factors (27 studies) [18,21,22,24,29,32,36,44–47,49,50,52,54–58,61,62,64,67–69,72,73]. There were a total of 7 studies conducted in women with hypertension[18,26,53,60,65,70,71], 1 study in women with dyslipidaemia[21], 1 study in women with osteopenia[51], and 1 study in women with dynapenia[63]. The remaining 3 studies were in healthy women of normal weight[28,48,59].

A total of 2,132 participants were included, with 1,069 and 1,023 participants in the exercise and control groups respectively. Each MetS variable encompassed the following number of studies and total participants: waist circumference: 21 studies, 1,198 participants; triglycerides: 25 studies, 1,064 participants; HDL: 26 studies, 1,035 participants; glucose: 20 studies, 1,103 participants; SBP: 23 studies, 877 participants; DBP: 23 studies, 877 participants. In 1 study[21], two different cohorts of women (women with or without dyslipidaemia) were analysed separately.

The exercise interventions were diverse amongst the studies. They consisted of a range of intensities classified by Table 1. Exercise modalities were categorised into continuous, resistance, combined (continuous and resistance) and interval training. The duration of the

interventions ranged from 8 weeks to 12 months. The intensity of the exercise sessions increased periodically over the course of the program, with measurements of heart rate and intensity regularly monitored.

3.3. Risk of bias

The risk of bias for selected studies are provided in Supplementary Materials Table S2. Overall, 3 studies were reported as low risk, 22 studies as some concerns and 15 studies as high risk of bias. Blinding of participants to their allocation of exercise intervention is not possible in exercise-related studies. Hence, allocation concealment under the domain “bias from randomisation process” was not described in detail in all studies. We therefore evaluated this aspect as “some concerns”. 10 studies reported acceptable method of random sequence generation (i.e. computer generated), whilst the remaining 30 studies were judged as “some concerns” due to insufficient detail reported for randomisation method.

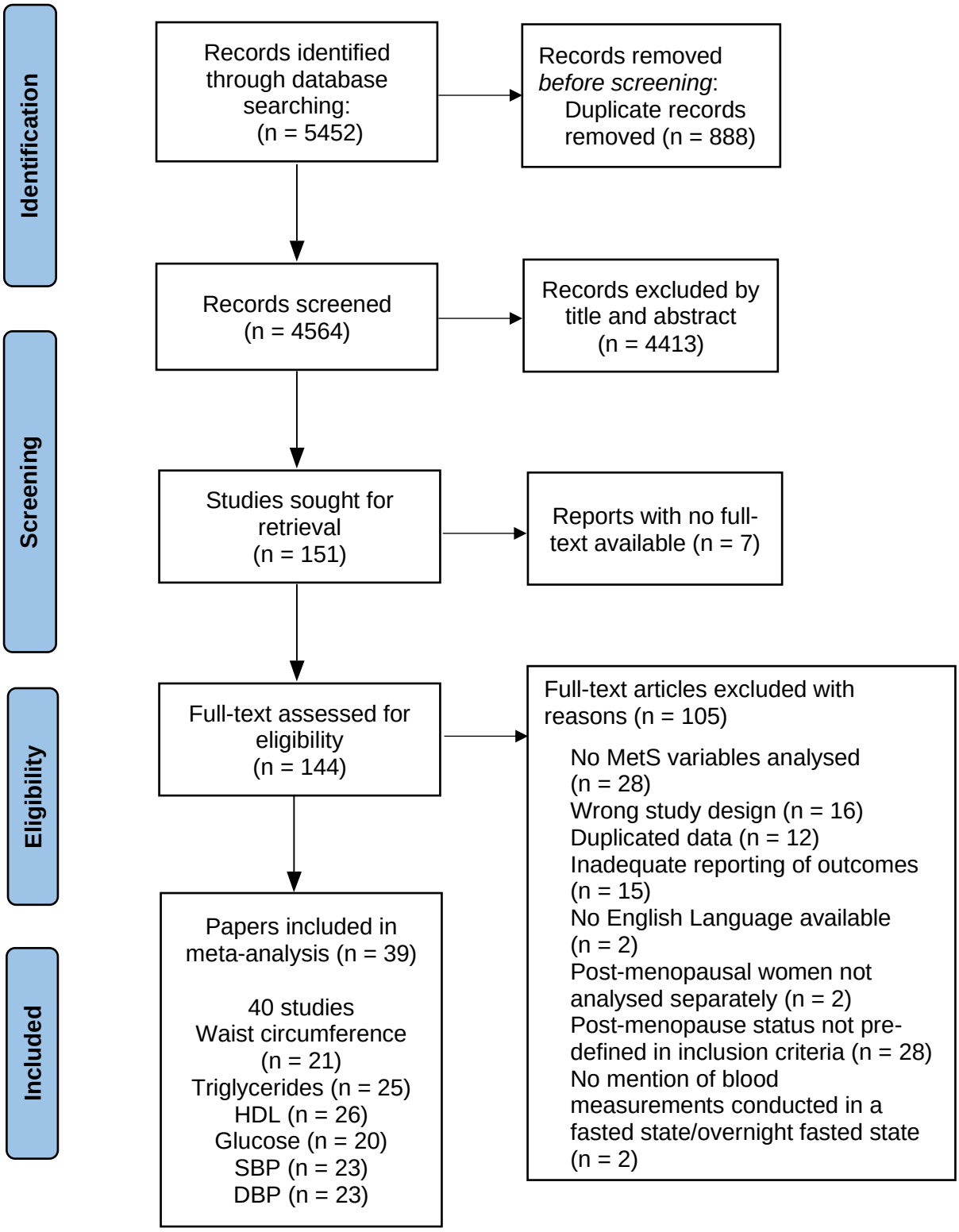

Figure 1. PRISMA flow diagram of the study selection process.

Table 2. Summary of characteristics of participants and interventions in 40 studies.

Study (Country)	Participants characteristics	Age (years); BMI (kg/m^2)	No. of Participants	Exercise Intervention			MetS Risk Factors
				Duration	Frequency	Modality (intensity)	
Akwa et al., 2017[73] (Ghana)	Healthy	EX: 61.3 ± 7.5; 31.2 ± 7.5 CON: 61.3 ± 7.8; 29.0 ± 5.4	EX: 8 CON: 10	8 weeks	3 days	Continuous (light-moderate intensity)	HDL, TG, SBP, DBP
Azadpour et al., 2017[26] (Turkey)	Obese with prehypertension	EX: 57.6 ± 4.3; 32.2 ± 1.8 CON: 56.6 ± 4.2; 31.3 ± 1.4	EX: 12 CON: 8	10 weeks	3 days	Continuous (moderate-vigorous intensity)	SBP, DBP, WC
Bergström et al., 2009[44] (Sweden)	Healthy overweight	EX: 58.5 ± 4.2; 24.2 ± 2.5 CON: 59.4 ± 3.6; 25.0 ± 2.2	EX: 48 CON: 44	12 months	4-5 days	Continuous (moderate intensity)	HDL, SBP, DBP, WC
Biteli et al., 2021[a][21] (Brazil)	Dyslipidaemic obese	EX: 62.3 ± 6.7; N/A CON: 59.3 ± 6.2; N/A	EX: 24 CON: 22	20 weeks	3 days	Combined (moderate intensity)	BG, HDL, TG, WC
Biteli et al., 2021[b][21] (Brazil)	Obese	EX: 58.5 ± 6.5; N/A CON: 61.2 ± 7.7; N/A	EX: 11 CON: 13	20 weeks	3 days	Combined (moderate intensity)	BG, HDL, TG, WC
Chagas et al., 2017[22] (Brazil)	Healthy obese	EX: 61.3 ± 6.4; 30.6 ± 5.0 CON: 59.8 ± 7.1; 32.8 ± 4.9	EX: 35 CON: 35	20 weeks	3 days	Combined (moderate intensity)	BG, HDL, TG, WC
Church et al., 2007[36] (USA)	Overweight/obese	EX: 56.6 ± 6.6; 31.3 ± 3.6 CON: 57.2 ± 5.8; 32.3 ± 3.9	EX: 103 CON: 102	6 months	3-5 days	Continuous (Moderate intensity)	BG, HDL, TG, SBP, DBP, WC
Colado et al., 2009[45] (Spain)	Healthy	EX: 54.0 ± 2.8; 29.5 ± 3.3 CON: 52.9 ± 1.9; 27.5 ± 3.3	EX: 21 CON: 10	24 weeks	3 days	Resistance (Moderate intensity)	BG, HDL, TG, SBP, DBP, WC
Conceição et al., 2013[46] (Brazil)	Healthy	EX: 53.4 ± 4.0; 26.2 ± 3.3 CON: 53.0 ± 5.7; 25.3 ± 1.8	EX: 10 CON: 10	16 weeks	3 days	Resistance (moderate-vigorous intensity)	BG, HDL, TG, SBP, DBP, WC
Dalleck et al., 2009[47] (USA)	Healthy	EX: 55.4 ± 3.2; 28.1 ± 4.5 CON: 57.4 ± 4.6; 30.0 ± 8.7	EX: 8 CON: 10	12 weeks	5 days	Continuous (moderate intensity)	BG, HDL, TG, SBP, DBP, WC
Figueroa et al., 2011[48] (Korea)	Healthy	EX: 54.0 ± 2.0; 24.2 ± 0.7 CON: 54.0 ± 1.0; 23.1 ± 0.7	EX: 12 CON:12	12 weeks	3 days	Combined (moderate intensity)	SBP, DBP
Frank et al., 2005[49] (USA)	Overweight	EX: 60.7 ± 6.7; 30.4 ± 4.1 CON: 60.6 ± 6.8; 30.5 ± 3.7	EX: 87 CON: 86	12 months	5 days	Continuous (moderate intensity)	BG, TG
Friedenreich et al., 2011[29] (Canada)	Healthy	EX: 61.2 ± 5.4; 29.1 ± 4.5 CON: 60.6 ± 5.7; 29.2 ± 4.3	EX: 160 CON: 160	12 months	5 days	Continuous (moderate-vigorous intensity)	WC

Table 2 (continued)

Gomez-Tomas et al., 2018[50] (Spain)	Healthy	EX: 70.9 ± 4.4; 28.7 ± 4.5 CON: 70.5 ± 5.4; 30.2 ± 5.6	EX: 18 CON: 20	12 months	3 days	Resistance (light-moderate intensity)	HDL, TG, WC
Hettchen et al., 2021[51] (Germany)	Osteopenic	EX: 53.6 ± 2.0; 23.7 ± 3.4 CON: 54.5 ± 1.6; 24.9 ± 4.8	EX: 27 CON:27	13 months	3 days	Continuous (vigorous intensity)	BG, HDL, TG, WC
Jaime et al., 2019[28] (USA)	Healthy	EX: 64.0 ± 1.0; 24.0 ± 0.6 CON: 67.0 ± 1.0; 22.5 ± 0.9	EX: 21 CON: 14	12 weeks	N/A	Resistance (light intensity)	SBP, DBP
Kim and Kim., 2012[18] (Korea)	Obese	EX: 53.4 ± 2.4; 25.0 ± 1.3 CON: 54.5 ± 2.8; 25.1 ± 1.5	EX: 15 CON: 15	16 weeks	3 days	Continuous (moderate-vigorous intensity)	BG, HDL, TG, SBP, DBP, WC
Keyhani et al., 2020[52] (Iran)	Healthy	EX: 54.9 ± 1.0; 27.9 ± 1.3 CON: 56.2 ± 0.7; 27.8 ± 1.2	EX: 10 CON: 10	8 weeks	3 days	Interval (vigorous intensity)	HDL, TG, SBP, DBP
Latosik et al., 2014[53] (N/A)	Hypertensive	EX: N/A; 28.2 ± 5.8 CON: N/A; 28.2 ± 4.5	EX: 15 CON: 10	8 weeks	N/A	Continuous (light-vigorous)	HDL, TG, SBP, DBP, WC
Lee et al., 2012[54] (Korea)	Obese	EX: 54.8 ± 2.8; 25.1 ± 1.6 CON: 54.3 ± 2.9; 25.2 ± 1.7	EX: 8 CON: 8	16 weeks	3 days	Continuous (light intensity)	BG, HDL, TG, SBP, DBP, WC
Lee et al., 2021[55] (Korea)	Obese	EX: 56.0 ± 2.9; 25.8 ± 2.0 CON: 57.5 ± 2.9; 25.5 ± 1.7	EX: 12 CON:12	16 weeks	5 days	Continuous (light-vigorous intensity)	HDL, TG
Lesser et al., 2016[56] (Canada)	Healthy	EX: 56.4 ± 6.9; 29.9 ± 3.5 CON: 57.7 ± 6.1; 28.9 ± 3.5	EX: 23 CON: 26	12 weeks	3 days	Continuous (light-vigorous intensity)	BG, WC
Libardi et al., 2012[57] (Brazil)	Healthy	EX: 53.7 ± 3.7; 26.1 ± 3.0 CON: 51.2 ± 6.4; 25.9 ± 2.3	EX: 12 CON: 12	16 weeks	3 days	Resistance (moderate-vigorous intensity)	HDL, TG
Marcus et al., 2009[58] (USA)	Healthy	EX: 56.3 ± 6.4; 28.5 ± 3.7 CON: 53.2 ± 6.5; 32.2 ± 4.0	EX: 10 CON: 6	12 weeks	3 days	Resistance (light-moderate)	WC
Miyaki et al., 2012[59] (Japan)	Healthy	EX: 60.0 ± 6.0; 22.2 ± 2.0 CON: 60.0 ± 7.0; 22.4 ± 2.6	EX: 11 CON: 11	8 weeks	3-5 days	Continuous (light-moderate intensity)	HDL, TG, SBP, DBP
Moreau et al., 2001[60] (USA)	Borderline to stage 1 hypertensive	EX: 53.0 ± 7.7; N/A CON: 55.0 ± 3.0; N/A	EX: 15 CON: 9	24 weeks	7 days	Continuous (moderate intensity)	BG, SBP, DBP
Neves et al., 2017[61] (Brazil)	Healthy	EX: 58.6 ± 3.9; 27.1 ± 3.7 CON: 57.7 ± 4.8; 27.5 ± 4.6	EX: 27 CON: 19	16 weeks	3 days	Combined (moderate intensity)	BG, TG

Table 2 (continued)

Nunes et al., 2016[24] (Brazil)	Healthy	EX: 62.0 ± 10.8; 27.4 ± 7.7 CON: 60.0 ± 7.8; 32.4 ± 6.3	EX: 11 CON: 11	16 weeks	3 days	Resistance (moderate intensity)	HDL, TG, WC
Rezende Barbosa et al., 2019[62] (Brazil)	Healthy	EX: 60.0 ± 4.5; 27.3 ± 4.2 CON: 58.5 ± 4.8; 27.6 ± 4.8	EX: 19 CON: 20	18 weeks	3 days	Continuous (moderate intensity)	SBP, DBP
Senechal et al., 2012[63] (Canada)	Dynapenic-obese	62.6 ± 4.1*; N/A	EX: 10 CON: 10	12 weeks	3 days	Resistance (vigorous intensity)	BG, HDL, TG, SBP, DBP, WC
Seo et al., 2010[64] (Korea)	Healthy	EX: 54.0 ± 3.6; 24.0 ± 1.9 CON: 58.0 ± 4.2; 24.0 ± 2.6	EX: 8 CON: 7	12 weeks	3 days	Continuous (vigorous intensity)	BG, HDL, TG, SBP, DBP, WC
Son and Park, 2021[32] (Korea)	Obese	EX: 68.2 ± 1.6; 26.7 ± 3.2 68.2 ± 1.4; 27.1 ± 1.4	EX: 18 CON: 17	12 weeks	3 days	Resistance (light-moderate intensity)	BG, HDL, TG, SBP, DBP, WC
Son et al., 2017[65] (Korea)	Stage 1 hypertensive	EX: 76.0 ± 5.0; 22.8 ± 0.7 CON: 74.7 ± 2.0; 24.1 ± 0.2	EX: 10 CON:10	12 weeks	3 days	Combined (light-moderate intensity)	SBP, DBP
Staffileno et al., 2001[66] (USA)	Hypertensive	EX: 57.1 ± 8.7; 31.1 ± 4.8 CON: 62.3 ± 8.7; 31.9 ± 5.7	EX: 9 CON: 9	8 weeks	5 days	Continuous (moderate intensity)	SBP, DBP
Trabka et al., 2013[67] (N/A)	Obese	EX: N/A; 31.6 ± 4.1 CON: N/A; 31.7 ± 4.9	EX: 23 CON: 21	10 weeks	3 days	Combined (moderate-vigorous)	HDL, TG, WC
van Gemert et al., 2014[68] (Netherlands)	Healthy	EX: 58.9 ± 4.6; 26.6 ± 2.9 CON: 58.4 ± 4.2; 27.3 ± 3.6	EX: 96 CON: 93	12 months	2 days	Combined (moderate -vigorous)	BG
Ward et al., 2020[69] (Sweden)	Healthy	EX: 55.7 ± 5.1; 28.1 ± 3.9 CON: 55.4 ± 5.0; 26.7 ± 3.6	EX: 26 CON: 29	15 weeks	3 days	Resistance (moderate intensity)	HDL, TG
Wong et al., 2018[70] (Korea)	Stage II hypertensive	EX: 59.0 ± 1.0; 24.2 ± 0.8 CON: 59.0 ± 1.0; 23.8 ± 0.8	EX: 21 CON: 20	12 weeks	5 days	Combined (light-moderate intensity)	SBP, DBP
Wong et al., 2019[71] (Korea)	Stage II hypertensive	EX: 74.0 ± 4.0; 26.0 ± 2.8 CON: 73.0 ± 4.0; 26.9 ± 2.9	EX: 52 CON: 48	20 weeks	3-4 days	Continuous (light-moderate intensity)	SBP, DBP
Wooten et al., 2011[72] (USA)	Obese	EX: 64.4 ± 0.7; 31.0 ± 0.5 CON: 67.0 ± 0.6; 34.0 ± 1.3	EX: 12 CON: 9	12 weeks	3 days	Resistance (moderate intensity)	HDL, TG

Data expressed as mean ± SD. [a,b] denotes sub-studies; *denotes combined value of participants; N/A: not applicable as not mentioned; BMI: body mass index; EX: exercise group; CON: control group; MetS: Metabolic Syndrome; T2D: type 2 diabetes; BG: blood glucose; HDL: high-density lipoprotein; TG: triglycerides; SBP: systolic blood pressure; DBP: diastolic blood pressure.

3.4. Meta-analysis

3.4.1. Waist circumference

The pooled meta-analysis of the 21 studies that included WC as an outcome suggest a large effect size of exercise training significantly reducing WC by 2.62 cm (95% CI: -3.39 to -1.86 cm; $p < 0.001$). I^2 demonstrated large heterogeneity present between studies ($I^2 = 74\%$, $p < 0.001$) (Figure 2). Sub-group analyses for exercise training intensities, modalities and duration were conducted and are presented in Table 3. The different exercise training intensities showed significant reductions in WC for light-moderate intensity (MD: -3.49 cm; 95% CI: -5.15 to -1.82 cm; $p < 0.001$; n = 3), moderate intensity (MD: -3.66 cm; 95% CI: -5.61to -1.72 cm; $p < 0.001$; n = 8), light-vigorous intensity (SMD: -4.00 cm; 95% CI: -6.91 to -1.10 cm; p = 0.007; n = 2). Likewise, the different exercise training modalities showed significant reductions for continuous training (MD: -1.74cm; 95% CI: -2.36 to -1.12 cm; $p < 0.001$; n = 8), resistance training (MD: -3.37 cm; 95% CI: -5.83 to -0.91 cm; p = 0.007; n = 6) and combined training (MD: -2.84 cm; 95% CI: -3.88 to -1.80 cm; $p < 0.001$; n = 7). Exercise training duration showed significant reductions with short term (MD: -2.18 cm; 95% CI: -4.15 to -0.21 cm; p = 0.03; n = 3), long term (MD: -2.77 cm; 95% CI: -3.83 to -1.71 cm; $p < 0.001$; n = 12) and very long-term exercise training (MD: -2.55 cm; 95% CI: -3.99 to -1.12 cm; $p < 0.001$; n = 6). I^2 was significantly reduced after sub-group analyses (intensity: 42.0%; modality: 53.0%; duration: 0%).

3.4.2. Triglycerides

Of the 25 studies including measurements of TG, the pooled meta-analysis showed exercise training had a small effect reducing TG by 0.40 mmol/L (95% CI: -0.71 to -0.09 mmol/L; p = 0.01). I^2 demonstrated large heterogeneity present between studies ($I^2 = 81\%$, $p < 0.001$) (Figure 3). The different exercise training intensities showed reductions in TG for moderate intensity (SMD: -0.54 mmol/L; 95% CI: -1.05 to -0.02 mmol/L; p = 0.04; n = 10). In addition, different exercise training modalities showed reductions for combined training (SMD: -1.08 mmol/L; 95% CI: -1.86 to -0.30 mmol/L; p = 0.007; n = 6) and exercise training duration showed

reductions with short term (SMD: -0.96 mmol/L; 95% CI: -1.66 to -0.26 mmol/L; p = 0.007; n = 5). Sub-group analyses revealed no heterogeneity for intensity (I^2 = 0%), a slight increase for modality (I^2 = 81.8%) and slight decrease for duration (I^2 = 71.1%).

3.4.3. HDL

Of the 26 studies that included HDL, the pooled meta-analysis showed exercise training had a large effect increasing HDL by 0.84 mmol/L (95% CI: 0.41 to 1.27 mmol/L; p < 0.001). I^2 demonstrated large heterogeneity present between studies (I^2 = 90%, p < 0.001) (Figure 4). The different exercise training intensities showed increases in HDL for light-moderate intensity (SMD: 1.97 mmol/L; 95% CI: 0.46 to 3.48 mmol/L; p = 0.01; n = 5). In addition, different exercise training modalities showed increases in HDL for continuous training (SMD: 1.12 mmol/L; 95% CI: 0.20 to 2.03 mmol/L; p = 0.02; n = 9) and resistance training (SMD: 0.96 mmol/L; 95% CI: 0.07 to 1.84 mmol/L; p = 0.04; n = 9). Exercise training duration showed reductions with short term (SMD: 1.04 mmol/L; 95% CI: 0.00 to 2.07 mmol/L; p = 0.05; n = 5) and long term (SMD: 0.81 mmol/L; 95% CI: 0.29 to 1.33 mmol/L; p = 0.002; n = 16). Sub-group analyses revealed no heterogeneity for intensity and duration (I^2 = 0%), and a slight decrease for modality (I^2 = 87.7%)

3.4.4. Glucose

Of the 20 studies including glucose, the pooled meta-analysis showed exercise training had a small effect decreasing glucose by -0.38 mmol/L (95% CI: -0.60 to -0.16 mmol/L; p < 0.001). I^2 demonstrated large heterogeneity present between studies (I^2 = 63%, p < 0.001) (Figure 5). The different exercise training intensities showed a reduction in glucose with moderate intensity (SMD: -0.54 mmol/L; 95% CI: -0.85 to -0.24 mmol/L; p < 0.001; n = 9), In addition, different exercise training modalities showed a significant reduction in glucose with combined training (SMD: -0.59 mmol/L; 95% CI: -1.01 to -0.16 mmol/L; p = 0.007; n = 7) and exercise training duration showed reductions with long term (SMD: -0.60 mmol/L; 95% CI: -0.90 to -0.31 mmol/L; p < 0.001; n = 13). Sub-group analyses revealed no heterogeneity for intensity (I^2 = 0%), slight decrease for modality (I^2 = 62.7%) and an increase for duration (I^2 = 83.4%).

3.4.5. SBP

Of the 23 studies including SBP, the pooled meta-analysis showed exercise training had a large effect decreasing SBP by 5.95 mmHg (95% CI: -7.98 to -3.92 mmHg; $p < 0.001$). I^2 demonstrated large heterogeneity present between studies ($I^2 = 99\%$, $p < 0.001$) (Figure 6). The different exercise training intensities showed significant reductions in SBP with light-moderate intensity (MD: -822 mmHg; 95% CI: -11.79 to -4.65 mmHg; $p < 0.001$; $n = 7$) and moderate intensity (MD: -5.44; 95% CI: -8.38 to -2.50 mmHg; $p < 0.001$; $n = 9$). In addition, different exercise training modalities showed reductions in SBP with continuous training (MD: -7.53 mmHg; 95% CI: -9.95 to -5.10 mmHg; $p < 0.001$; $n = 13$) and combined training (MD: -7.28 mmHg: 95% CI: -10.14 to -4.41 mmHg; $p < 0.001$; $n = 4$). Exercise training duration showed reductions with short term (MD: -6.10 mmHg; 95% CI: -7.96 to -4.24 mmHg; $p < 0.001$; $n = 6$) and long term (MD: -6.90 mmHg; 95% CI: -9.60 to -4.21 mmHg; $p < 0.001$; $n = 13$). I^2 was significantly decreased after sub-group analyses (intensity: 0%; modality: 54.1%; duration: 0%).

3.4.6. DBP

Of the 23 studies including DBP, the pooled meta-analysis showed exercise training had a large effect decreasing DBP by 4.14 mmHg (95% CI: -6.19 to -2.08 mmHg; $p < 0.001$). I^2 demonstrated large heterogeneity present between studies ($I^2 = 100\%$, $p < 0.001$) (Figure 7). The different exercise training intensities showed reductions in DBP with light-moderate intensity (MD: -5.98; 95% CI: -9.86 to -2.11 mmHg; $p = 0.002$; $n = 7$) and moderate intensity (MD: -3.70; 95% CI: -5.42 to -1.98 mmHg; $p < 0.001$; $n = 9$). In addition, different exercise training modalities showed reductions in DBP with continuous training (MD: -4.78 mmHg; 95% CI: -7.41 to -2.16 mmHg; $p < 0.001$; $n = 13$) and combined training (MD: -4.16 mmHg: 95% CI: -7.03 to -1.29 mmHg; $p = 0.005$; $n = 4$). Exercise training duration showed reductions with short term (MD: -4.61 mmHg; 95% CI: -7.82 to -1.39 mmHg; $p = 0.005$; $n = 6$) and long term (MD: -4.41 mmHg; 95% CI: -7.35 to -1.46 mmHg; $p = 0.003$; $n = 13$). I^2 decreased significantly

after sub-group analyses for intensity (11.0%) and duration (0%), and slightly decreased for modality (90.6%).

3.5. Meta-regression

Across the six meta-analyses, random-effects meta-regression revealed no significant moderator effects of BMI or health status (Supplementary Materials Table 3).

3.6. Publication bias and sensitivity analysis

To ascertain publication bias, we used funnel plots and Egger's test. Visual inspection of the funnel plots reveal asymmetry, denoting a certain degree of publication bias (Supplementary Materials Figure S1). Egger's test found no evidence of publication bias in waist circumference ($p = 0.157$), triglycerides ($p = 0.688$), SBP ($p = 0.316$) and DBP ($p = 0.826$), except for HDL ($p < 0.001$) and BG ($p = 0.15$) (Supplementary Materials Figures S1a-f). Trim-fill analysis were performed, although no significant changes were found to the data. Sensitivity analysis for pooled analyses revealed that no single trial affected the significance of the SMD, MD or heterogeneity.

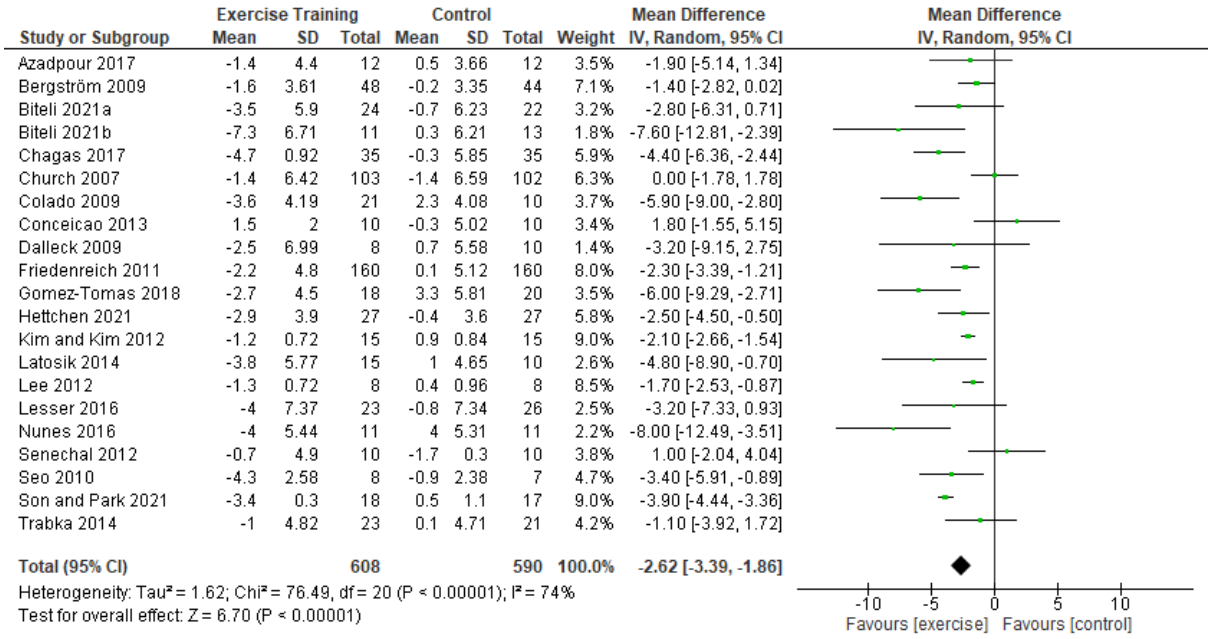

Figure 2. Forest plot of randomised controls trials investigating the effect of exercise training vs control on waist circumference using the random effects model. There are a total of 21 studies reporting changes in waist circumference (cm). Negative values favour exercise intervention on the left side. 95% CI: 95% confidence interval; MD: mean difference; SD: standard deviation.

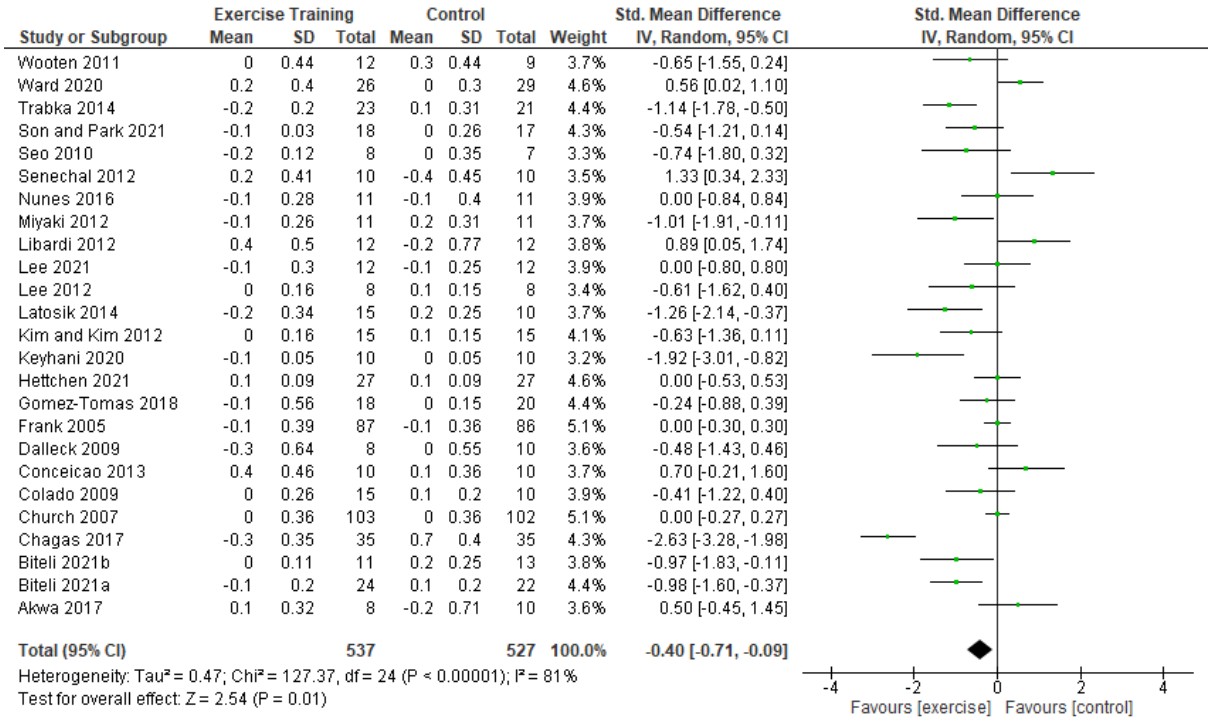

Figure 3. Forest plot of randomised controls trials investigating the effect of exercise training vs control on triglycerides using the random effects model. There are a total of 25 studies reporting changes in triglycerides (mmol/L). Negative values favour exercise intervention on the left side. 95% CI: 95% confidence interval; SMD: standardised mean difference; SD: standard deviation.

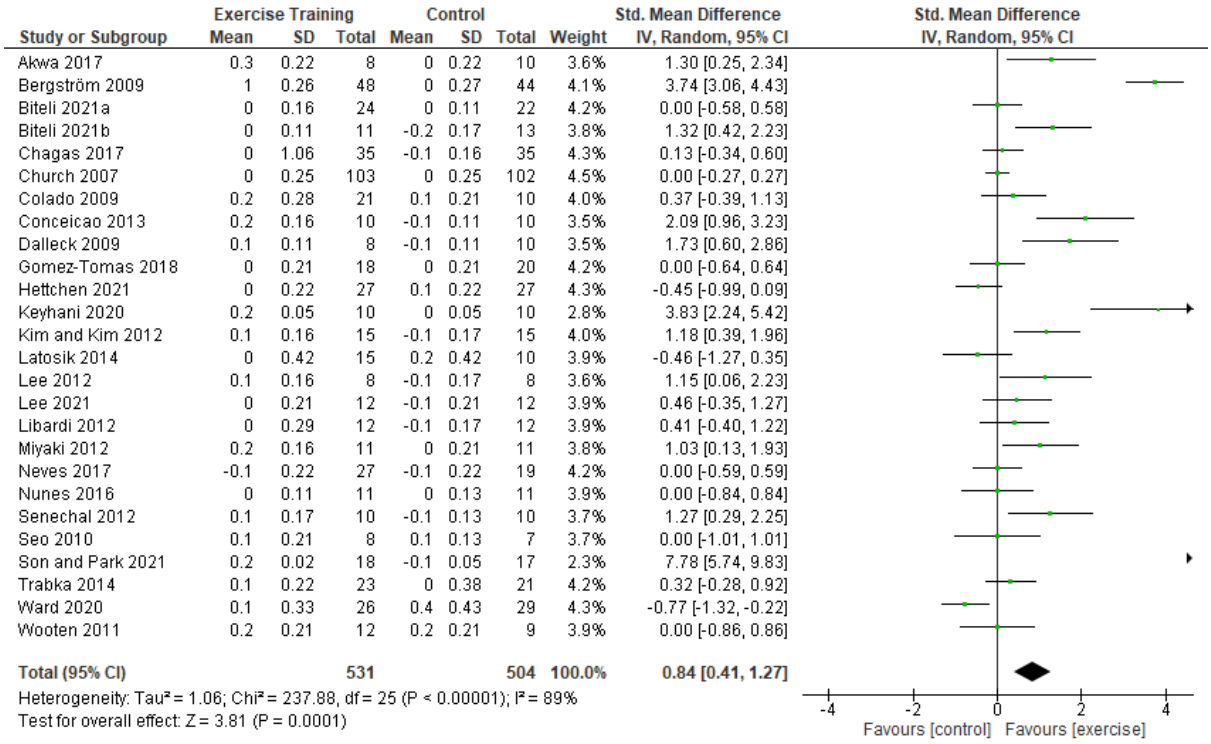

Figure 4. Forest plot of sub-analysis on the effects of exercise training intensities on HDL using the random effects model. There are a total of 26 studies reporting changes in HDL (mmol/L). Positive values favour exercise intervention on the right side. Data are reported as SMD (95% CI). HDL: high-density lipoprotein; 95% CI: 95% confidence interval; SMD: standardised mean difference; SD: standard deviation.

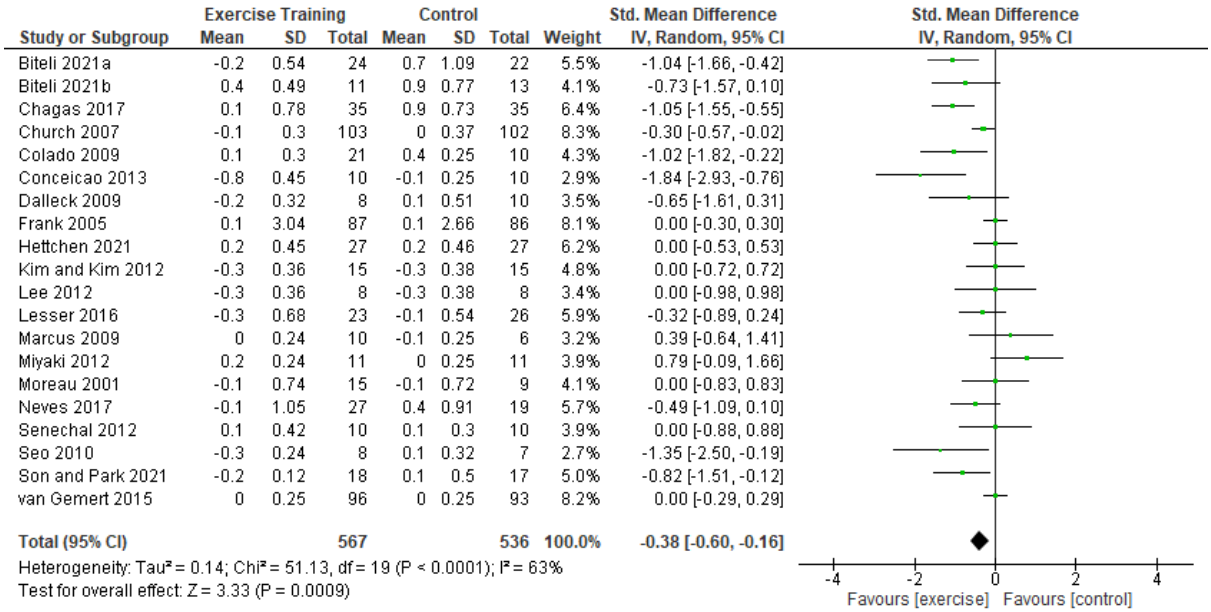

Figure 5. Forest plot of randomised controls trials investigating the effect of exercise training vs control on blood glucose using the random effects model. There are a total of 20 studies reporting changes in glucose (mmol/L). Negative values favour exercise intervention on the left side. 95% CI: 95% confidence interval; SMD: standardised mean difference; SD: standard deviation.

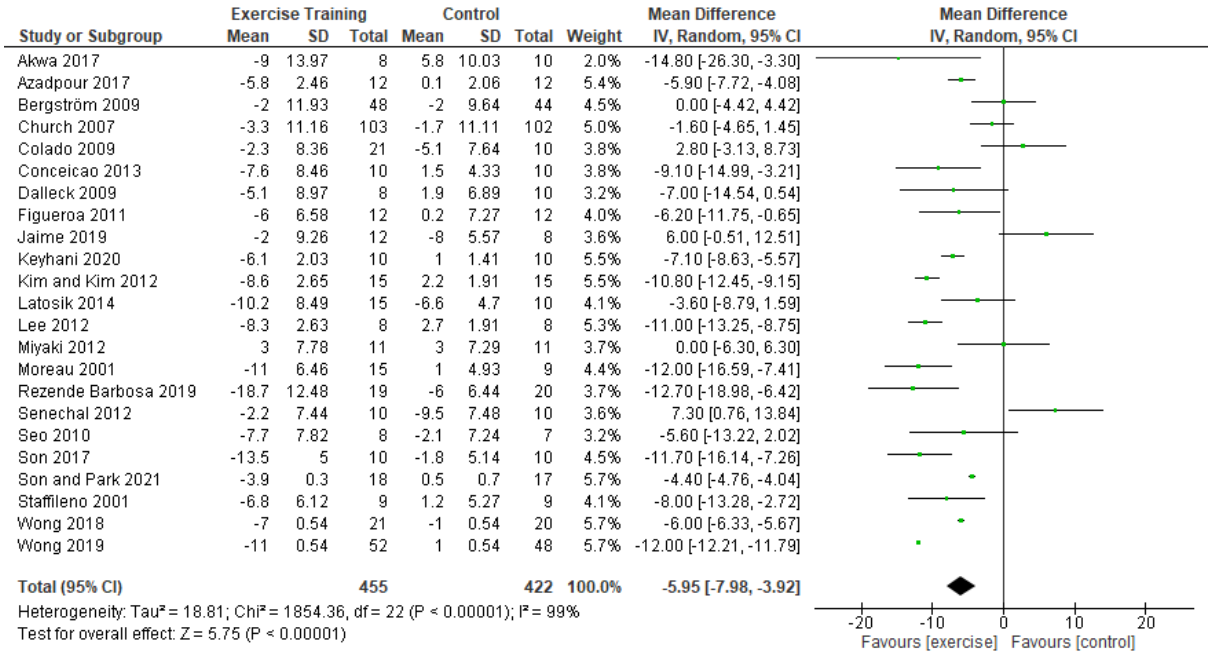

Figure 6. Forest plot of randomised controls trials investigating the effect of exercise training vs control on SBP using the random effects model. There are a total of 23 studies reporting changes in SBP (mmHg). Negative values favour exercise intervention on the left side. 95% CI: 95% confidence interval; MD: mean difference; SBP: systolic blood pressure; SD: standard deviation.

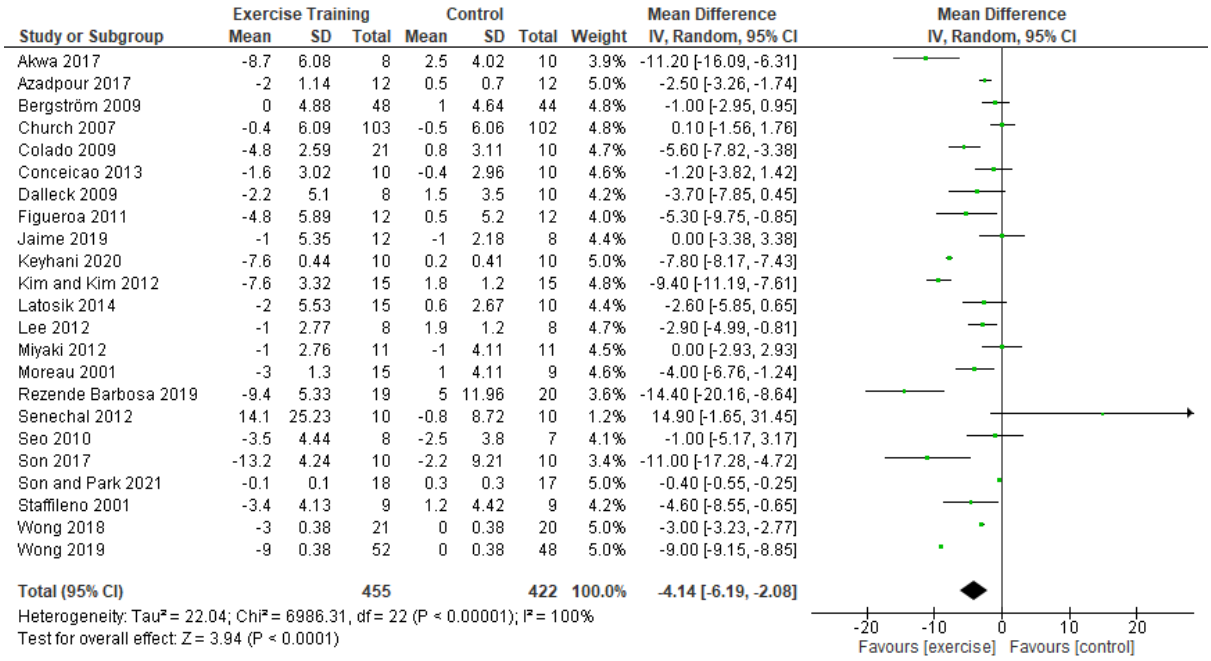

Figure 7. Forest plot of randomised controls trials investigating the effect of exercise training vs control on DBP using the random effects model. There are a total of 23 studies reporting changes in DBP (mmHg). Negative values favour exercise intervention on the left side. 95% CI: 95% confidence interval; MD: mean difference; DBP: diastolic blood pressure; SD: standard deviation.

Table 3. Sub-group analysis of 40 studies.

Groups	WC (cm)				TG (mmol/L)				HDL (mmol/L)			
	n	MD (95% CI)	*P*	I^2 (%)	n	SMD (95% CI)	*P*	I^2 (%)	n	SMD (95% CI)	*P*	I^2 (%)
Intensity												
Light	1	-1.70 [-2.53, -0.87]	**<0.001***	N/A	1	-0.61 [-1.62, 0.40]	0.24	N/A	1	1.15 [0.06, 2.23]	**0.04***	N/A
Light-to-moderate	3	-3.49 [-5.15, -1.82]	**<0.001***	92%	5	-0.41 [-0.82, 0.01]	0.06	33%	5	1.97 [0.46, 3.48]	**0.01***	92%
Moderate	8	-3.66 [-5.61, -1.72]	**<0.001***	75%	10	-0.54 [-1.05, -0.02]	**0.04***	88%	11	0.56 [-0.09, 1.21]	0.09	92%
Light-to-vigorous	2	-4.00 [-6.91, -1.10]	**0.007***	0%	3	-0.11 [-1.30, 1.07]	0.85	83%	2	-0.00 [-0.90, 0.90]	1	59%
Moderate-to-vigorous	4	-1.29 [-2.93, 0.36]	0.12	45%	2	-0.25 [-2.05, 1.55]	0.78	90%	3	0.83 [-0.10, 1.77]	0.08	74%
Vigorous	3	-1.82 [-4.13, 0.49]	0.12	61%	4	-0.30 [-1.45, 0.85]	0.61	85%	4	1.03 [-0.47, 2.53]	0.18	90%
Modality												
Continuous	8	-1.74 [-2.36, -1.12]	**<0.001***	10%	9	-0.29 [-0.59, 0.02]	0.06	51%	9	1.12 [0.20, 2.03]	**0.02***	90%
Resistance	6	-3.37 [-5.83, -0.91]	**0.007***	82%	9	0.16 [-0.28, 0.59]	0.48	65%	9	0.96 [0.07, 1.84]	**0.04***	90%
Combined	7	-2.84 [-3.88, -1.80]	**<0.001***	42%	6	-1.08 [-1.86, -0.30]	**0.007***	87%	7	0.12 [-0.21, 0.46]	0.47	49%
Interval	0	Not Estimable	N/A	N/A	1	-1.92 [-3.01, -0.82]	**<0.001***	N/A	1	3.83 [2.24, 5.42]	**<0.001***	N/A
Duration												
< 12 weeks	3	-2.18 [-4.15, -0.21]	**0.03***	7%	5	-0.96 [-1.66, -0.26]	**0.007***	69%	5	1.04 [0.00, 2.07]	**0.05***	85%
≥ 12 weeks	12	-2.77 [-3.83, -1.71]	**<0.001***	79%	15	-0.33 [-0.86, 0.19]	0.22	85%	16	0.81 [0.29, 1.33]	**0.002***	85%
≥ 6 months	6	-2.55 [-3.99, -1.12]	**<0.001***	72%	5	-0.04 [-0.21, 0.14]	0.67	0%	5	0.72 [-0.52, 1.96]	0.26	96%

Table 3 continued.

Groups	BG (mmol/L)				SBP (mmHg)				DBP (mmHg)			
	n	SMD (95% CI)	*P*	I^2 (%)	n	MD (95% CI)	*P*	I^2 (%)	n	MD (95% CI)	*P*	I^2 (%)
Intensity												
Light	1	0.00 [-0.98, 0.98]	1	N/A	2	-2.79 [-19.44, 13.86]	0.74	96%	2	-1.77 [-4.54, 1.01]	0.35	51%
Light-to-moderate	4	0.04 [-0.66, 0.74]	0.91	66%	7	-8.22 [-11.79, -4.65]	**<0.001***	100%	7	-5.98 [-9.86, -2.11]	**0.002***	100%
Moderate	9	-0.54 [-0.85, -0.24]	**<0.001***	64%	9	-5.44 [-8.38, -2.50]	**<0.001***	76%	9	-3.70 [-5.42, -1.98]	**<0.001***	80%
Light-to-vigorous	1	-0.32 [-0.89, 0.24]	0.26	N/A	1	-3.60 [-8.79, 1.59]	0.17	N/A	1	-2.60 [-5.85, 0.65]	0.12	N/A
Moderate-to-vigorous	3	-0.51 [-1.48, 0.46]	0.3	81%	1	-9.10 [-14.99, -3.21]	**0.002***	N/A	1	-1.20 [-3.82, 1.42]	0.37	N/A
Vigorous	2	-0.57 [-1.87, 0.73]	0.39	77%	3	-2.06 [-10.98, 6.87]	0.65	89%	3	-1.81 [-9.40, 5.78]	0.64	88%
Modality												
Continuous	8	-0.12 [-0.32, 0.08]	0.24	15%	13	-7.53 [-9.95, -5.10]	**<0.001***	92%	13	-4.78 [-7.41, -2.16]	**<0.001***	98%
Resistance	5	-0.65 [-1.33, 0.02]	0.06	66%	5	0.15 [-5.42, 5.72]	0.96	87%	5	-1.42 [-4.08, 1.23]	0.29	84%
Combined	7	-0.59 [-1.01, -0.16]	**0.007***	74%	4	-7.28 [-10.14, -4.41]	**<0.001***	52%	4	-4.16 [-7.03, -1.29]	**0.005***	63%
Interval	0	Not estimable	N/A	N/A	1	-7.10 [-8.63, -5.57]	**<0.001***	N/A	1	-7.80 [-8.17, -7.43]	**<0.001***	N/A
Duration												
< 12 weeks	1	0.79 [-0.09, 1.66]	0.08	N/A	6	-7.10 [-8.63, -5.57]	**<0.001***	42%	6	-4.61 [-7.82, -1.39]	**0.005***	97%
≥ 12 weeks	13	-0.60 [-0.90, -0.31]	**<0.001***	47%	13	-6.90 [-9.60, -4.21]	**<0.001***	99%	13	-4.41 [-7.35, -1.46]	**0.003***	100%
≥ 6 months	6	-0.14 [-0.35, 0.07]	0.19	38%	4	-2.80 [-8.55, 2.95]	0.34	86%	4	-2.52 [-5.18, 0.13]	0.06	84%

SMD: standardised mean difference; MD: mean difference; 95% CI: 95% confidence interval; N/A: not applicable; WC: waist circumference; TG: triglycerides; HDL: high-density lipoprotein; BG: blood glucose; SBP: systolic blood pressure; DBP: diastolic blood pressure.

4. Discussion

This systematic review and meta-analysis evaluated 40 studies, involving 2,132 participants, producing novel exploration to assess the mediating impact of exercise training duration, modality and intensity on MetS risk factors in post-menopausal women. Studies that evaluated exercise training of ≥8 weeks i post-menopausal women who reported at least one MetS risk variable were meta-analysed. Sub-group analyses of exercise intensity, modality and duration were employed to assess the effectiveness of exercise dosing in ameliorating MetS risk. Overall, exercise training was reported to significantly improve MetS risk factors in post-menopausal women, with the largest effect prevalent on SBP and DBP and smallest on BG. This review also concluded that long term training significantly benefited MetS risk factors except for TG, and moderate intensity and combined exercise training significantly reduced MetS risk factors, except for HDL.

It is well understood that regular exercise can be used as a non-pharmacological tool to improve metabolic health. The World Health Organisation (WHO)[74], American College of Sports Medicine (ACSM)[43] and the UK Chief Medical Officers (CMO)[75] recommend at least 150 minutes of moderate-intensity physical activity or 75 minutes of vigorous-intensity physical activity per week for healthy adults to maintain or improve health[76,77]. Our findings support current guidance, based on the favourable effects of moderate intensity exercise on MetS risk variables except for HDL, with largest effect on WC, SBP and DBP. However, results for vigorous intensity training were inconclusive due to limited studies. Various studies conducted have evaluated the benefit of exercise training on MetS and cardiovascular risk parameters in middle-aged adults. A meta-analysis by Ashton *et al*. found that medium term (7 – 24 weeks) resistance exercise training can be effective in improving cardiometabolic health markers in middle-aged adults, specifically in SBP, DBP, HDL, TG and BG[78]. Ashton *et al*. indicates greater benefit is reported in those with elevated cardiometabolic risk, yet our findings present significant benefit in WC and HDL only in post-menopausal women. However,

these inconsistencies could be attributed to population of interest and the limited studies evaluating resistance training.

Endurance training (any activity that utilises large muscle groups that can be continuously maintained) with supplementation of occasional resistance training is recommended by the ACSM for adults with hypertension[79]. It has been shown that a 10 mmHg reduction in SBP is associated with a 20% risk reduction in major CVD events[80]. This meta-analysis evaluated 7 studies (17.5%) which included post-menopausal women with clinical hypertension, supporting that exercise modalities of continuous and combined exercise training elicited a large effect on SBP and DBP improvements and supports previous published findings[19]. Similarly, this positive effect was consistent in published literature conducted in both menopausal and post-menopausal women[81]. Interestingly, our results showed significant improvements in BP; reductions of 8 mmHg and 6 mmHg for SBP and DBP respectively, even with light-moderate intensity training. Furthermore, we saw benefits in BP with exercise training in just 8 – 10 weeks. This is supported by a meta-analysis that found hypotensive effects with just a single bout of resistance exercise in healthy adults[82]. This further highlights the benefits of exercise in controlling BP in a relatively short duration in post-menopausal women, and for those who may find a lower intensity of exercise more tolerable.

VAT deposition is known to increase during the menopausal transition due to the decline in oestrogen, which contributes to increased WC and consequently elevates cardiovascular risk[11,83]. Collectively, findings indicate that exercise training show effectiveness in reducing WC, with the largest effect particularly with intensities of light-moderate and moderate, modalities of resistance and combined exercise training, and durations of ≥12 weeks. The effects of exercise training dosage on WC or VAT in post-menopausal women are limited and inconclusive across literature. However, findings are further supported by the only other meta-analysis conducted in post-menopausal women, showing significant reductions in WC with aerobic exercise training of ≥12 weeks[84]. These findings share similarities with other previous meta-analyses conducted in adults, where they found aerobic exercise of at least

moderate intensity[31,85,86] was effective in reducing VAT and WC[87], specifically three times per week for 12 – 16 weeks[86]. It is understood that WC is surrogate marker for VAT and cannot depict true representation of VAT reductions within this study, which warrants further research required to ascertain the effects of exercise training on VAT in post-menopausal women. Nevertheless, VAT as well as subcutaneous adipose tissue (SAT) are contributors to abdominal obesity which is reflected through WC[88]. The ability for exercise to decrease WC are potentially owed to improvements in insulin sensitivity, BG and lipid profiles. Since excess VAT is strongly correlated with impaired glucose and lipid metabolism[89], we theorise to see mediation in these parameters.

TG and HDL collectively and independently are known to be associated with CVD risk. Hence, the use of TG to HDL ratio, particularly a ratio >3.5, is used to predict heart disease mortality [90]. Additionally, for every 0.26 mmol/L increment in HDL, it has been found to be associated with a 2 – 3% decrease in coronary artery disease risk[91]. We found favourable changes in MetS related blood lipids markers that were most apparent with HDL, and the least with TG. Overall, this is supported and consistent with a review by Wang and Xu, who found HDL sensitivity to aerobic exercise to be higher than that of TG[92]. A meta-analysis by Wood *et al.* have shown HIIT to be superior to moderate intensity continuous training (MICT) in improving HDL levels[93]. Contrastingly, they found no differences in HIIT nor MICT on the influence of TG. Although there were limited studies included in our meta-analysis for HIIT, our results were dissimilar for the effects of moderate intensity and continuous training on TG and HDL levels. We observed a significant decrease in TG but none in HDL with moderate intensity, of which this was contrasted with continuous training. Moreover, reductions in TG were seen with combined training but not for HDL. It has been proposed through previous studies that exercise duration, intensity and volume positively correlate with exercise-induced changes in dyslipidaemia, particularly if reductions in TG are to be achieved[92,94–96]. Interestingly, sub-group analysis for duration contradicts and showed that improvements in these parameters were diminished for exercise training conducted for ≥12 weeks for TG, and

≥6 months for HDL. This may be contributed mainly by the high heterogeneity and limited studies, resulting in the inconclusion to ascertain the effect of exercise training on these blood lipids measures.

Exercise training of moderate intensity and combined training can have small to moderate mediation in glycaemia, reflected also with exercise training durations of ≥12 weeks. Combined exercise training comprises of resistance exercises which contribute to muscle strength and hypertrophy[97]. Promotion of glucose cell uptake from skeletal muscle during exercise have been proposed to increase insulin sensitivity[98], and this was seen with aerobic exercise of 3 – 4 months in post-menopausal women[84]. However, continuous exercise training did not elicit reductions in BG. Furthermore, caution is required in the interpretation of these findings as participants of included studies for this meta-analysis had no declarations of having impaired glucose or insulin resistance. We hypothesise that this modality of exercise training is associated with significant improvements in other MetS parameters and may mediate glycaemic regulation through the prevention of insulin resistance development. Further studies are warranted to elucidate exercise training dosage on insulin sensitivity in post-menopausal women.

4.1 Strengths and limitations

This systematic review and meta-analysis contribute novel findings to literature on the metabolic benefits of exercise training in post-menopausal women. There are many strengths in this study, which are attributed to the inclusion of RCTs only relevant to the meta-analysis and utilising studies with an “intention-to-treat” approach or with ≥80% adherence rate. Sub-group analyses based on exercise training intensities, modalities and duration were also conducted to assess the efficacy of exercise training type on MetS risk variables. However, there are some limitations. Firstly, despite being able to ascertain heterogeneity sources through performing sub-group analyses and meta-regression, there was still a lack of homogeneity across the studies. Participants physical activity status was not included in the meta-regression due to the lack of reporting across numerous studies.

Other confounding factors such as diversity in participants' demographics may be a contributing source of heterogeneity. Further work investigating the effects of exercise on MetS risk factors should look to prioritise the influence of participants' characteristics to evaluate the response of exercise on different sub-populations of post-menopausal women. Secondly, due to discrepancies in exercise intervention frequency across the studies, with several studies not fully reporting the frequency, this was therefore not included in the sub-analyses. Thirdly, we acknowledge the exclusion of a considerably large body of research that have investigated exercise training in post-menopausal women. Post-menopause occurs after menopause and is defined by the cessation of menstruation for at least 1 year. However, to encapsulate the effects of exercise training in post-menopausal women, we only included studies with specific pre-defined post-menopausal status and excluded studies that were ambiguous or did not specify. It was unexpected that this resulted in the loss of a third of eligible studies for inclusion in this meta-analysis (Figure 1). It is crucial to specify parameters for certain cohorts of interest in research to draw conclusive findings for these populations. Lastly, certain outcomes of interests were underreported in numerous studies, of which there were no response from contacted authors. To allow future researchers to ascertain the full effects of exercise training in future meta-analyses, we express our concurrence with Hurst *et al.* and Straight *et al.* in the standardisation of reportion exercise training protocols[99,100]. This encompass mainly training modality, intensity, volume, frequency, duration, adherence rate and fidelity. Consequently, this present review is underpowered and inconclusive for detection of effects for several sub-groups analyses of interest. Therefore, future work that continues to develop precise exercise doses in the prevention or amelioration of MetS risk factors across different populations of post-menopausal women is warranted.

5. Conclusion

Physical inactivity and sedentary activity are precursors to metabolic dysfunction that can progress into a plethora of cardiometabolic conditions. The menopausal transition in women

results in hormonal imbalances that can further exacerbate these metabolic risks. There is no "one-size fits all" approach; however this review reinforces the importance of regular physical activity as a non-pharmacological tool in the improvement of MetS risk parameters within post-menopausal women, with significant improvements seen in interventions spanning 8 – 10 weeks. Our novel findings further extend the evidence of moderate intensity and combined training in significantly benefitting abdominal obesity, dyslipidaemia, dysglycaemia and hypertension in post-menopausal women. This review demonstrates that other modalities and intensities can elicit benefits in at least one aspect of metabolic risk and should not be overlooked. Due to disparities within technical and publication methodologies, there was insufficient data to determine if this effect was a result of total exercise dose or independent factors. We hypothesise that benefits with light-moderate and combined training are prevalent because they are sustainable methods for delivering exercise in post-menopausal women. Giving the nature of studies included, findings from this study should be interpreted with caution as the generalisability of these results do not encompass the wider population of post-menopausal women who are elderly or have chronic conditions. Further work is needed to investigate non-pharmacological therapeutic interventions within these population groups.

DECLARATIONS

Authorship contributions. A.T and R.C performed database searches, screening and assessment quality of studies. A.T extracted data and performed statistical analyses. A.T, R.T and R.C interpreted the data from the result. All authors (A.T, R.T, M.S, S.P, R.B, R.C) reviewed and contributed to the drafting of the final version of the manuscript. All authors (A.T, R.T, M.S, S.P, R.B, R.C) read and approved on the final version of the manuscript.

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