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Meta-analysis

Supervised lifestyle intervention for people with metabolic syndrome improves outcomes and reduces individual risk factors of metabolic syndrome: A systematic review and meta-analysis

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ABSTRACT

Background: Metabolic syndrome is characterised by a clustering of metabolic risk factors including abdominal obesity, raised triglycerides, lowered HDL cholesterol, hypertension and impaired glucose tolerance. Multifaceted lifestyle interventions including diet and exercise are recommended as the first-line treatment for the metabolic syndrome.
Objective: To investigate the effects of lifestyle interventions that include both diet interventions and supervised exercise on outcomes for people with metabolic syndrome.
Methods: A systematic review and meta-regression was conducted. PubMed, EMBASE, MEDLINE and CINAHL were searched from the earliest date possible until November 2018 to identify randomised controlled trials examining the effects of lifestyle interventions compared to usual care on patient health outcomes and components of metabolic syndrome. Post-intervention means and standard deviations were pooled using inverse variance methods and random-effects models to calculate mean differences (MD), standardised mean differences (SMD) and 95% confidence intervals (CI).
Results: Searching identified 2598 articles, of which 15 articles reporting data from 10 trials, with 1160 participants were included in this review. Compared to usual care, supervised lifestyle intervention demonstrated significant improvements in all but one of the components of metabolic syndrome. Reductions were seen in waist circumference (−4.9 cm, 95%CI −8.0 to −1.7), systolic blood pressure (−6.5 mmHg, 95%CI −10.7 to −2.3), diastolic blood pressure (−1.9 mmHg, 95%CI −3.6 to −0.2), triglycerides (SMD −0.46, 95%CI −0.88 to −0.04) and fasting glucose (SMD -0.68, 95%CI −1.20 to −0.15). Prevalence of metabolic syndrome was reduced by 39% in intervention group participants compared to control group participants (Risk Ratio 0.61, 95%CI 0.38 to 0.96). Improvements in quality of life were not statistically significant.
Conclusion: There is low to moderate quality evidence that supervised multifaceted lifestyle intervention improves multiple risk factors of metabolic syndrome, as well as reducing prevalence of the disease. Health services should consider implementing lifestyle intervention programs for people with metabolic syndrome to improve health outcomes and prevent progression to chronic disease.

Contents

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1. Introduction

Approximately 25% of adults worldwide have metabolic syndrome [1,2]. It is an increasingly prevalent condition characterised by a clustering of metabolic risk factors including abdominal obesity, raised triglycerides, lowered HDL cholesterol, hypertension and impaired glucose tolerance. There are several definitions of metabolic syndrome, but it is generally diagnosed when three or more of these risk factors are present. Metabolic syndrome doubles the risk for atherosclerotic cardiovascular disease and increases risk for type 2 diabetes five-fold [3]. People with metabolic syndrome also have higher healthcare utilisation and costs when compared to people without metabolic syndrome [4]. It is therefore important to proactively manage people with metabolic syndrome before they develop further chronic disease.

People with metabolic syndrome are often obese and sedentary [3]. One effective management strategy for metabolic syndrome is thought to be calorie restriction and exercise with therapeutic guidelines advocating for multifactorial lifestyle changes as primary treatment [3]. Current guidelines are based on evidence available for the individual risk factors that contribute to metabolic syndrome. For example, weight loss has a positive impact on all the risk factors for metabolic syndrome and physical activity improves energy balance, reduces insulin resistance and increases physical fitness, which in turn reduces the risk of cardiovascular disease [5]. For the purposes of this review, lifestyle intervention will be defined as multifaceted lifestyle modification programs that include at a minimum diet and exercise intervention and may also include other components such as counselling or behaviour change techniques. The efficacy of multidisciplinary lifestyle modification programs for secondary prevention of cardiovascular disease and type 2 diabetes mellitus has been well established [6,7]. Given the same risk factors are implicated in metabolic syndrome, it would be reasonable to hypothesise that a lifestyle modification program would have positive outcomes on the metabolic syndrome.

A number of previous systematic reviews have considered the effect of lifestyle interventions on metabolic syndrome [8–10]. Results of these reviews indicate that lifestyle modification is effective in reducing metabolic syndrome prevalence and reducing the severity of its individual components. However, none of these reviews were limited to supervised multifaceted lifestyle interventions, all included trials in which not all participants had metabolic syndrome and all included studies which did not have supervised exercise as an intervention. The most recent of these reviews was conducted in 2016 and included studies which were not randomised controlled trials [9]. As a result of these limitations, it may be difficult for health service providers to make decisions regarding implementation of supervised, multifaceted lifestyle interventions for people with metabolic syndrome. Therefore, the objective of this systematic review is to determine whether a supervised, multifaceted lifestyle intervention, compared to usual care, improves health outcomes and the modifiable risk factors for people with metabolic syndrome.

2. Methods

This systematic review was prospectively registered with the PROSPERO international register of systematic reviews (CRD42018108864) and was conducted and reported with reference to PRISMA guidelines for high quality reporting of systematic reviews and meta-analyses [11].

2.1. Identification and selection of trials

Articles were identified through searching the following electronic databases: CINAHL (EBSDCO), PubMed, MEDLINE (Ovid) and EMBASE (Ovid) from the earliest date available until November 2018. The search strategy included population and intervention keywords (metabolic syndrome and lifestyle intervention program) as well as synonyms of these terms (see Appendix A). A manual search of reference lists of included articles was also conducted to ensure that all relevant articles were identified. The search was restricted to studies published in English.

Two reviewers (MvN, CP) independently applied the inclusion and exclusion criteria to the titles and abstracts of all articles to identify relevant studies. Any trials that were not clearly excluded based on title and abstract were reviewed in full-text by both reviewers. Any discrepancies between reviewers at each step were resolved through discussion until consensus was reached. The agreement between the two reviewers was calculated using the kappa statistic [12] with a kappa of 0.21 to 0.40 suggesting fair agreement, 0.41 to 0.60 suggesting moderate agreement, 0.61 to 0.80 suggesting substantial agreement; and 0.81 to 0.99 suggesting almost perfect agreement [12].

2.2. Inclusion and exclusion criteria

Randomised controlled trials published in English were eligible for inclusion if they evaluated the effect of a supervised lifestyle intervention compared to usual care in adults (aged 18+ years) with metabolic syndrome. We defined lifestyle intervention as involving both diet and exercise interventions with or without other components such as counselling. Accepted definitions of metabolic syndrome included the International Diabetes Federation worldwide definition [13] of the metabolic syndrome and National Cholesterol Education Program and Adult Treatment Panel III (NCEP-ATP III) diagnostic criteria [14] or criteria closely aligned to these definitions prior to publication of these definitions in 2001 (i.e. 3 of 5 of the risk factors for metabolic syndrome present). For the purposes of this review usual care included no intervention, standard care, sham exercise control group or brief advice/recommendation only. Trials were excluded if the participants were pregnant women with gestational diabetes or if participants had only one or two components of metabolic syndrome, therefore not fulfilling the diagnostic criteria of metabolic syndrome. Trials were also excluded if the intervention consisted of exercise or dietary intervention only, brochures only, single session or unsupervised exercise.

2.3. Data extraction

Data extraction was completed by one reviewer (MvN) and was checked for accuracy by another reviewer (CP). A data extraction form based on the Cochrane Data Collection was used. Data was extracted on participant characteristics (number of participants in each group, male:female ratio, age); anthropometric data (weight, body mass index, waist circumference, waist hip ratio), metabolic risk factors (cholesterol, glucose, blood pressure); intervention details (types, delivery, setting, number and frequency of sessions, duration of interventions); outcomes (anthropological and metabolic outcomes, functional outcomes and outcomes related to quality of life), results, dropouts and adverse events.

2.4. Quality assessment

The methodological quality of the included studies was assessed using the PEDro scale [15]; an 11-point scale used to assess risk of bias in randomised controlled trials. The PEDro scale awards 1 point per criteria (the first criterion is not scored), and includes random allocation, concealed allocation, group similarity at baseline, participant/therapist/assessor blinding, dropout number, intention-to-treat, between-group difference and point estimate and variability. The PEDro scale is a valid and reliable measure of methodological quality of randomised controlled trials [16]. Two reviewers (MvN, CP) independently assessed the studies according to the PEDro criteria. Agreement between the reviewers was recorded and evaluated using the kappa statistic [12]. For lifestyle intervention trials where it is not possible to blind the participants or therapists, a score of 8 is the highest possible score. Therefore, a trial with a score < 4 was categorised as being of poor methodological quality; a score of 4–6 was considered moderate quality and a score > 6 was considered good quality [17,18].

2.5. Outcomes

Our outcomes of interest were patient health outcomes classified according to the International Classification of Functioning, Disability and Health into the domains of: body structure and function, activity and participation [19]. Body structure and function outcomes included metabolic syndrome risk factors and other anthropometric measures, activity measures related to physical functioning, and participation measures were measures such as quality of life. Secondary outcomes related to safety and adverse events.

2.6. Data analysis

Where possible, meta-analyses were completed by pooling post-intervention means and standard deviations using Hedges' g. Meta-analyses were conducted using a random-effects model and inverse variance methods to calculate the mean difference (MD) or standardised mean difference (SMD) and 95% confidence interval (CI). The variance term of the random effect was estimated using the DerSimonian-Laird estimator. When analysing the SMDs, a meta-test of the required equal variances assumption was carried out to assess for possible violations [20]. Only the fasting glucose outcome indicated potential violations although a sensitivity analysis using log ratio of means without the assumption of equal variances returned similar results. Statistical heterogeneity was assessed using the I^2 statistic where I^2 values >50% are considered to represent substantial heterogeneity [21]. Where there were high levels of heterogeneity present in a meta-analysis, study characteristics and data-related factors were explored to identify a cause of the heterogeneity. This was carried out using meta-regression analyses where potential moderators were included one at a time in the analysis to assess the effect on heterogeneity. All continuous moderators were mean-centred so that the intercept from the meta-regression model could be interpreted as the estimated outcome effect for an average study. Where a study reported change scores only these were also included in meta-analyses despite the risk of increased heterogeneity as per the Cochrane Handbook for Systematic Reviews [21]. Meta-analyses and forest plots were created using RevMan 5 [22] and meta-regression analyses were carried out using the metafor package [23] in the R statistical software package [24].

To determine clinical significance of results some data conversions were performed. Fasting glucose levels were converted to glycosylated haemoglobin (HbA1c) values using the American Diabetes Association calculator (https://professional.diabetes.org/diapro/glucose_calc) [25] and triglyceride levels were converted to mmol/L using another online calculator (https://www.omnicalculator.com/health/cholesterol-units) [26].

The Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach was applied to each meta-analysis to determine the quality of each body of evidence. Trials were downgraded one place if: 1. Risk of bias was evident (majority of trials scored <6 on PEDro); 2. There was evidence of unexplained heterogeneity ($I^2 > 50\%$); 3. There was evidence of indirectness in population or outcome; 4. There was evidence of imprecision (wide 95%CI >0.8 for SMD and >minimal clinically important difference for MD); or 5. Publication bias (visual inspection of funnel plots when there were at least 10 trials in the meta-analysis). Meta-analyses were subsequently graded as high (4), medium (3), low (2) or very low quality (1).

3. Results

3.1. Study selection

The search identified 2598 articles and following removal of duplicates there were 1954 articles to screen on title and abstract. The agreement between the two reviewers was 'good' (kappa 0.78, 95% CI, 0.66 to 0.91) when screening title and abstract and 25 articles were identified for review in full text (Fig. 1). The two reviewers worked together to determine that 15 articles were eligible to be included in the review.

This systematic review includes 15 published papers from 10 randomised controlled trials. Three studies by Straznicky et al. [27–29] report data from one trial and two studies by Anderssen et al. [30,31], as well as the study by Torjesen et al. [32] all report data from the Oslo Diet and Exercise Study (ODES) [33]. Two studies by Tran et al. [34,35] also report results from the same trial. Data were only included once in any meta-analysis for participant data reported in multiple trials. The most complete data (i.e. not sub-group data) was selected for inclusion in meta-analyses.

3.2. Study characteristics

The mean PEDro score of included trials was 4.5 out of 10, ranging from 3 [32,36,37] to 7 [38] (Table 1, Appendix B). Inter-rater agreement between reviewers was very good (kappa 0.90, 95% CI 0.80 to 1.0) when rating methodological quality. All included trials were randomised controlled trials, one trial had concealed allocation [38] and three trials used intention-to-treat analysis [34,38,39].

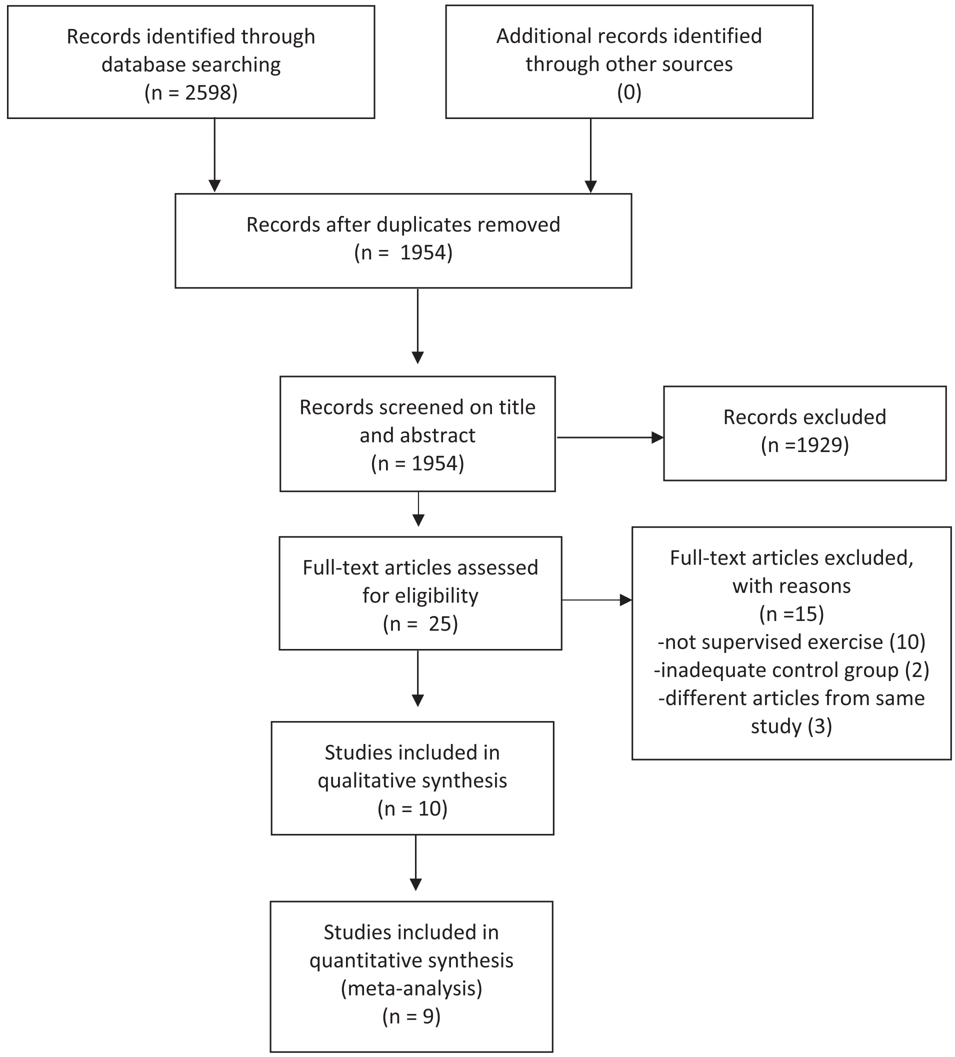

Fig. 1. Overview of systematic review process..

3.2.1. Participants

The review included 1160 participants from 10 trials of which data from 831 participants are included in meta-analyses. A total of 337 participants were from one study [34]. Four of the studies included only female participants [37,39–41] and of the rest, 78% of the participants were female. The mean age of participants ranged from 40 [37] to 67 years [40]. Four of the studies were conducted in Asia, two in Australia, two in Europe/United Kingdom, one in the USA and one in South America (Table 1).

3.2.2. Intervention

As per the inclusion criteria, all trials included both dietary intervention and a supervised exercise intervention. Dietary interventions included education or behavioural counselling on healthy eating [34,37,38], intensive nutritional education course [37], calorie reduction [28,32,36,39–41], reducing carbohydrates [39,40] and fats [31,36,40,41], daily food diary [40,41], recipes [28,34], supermarket tour and cooking sessions [38]. In general, dietary interventions targeted either calorie restriction [28,32,36,39–41] or healthy eating [35,37,38,42].

All supervised exercise sessions were group based, but group size was not reported in any study. There were a wide range of exercise interventions utilised including: circuit classes [32,37,38], Tai Chi [37], aqua aerobics [37], strength training [34,38,40,41], rhythmic dance or aerobics [32,38,40,41], yoga [39], Tai Bo [39], walking [32,34,36,38,42], jogging/running [32,36], cycling [28] and cycle ergometry [36]. Most studies reported individual tailoring of exercises to suit participant's needs. Three trials included supervised walking or jogging only [35,36,42]. The duration of exercise interventions ranged from 4 weeks [40,41] to 1 year [32]. Exercise sessions ranged from 60 [28,32,36,38,42] to 120 min [40,41] in duration (Table 2). Session frequency ranged from once a week [28,38] to daily walking [34], with 6 of the other studies having at least 3 supervised sessions per week [32,36,39–42].

Other interventions included health education [34,39–42], health screening (BP and body weight checks) [28,40,41], health counselling [37,39–41], and behavioural interventions [36,37].

3.3. Effects of lifestyle interventions on body structure and function

3.3.1. Metabolic syndrome risk factors

Outcomes measures included anthropometric measures of waist circumference (measured in 6 trials) [28,34,38,39,41,42]; BMI (measured in 9 trials) [29,32,34,36–39,41,42] and body weight (measured in 7 trials) [28,34,36–39,41]. Systolic and diastolic blood pressure were both measured in 8 trials [28,34,36–39,41,42]. Metabolic measures of HDL cholesterol and triglycerides were both assessed in 9 trials [28,32,34,36–39,41,42], while LDL cholesterol was reported in 5 trials [28,34,36,38,41].

Table 1
Study characteristics.

Study (country)	Population	PEDro score	Participants (int/cont)	Male:female (int/cont)	Age range	Outcomes	Metabolic syndrome criteria used	Timing of outcomes
Carroll et al., 2007 [37] (UK)	Healthy, premenopausal, women over 18 years who were obese and sedentary	3	17:14	100% female	Int: 40 ± 7 Cont: 42 ± 8	Physical: VO_2, VCO_2, Respiratory exchange ratio, expired volume of gas, tidal volume, BP, BMI, fasting glucose, cholesterol Psychological: General well-being schedule	IDF, 2005	Baseline, 12 weeks and 12 months
Oh et al., 2008 [41] (Korea)	Rural women with metabolic syndrome	4	16:16	100% female	Int: 65 ± 10 Cont: 70 ± 8	Physical: Weight, waist circumference, BMI, BP, fasting glucose, cholesterol Psychological: Self-efficacy, Quality of life	NCEP-ATP III Waist circumference as per Asia Pacific	Baseline, 4 weeks
Oh et al., 2010 [39] (Korea)	Women 40 years or older with MetS	6	31:21	100% female	Int: 60 ± 8 Cont: 67 ± 9	Physical: Weight, waist circumference, BP, fasting glucose, cholesterol, insulin resistance Psychological: Quality of life	NCEP-ATP III Waist circumference as per Asia Pacific	Baseline, 3,6, and 12 months
Oh et al., 2011 [40] (Korea)	Post-menopausal women MetS	4	16:13	100% female	Int: 65 ± 11 Cont: 70 ± 5	Inflammatory chemokines and insulin resistance	NCEP-ATP 2001, WHO-Asia Pacific 2004	Baseline, 4 weeks
Pettman et al., 2009 [38] (Australia)	Volunteers with MetS, not taking medications for cholesterol, glucose or BP	7	103:50	29:74/ 14:36	Mean age 45 years (no other info given)	Physical: Weight, BMI, waist circumference, body composition, cholesterol, glucose tolerance, BP, HR, fitness, handgrip strength, dietary intake, energy expenditure	IDF, 2005	Baseline, 16 weeks
Saboya et al., 2017 [42] (Brazil)	Subjects with MetS	4	41:41	12:13/ 12:7	Int: 51 ± 8 Cont: 52 ± 7	Physical: Waist circumference, BMI, BP, fasting glucose, cholesterol Psychological: Depression and anxiety (adult self-report), quality of life	Combination of NCEP-ATP and IDF	Baseline, 3 months and 9 months
Straznicky et al., 2011 [27] Straznicky et al., 2011 [28] Straznicky et al., 2012 [29] (Australia)	Men and post-menopausal women aged 45–65, overweight, non-smokers, sedentary, unmedicated with MetS	6	13:12	9:4 6:6	Int: 52 ± 1 Cont: 56 ± 2	Physical: Weight, BMI, Waist circumference, waist hip ratio, cholesterol, BP, fasting glucose, insulin, renal parameters, VO_2 max	NCEP - ATP III	Baseline, 12 weeks and 7 months
Torjesen et al., 2017 [32] Anderssen et al., 1996 [30] Anderssen et al., 2007 [31] (Norway)	Inactive people with MetS. No cardiovascular disease or diabetes, no medications	5	67:43	100% male	40 years old (no other information given)	Physical: Insulin resistance, fasting glucose, biomarkers, cholesterol, weight, BP	All of the below BMI > 24 kg/m2 DBP 86–99 TC -5.2-7.74 mmol/L HDL-C < 1.2 mmol/L FT - >1.4 mmol/L Anderssen 2007 – IDF criteria	Baseline, 12 months
Tran et al. 2017 [34] Tran et al. 2017 [35] (Vietnam)	Adults aged 50–65 years with MetS	5	214:203	31:144/ 35:127	Int: 58 ± 5 Cont: 57 ± 5	Physical: Weight, BMI, Waist circumference, BP, cholesterol, glucose, physical activity levels, dietary intake	NCEP-ATP III	Baseline, 6 months
Watkins et al., 2003 [36] (USA)	Adults >29 years with MetS	3	21:11	Not reported	Not reported	Physical: Fasting glucose, Cholesterol, BP Aerobic fitness (VO_2 max), weight loss	SBP 130–179 DBP >85 mmHg BMI >25 Insulin >80μU/mL 2 h after ingestion of 75 g glucose TG >150 mg/dL OR HDL-C < 40 mg/dL	Baseline, 26 weeks

Note: int = intervention; con = control; MetS = metabolic syndrome; VO2 = maximal oxygen consumption; VCO2 = rate of elimination of Carbon Dioxide; SBP = systolic blood pressure, DBP = diastolic blood pressure; BP = blood pressure; HR = heart rate; IDF = International Diabetes Federation; NCEP-ATP = National Cholesterol Education Program-Adult Treatment Panel; HDL = High Density lipoprotein; BMI = body mass index; HOMA = homeostasis Model Assessment of Insulin Resistance; WHO = World Health Organisation; TC = total cholesterol; FT = fasting triglycerides; TG = triglyceride.

3.3.1.1. Waist circumference. A meta-analysis of 6 trials [28,34,38,39,41,42] with 643 participants found medium quality evidence that compared to usual care, lifestyle intervention reduced waist circumference by 4.9 cm (95% CI −8.0 to −1.7, $I^2 = 81\%$) (Fig. 2, Table 3).

The only significant moderator from the regression analysis was the dichotomous moderator of whether the dietary intervention was targeted at weight loss via calorie restriction and this moderator also accounted for approximately 27% of the heterogeneity (Table 4). On average weight circumference decreased more if the dietary intervention was aimed at weight loss (difference in MD −4.6 cm, 95% CI −9.2 to −0.1) with strong evidence overall for reduction in waist circumference for this intervention (MD −7.4 cm, 95% CI −11.0 to −3.9, I^2 54%). However, results were still significant when the dietary intervention was not aimed at weight loss (MD −2.8 cm, 95% CI −5.6 to 0.0, I^2 54%). Results were no longer significant if the intervention was walking–based exercise only (MD −3.0 cm, 95%CI −6.9 to 0.9, I^2 15%). While amount of supervised exercise and total education provided were not significant moderators, they did absorb some of the heterogeneity ($I^2 = 58\%$ and $I^2 = 55\%$) and the overall effect for the MD was similar and remained significant.

3.3.1.2. HDL-cholesterol. A meta-analysis of 9 trials [28,32,34,36–39,41,42] with 797 participants found very low quality evidence that compared to usual care, multifaceted lifestyle intervention did not have a significant impact on HDL Cholesterol (SMD 0.70, 95% CI −0.09 to 1.49, $I^2 = 95\%$) (Fig. 3, Table 3).

Significant moderators from the meta-regression analysis were intervention duration, amount of supervised exercise and percentage women. When adjusting for these significant moderators, the mean effects were similar but became statistically significant (Table 4).

Table 2
Intervention characteristics.

Study	Duration and frequency of sessions	Disciplines involved	Exercise intervention	Dietary intervention	Other intervention
Carroll et al., 2007 [37]	12 weeks 1-hour education 1×/week (12 sessions) 1-h exercise 2×/week (24 sessions)	Dietitian Cognitive Behavioural Therapist Fitness instructor	Supervised structured exercise including circuit training, Tai Chi, aqua aerobics etc.	Intensive 3-week nutritional education course. Booklet on healthy eating principles	Sessions addressing behaviour change: goal setting, problem solving and coping skills
Oh et al., 2008 [41]	4 weeks 1-hour education and 1-hour exercise, 3×/week (12 sessions)	Exercise physiologist Nurse	Supervised stretching, strength training, rhythmic dance, warm up and cool down	Dietary counselling. Aim to reduce diet by 300 kcal; increase intake of fruit, vegetables, low fat dairy and whole grains; reduce intake of fat, refined grains, sweets and red meats. Daily food diary	Health screening and health education on: MetS and hypertension/obesity/diabetes etc.
Oh et al., 2010 [39]	26 weeks 50-minute education and 40-minute exercise 3×/week for first 13 weeks then 2×/week for next 13 weeks (60 sessions)	Nurse practitioner Exercise physiologist Nurse researcher	Supervised yoga, stretching and Tae-Bo (rhythmic aerobic dance). Daily brisk walking encouraged	Low-calorie, low-carbohydrate diet. Monitored to maintain <1500 kcal/day and limit carbohydrates to 60% of caloric intake	Health monitoring (BP, body weight), individual counselling, health education on MetS and lifestyle modification
Oh et al., 2011 [40]	4 weeks 1-hour education/counselling and 1-hour exercise 3×/week (12 sessions)	Exercise physiologist Researchers	Supervised stretching, strength training, aerobic dance and warm up and cool down exercises	Advice to reduce food intake by 300 kcal. Focus on reducing carbohydrates and fats and increasing fibre rich foods (fruits/vegetables). Daily food diary.	Health screening (BP and body weight check) Health education: risk factors, complications of MetS Health counselling
Pettman et al., 2009 [38]	16 weeks 1-hour lifestyle intervention session and 1-hour exercise 1×/week (16 sessions)	Study coordinator – health nutrition background Peer leader/study coordinator – experienced in adult training and self-management programs	Supervised exercise session including walking, walk-aerobics, dance-aerobics, strength training with dumbbells/resistance bands and circuit training. Encouraged to achieve national physical activity guidelines – 30 mins mod intensity physical activity most days	Dietary education sessions based on dietary guidelines for Australian adults (rather than energy restriction) Supermarket tour with education on food labels Practical cooking sessions	Sessions including lifestyle related topics such as self-management techniques
Saboya et al., 2017 [42]	12 weeks 1:1 sessions with psychology and nutritional teams 1×/week 1-hour treadmill sessions 3×/week (36 sessions)	Psychologist Nurse Physical Therapist Nutritionist	Treadmill - training range between 75 and 85% of maximal heart rate for each individual	Nutrition: Body weight measurement, adhesion to dietary program assessed, strategies and goals discussed	Psychology: based on transtheoretical model of change
Straznicky et al., 2011 [27] Straznicky et al., 2011 [28] Straznicky et al., 2012 [29]	12 weeks Dietary counselling 1×/fortnight 40-minute supervised bicycle riding 1×/week (12 sessions)	Nutritionist Exercise performed under supervision at Alfred Hospital Heart Centre	40 min of bicycle riding on alternate days, supervised exercise once weekly	Modified DASH diet, relative protein content 22% of energy intake. Calorie reduction of 600 cal/day; given 14-day menu plans and recipes;	Body weight measurement fortnightly
Torjesen et al., 2017 [32] Anderssen et al., 1996 [30] Anderssen et al., 2007 [31]	52 weeks 3 dietary counselling sessions, at baseline, 3 and 9 months 1-hour exercise 3×/week (156 sessions)	Diet – not specified Exercise – highly qualified instructors	Supervised workouts at 60–80% of peak heart rate. Aerobics, circuit training, jogging, fast walking. Progressed for 8 weeks, and then maintenance program	Individualized dietary counselling, energy restriction, increased fish and fish products, decreased fat and cholesterol	
Tran et al., 2017 [34] Tran et al., 2017 [35]	26 weeks 2-hour education sessions 1×/month for 4 months (4 sessions) Daily walking in commune (up to 182 sessions)	Program staff – medical doctors or nurses -conducted education sessions and led walking groups	Participated in supervised walking groups established at each commune	Booklet including suggested meal plans, recipes and tips for healthy eating (based on Food Based Dietary Guidelines in Vietnam)	Provided with health promotion booklet
Watkins et al. 2003 [36]	26 weeks Weight management program ×1 session/week (26 sessions) 1-hour exercise 3–4×/week (78–104 sessions)	Dietitian Exercise physiologist	1-hour sessions 3–4× per week. Mostly walking or jogging, cycle ergometry if unable to walk	Weight management program (groups of 3–4). Goal of 0.5–1 kg/week by decreasing calorie and fat intake. Dietary goals 1200/1500 cal for women/men, <20% calories from fat	Behavioural intervention based on LEARN manual – lifestyle, attitudes, relationships

Note: MetS = metabolic syndrome.

Increases in intervention duration and amount of supervised exercise were associated with greater increases in HDL cholesterol for the intervention group while higher percentage of women was negatively associated with improvements in HDL cholesterol for intervention. While it was not a significant moderator, weight loss did absorb some of the heterogeneity (I^2 58%). For the dichotomous moderators, results were only significant when the dietary interventions were aimed at weight loss (SMD 1.26, 95%CI 0.13 to 2.40, I^2 96%).

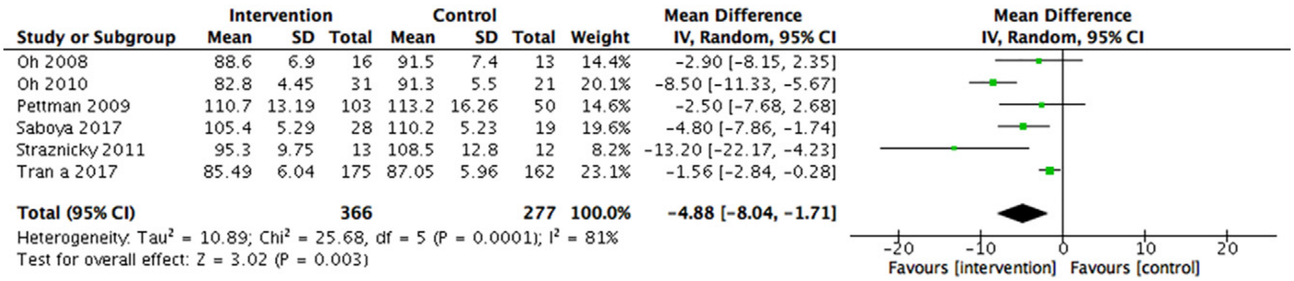

Fig. 2. Waist circumference.

3.3.1.3. Triglycerides. A meta-analysis of 9 trials [28,32,34,36–39,41,42] with 797 participants found that compared to usual care, there was low quality evidence that lifestyle intervention reduced triglycerides by a moderate and significant amount (SMD −0.46, 95%CI −0.88 to −0.04, $I^2 = 84\%$) (Fig. 4, Table 3).

When data is converted to mmol/L, compared to usual care, lifestyle intervention reduced triglycerides by 0.2 mmol/L (95%CI −0.4 to −0), $I^2 = 22\%$.

The only significant moderator in regression analyses was the percentage of women in each study. Results remained significant when accounting for this variable (SMD −0.48, 95%CI −0.74 to −0.21, I^2 55%) but higher proportion of women in the studies was associated with less reductions in triglyceride levels for intervention versus control (e.g. 0.014 increase in SMD per 1% change in percentage women, 95% CI 0.01 to 0.02). The moderator of weight loss was the only one to substantially reduce the heterogeneity to <50% (I^2 33%). The effect on triglycerides was only significant when the dietary interventions were aimed at weight loss and when the exercise intervention was not walking-based.

3.3.1.4. Blood pressure. A meta-analysis of 8 trials [28,34,36–39,41,42] with 689 participants found high quality evidence that compared to usual care, lifestyle intervention reduced systolic blood pressure by 6.5 mmHg (95% CI –10.7 to −2.3, $I^2 = 59\%$) (Fig. 5, Table 3). The moderator of weight loss reduced the I^2 to 0%. For every additional 1 kg of weight loss for the intervention group compared to control, there was an additional decrease in systolic blood pressure of 0.9 mmHg (95%CI 0.1 to 1.7). For the dichotomous outcomes, results remained significant for dietary interventions aimed at weight loss and non-walking-based exercise programs. A meta-analysis of 8 trials [28,34,36–39,41,42] with 691 participants found medium quality evidence that compared to usual care, multifaceted lifestyle intervention reduced diastolic blood pressure by 1.9 mmHg (95% CI −3.6 to −0.2, $I^2 = 12\%$) (Fig. 6, Table 3). Significant moderators on meta-regression were amount of supervised exercise, whether the intervention was walking-based and quality score. When adjusting for quality score, results remain significant with increased magnitude (MD −2.6 mmHg, 95%CI −4.3 to −0.9, I^2 0%) but when adjusting for amount of exercise, results become non-significant although with evidence still in the direction of an effect (MD −1.5 mmHg, 95%CI −3.5 to 0.5, I^2 0%). Results remained significant when considering the studies with only walking-based exercise (MD −3.3 mmHg, 95%CI −5.4 to −1.3, I^2 0%).

3.3.1.5. Fasting glucose. A meta-analysis of 10 trials [28,34,36–42] with 816 participants found low quality evidence that compared to usual care, lifestyle intervention decreased fasting glucose by a moderate and significant amount (SMD -0.68, 95% CI −1.20 to −0.15, $I^2 = 90\%$) (Fig. 7, Table 3). When including only trials that measured glucose in

Table 3
GRADE quality assessment.

		Bias	Inconsistency	Indirectness	Imprecision	Publication bias	Rating
Waist circumference 6 RCTs (n = 643)	MD 4.9 cm, 95%CI −8.0 to −1.7, I^2 81%	0	−1[b]	0	0	0[d]	3: medium
HDL cholesterol 9 RCTs (n = 797)	SMD 0.70, 95%CI −0.09 to 1.49, I^2 95%	−1[a]	−1[b]	0	−1[c]	0[d]	1: very low
Triglycerides 9 RCTs (n = 797)	SMD −0.46, 95%CI −0.88 to −0.04, I^2 84%	−1[a]	0	0	−1[c]	0[d]	2: low
Systolic BP 8 RCTs (n = 689)	MD 6.5 mmHg, 95%CI −10.7 to −2.3, I^2 59%	0	0	0	0	0[d]	4: high
Diastolic BP 8 RCTs (n = 691)	MD 1.9 mmHg, 95%CI −3.6 to −0.2, I^2 12%	−1[a]	0	0	0	0[d]	3: medium
Fasting glucose 10 RCTs (n = 816)	SMD −0.68, 95%CI −1.20 to −0.15, I^2 90%	−1[a]	0	0	−1[c]	0	2: low
Prevalence of MetS 4RCTs (n = 463)	RR 0.61, 95%CI 0.38 to 0.96, I^2 73%	−1[a]	0	0	0	0[d]	3: medium
Body Mass Index 9 RCTs (798)	SMD −1.30, 95%CI −2.18 to −0.44, I^2 96%	−1[a]	-1[b]	0	−1[c]	0[d]	1: very low
Weight 7 RCTs (n = 643)	MD 2.1 kg, 95%CI −3.3 to −0.8, I^2 7%	−1[a]	0	0	0	0[d]	3: medium
Physical fitness 4 RCTs (n = 225)	SMD 1.64, 95% CI 0.40 to 2.87, I^2 89%	0	0	0	−1[c]	0[d]	3: medium
Quality of Life 3 RCTs (n = 97)	SMD 1.68, 95% CI −0.23 to 3.58, $I^2 = 95\%$	−1[a]	−1[b]	0	−1[c]	0[d]	1: very low

NB: 0 = not downgraded. BP = blood pressure; MetS = metabolic syndrome.
[a] Downgraded one place due majority of trials scoring <6 on the PEDro scale.
[b] Downgraded one place due to unexplained heterogeneity.
[c] Downgraded one place due to wide confidence interval.
[d] Funnel plots not completed due to <10 studies in meta-analysis.

Table 4
Meta-regression results for significant moderators and moderators with more than a moderate effect on heterogeneity.

Outcome	Moderator	Estimate	95% CI	P	I^2	I^2 difference	Effect	95% CI of effect	P
Body mass index	Intervention duration	−0.14	(−0.20, −0.07)	0	95	1	−1.34	(−2.16, −0.52)	0.001
	Amount of supervised exercise	−0.04	(−0.06, −0.03)	0	89	7	−1.49	(−2.20, −0.79)	0
	Percentage women	0.05	(0.03, 0.08)	0	94	2	−1.41	(−2.15, −0.66)	0
	Weight loss difference	−0.09	(−0.16, −0.02)	0.008	51	45	−0.50	(−0.79, −0.22)	0.001
	Diet aimed at weight loss	−1.76	(−3.44, −0.08)	0.04	95	1	−0.36	(−1.60, 0.88)	0.573
Diastolic blood pressure	Amount of supervised exercise	−0.08	(−0.15, −0.01)	0.036	0	12	−1.46	(−3.44, 0.52)	0.149
	Walking-based exercise	−3.48	(−6.57, −0.39)	0.027	0	12	0.13	(−2.19, 2.44)	0.913
	Quality score	1.46	(0.31, 2.62)	0.013	0	12	−2.60	(−4.25, −0.95)	0.002
Fasting glucose	Intervention duration	−0.05	(−0.08, −0.02)	0.001	79	11	−0.62	(−0.99, −0.25)	0.001
	Amount of supervised exercise	−0.02	(−0.02, −0.01)	0	57	33	−0.67	(−1.0, −0.34)	0
	Percentage women	0.02	(0.01, 0.03)	0	78	12	−0.63	(−1.01, −0.26)	0.001
	Weight loss difference	−0.05	(−0.11, 0.001)	0.056	0	90	−0.44	(−0.62, −0.26)	0
HDL cholesterol	Intervention duration	0.12	(0.07, 0.17)	0	92	4	0.70	(0.08, 1.32)	0.027
	Amount of supervised exercise	0.04	(0.02, 0.05)	0	89	7	0.77	(0.10, 1.44)	0.025
	Percentage women	−0.04	(−0.07, −0.02)	0	94	1	0.81	(0.10, 1.52)	0.026
	Weight loss difference	−0.01	(−0.08, 0.06)	0.782	58	37	0.06	(−0.30, 0.41)	0.76
Physical fitness	Age	0.39	(0.13, 0.65)	0.004	89	1	2.07	(0.74, 3.40)	0.002
	Weight loss difference	0.22	(0.07, 0.38)	0.004	84	6	1.78	(0.81, 2.75)	0
Systolic blood pressure	Weight loss difference	−0.93	(−1.73, −0.13)	0.022	0	59	−4.21	(−6.81, −1.62)	0.001
Triglycerides	Percentage women	0.01	(0.01, 0.02)	0.001	55	28	−0.48	(−0.74, −0.21)	0
	Weight loss difference	−0.02	(−0.07, 0.04)	0.616	33	51	−0.19	(−0.42, 0.05)	0.118
Weight	Weight loss difference	−1	(−1.77, −0.23)	0.011	0	7	−3.30	(−4.71, −1.89)	0
Waist circumference	Amount of education	−0.11	(−0.23, 0.02)	0.092	55	26	−4.38	(−6.66, −2.1)	0
	Diet aimed at weight loss	−4.64	(−9.18, −0.11)	0.045	54	27	−2.80	(−5.60, 0.001)	0.05

mmol/L [28,32,35,37,38] so that data could be converted to %HbA1c for clinical interpretability, lifestyle intervention reduced fasting glucose by 0.3 mmol/L which is equivalent to a reduction in HbA1c of 1.8%.

Significant moderators from the meta-regression analysis were intervention duration, amount of supervised exercise and percentage women. However, when adjusting for these significant moderators, the mean effects were similar (Table 4). Increases in intervention duration and amount of supervised exercise were associated with larger reductions in the fasting glucose SMD (i.e. more evidence in favour of intervention), while for percentage women the association was positive (e.g. an 0.02 increase in SMD per 1% increase in percentage women, 95% CI 0.01 to 0.03). The moderator of weight loss was close to significant ($p = .056$) and was the only one that resulted in a substantial reduction in detected heterogeneity ($I^2 = 0\%$). For the dichotomous moderators, the fasting glucose SMD was only significant for non-walking-based interventions and for the studies where the diet was aimed at weight loss.

3.3.2. Prevalence of metabolic syndrome

In all studies, all participants had metabolic syndrome at baseline. Four studies [31,34,37,39] with 463 participants reported prevalence of metabolic syndrome following the intervention. All reported reductions in metabolic syndrome prevalence after the intervention with an overall 39% risk reduction in the intervention group (RR 0.61, 95%CI 0.30to 0.96, I^2 73%) (Table 3).

From the meta-regression analysis, significant moderators were intervention duration, percentage of women participants and whether the intervention included a diet aimed at weight loss. These moderators, and also weight loss, significantly reduced heterogeneity (I^2 0%, 12%, 0% and 0% respectively) and mean effects remained similar despite the small number of trials in the meta-regression analysis. Results remained significant regardless of whether the diet intervention was targeted at weight loss or not but was no longer significant for walking-based interventions.

3.3.3. Other anthropometric outcomes

3.3.3.1. Body mass index (BMI). A meta-analysis of 9 trials [28,32,34,36–39,41,42] with 798 participants found very low quality evidence that compared to usual care, lifestyle intervention reduced body mass index by a large and significant amount with a large degree of unexplained heterogeneity (SMD −1.30, 95% CI −2.18 to −0.44, $I^2 = 96\%$).

From the meta-regression analysis, the duration of the intervention, the amount of supervised exercise, percentage women participants and weight loss were all significant moderators. Accounting for the moderators did not alter the results nor reduce I^2 below 50%. For dichotomous moderators, results were significant for non-walking-based exercise interventions and dietary interventions aimed at weight loss.

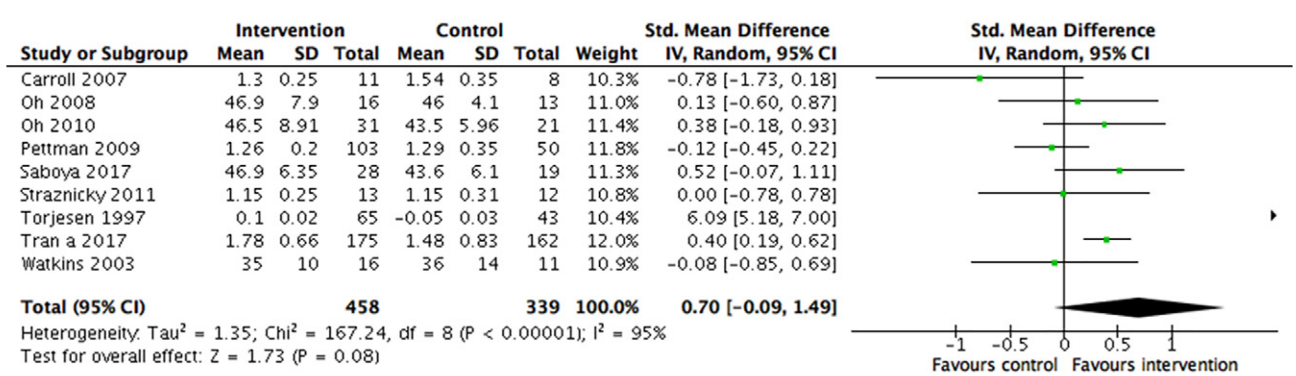

Fig. 3. HDL cholesterol.

Study or Subgroup	Intervention Mean	Intervention SD	Intervention Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI
Carroll 2007	1.8	0.69	11	1.91	0.49	8	8.6%	−0.17 [−1.08, 0.74]
Oh 2008	89.7	25	16	141.3	75.5	13	9.7%	−0.93 [−1.71, −0.16]
Oh 2010	179.2	61.25	31	189.5	139.31	21	11.6%	−0.10 [−0.66, 0.45]
Pettman 2009	1.62	1.01	103	1.62	0.78	50	13.3%	0.00 [−0.34, 0.34]
Saboya 2017	176.2	65.09	28	215	63.2	19	11.2%	−0.59 [−1.19, 0.00]
Straznicky 2011	1.2	0.72	13	2.2	1.73	12	9.3%	−0.74 [−1.56, 0.07]
Torjesen 1997	−0.7	0.2	65	−0.1	0.5	43	12.5%	−1.70 [−2.15, −1.25]
Tran a 2017	2.32	1.09	175	2.52	1.8	162	14.1%	−0.14 [−0.35, 0.08]
Watkins 2003	217	178	16	180	99	11	9.7%	0.24 [−0.53, 1.01]
Total (95% CI)			**458**			**339**	**100.0%**	**−0.46 [−0.88, −0.04]**

Heterogeneity: Tau² = 0.31; Chi² = 49.37, df = 8 (P < 0.00001); I² = 84%
Test for overall effect: Z = 2.17 (P = 0.03)

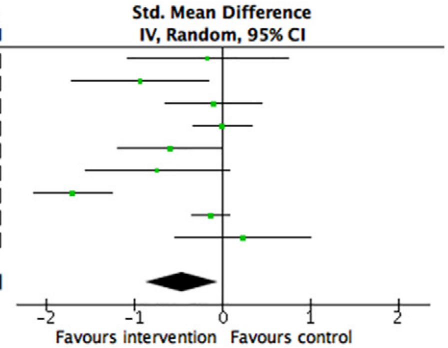

Fig. 4. Triglycerides.

3.3.3.2. Body weight. A meta-analysis of 7 trials [28,34,36–39,41] with 643 participants found medium quality evidence that compared to usual care, lifestyle intervention reduced body weight by 2.1 kg (95% CI −3.3 to −0.8, $I^2 = 7\%$) (Table 3). Apart from weight loss, there were no significant moderators on meta-regression analysis.

3.4. Effect of lifestyle intervention on measures of activity

3.4.1. Fitness

A meta-analysis of 4 trials [28,36–38] with 225 participants found medium quality evidence that compared to usual care, lifestyle intervention improved physical fitness by a large and significant amount (SMD 1.64, 95% CI 0.40 to 2.87, I^2 89%).

Meta-regression analysis found that age and weight loss were significant moderators. When adjusting for age, overall fitness SMD was similar, although an increase in age was associated with a greater difference between the intervention and control groups (increase in one year associated increase in SMD of 0.4, 95% CI 0.1 to 0.7). When adjusting for weight loss, the effect also remained significant and every extra kilogram difference lost in favour of the intervention group was associated with an increase in fitness of SMD (95%CI 0.1 to 0.4).

3.4.2. Behaviour change

Two studies reported significant positive behaviour change in relation to physical activity in the intervention group [35,41], with one reporting significant increases in moderate intensity activity, walking and total physical activity, and decreased mean sitting time [35]. Six studies reported significant positive behaviour changes related to food intake in the intervention groups [28,31,35,36,38,41]. Intervention groups showed greater intake of polyunsaturated fatty acids and protein [38]; reduced energy intake [31,36] and saturated fat intake [28,31,36]; and reduced intake of animal organs and use of cooking oil [35].

3.5. Effect of lifestyle intervention on measures of participation

Four studies investigated the effect of a multidisciplinary lifestyle intervention on health-related quality of life [37,39,41,42]. Two studies used the Medical Outcomes Study Short Form [39,42], one used the EQ-5D-5 L [41] and one used the General Well-Being Schedule [37]. Meta-analysis of 3 trials [37,41,42] including 97 participants found a non-significant but large improvement in quality of life (SMD 1.68, 95% CI −0.23 to 3.58, $I^2 = 95\%$). One study included long-term follow-up of quality of life [42] and found that improvements in QoL were not sustained at 12 months.

Adverse events were not reported in any trials.

4. Discussion

This systematic review of 15 papers reporting data on 1160 participants from 10 randomised controlled trials found that compared to usual care, supervised multifaceted lifestyle interventions significantly reduced metabolic risk factors, increased physical fitness and decreased prevalence of metabolic syndrome. There were no significant changes for HDL cholesterol and a non-significant improvement in quality of life. The results from this systematic review were similar to those reported in previous systematic reviews [7–10,26] in groups of people with and without metabolic syndrome. Our review demonstrates that supervised lifestyle intervention (comprising at least diet and exercise) is beneficial for people who have a diagnosis of metabolic syndrome.

The magnitude of improvements seen in metabolic risk factors are likely to be clinically significant. A 1 cm increase in waist circumference is associated with a 2% increase in risk of cardiovascular events [43] and, for people with diabetes, a 5 cm higher waist circumference is associated with higher all-cause mortality [44]. Therefore, the 4.9 cm reduction in waist circumference found on meta-analysis or 7.4 cm on meta-regression for dietary interventions aimed at weight loss is likely

Study or Subgroup	Intervention Mean	Intervention SD	Intervention Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Random, 95% CI
Carroll 2007	134.2	17.3	11	136.6	19.2	8	5.0%	−2.40 [−19.18, 14.38]
Oh 2008	122.6	11.2	16	133.5	18	13	9.0%	−10.90 [−22.12, 0.32]
Oh 2010	120.8	11.14	31	127.1	18.79	21	11.7%	−6.30 [−15.24, 2.64]
Pettman 2009	126.5	13.19	103	128.6	12.02	50	19.9%	−2.10 [−6.29, 2.09]
Saboya 2017	120.6	12.17	28	134.3	12.21	19	14.5%	−13.70 [−20.80, −6.60]
Straznicky 2011	119	14.42	13	135	17.3	12	7.7%	−16.00 [−28.54, −3.46]
Tran a 2017	133.29	10.64	175	133.87	21.67	162	20.8%	−0.58 [−4.27, 3.11]
Watkins 2003	130	10	16	138	13	11	11.4%	−8.00 [−17.11, 1.11]
Total (95% CI)			**393**			**296**	**100.0%**	**−6.51 [−10.71, −2.31]**

Heterogeneity: Tau² = 18.55; Chi² = 17.23, df = 7 (P = 0.02); I² = 59%
Test for overall effect: Z = 3.04 (P = 0.002)

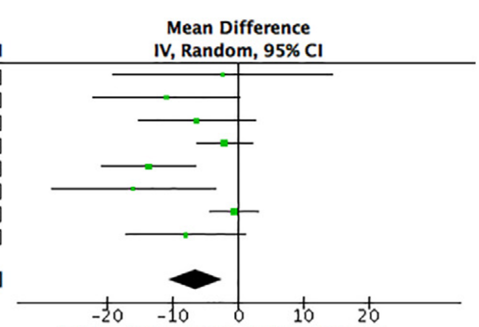

Fig. 5. Systolic blood pressure.

Study or Subgroup	Intervention Mean	Intervention SD	Intervention Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Random, 95% CI
Carroll 2007	84	11.5	11	85	8.3	10	4.0%	−1.00 [−9.52, 7.52]
Oh 2008	75.7	10.6	16	77.8	11.1	13	4.6%	−2.10 [−10.06, 5.86]
Oh 2010	74.3	8.91	31	73.6	12.83	21	7.1%	0.70 [−5.62, 7.02]
Pettman 2009	74.1	10.15	103	73.4	7.78	50	26.7%	0.70 [−2.21, 3.61]
Saboya 2017	80.9	10.58	28	86.4	10.9	19	7.2%	−5.50 [−11.78, 0.78]
Straznicky 2011	71	10.82	13	73	10.39	12	4.2%	−2.00 [−10.32, 6.32]
Tran a 2017	83.69	10.73	175	86.04	11.93	162	34.5%	−2.35 [−4.78, 0.08]
Watkins 2003	87	5	16	93	7	11	11.7%	−6.00 [−10.81, −1.19]
Total (95% CI)			**393**			**298**	**100.0%**	**−1.89 [−3.64, −0.15]**

Heterogeneity: Tau² = 0.77; Chi² = 7.93, df = 7 (P = 0.34); I² = 12%
Test for overall effect: Z = 2.12 (P = 0.03)

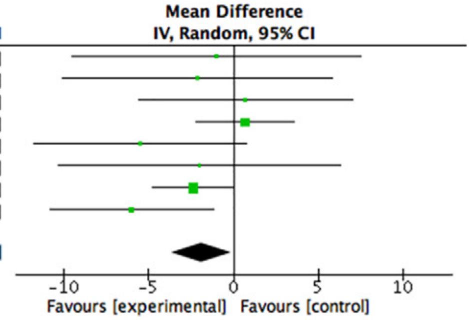

Fig. 6. Diastolic blood pressure.

to be clinically significant for people with metabolic syndrome. For glycaemic control, considering a 0.3% reduction in HbA1c is clinically meaningful [45,46], results of the meta-analysis are approaching clinical significance with a 0.22% reduction in HbA1c observed. Achieving a target of 120–124 mmHg for systolic blood pressure is associated with the lowest risk of cardiovascular disease and all-cause mortality [46]. This review found significant reductions in systolic blood pressure following lifestyle intervention and the mean systolic blood pressure in intervention participants in 4 trials was within the target range of 120–124 mmHg while none of the control group means were within the target range. Therefore, results are again likely to be clinically significant.

In contrast to other studies which reported an increase in HDL cholesterol with lifestyle modification in diabetic [47] or stroke [48] populations, our review did not find any effect on HDL cholesterol. Other studies have reported that HDL cholesterol is correlated with physical fitness [49]. It may be possible that some of the studies included in this review did not include exercise interventions of a high enough intensity to beneficially affect HDL cholesterol. On meta-regression analysis, trials of longer duration and with more supervised exercise had a greater positive effect on HDL cholesterol. Conversely, significant reductions in triglycerides were observed. For each 1 mmol/L increase in triglycerides there is a 32% increase in risk of cardiovascular disease in men and a 76% increase in risk of disease in women [50]. Given this significant increase in cardiovascular disease risk for each 1 mmol/L, a reduction of 0.3 mmol/L found in this review is likely to be clinically significant.

Specific intervention characteristics may have played an important role in the effectiveness of interventions on important outcomes. Dietary interventions that targeted weight loss through calorie restriction [28,32,36,39–41] appear to have had a more significant impact on the majority of outcomes. In addition, weight loss was a significant moderator in many of the outcomes and had a significant impact on heterogeneity suggesting that weight loss may be an important factor in the effectiveness of interventions. However, results were still significant when adjusting for weight loss indicating that participants can still have benefits in the absence of weight loss. Walking-based exercise programs may have been insufficient to produce significant differences between intervention and control groups. However, these results should be interpreted with caution as they are based on only three low to moderate quality trials [35,36,42]. The percentage of women in the trials was also often a significant moderator. An increase in the percentage of women in a trial was associated with reduced between group differences for HDL cholesterol, triglycerides and fasting glucose. However, these effects were small.

The statistically and clinically significant results found should encourage health service providers to consider providing lifestyle intervention programs for people with metabolic syndrome. The diagnosis of metabolic syndrome provides the opportunity to intervene early with lifestyle intervention to prevent progression to chronic disease. Improvements in patient health outcomes found in this review are likely to lead to improved health service outcomes. For example, a retrospective study found that a lifestyle intervention program was associated with reduced emergency department presentations for people with metabolic syndrome [51]. Health services should consider implementing lifestyle intervention programs for people with metabolic syndrome to reduce risk factors and prevent progression to chronic disease to ultimately improve both patient health outcomes and health service outcomes.

A limitation of the review is that most of the studies included were of low to moderate methodological quality. This may have increased risk of bias in analyses and therefore only low to medium level evidence can be established. However, we did adjust for study quality in meta-regression analysis and found that it was not a significant moderator. A number of the meta-analyses also demonstrated statistical heterogeneity. Meta-regression and sub-group analyses were conducted as appropriate, and in most cases were able to account for this heterogeneity. It should also be noted that although all interventions included supervised exercise, the intensity and content of dietary interventions varied widely. This was, however, explored in meta-regression analyses. None of the trials reported follow-up beyond one year of intervention. Information on maintenance of lifestyle change and long-term effects

Study or Subgroup	Intervention Mean	Intervention SD	Intervention Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI
Carroll 2007	5.71	0.79	11	5.88	0.93	8	8.7%	−0.19 [−1.10, 0.72]
Oh 2008	100.8	9.3	16	111.4	33.5	13	9.6%	−0.44 [−1.18, 0.30]
Oh 2010	94.2	11.14	31	95.9	12.37	21	10.5%	−0.14 [−0.70, 0.41]
Oh 2011	104.9	14.22	14	111.6	14.43	8	8.9%	−0.45 [−1.33, 0.43]
Pettman 2009	5.46	0.7	103	5.5	0.8	50	11.4%	−0.05 [−0.39, 0.28]
Saboya 2017	107.7	18	25	111	18.75	19	10.3%	−0.18 [−0.77, 0.42]
Straznicky 2011	4.9	0.36	13	5.3	0.35	12	9.1%	−1.09 [−1.94, −0.24]
Torjesen 1997	−0.3	0.1	65	0	0.1	43	10.5%	−2.98 [−3.54, −2.42]
Tran a 2017	6	1.23	175	6.67	1.75	162	11.7%	−0.44 [−0.66, −0.23]
Watkins 2003	84	8	16	92	12	11	9.3%	−0.79 [−1.59, 0.01]
Total (95% CI)			**469**			**347**	**100.0%**	**−0.68 [−1.20, −0.15]**

Heterogeneity: Tau² = 0.60; Chi² = 87.88, df = 9 (P < 0.00001); I² = 90%
Test for overall effect: Z = 2.53 (P = 0.01)

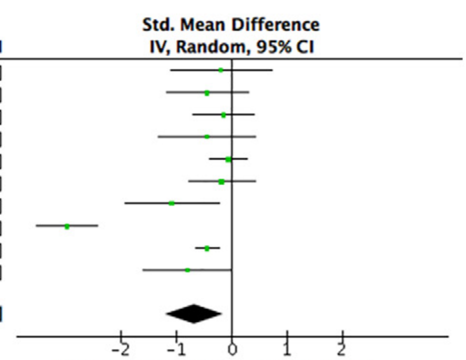

Fig. 7. Fasting glucose.

on morbidity and mortality would be beneficial. The strengths of this review are that it followed PRISMA reporting guidelines and only included randomised controlled trials evaluating multifaceted lifestyle interventions with supervised exercise for participants with metabolic syndrome.

This review demonstrates that multifaceted lifestyle interventions reduce the prevalence of metabolic syndrome and improve most metabolic risk factors. Given the high prevalence of the disease worldwide, and the increased cardiovascular risks associated with the disease, implementing a multifaceted lifestyle intervention for those with metabolic syndrome is likely to improve patient health outcomes and may reduce healthcare costs associated with hospitalisation and emergency department presentations for cardiovascular and metabolic disorders. Such lifestyle interventions may therefore be cost effective for health services to implement. Further research with longer term follow-up is needed to determine whether these changes are maintained and the impact on morbidity and mortality. Future research should also consider health service outcomes such as emergency department presentations and hospitalisations as well as health economic analyses. It may also be useful to establish whether multifaceted programs without supervision (e.g. telehealth, home exercise programs etc.) are also effective in reducing prevalence and risk factors for metabolic syndrome as these interventions may be less costly and more accessible.

5. Conclusions

This systematic review has demonstrated low to moderate quality evidence that multifaceted lifestyle intervention, including supervised exercise, is effective in reducing the prevalence of metabolic syndrome as well as treating its individual components.

Author contribution

MvN and CP contributed significantly to conception, data collection, data analysis, data interpretation and manuscript preparation. Author LP contributed significantly to data analysis, data interpretation an/d manuscript preparation.

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Declaration of competing interest

The authors declare no conflict of interest.

Appendix A. Search strategy (Medline)

# ▲	Searches	Results
1	Metabolic syndrome/	28,495
2	Metabolic syndrome.mp.	50,558
3	syndrome x.mp.	2005
4	metS X.mp.	10
5	metS.mp.	9320
6	insulin resistance syndrome.mp.	1633
7	1 or 2 or 3 or 4 or 5 or 6	55,291
8	Cardiac Rehabilitation/	1785
9	cardiac rehab*.mp.	6484
10	cardiovascular exercise program*.mp.	14
11	cardiorespiratory exercise program*.mp.	0
12	Secondary Prevention/ or secondary prevention program*.mp.	18,995
13	lifestyle intervention program*.mp.	460
14	multidisciplinary rehabilitation program*.mp.	227
15	multidisciplinary intervention program*.mp.	59
16	(weight loss and exercise).mp. [mp = title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	9561
17	(diet and exercise).mp. [mp = title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	27,604
18	8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17	57,348
19	Randomised controlled trial.mp. or Randomised Controlled Trial/	498,217
20	RCT.mp.	18,800
21	random* control*.mp.	669,338
22	19 or 20 or 21	673,105
23	7 and 18 and 22	

Appendix B. Quality assessment: PEDro scores of included trials

Study	Eligibility Criteria	Random allocation	Concealed allocation	Groups similar at baseline	Participant blinding	Therapist blinding	Assessor blinding	<15% dropouts	Intention-to-treat analysis	Between-group difference reported	Point estimate and variability reported	Total
Carrol, 2008	Y	Y	N	N	N	N	N	N	N	Y	Y	3
Oh, 2008	Y	Y	N	Y	N	N	N	N	N	Y	Y	4
Oh, 2010	Y	Y	N	Y	N	N	N	Y	Y	Y	Y	6
Oh, 2011	Y	Y	N	Y	N	N	N	N	N	Y	Y	4
Pettman, 2009	Y	Y	Y	Y	N	N	N	Y	Y	Y	Y	7

(continued on next page)

(*continued*)

Study	Eligibility Criteria	Random allocation	Concealed allocation	Groups similar at baseline	Participant blinding	Therapist blinding	Assessor blinding	<15% dropouts	Intention-to-treat analysis	Between-group difference reported	Point estimate and variability reported	Total
Saboya, 2017	Y	Y	N	Y	N	N	N	N	N	Y	Y	4
Straznicky, 2011 Straznicky, 2011 Straznicky, 2010	Y	Y	N	Y	N	N	Y	Y	N	Y	Y	6
Tran, 2017 Tran 2017	Y	Y	N	Y	N	N	N	N	Y	Y	Y	5
Torjesen, 1997	Y	Y	N	Y	N	N	N	Y	N	Y	Y	5
Watkins, 2003	Y	Y	N	N	N	N	N	N	N	Y	Y	3

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