# **BMJ Open** Effects of lifestyle interventions on cardiovascular risk factors in South Asians: a systematic review and metaanalysis

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#### ABSTRACT

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Professor Sonia S Anand; anands@mcmaster.ca **Background** The cardiovascular disease (CVD) burden among South Asians is high. Lifestyle interventions have been effective in the primary prevention of CVD, but this has not been replicated, through a synthesis of randomised trials, in South Asians.

Methods Four electronic databases (MEDLINE, Embase, CENTRAL and CINAHL), two clinical trial registries and references of included articles were searched through June 2022 (featuring ≥90% South Asian participants). Random-effects pairwise meta-analyses were performed, and heterogeneity was quantified with the I<sup>2</sup> statistic. The Grades of Recommendation, Assessment, Development, and Evaluation (GRADE) framework was used to report on the quality of evidence (International Prospective Register of Systematic Reviews registration (PROSPERO).

Results Thirty-five studies were included. Twelve tested diet and physical activity interventions; 18 tested diet alone; and 5 tested physical activity alone. All reported effects of the intervention(s) on at least one established risk factor for CVD, including blood pressure (systolic blood pressure (SBP), diastolic blood pressure (DBP) and blood lipids (high-density lipoprotein cholesterol (HDLc), low-density lipoprotein cholesterol (LDLc) or triglycerides). No trials reported clinical CVD. There is moderatequality evidence that diet and physical activity interventions improve SBP (mean difference (MD) -2.72 mm Hg, 95% Cl -4.11 to -1.33) and DBP (MD -1.53 mm Hg, 95% Cl -2.57 to -0.48); high-quality to moderate-quality evidence that diet-only interventions improve DBP (MD -2.05 mm Hg, 95% Cl -2.93 to -1.16) and blood lipids (triglycerides (MD -0.10 mmol/L, 95% CI -0.14 to -0.06) and LDLc (MD -0.19 mmol/L, 95% CI -0.32 to -0.06)); and moderate-quality evidence that physical activity-only interventions improve SBP (MD -9.7 mm Hg, 95% CI -11.05 to -8.35), DBP (MD -7.29 mm Hg, 95% CI -8.42 to -6.16) and HDLc (MD 0.08 mmol/L, 95% CI 0.04 to 0.11) compared with usual care.

**Conclusions** Lifestyle interventions improve blood pressure and blood lipid profiles in adult South Asians at risk of CVD. Tailored interventions should be used to modify cardiovascular risk factors in this at-risk group.

PROSPERO registration number CRD42018090419.

#### **INTRODUCTION**

More people die worldwide from cardiovascular disease (CVD) than from any other

#### STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ This review is the first to compile evidence from randomised trials conducted to assess the effect of lifestyle interventions that include diet and/or physical activity components on cardiovascular risk in South Asians.
- ⇒ None of the included trials reported on any clinical endpoint of cardiovascular disease (CVD) (incidence of myocardial infarction or stroke). Whether lifestyle interventions can prevent clinical CVD in South Asians remains unclear.
- ⇒ There were not enough physical activity intervention studies to adequately assess the effect of that particular lifestyle intervention on cardiovascular risk in South Asians.
- $\Rightarrow$  The diet-only interventions included in the review were variable in design and could have contributed to the unaccounted-for heterogeneity in the meta-analyses.

cause.<sup>1</sup> South Asians (individuals originating from India, Pakistan, Bangladesh, Sri Lanka, Nepal and/or Bhutan) are quickly becoming one of the largest populations worldwide.<sup>2</sup> Currently, South Asians make up 24.8% of the world's population.<sup>3</sup> By 2025, it is expected that this will rise to 26.2% of the world's population.<sup>3</sup> In Western countries, the prevalence of CVD among South Asians is three to four times higher and more aggressive than non-South Asians due to earlier (<50 vears) development of cardiovascular risk factors such as abdominal adiposity, dyslipidaemia and dysglycaemia.<sup>4-9</sup> Improving established cardiometabolic risk factors for CVD including abnormal lipid profiles, high blood pressure and type 2 diabetes early, which together account for over twothirds of the population attributable risk of myocardial infarction (MI),<sup>10</sup> may lower the burden of CVD, improve quality of life and reduce healthcare costs attributable to CVD. According to the WHO, a healthy diet and regular physical activity can substantially reduce the risk of CVD, largely through modifying these risk factors.<sup>1</sup> These strategies will likely be beneficial in lowering the burden of CVD among South Asians.

Although pharmacological approaches are useful for patients, many individuals with cardiovascular risk factors prefer non-pharmacological approaches to CVD risk management.<sup>11</sup> <sup>12</sup> Interventions that improve diet and/ or increase physical activity are typically less expensive, improve individual well-being and are less likely to be associated with negative side effects compared with some drug therapies.<sup>11</sup> <sup>13</sup> Diet and physical activity interventions are effective in reducing cardiovascular risk factors (ie, diabetes) and CVD incidence.<sup>8</sup> <sup>14–17</sup> Canadian and European clinical guidelines propose healthy behavioural changes through diet and physical activity as the first line of treatment for individuals with cardiovascular risk factors.<sup>18</sup> <sup>19</sup>

The effectiveness of diet and physical activity interventions in improving cardiovascular health in the general population has been extensively reviewed,<sup>8 20-23</sup> but no systematic reviews have assessed the effectiveness of such interventions in the South Asian population. There are several physiological, cultural and socioeconomic factors that may contribute to differences when assessing healthy active living interventions in ethnic populations compared with non-ethnic populations. For example, physiological measures such as body mass index (BMI) thresholds and waist circumference cut-offs are different for South Asians due to a differential body fat distribution.<sup>24-26</sup> In addition, the dietary habits of South Asians are affected by cultural customs, beliefs, food availability and generational preferences.<sup>26</sup> While beneficial effects of diet and physical activity interventions have been well documented, findings from studies conducted in non-South Asian populations must be replicated in such an ethnically diverse population, given the variable risk factor profiles and cultural context. In this review, we synthesise data from randomised controlled trials (RCTs) assessing the effect of diet and/or physical activity interventions on cardiovascular risk in adult South Asian populations. Our primary objective is to determine if dietary modifications, physical activity or a combination of both improves cardiovascular risk factors in randomised trials involving adult South Asians (International Prospective Register of Systematic Reviews registration ID: CRD42018090419).

#### **METHODS**

#### Search strategy and selection criteria

The authors worked with an experienced research librarian to develop subject-specific and keyword approaches to search strategies across all databases (online supplemental appendix 1). We searched four databases through June 2022 including MEDLINE, Embase, Cochrane Central Register of Controlled Trials (The Cochrane Library) and CINAHL. We also searched for ongoing or completed trials using the clinical trials registry platform (www.ClinicalTrials.gov) and the WHO International Clinical Trials Registry Platform Search Portal (http://apps.who.int/trialsearch/) and manually searched the references of included studies.

RCTs aimed at primary prevention of CVD of any duration, including cluster randomised and/or factorial 2×2 designs, involving at least one diet and/or physical activity component, among adult (18 years or older) South Asians originating from India, Pakistan, Sri Lanka, Bangladesh, Bhutan and/or Nepal, regardless of their place of residence (including outside of South Asia), were eligible for this review. No language or publication status restrictions were applied. A native speaker or a professional translator would have been contacted if the search resulted in any non-English papers. The comparator was defined as no intervention or usual diet/physical activity advice through leaflets, websites or other modes of communication. Eligible studies must have reported one or more of the following outcomes: incidence of MI (fatal and/or non-fatal), incidence of stroke (fatal and/or non-fatal), blood lipids (low-density lipoprotein cholesterol (LDLc, mmol/L), high-density lipoprotein cholesterol (HDLc, mmol/L), non-HDLc (mmol/L, if reported directly), triglycerides (mmol/L), blood pressure (systolic blood pressure (SBP) and diastolic blood pressure (DBP) (mm Hg)), hypertension (dichotomous, reported as n (%) based on a threshold of 140/90 mm Hg), visceral adipose tissue volume (cm<sup>3</sup>, MRI or CT reported) and incidence of type 2 diabetes (self-reported, n (%)). However, since no important CVD clinical endpoints were reported in the trials included, additional data on BMI  $(kg/m^2)$ , weight (kg), waist circumference (cm), homeostatic model assessment of insulin resistance (HOMA-IR), fasting plasma glucose (FPG, mmol/L) and insulin sensitivity (IS) were also extracted to better understand the effects of diet and/or physical activity interventions on cardiovascular risk. Studies of secondary prevention (ie, in populations that had experienced a prior CVD event such as a MI, stroke, coronary heart disease, etc) and studies in which <90% of the sample were South Asians were excluded (tables 1 and 2).

#### Study selection and data extraction

Two review authors (JL and MA) independently reviewed studies in duplicate at the title and abstract screening stage using Distiller SR (Evidence Partners, Ottawa, Canada).<sup>27</sup> The authors (JL and MA) resolved conflicts internally on discussion and consulted a senior author (RJdS) to resolve any discrepancies. Once the full-text articles were identified, two review authors (JL, working with either MA or BJK) independently and in duplicate screened full-text of studies for inclusion, again using Distiller SR, with discrepancies resolved by consensus or discussion with a third author (RJdS). There was excellent agreement between the screeners (kappa=0.95).

The authors (JL, working with either MA or BJK) independently and in duplicate extracted information on

PICO criteria	Definition
Population	Adult (18 years or older) South Asians originating from India, Pakistan, Sri Lanka, Bangladesh, Bhutan and/o Nepal, regardless of their place of residence
Intervention	Lifestyle interventions that target either a diet or a physical exercise component through a multimedia or a behavioural support strategy
Comparator	Routine/standard care
Outcome	Cardiovascular outcomes including incidence of myocardial infarction (fatal and/or non-fatal), incidence of stroke (fatal and/or non-fatal), blood lipids (LDLc (mmol/L), HDLc (mmol/L), non-HDLc (mmol/L if reported directly) and triglycerides (mmol/L)), blood pressure (SBP and DBP (mm Hg)), hypertension (dichotomous, reported as n (%) based on a threshold of 140/90 mm Hg), visceral adipose tissue volume (cm <sup>3</sup> , MRI or CT reported) and incidence of type 2 diabetes self-reported, n (%))

DBP, diastolic blood pressure; HDLc, high-density lipoprotein cholesterol; LDLc, low-density lipoprotein cholesterol; SBP, systolic blood pressure.

study design, focus of intervention, study setting, unit of randomisation, unit of analysis, sample ethnicity, sample size, mean age, age range, sex (% female), baseline health status, intervention, comparator, and main and additional outcomes onto a piloted extraction form. Where necessary, study investigators were contacted via email to obtain further data if such data were not reported in the published paper. The primary author (JL) transferred the extracted data into a review manager (RevMan V.5.3)<sup>28</sup> file, and both MA and BJK independently verified the fidelity of the transfer.

#### Patient and public involvement

No patients or members of the public were included in the design, conduct, reporting or dissemination of this work.

#### **Statistical analysis**

Data for meta-analyses were prepared based on the *Cochrane Handbook for Systematic Reviews*.<sup>29</sup> For continuous outcomes, postintervention scores were used to calculate the mean differences (MDs), along with 95% CIs. However, within-group change scores were used in

Table 2         Study Inclusion/exclusion criteria	
Inclusion criteria	Exclusion criteria
Human studies	Study assesses primary prevention of diabetes, obesity or metabolic syndrome
Study assesses primary prevention of CVD and risk reduction in patients without any history of CVD	Minimum age restriction less than 18
Randomised controlled trials, both individual and cluster randomised and/or factorial 2×2 designs	Active intervention as a comparator, or only one arm or no comparator
Adult (18 years or older) South Asians originating from India, Pakistan, Sri Lanka, Bangladesh, Bhutan and/or Nepal, regardless of their place of residence	Non-inert placebo
Lifestyle intervention must have one diet or physical exercise component or both combined	Study includes a population that is not primarily South Asian (less than 90%)
Lifestyle interventions that have a multimedia component (eg, text messaging) or a behavioural component if it affects at least one of diet or a physical activity component change	
Addresses at least one of the following: incidence of myocardial infarction (fatal and/ or non-fatal), incidence of stroke (fatal and/or non-fatal), blood lipids (LDLc (mmol/L), HDLc (mmol/L), non-HDLc (mmol/L, if reported directly) and triglycerides (mmol/L)), blood pressure (SBP and DBP (mm Hg)), hypertension (dichotomous, reported as n (%) based on a threshold of 140/90 mm Hg), visceral adipose tissue volume (cm <sup>3</sup> , MRI or CT reported) and incidence of type 2 diabetes (self-reported, n (%))	
CVD, cardiovascular disease; DBP, diastolic blood pressure; HDLc, high-density lipoprotein; LDLc, low-blood pressure.	density lipoprotein; SBP, systolic

cases where the statistical treatment of postintervention scores did not accurately represent the true treatment effect reported in the original publication, using the analytical plan (eg, analysis of covariance). For dichotomous outcomes, relative risk (RR) estimates with 95% CIs were used. To help provide clinical context and aid in our quality of evidence assessment, we established minimally important differences (MIDs) for each risk factor that was affected by the intervention.

The authors encountered two main unit of analysis issues: (1) multiple intervention arms and 2) cluster randomised trials. For one of the studies with multiple trial arms/intervention groups,<sup>30</sup> data from the trial arm judged to be the most relevant to the review authors' definition of 'lifestyle (diet and/or physical activity) interventions' in the pairwise comparison (meta-analysis) were used because each trial arm had a unique group of participants allocated to it.<sup>31</sup> For the other two studies with multiple trial arms,<sup>32,33</sup> the effects of the two exercise arms were different from each other for many outcomes, so rather than combining the groups into a single pairwise comparison versus control, the control group was split into half. This was preferable to combining two heterogenous activity arms. Cluster randomised trials were also assessed based on Cochrane guidelines.<sup>31</sup> Most included cluster randomised trials reported individual participant data,<sup>30 34-39</sup> adjusted for the clustering effect, which made it possible to use directly in the authors' meta-analyses. Generic inverse variance meta-analysis was conducted for one of the cluster trials which reported effect estimates adjusted for clustering but not individual participant data.<sup>40</sup> No ongoing studies that have not published/provided results were included in the review. The RevMan calculator<sup>28</sup> was used to calculate SD, SEs or 95% CIs, where necessary. Where these data were not available, values were imputed based on recommendations made by the *Cochrane Handbook*,<sup>31</sup> such as imputing missing SDs for an included study based on SDs from other similarly powered included studies reporting that same outcome.

Where at least two studies were available, Dersimonian and Laird random-effects meta-analyses were performed in RevMan V.5.3.<sup>28</sup> The review authors used the randomeffects model based on prior assumptions of variability across the studies. A fixed-effects model was conducted when fewer than five studies were combined in a metaanalysis because the estimated SD of underlying true effects across studies (tau) cannot be reliably estimated when the number of studies is small.<sup>41</sup> For each metaanalysis, the Cochrane's Q and the  $I^2$  statistic were used to detect and quantify heterogeneity, respectively. If the  $I^2$  statistic was more than 50% and the p value for the  $\chi^2$ test was <0.05, the studies were judged to have substantial heterogeneity between them.<sup>42</sup> Overlaps between CIs of effect estimates were also considered to further assess clinical heterogeneity between trials. Lastly, a funnel plot was created to assess the small study reporting bias when there were 10 or more trials reporting on an outcome.

The funnel plot was examined using Egger's test to ascertain if there was any publication bias.

#### Assessment of risk of bias (ROB) of included studies

Two review authors (JL, working with either MA or BJK) independently assessed study ROB on each of the following domains: random sequence generation, allocation concealment, blinding of participants, personnel and outcome assessors, the proportion of missing outcome data, and whether there was selective reporting of outcomes using the *Cochrane Handbook for Systematic Reviews*<sup>29</sup> (online supplemental appendix 2).

#### **Subgroup analyses**

The authors stratified the pooled effects by the type of intervention to evaluate whether the effect differed between (1) combined diet and physical activity versus usual care interventions, (2) diet-only versus usual care interventions and (3) physical activity only versus usual care interventions. Initially, several subgroup analyses were planned to discern if the effects of the interventions varied across sex (male vs female), age (over 65 vs under 65), nationality, immigration status (SA living in South Asia vs SA living abroad), baseline risk factors (none vs some) and medication use (no drugs vs some drug use). However, subgroup analyses were only undertaken for outcomes that were reported by more than 10 studies to ensure adequate power within each subgroup.<sup>41</sup> In addition, three sensitivity analyses were carried out: (1) excluding studies that were judged to be of high risk based on ROB domains; (2) excluding studies that reported values that were likely erroneously reported (eg, triglyceride levels of 0.8 mmol/L in baseline intervention compared with 4.98 mmol/L in the baseline control (3) group)<sup>43</sup>; and (3) excluding studies led by an author (RB) Singh), which have had a letter of concern published questioning the veracity of data collection, but no formal retraction being issued.<sup>44 45</sup>

#### Assessment of the quality of evidence

The quality of evidence presented in this review was evaluated using GRADE.<sup>46</sup> Two review authors (JL, working with MA or BJK) evaluated the evidence based on ROB, inconsistency, indirectness, imprecision and publication bias for all outcomes reported in the meta-analyses. The following were considered to be MIDs, based on literature: HDLc=minimum of 10% increase,<sup>47</sup> LDLc=0.28 mmol/L,<sup>48</sup> triglycerides=0.90 mmol/L,<sup>48</sup> SBP=5 mm Hg,<sup>49</sup> DBP=5 mm Hg,<sup>49</sup> FPG=0.6 mmol/L,<sup>50</sup> weight change=5–6 kg<sup>51</sup> and BMI=2.3 units. A minimum important change of 2.3 units for BMI corresponds to a 13 lb weight loss, which would bring a 5 ft 5 inches South Asian person with an above ideal BMI ( $\geq$ 23) into the middle of the normal range (18.5–23.0).

#### RESULTS

An electronic search of the databases identified 34 eligible publications (reporting on 33 trials), and one additional study through a manual reference check of included

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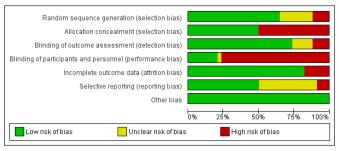
## Additional records identified through other ecords identified Identificatio through datab searching N = 6688 I Records after duplicates removed N = 4439 Records screened N = 4439 Title and Abstract Screening - Records excluded N = 4246 Screening Weighted Kappa = 0.73 Full-text articles as for eligibility N = 193 Full-text articles excluded, with reasons N = 158 Eligibility Weighted Kappa = 0.95 Not a randomized controlled trial (N = 40) Does not include South Asiams (N = 29) Does not include primary prevention of ardiovascular disease or reduction of risk (N = 35) Participants are not adults (N = 4) Does not involve usual care as a comparator (N = 10) Does not involve usual care as a comparator (N = 25) Outcomes of interest not reported (N = 3) Does not have any results reported (N = 12)\* \*note: this includes protocols for studies (N=9) Studies included in qualitative synthesi Include (meta-analysis) N = 35 Studies included in quantitative synthesis (meta-analysis)

**Figure 1** Study Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram.

studies was found (figure 1 and online supplemental appendix 3). The main reasons for exclusion of the 158 out of 193 full-text studies included the study not being an RCT (n=40, 25.3%) and studies not assessing primary prevention of CVD (n=35, 22.2%) (online supplemental appendix 4).

Of the 35 included studies (online supplemental table S1), 26 were parallel-arm RCTs,<sup>10 32 33 43–45 52–72</sup> and 8 were cluster RCTs.<sup>30 34–40</sup> Thirty-one studies were conducted in South Asian countries (20 in India, 5 in Pakistan, 3 in Nepal, 2 in Sri Lanka and 1 in Bangladesh)<sup>30 32-40 43-45 53-60 62-64 6</sup> and 4 studies were conducted outside of Asia (1 in the USA and 3 in Canada).<sup>10 32 52 61</sup> Most participants in the studies had at least one major risk factor for CVD such as diabetes, <sup>33 54 60 63 67-69 71</sup> dyslipidaemia, <sup>43 55 64</sup> hyperten-sion, <sup>35 40 44 45 65 66 70 72</sup> obesity <sup>53 57</sup> or metabolic syndrome. <sup>36 56</sup> Eighteen studies assessed diet alone<sup>34 39 43-45 53-59 62 64 67-69 71</sup>: 5 studies assessed physical activity alone<sup>32 33 60 65 72</sup>; and 12 studies assessed a combination of diet and physical activity modifications.<sup>10</sup> <sup>30</sup> <sup>35–38</sup> <sup>40</sup> <sup>52</sup> <sup>61</sup> <sup>63</sup> <sup>66</sup> <sup>70</sup> The comparator in all of the trials was usual lifestyle/dietary advice, with the exception of three trials in which the comparator was no intervention.<sup>37 58 71</sup> No studies reported on the incidence of fatal or non-fatal MI and/or stroke. Twenty studies reported on blood lipids (HDLc, LDLc and triglycerides)<sup>30363943-4553-60626467-6971</sup>;26studiesreportedonblood pressure (SBP and DBP)<sup>10 30 33-40 43-45 52-55 57 61 62 65-67 69 71 72</sup>:3 studies reported on hypertension<sup>10 52 63</sup>; 2 studies reported on visceral adipose tissue volume<sup>32 56</sup>; and 2 studies

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**Figure 2** ROB graph: review authors' judgements about each ROB item presented as percentages across all included studies. ROB, risk of bias.

reported on the incidence of type 2 diabetes.<sup>10 52</sup> No studies directly reported on non-HDLc.

Figures 2 and 3 present summary ROB assessments. A detailed ROB assessment for each study appears in online supplemental appendix 2. The domains for which the studies were judged to be at the lowest ROB were random sequence generation (70% low risk), blinding of outcome assessment (72% low risk) and incomplete outcome data across most of the outcomes (78% low risk), while the highest ROB was associated with blinding of participants and personnel across all outcomes (82% high risk). Blinding of participants and personnel is typically not feasible for complex, food-based diet and physical activity interventions. We identified the domain of selective reporting to have the highest proportion of unclear bias as we were unable to find relevant information in registered protocols or other study-related sources (none of the authors we contacted for missing protocols provided any additional information). We present the GRADE assessment with reasons for downgrading in the 'summary of findings' tables (tables 3-8), created using the GRADEpro Guideline Development Tool.<sup>73</sup>

## Diet and physical activity interventions versus usual care Blood pressure

## Systolic blood pressure

Based on the pooled data from 12 studies (14 589 participants), with an average follow-up length of 11 months (minimum (min)=3, maximum (max)=24) diet and physical activity interventions significantly reduce SBP (MD -2.72 mm Hg, 95% CI -4.11 to -1.33 mm Hg), compared with usual care (online supplemental appendix 5, eFigure 1.1;  $\bigoplus \bigoplus \bigoplus \bigcirc$ , moderate). However, the upper bound of the CI, which is -4.11 mm Hg, still does not meet the MID of -5.0 mm Hg and therefore is not clinically significant. There is no significant funnel plot asymmetry (Egger's p=0.34) (online supplemental appendix 5, eFigure 1.1b). The reported heterogeneity is high  $(I^2=54\%, p=0.01)$ after removing one study<sup>10</sup> from the sensitivity analysis. There is no statistically significant heterogeneity between the subgroups of people taking medications and those who did not take any medications throughout the trials (I<sup>2</sup>=41.8%, p=0.19).

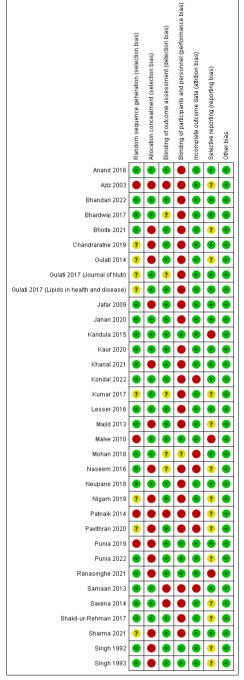


Figure 3 ROB summary: review authors' judgements about each ROB item for each included study. ROB, risk of bias.

#### Diastolic blood pressure

Based on the pooled data from 11 studies (14 527 participants), with an average follow-up length of 11 months (min=3, max=24), diet and physical activity interventions significantly reduce DBP (MD –1.53 mm Hg, 95% CI –2.57 to –1.01 mm Hg), compared with usual care (online supplemental appendix 5, eFigure 1.2;  $\bigoplus \bigoplus \bigcirc \bigcirc$ , low). However, the upper bound of the CI, which is –2.57 mm Hg, still does not meet the MID of –5.0 mm Hg and therefore is not clinically significant. There is significant funnel plot asymmetry (Egger's p=0.013) (online supplemental eFigure 1.2b). The reported heterogeneity is high <u>d</u>

 $(I^2=67\%, p=0.0008)$  after removing one study<sup>10</sup> from the sensitivity analysis. There is no statistically significant heterogeneity between the two subgroups of people taking medications and those who did not take any medications throughout the studies ( $I^2=38.3\%, p=0.20$ ).

#### Hypertension

Based on the pooled data from two studies with low heterogeneity ( $I^2=0\%$ , p=0.84; 635 participants), and an average follow-up length of 7.5 (min=3, max-12) months, there is no statistically significant difference in hypertension with provision of a combined diet and physical activity intervention (RR=0.47, 95% CI 0.17 to 1.35) compared with usual care in this sensitivity analysis (online supplemental appendix 5, eFigure 1.3;  $\bigoplus \bigoplus \bigoplus \bigcirc$ , moderate).

#### **Blood lipids**

None of the 12 combined diet and physical activity interventions reported on any of the blood lipid parameters (HDLc, LDLc and triglycerides).

#### Incidence of type 2 diabetes

Based on the pooled data from two studies with low heterogeneity ( $I^2=0\%$ , p=0.40; 661 participants) and an average follow-up length of 9 (min=6, max=12) months, there is no statistically significant difference in the incidence of type 2 diabetes with provision of a combined diet and physical activity intervention (RR=1.25, 95% CI 0.39 to 4.06) compared with usual care (online supplemental appendix 5, eFigure 1.4;  $\bigoplus \bigoplus \bigcirc$ , moderate).

#### Additional outcomes

Diet and physical activity interventions significantly reduced BMI (MD -1.07 kg/m<sup>2</sup>, 95% CI -1.27 kg/m<sup>2</sup> to  $-0.88 \text{ kg/m}^2$ ) (online supplemental appendix 5, eFigure 1.5;  $\bigoplus \bigoplus \bigoplus \bigoplus$ , high; average follow-up length=8.25 months (min=3, max=12)), weight (MD -2.70 kg, 95%CI -3.17 to -2.27 kg) (online supplemental appendix 5, eFigure 1.6;  $\bigoplus \bigoplus \bigoplus \bigoplus$ , high; average follow-up length=10 months (min=6, max=12)), waist circumference (MD -3.07 cm, 95% CI -5.15 to -0.98 cm) (online supplemental appendix 5, eFigure 1.7;  $\bigoplus \bigoplus \bigoplus \bigcirc$ , moderate; average follow-up length=8 months (min=6, max=12) and FPG levels (MD -0.77 mmol/L, 95% CI -1.2 to -0.35 mmol/L) (online supplemental appendix 5, eFigure 1.8;  $\oplus \oplus \oplus \odot$ , moderate; average follow-up length: 9 months (min=6, max=12)), compared with usual care. The CI for FPG includes the MID (0.6 mmol/L). Therefore, we do not have enough evidence to say if it is clinically significant. However, for the other additional outcomes, CIs lie to the right of the MIDs and therefore are not clinically significant. None of the trials reported on IS or insulin resistance (HOMA-IR).

#### Diet-only interventions versus usual care Blood pressure

#### Systolic blood pressure

Based on the pooled data from eight studies (1495 participants), with an average follow-up length of 4 months

Outcomes	Anticipated absolute effects* (95% CI)		Relative		Certainty of the
	Risk with usual care	Risk with diet+physical	effect (95% CI)	Participants, n (studies)	evidence (GRADE)
SBP (mm Hg)	The mean SBP was 130.63 mm Hg.	MD 2.72 mm Hg lower (from 4.11 lower to 1.33 lower)	-	14 589 (12 RCTs)	⊕⊕⊕⊖ Moderate†
SBP (mm Hg), no medications	The mean SBP, no medications, was 127.4 mm Hg.	MD 1.72 mm Hg lower (from 3.71 lower to 0.27 higher)	-	11 715 (5 RCTs)	⊕⊕⊕⊕High
SBP (mm Hg), medications	The mean SBP, medications, was 133.86 mm Hg.	MD 3.61 mm Hg lower (from 5.63 lower to 1.59 lower)	-	2874 (7 RCTs)	⊕⊕⊕ ⊖ Moderate‡
DBP (mm Hg)	The mean DBP was 85.39 mm Hg.	MD 1.53 mm Hg lower (from 2.57 lower to 0.48 lower)	-	14 527 (11 RCTs)	⊕⊕ ○○ Low§¶
DBP (mm Hg), no medications	The mean DBP, no medications, was 84.93 mm Hg.	MD 0.67 mm Hg lower (from 2.36 lower to 1.01 higher)	_	11 653 (4 RCTs)	⊕⊕⊕ ⊖ Moderate**
DBP (mm Hg), medications	The mean DBP, medications, was 85.85 mm Hg.	MD 2.05 mm Hg lower (from 3.35 lower to 0.75 lower)	-	2874 (7 RCTs)	⊕⊕⊕ ⊖ Moderate¶
Hypertension (yes/ no)	34 per 1000	16 per 1000 (6–46)	RR 0.47 (0.17– 1.35)	635 (2 RCTs)	⊕⊕⊕ ⊖ Moderate‡‡
Incidence of diabetes (yes/no)	15 per 1000	18 per 1000 (6–60)	RR 1.25 (0.39– 4.06)	661 (2 RCTs)	⊕⊕⊕ ⊖ Moderate‡‡

\*I<sup>2</sup> statistic=54%, p=0.01, implying significant heterogeneity between studies without a lot of overlap in CIs.

+1<sup>2</sup> statistic=58%, p=0.03, implying significant heterogeneity between studies without a lot of overlap in Cls.

↓1<sup>2</sup> statistic=67%, p=0.0008, implying significant heterogeneity between studies without a lot of overlap in Cls.

§Egger's test: p=0.013.

¶I<sup>2</sup> statistic=61%, p=0.02, implying significant heterogeneity between studies without a lot of overlap in Cls.

\*\*1<sup>2</sup> statistic=69%, p=0.02, implying significant heterogeneity between studies without a lot of overlap in CIs.

††Optimal Information Size (OIS) not met.

CI, confidence interval; DBP, diastolic blood pressure; MD, mean difference; RCT, randomised controlled trial; RR, relative risk; SBP, systolic blood pressure.

(min=1, max=12), diet-only interventions do not significantly reduce SBP (MD –1.25 mm Hg, 95% CI –2.66 to 0.16 mm Hg), compared with usual care (online supplemental appendix 5, eFigure 2.1;  $\bigoplus \bigoplus \bigoplus \bigoplus$ , high). The reported heterogeneity is not of concern (I<sup>2</sup>=0%, p=0.63) after removing two high ROB studies<sup>34</sup> <sup>62</sup> and two other studies (Singh *et al*<sup>44</sup> <sup>45</sup>) with suspected incorrect data<sup>74</sup> in this sensitivity analysis (online supplemental appendix 5, eFigure 2.1). There is no statistically significant heterogeneity between the two subgroups of people taking medications and those who did not take any medications throughout the studies (I<sup>2</sup>=0%, p=0.88).

#### Diastolic blood pressure

Based on the pooled data from eight studies (1495 participants), with an average follow-up length of 4 months (min=1, max=12), diet-only interventions significantly reduce DBP (MD -2.05 mm Hg, 95% CI -2.93 to -1.16 mm Hg), compared with usual care (online supplemental appendix 5, eFigure 2.2;  $\bigoplus \bigoplus \bigoplus \bigoplus$ , high). However, the upper bound of the CI, which is -2.9 mm Hg, still does not meet the MID of -5.0 mm Hg and therefore is not clinically significant. The reported heterogeneity is not of concern (I<sup>2</sup>=0%, p=0.66) after removing the high-risk studies<sup>34 44 45 62</sup> in this sensitivity analysis (online supplemental appendix 5, eFigure 2.2). There is no statistically significant heterogeneity between the two subgroups of people taking medications and those who did not take any medications throughout the studies (I<sup>2</sup>=0%, p=0.53).

# Blood lipids

#### Triglycerides

Based on the pooled data from seven studies (1337 participants), with an average follow-up length of 4 months (min=1, max=6), there is a statistically significant difference in triglyceride concentrations with the

	Anticipated absolute effects* (95% CI)		Relative		Certainty of the	
Outcomes	Risk with usual care	Risk with diet+physical	effect (95% CI)	Participants, n (studies)	evidence (GRADE)	
BMI (kg/m²)	The mean BMI was 24.75 kg/m <sup>2</sup> .	Mean 1.07 kg/m <sup>2</sup> lower (from 1.27 lower to 0.88 lower)	-	871 (3 RCTs)	⊕⊕⊕⊕High	
Weight change (kg)	The mean weight was 70.45 kg.	Mean 2.72 kg lower (from 3.17 lower to 2.27 lower)	-	814 (3 RCTs)	⊕⊕⊕High	
Waist circumference (cm)	The mean waist circumference was 94.43 cm.	MD 3.07 cm lower (from 5.15 lower to 0.98 lower)	-	451 (3 RCTs)	⊕⊕⊕⊖ Moderate†	
FPG (mmol/L)	The mean FPG was 6.55 mmol/L.	MD 0.77 mmol/L lower (from 1.2 lower to 0.35 lower)	-	331 (2 RCTs)	⊕⊕⊕⊖ Moderate†	

Table 4 Comparison 1: diet and physical activity interventions versus usual care (additional outcomes)

\*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).

†OIS not met.

BMI, body mass index; CI, confidence interval; FPG, fasting plasma glucose; MD, mean difference; RCT, randomised controlled trial.

provision of diet only interventions (MD –0.12 mmol/L, 95% CI –0.19 to –0.06 mmol/L), compared with usual care (online supplemental appendix 5, eFigure 2.3;  $\oplus \oplus \oplus \odot$ , moderate). However, the upper bound of the 95% CI, –0.19 mmol/L, still does not meet the MID of 0.90 mmol/L and therefore is not clinically significant. The reported heterogeneity is low (I<sup>2</sup>=50%, p=0.06) after removing three studies<sup>44 45 68</sup> from the sensitivity analysis (online supplemental appendix 5, eFigure 2.3). There is statistically significant heterogeneity between the two subgroups of people taking medications and those who did not take any medications throughout the studies (I<sup>2</sup>=76.2%, p=0.04).

#### High-density lipoprotein cholesterol

Based on the pooled data from 10 studies (1620 participants), with an average follow-up length of 3 months (min=1, max=6), there is no statistically significant difference in HDLc concentrations with the provision of diet-only interventions (MD 0.03 mmol/L, 95% CI -0.02 mmol/L to 0.07 mmol/L), compared with usual care (online supplemental appendix 5, eFigure 2.4;  $\oplus \oplus \odot$ , low). There is significant heterogeneity (I<sup>2</sup>=84%, p=<0.001) and funnel plot asymmetry (Egger's p=0.003) (online supplemental appendix 5, eFigure 2.4b) even after removing high ROB studies<sup>44 45 62 68</sup> (online supplemental appendix 5, eFigure 2.4). There is no statistically significant heterogeneity between the two subgroups of people taking medications and those who did not take any medications throughout the trials (I<sup>2</sup>=0%, p=0.59).

#### Low-density lipoprotein cholesterol

Based on the pooled data from 11 trials (1701 participants), with an average follow-up length of 3 months (min=1, max=6), diet-only interventions significantly lowered LDLc concentration (MD -0.19 mmol/L, 95% CI -0.32 to -0.06 mmol/L), compared with usual care (online supplemental appendix 5, eFigure 2.5;  $\oplus \oplus^{\circ\circ}$ , low). The CI for LDLc includes the MID (0.28 mmol/L).<sup>48</sup> Therefore, we do not have enough evidence to say if it is clinically significant. There is significant funnel plot asymmetry (Egger's p=0.03) (online supplemental appendix 5, eFigure 2.5b). The reported heterogeneity persists (I<sup>2</sup>=80%, p=<0.001) even after removing two high-risk studies<sup>62 68</sup> (online supplemental appendix 5, eFigure 2.5). However, there is no statistically significant heterogeneity between the two subgroups of people taking medications and those who did not take any medications throughout the trials (I<sup>2</sup>=48.1%, p=0.17).

#### Additional outcomes

Diet-only interventions significantly reduce BMI (MD  $-0.39 \text{ kg/m}^2$ , 95% CI  $-0.64 \text{ to } -0.14 \text{ kg/m}^2$ ) (online supplemental appendix 5, eFigure 2.6;  $\oplus \oplus \oplus \oplus$ , high), weight (MD -1.35 kg, 95% CI -2.38 to -0.32 kg) (online supplemental appendix 5, eFigure 2.7;  $\oplus \oplus \oplus \odot$ , moderate; and FPG levels (MD -0.8 mmol/L; 95% CI -0.33 to -0.03 mmol/L) (online supplemental appendix 5, eFigure 2.8;  $\oplus \oplus \oplus \odot$ , moderate), with an average length of follow-up being 3-4 months (min=1, max=6), compared with usual care. However, the upper bounds of the CIs for BMI, weight change or FPG still do not meet their MIDs and therefore are not clinically significant. Diet-only interventions did not reduce waist circumference (online supplemental appendix 5, eFigure 2.9;  $\bigoplus \bigoplus \bigoplus \bigoplus$ , high; average length of follow-up: 4 months, min=1, max=6) or insulin resistance (HOMA-IR) (online supplemental appendix 5, eFigure 2.10;  $\oplus \oplus \oplus \odot$ , moderate; average length of follow-up: 4 months, min=2, max-6). There were no studies which reported on IS.

Table 5         Comparison 2: diet-only intervention versus usual care (main outcomes)					
	Anticipated absolute effects* (	95% CI)	Relative effect	Participants,	Certainty of the
Outcomes	Risk with usual care	Risk with diet	(95% CI)	n (studies)	evidence (GRADE)
Triglycerides (mmol/L)	The mean triglycerides was 1.59 mmol/L.	MD 0.12 mmol/L lower (0.10 lower to 0.06 lower)	-	1337 (7 RCTs)	⊕⊕⊕⊖ Moderate†
Triglycerides (mmol/L), no medications	The mean triglycerides, no medications, was 1.57 mmol/L.	MD 0.16 mmol/L lower (0.24 lower to 0.08 lower)	-	1003 (5 RCTs)	⊕⊕⊕⊕High
Triglycerides (mmol/L) - medications	The mean triglycerides, medications, was 1.24 mmol/L.	MD 0.01 mmol/L lower (0.13 lower to 0.06 lower)	-	334 (2 RCTs)	⊕⊕⊕⊖ Moderate‡
HDLc (mmol/L)	The mean HDLc was 1.06 mmol/L.	MD 0.03 mmol/L higher (0.02 lower to 0.07 higher)	-	1620 (10 RCTs)	⊕⊕⊖⊖ Low§¶
HDLc (mmol/L), no medications	The mean HDLc, no medications, was 1.06 mmol/L.	MD 0.02 mmol/L higher (0.03 lower to 0.08 higher)	-	1286 (8 RCTs)	⊕⊕⊕⊖ Moderate**
HDLc (mmol/L), medications	The mean HDLc, medications, was 0.54 mmol/L.	MD 0.04 mmol/L higher (0.01 lower to 0.07 higher)	-	334 (2 RCTs)	⊕⊕⊕⊖ Moderate‡
LDLc (mmol/L)	The mean LDLc was 2.92 mmol/L.	MD 0.19 mmol/L lower (0.32 lower to 0.06 lower)	-	1701 (11 RCTs)	⊕⊕⊖⊖ Low††‡‡
LDLc, (mmol/L) no medications	The mean LDLc, no medications, was 3.13 mmol/L.	MD 0.23 mmol/L lower (0.37 lower to 0.08 lower)	-	1352 (9 RCTs)	⊕⊕⊕⊖ Moderate††
LDLc (mmol/L), medications	The mean LDLc, medications, was 2.70 mmol/L.	MD 0.2 mmol/L lower (0.3 lower to 0.34 higher)	-	334 (2 RCTs)	⊕⊕⊕⊖ Moderate‡
SBP (mm Hg)	The mean SBP was 129.54 mm Hg.	MD 1.25 mm Hg lower (2.66 lower to 0.16 higher)	-	1495 (8 RCTs)	⊕⊕⊕⊕High
SBP (mm Hg), no medications	The mean SBP, no medications, was 132.16 mm Hg.	MD 1.19 mm Hg lower (2.78 lower to 0.39 higher)	-	1146 (6 RCTs)	⊕⊕⊕⊕High
SBP (mm Hg), medications	The mean SBP, medications was 126.92 mm Hg.	MD 1.47 mm Hg lower (4.57 lower to 1.64 higher)	-	349 (2 RCTs)	⊕⊕⊕⊖ Moderate‡
DBP (mm Hg)	The mean DBP was 81.67 mm Hg.	MD 2.05 mm Hg lower (from 2.93 lower to 1.16 lower)	-	1495 (8 RCTs)	⊕⊕⊕High
DBP (mm Hg), no medications	The mean DBP, no medications, was 82.34 mm Hg.	2.22 mm Hg lower (from 3.26 lower to 1.19 lower)	-	1146 (6 RCTs)	⊕⊕⊕⊕High
DBP (mm Hg), medications	The mean DBP, medications, was 81 mm Hg.	MD 1.59 mm Hg lower (from 3.27 lower to 0.1 higher)	-	349 (2 RCTs)	⊕⊕⊕⊖ Moderate‡

.I<sup>2</sup> statistic for subgroup differences is 76.2%, (P=0.04), implying there is significant heterogeneity between the two subgroups of medication use

‡OIS is not met when high-risk studies are removed.

 $I^2$  statistic =84%, p=<0.00001, implying significant heterogeneity between studies without a lot of overlap in CIs. ¶Egger's test: p=0.003.

\*\*1<sup>2</sup> statistic =84%, p=<0.00001, implying significant heterogeneity between studies without a lot of overlap in CIs.

++1<sup>2</sup> statistic =80%, p=<0.00001, implying significant heterogeneity between studies without a lot of overlap in CIs.

‡‡Egger's test: p=0.03.

§§

CI, confidence interval; DBP, diastolic blood pressure; HDLc, high-density lipoprotein; LDLc, low-density lipoprotein; MD, mean difference; RCT, randomised controlled trial; SBP, systolic blood pressure.

Physical activity only versus usual care Blood pressure Systolic blood pressure Based on the pooled data from two studies with low heterogeneity ( $I^2 = 18\%$ , p=0.27; 103 participants), and an average follow-up length of 2 months (min=2, max=2),

Outcomes	Anticipated absolute effects* (95% CI)		Relative		Certainty of the
	Risk with usual care	Risk with diet	effect (95% CI)	Participants, n (studies)	evidence (GRADE)
BMI (kg/m²)	The mean BMI was 27.86 kg/ m <sup>2</sup> .	MD 0.39 kg/m <sup>2</sup> lower (from 0.64 lower to 0.14 lower)	-	1415 (7 RCTs)	⊕⊕⊕⊕High
Weight change (kg)	The mean weight was 73.37 kg.	MD 1.35 kg lower (from 2.38 lower to 0.32 lower)	-	1563 (9 RCTs)	⊕⊕⊕⊖ Moderate†
Weight change (kg), medications	The mean weight, medications was 70.00 kg.	MD 1.06 kg lower (from 4.07 lower to 1.95 higher)	-	349 (2 RCTs)	⊕○○○ Very lowद
Weight change (kg), no medications	The mean weight, no medications was 76.75 kg.	MD 0.74 kg lower (from 1.22 lower to 0.26 lower)	-	1154 (6 RCTs)	⊕⊕⊕⊕High
FPG (mmol/L)	The mean FPG was 5.17 mmol/L.	MD 0.18 mmol/L lower (from 0.33 lower to 0.03 lower)	-	1412 (7 RCTs)	⊕⊕⊕⊖ Moderate†
Waist circumference (cm)	The mean waist circumference was 97.34 cm.	MD 0.25 cm lower (from 0.82 lower to 0.31 higher)	-	641 (5 RCTs)	⊕⊕⊕High
Homa-Ir	The mean HOMA-IR was 4.70	MD 0.02 lower (from 0.48 lower to 0.43 higher)	-	371 (2 RCTs)	⊕⊕⊕⊖ Moderate‡

<sup>†</sup>Pavithran et al<sup>69</sup> has a high ROB with some uncertainties in the assessment. ROB, risk of bias

‡OIS is not met when high-risk studies are removed.

High ROB that possibly contributes to the inconsistency with  $l^2$  statistic = 81%,

 $|||^2$  statistic = 81%, p=0.02, implying significant heterogeneity without a lot of overlap in CIs.

BMI, body mass index; CI, confidence interval; FPG, fasting plasma glucose; HOMA-IR, homeostatic model assessment of insulin resistance; MD, mean difference; RCT, randomised controlled trial; ROB, risk of bias.

there is a statistically significant difference in SBP (MD –9.7 mm Hg; 95% CI –11.05 to –8.35 mm Hg), between the provision of a physical activity intervention and usual care (online supplemental appendix 5, eFigure 3.1  $\oplus \oplus \oplus \odot$ , moderate). The CI lies completely to the left of the MID (5 mm Hg) and is therefore clinically and statistically significant.

#### Diastolic blood pressure

Based on the pooled data from two studies with low heterogeneity (I<sup>2</sup>=17%, p=0.27; 103 participants) and an average follow-up length of 2 months (min=2, max=2), there is a statistically significant difference in DBP (MD -7.29 mm Hg, 95% CI -8.42 to -6.16 mm Hg) between the provision of a physical activity intervention and usual care (online supplemental appendix 5, eFigure 3.2;  $\oplus \oplus \oplus \odot$ , moderate). The CI lies completely to the left of the MID (5 mm Hg) and is therefore clinically and statistically significant.

#### **Blood lipids**

#### High-density lipoprotein cholesterol

Based on the pooled data from two studies with low heterogeneity ( $I^2=0\%$ , p=0.49; 183 participants), and an

average follow-up length of 3 months (min=3, max=3), there is a statistically significant increase in HDLc (MD 0.08 mmol/L, 95% CI 0.04 to 0.11 mmol/L) between the provision of a physical activity intervention and usual care (online supplemental appendix 5, eFigure 3.3;  $\oplus \oplus \oplus \odot$ , moderate). However, the CI includes the MID (a minimum 10% increase in HDLc). Therefore, we do not have enough evidence to suggest whether it is clinically significant.

## Low-density lipoprotein cholesterol

Based on the pooled data from two studies with low heterogeneity (I<sup>2</sup>=77%, p=0.01; 183 participants) and an average follow-up length of 3 months (min=3, max=3), there is no statistically significant difference in LDLc (MD –0.02 mmol/L; 95% CI –0.10 to 0.05 mmol/L) between the provision of a physical activity intervention and usual care (online supplemental appendix 5, eFigure 3.4;  $\oplus \oplus^{OO}$ , low).

#### Additional outcomes

Physical activity only interventions did not reduce BMI, weight, waist circumference or FPG levels (online supplemental appendix 5, eFigures 3.5-3.8;  $\bigoplus \bigoplus \bigoplus \bigcirc$ , moderate;

Outcomes	Anticipated absolute effects* (95% CI)		Relative		Certainty of the
	Risk with (usual care)	Risk with (physical activity <b>)</b>	effect (95% CI)	Participants, n (studies)	evidence (GRADE)
SBP (mm Hg)	The mean SBP was 145.8 mm Hg.	MD 9.7 mm Hg lower (from 11.05 lower to 8.35 lower)	-	103 (2 RCTs)	⊕⊕⊕⊖ Moderate†
DBP (mm Hg)	The mean DBP was 93.1 mm Hg.	MD 7.29 mm Hg lower (from 8.42 lower to 6.16 lower)	-	103 (2 RCTs)	⊕⊕⊕⊖ Moderate†
HDLc (mmol/L)	The mean HDL was 1.17 mmol/L.	MD 0.08 mmol/L higher (from 0.04 higher to 0.11 higher)	-	183 (2 RCTs)	⊕⊕⊕⊖ Moderate†
LDLc (mmol/L)	The mean LDL was 2.73 mmol/L	MD 0.02 mmol/L lower (from 0.1 lower to 0.05 higher)	-	183 (2 RCTs)	⊕⊕○○ Low†‡

†OIS not met.

↓l<sup>2</sup>statistitc =77%, p=0.01, implying significant heterogeneity between studies without a lot of overlap in Cls.

.. ..

CI, confidence interval; DBP, diastolic blood pressure; HDLc, high-density lipoprotein; LDLc, low-density lipoprotein; MD, mean difference; RCT, randomised condtrolled trial; SBP, systolic blood pressure.

average length of follow-up: 3 months, min=3, max=3). There were no studies which reported on insulin resistance (HOMA-IR) or IS in this review.

#### **Other main outcomes**

#### Visceral adipose tissue volume

In two studies (143 participants),<sup>32 56</sup> there is no significant effect of diet or physical activity interventions on visceral adipose tissue volume (p=0.90 and p=0.35, respectively) ( $\bigoplus \bigoplus \bigcirc$ , moderate; average follow-up length of 4.5 months; min=3, max=6).

#### DISCUSSION

In thirty-five studies assessing the effect of diet and/or physical activity interventions in adult South Asians at risk for CVD, combined diet and physical activity interventions (n=12) significantly lowered SBP and DBP, BMI, weight, waist circumference and FPG. Studies that used a diet only intervention approach (n=18) significantly lowered DBP, triglycerides, LDLc, BMI, weight and FPG levels. Studies which used a physical activity only intervention (n=5) significantly lowered SBP and DBP and

Table 8         Comparison 3: physical activity versus usual care (additional outcomes)						
	Anticipated absolute effects* (95% CI)		Relative	Participants,	Certainty of the	
Outcomes	Risk with (usual care <b>)</b>	Risk with (physical activity <b>)</b>	effect (95% CI)	n (studies)	evidence (GRADE)	
Weight change (kg)	The mean weight was 68.25 kg.	MD 0.43 kg higher (from 0.82 lower to 1.68 higher)	-	161 (2 RCTs)	⊕⊕⊕⊖ Moderate†	
BMI (kg/m <sup>2</sup> )	The mean BMI was 27.0 kg/m <sup>2</sup> .	MD 0.14 kg/m <sup>2</sup> lower (from 0.63 lower to 0.36 higher)	-	161 (2 RCTs)	⊕⊕⊕⊖ Moderate†	
Waist circumference (cm)	The mean waist circumference was 90.75 cm.	MD 0.2 cm lower (from 1.03 lower to 0.63 higher)	-	161 (2 RCTs)	⊕⊕⊕⊖ Moderate†	
FPG (mmol/L)	The mean FPG was 6.36 mmol/L.	MD 0.06 mmol/L higher (from 0.09 lower to 0.22 higher)	-	161 (2 RCTs)	⊕⊕⊕⊖ Moderate†	

\*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).

†OIS not met.

BMI, body mass index; CI, confidence interval; FPG, fasting plasma glucose; MD, mean difference; RCT, randomised controlled trial.

increased HDLc. The quality of evidence was moderate overall. However, improvements were of very modest effect size and were not clinically significant for the most part. Nonetheless, the results of the review suggest that diet and/or physical activity interventions likely result in a slight improvement in cardiovascular risk in adult South Asians.<sup>75</sup>

Findings from two recent systematic reviews that assessed the effects of diet and/or physical activity interventions on cardiovascular risk in non-South Asian adults without glucose impairment<sup>4</sup> and in a population at increased risk<sup>29</sup> are comparable to our study. Zhang *et al*<sup>p</sup> reviewed 79 studies, of which at least 21 studies used a combined diet and physical activity intervention, and showed that combined diet and physical activity interventions significantly improved all blood lipid (HDLc (0.03 mmol/L, 95% CI -0.01 to 0.04), LDLc (-0.09 mmol/L, 95% CI -0.13 to -0.04), triglycerides (-0.08 mmol/L, 95% CI - 0.14 to - 0.03) and blood pressure outcomes (SBP (-2.16 mm Hg, 95% CI -2.9 to -1.39) and DBP (-1.83 mm Hg, 95% CI -2.34 to -1.31)). Sisti *et al*<sup>76</sup> reviewed 36 studies administering a multifactorial intervention consisting of individual counselling and found that the intervention significantly improved blood lipid concentrations (LDLc (-0.21 mmol/L, 95% CI -0.36 to -0.05), blood pressure (SBP (-3.34 mm Hg, 95% CI -4.70 to -1.97) and DBP (-2.98 mm Hg, 95% CI -4.15 to -1.81)), similar to our study.

Most of the studies included in this review (n=31, 88.6%)were conducted within South Asia. Three of the four trials conducted outside South Asia assessed the effects of a combined diet and physical activity intervention on cardiovascular risk (38% of the eight trials that assessed this), while the fourth trial assessed the effects of a physical activity intervention only on a cardiovascular risk factor (33% of the three trials that assessed this). The results of the four trials conducted outside South Asia were consistent with the interventions on cardiovascular risk conducted within South Asia. In both locations, no effects were observed. However, our findings related to the effects of diet and/or physical activity interventions on cardiovascular risk are largely based on a homogeneous South Asian population residing in India and Pakistan. Thus, the generalisability of our findings to South Asian populations living outside of the Indian subcontinent is limited. In addition, most of the studies (n=31, 88.6%)were conducted within the last decade. Thus, the risk of temporality affecting the baseline risk and the relationship being assessed in this review is minimal.

Moreover, the included diet-only trials assessed very diverse nutrition interventions: a lower-carbohydrate diet (n=6 trials, 677 participants), a low sodium ratio (n=2 trials, 1818 participants), a lower saturated-fat diet (n=1 trial, 66 participants) or supplementing a regular diet with a single food such as oats, flaxseed, wheatgrass, guava, honey, high protein, highfibre supplement and/or *Aegle marmelos* leaf juice (n=8 trials, 661 participants). The blood pressure-lowering and/or lipid profile-improving effect we see in our review may be due to the nutrient profiles of such foods (ie, foods higher in dietary protein, fibre, unsaturated fats and/or potassium). Many other reviews and clinical trials conducted in South Asians have shown favourable effects of similar diet modifications on reducing CVD risk. For example, Dixit *et al*<sup>77</sup> showed that improving macronutrient quality, such as replacing refined carbohydrates like white rice with ancient grains such as brown rice, and adjusting macronutrient quantities (ie, lower carbohydrate intake) can improve risk factors for CVD such as blood lipid profiles and the onset of type 2 diabetes in South Asians, perhaps due to a combination of fibre, proteins, vitamins, phytochemicals and minerals found in grains. Kalita *et al*<sup>78</sup> showed that incorporating almonds in the diet improved blood lipid profiles of HDLc and LDLc in South Asians, attributing the beneficial effect to the healthy fatty acid composition of almonds that may prevent LDLc oxidation. One of the studies included in this review<sup>53</sup> tested the effect of a low-carbohydrate, vegetarian diet, which has also been shown to be associated with fewer cardiometabolic risk factors in non-South Asian and South Asian populations. A study conducted by Jenkins et al in a predominantly non-South Asian population showed a remarkable improvement in lipid concentrations (lower LDLc levels: -8.1% (p=0.002) and reduced blood pressure (SBP -1.9% (p=0.052) and DBP: -2.4% (p=0.02)) in hyperlipidaemic patients given a low-carbohydrate, vegetarian diet.<sup>79</sup> Similarly, according to the Mediators of Atherosclerosis in South Asians living in America prospective cohort study, vegetarians were more likely to have lower total cholesterol levels, LDLc levels, BMI and fasting glucose levels.<sup>80</sup> The protective effects of a vegetarian diet appear to persist across rural and urban environments; in a study conducted in India, both rural and urban participants consuming a vegetarian diet (one-third of them) were found to have lower levels of total cholesterol, LDLc, triglycerides, FPG and DBP than meat eaters.<sup>81</sup>

Only five relatively small trials that assessed the impact of physical activity only on cardiovascular risk factors in South Asians were identified in this review. Interventions focused on physical activity alone improved SBP, DBP and HDLc. The American Heart Association and the American College of Cardiology have shown a modest amount of evidence supporting physical activity's role in reducing the risk of CVD.<sup>82</sup> According to Nystoriak and Bhatnagar,<sup>83</sup> regular moderate to intense exercise can reduce SBP by 3.4 mm Hg and DBP by 2.4 mm Hg, while endurance training is associated with a particular increase in HDLc levels. This is similar to the findings of this review. A recommendation for physical activity in South Asians as an intervention to reduce cardiovascular risk seems appropriate.

Combined diet and physical activity interventions showed similar benefits in cardiovascular risk markers. A synergistic effect of combined diet plus physical activity interventions has been shown in other trials and reviews conducted in the more extensively studied non-South Asian populations.<sup>8 76 84</sup> For example, Gepner *et al*, found that during weight maintenance following weight loss on either a low-fat or a Mediterranean diet, the addition of exercise attenuated waist circumference rebound and the accompanying adverse changes in the lipid profile when the intervention ceased.<sup>84</sup> The addition of physical activity to weight loss diets may be of particular benefit to South Asians, who have a propensity for visceral fat storage even with a normal BMI. The postulated mechanism of action and efficacy for such combined interventions likely does not differ across ethnicities because the underlying biology of atherosclerosis and subsequent CVD is similar across South Asian and non-South Asian populations.<sup>85</sup> The added benefit of combined diet and physical activity interventions for cardiovascular risk factor management is more strongly related to the synergistic effects of the interventions, than to baseline characteristics of a given population.<sup>8</sup> Thus, even though South Asians may enter such studies with an increased risk factor burden compared with other groups, if their response to the intervention is typical, it is reasonable to expect a synergistic effect of combined diet and physical activity interventions in South Asians as well as any other population.

Furthermore, diet and physical activity in combination did not significantly reduce cardiovascular risk more than diet or physical activity interventions alone. The nature of the combined diet and physical activity interventions included in the review may have limited the large beneficial effects on cardiovascular risk factors often observed in other studies. Combined diet and physical activity interventions employed a multipronged approach to behavioural change. Eleven out of the 12 studies disseminated health messages either through a digital media platform (n=5) or through personnel (n=6), while the final study combined all such approaches in addition to administering behavioural change focused experiential activities in a controlled setting. It is plausible that multicomponent interventions, with digital and personnel involvement, have low adherence rates, compared with rigorously planned and delivered specific, targeted strategies (ie, making one small change in the diet or adding one component of physical activity). Several other studies have provided support for an active approach to behavioural change that focuses on changing the environment of individuals, modelling behaviours, and constant feedback to be more effective and improve adherence rates among the population.<sup>86 87</sup>

An encouraging finding of this review is that the improvement in CVD risk factors appears independent of baseline cardiovascular risk. In the 29 studies that enrolled participants at increased risk of CVD (eg, those with a diagnosis of metabolic syndrome, dyslipidaemia, obesity, diabetes and/ or hypertension), improvements in SBP, DBP, triglycerides, LDLc, BMI, weight and FPG were similar to those of the studies that did not enrol partipants at an increased risk. This is important because each of these risk factors independently contributes to CVD development,<sup>88 89</sup> so small improvements across several risk factors may prove to be beneficial. For example, a recent study found that a modest population-wide reduction of 1 mm Hg in SBP reduced the number of cardiovascular events, such as stroke, by 12.1 (95% CI 7.9 to 16.3) and 4.8 (95% CI 2.9 to 6.6) per 100 000 person-years in African Americans and white Europeans, respectively.<sup>90</sup> Similarly, a 1 mmol reduction in LDLc for 5 years can reduce the risk of CVD by 20% in middle-aged individuals.<sup>91</sup> Thus, it seems reasonable to continue recommending diet and physical activity interventions to reduce

cardiovascular risk in South Asians by targeting multiple cardiovascular risk factors based on the positive evidence from large-scale behavioural modification trials such as the Diabetes Prevention Program<sup>85</sup> and the Finnish trial.<sup>92</sup>

The strengths of this study include a comprehensive search strategy that included searching four major databases, ongoing trial registrations and references of included studies, with the screening, data extraction, ROB assessment and GRADE all conducted independently and in duplicate. The inclusion/exclusion criteria for this review was broad enough to avoid a paucity of evidence but specific enough to answer the research question adequately. Attempts were made to contact study authors of trials that did not have published protocols available.

There are some limitations to this review. First, studies included in the review were primarily small, short-term studies. Not many long-term studies (>12 months) or trial data were evaluated, which makes the long-term effectiveness and feasibility of diet and physical activity interventions to prevent CVD hard to assess through this review. Second, the unaccounted-for heterogeneity across diet-only studies may reflect heterogeneity of the strategies used by the dietonly interventions to modify dietary practices. While some trials focus on changing multiple aspects of a single diet including macronutrient ratios (such as low carbohydrate, low sodium and/or low saturated fat content), many of them administered a single nutrient (eg, oats, flaxseed powder, wheatgrass, guava and protein/fibre supplement), as an add-on and assessed its effectiveness in reducing cardiovascular risk. The heterogeneity of the diet studies also makes it difficult to translate the findings of this review to clinical practice. However, another point to be made here is that when it comes to dietary changes, there is no one-size-fits-all strategy. Several dietary modifications may be effective at improving cardiovascular risk factors, which allows for flexibility in dietary counselling. Finally, there is considerable unaccounted-for heterogeneity with regard to nationality and immigration status (most of the studies were conducted within South Asia, primarily in South Asians from India), baseline risk factors and length of trials in this review. The review authors were unable to conduct all the preplanned subgroup analyses due to a lack of data, limiting the generalisability of our findings.

#### **CONCLUSIONS**

Lifestyle interventions improve blood pressure (SBP and DBP) and blood lipid (triglycerides, HDLc and LDLc) profiles in adult South Asians. These findings suggest that diet and/or physical activity interventions be actively promoted among the South Asian population in order to lower their cardiovascular risk.

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#### REFERENCES

- WHO. Fact sheet: cardiovascular diseases (CVDs). WHO, 2017: 1–6.
   Ahmad S, Shanmugasegaram S, Walker KL, et al. Examining sedentary time as a risk factor for cardiometabolic diseases and their markers in South Asian adults: a systematic review. Int J Public
- Health 2017;62:503–15.
- 3 Worldometers. Southern Asia population, 2019.
- 4 Joshi P, Islam S, Pais P, et al. Risk factors for early myocardial infarction in South Asians compared with individuals in other countries. *JAMA* 2007;297:286–94.

- 5 Rana A, de Souza RJ, Kandasamy S, et al. Cardiovascular risk among South Asians living in Canada: a systematic review and metaanalysis. CMAJ Open 2014;2:E183–91.
- 6 Nag T, Ghosh A. Cardiovascular disease risk factors in Asian Indian population: A systematic review. J Cardiovasc Dis Res 2013;4:222–8.
- 7 Gupta M, Singh N, Verma S. South Asians and cardiovascular risk: what clinicians should know. *Circulation* 2006;113:e924–9.
- 8 Zhang X, Devlin HM, Smith B, *et al.* Effect of lifestyle interventions on cardiovascular risk factors among adults without impaired glucose tolerance or diabetes: a systematic review and meta-analysis. *PLoS One* 2017;12:e0176436.
- 9 Kalra D, Vijayaraghavan K, Sikand G, et al. Prevention of atherosclerotic cardiovascular disease in South Asians in the US: a clinical perspective from the National lipid association. J Clin Lipidol 2021;15:402–22.
- 10 Samaan Z, Schulze KM, Middleton C, et al. South Asian heart risk assessment (Sahara): randomized controlled trial design and pilot study. JMIR Res Protoc 2013;2:e33.
- 11 Stewart J, Manmathan G, Wilkinson P. Primary prevention of cardiovascular disease: a review of contemporary guidance and literature. JRSM Cardiovasc Dis 2017;6:204800401668721–21.
- 12 Chu P, Pandya A, Salomon JA, et al. Comparative effectiveness of personalized lifestyle management strategies for cardiovascular disease risk reduction. J Am Heart Assoc 2016;5:e002737–e37.
- 13 Guidelines P, Risk C. Prevention of cardiovascular disease prevention of cardiovascular disease. World Health Organization, 2007: 1–30.
- 14 Ijzelenberg W, Hellemans IM, van Tulder MW, et al. The effect of a comprehensive lifestyle intervention on cardiovascular risk factors in pharmacologically treated patients with stable cardiovascular disease compared to usual care: a randomised controlled trial. BMC Cardiovasc Disord 2012;12:71.
- 15 Hamdy O, Mottalib A, Morsi A, et al. Long-Term effect of intensive lifestyle intervention on cardiovascular risk factors in patients with diabetes in real-world clinical practice: a 5-year longitudinal study. BMJ Open Diabetes Res Care 2017;5:e000259–e59.
- 16 Blokstra A, van Dis I, Verschuren WM. Efficacy of multifactorial lifestyle interventions in patients with established cardiovascular diseases and high risk groups. *Eur J Cardiovasc Nurs* 2012;11:97–104.
- 17 Uthman OA, Hartley L, Rees K, et al. Multiple risk factor interventions for primary prevention of cardiovascular disease in low- and middleincome countries. *Cochrane Database Syst Rev* 2015;8:CD011163.
- 18 Anderson TJ, Grégoire J, Pearson GJ, *et al.* 2016 Canadian cardiovascular Society guidelines for the management of dyslipidemia for the prevention of cardiovascular disease in the adult. *Can J Cardiol* 2016;32:1263–82.
- 19 Piepoli MF, Hoes AW, Agewall S, et al. 2016 European guidelines on cardiovascular disease prevention in clinical practice, 2016: 2315–81.
- 20 Angermayr L, Melchart D, Linde K. Multifactorial lifestyle interventions in the primary and secondary prevention of cardiovascular disease and type 2 diabetes mellitus--a systematic review of randomized controlled trials. *Ann Behav Med* 2010;40:49–64.
- 21 Dunkley AJ, Charles K, Gray LJ, et al. Effectiveness of interventions for reducing diabetes and cardiovascular disease risk in people with metabolic syndrome: systematic review and mixed treatment comparison meta-analysis. *Diabetes Obes Metab* 2012;14:616–25.
- 22 Estruch R, Ros E, Salas-Salvadó J, et al. Primary prevention of cardiovascular disease with a Mediterranean diet supplemented with extra-virgin olive oil or nuts. N Engl J Med 2018;378:e34.
- 23 Jenkins DJA, Kendall CWC, Marchie A, et al. Effects of a dietary portfolio of cholesterol-lowering foods vs lovastatin on serum lipids and C-reactive protein. JAMA 2003;290:502–10.
- 24 Rush E, Plank L, Chandu V, et al. Body size, body composition, and fat distribution: a comparison of young New Zealand men of European, Pacific Island, and Asian Indian ethnicities. N Z Med J 2004;117:U1203.
- 25 Deurenberg P, Deurenberg-Yap M, Guricci S. Asians are different from Caucasians and from each other in their body mass index/body fat per cent relationship. *Obes Rev* 2002;3:141–6.
- 26 Patel N, Ferrer HB, Tyrer F, et al. Barriers and facilitators to healthy lifestyle changes in minority ethnic populations in the UK: a narrative review. J Racial Ethn Health Disparities 2017;4:1107–19.
- 27 Distiller SR [program]. Ottawa, Canada: Evidence Partners.
- 28 The Cochrane C. RevMan 5 | Cochrane community, 2014.
- 29 Higgins JPT, Altman DG. Higgins 2011. In: Higgins JPT, Green S, eds. Cochrane Handbook for Systematic Reviews of Interventions. Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 20112011.
- 30 Jafar TH, Islam M, Hatcher J, *et al*. Community based lifestyle intervention for blood pressure reduction in children and young

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# 

adults in developing country: cluster randomised controlled trial. *BMJ* 2010;340:c2641.

- 31 Higgins J, Green S. Chapter 16 : Special topics in statistics, 2008.
- 32 Lesser IA, Singer J, Hoogbruin A, et al. Effectiveness of exercise on visceral adipose tissue in older South Asian women. Med Sci Sports Exerc 2016;48:1371–8.
- 33 Ranasinghe C, Devage S, Constantine GR, et al. Glycemic and cardiometabolic effects of exercise in South Asian Sri Lankans with type 2 diabetes mellitus: a randomized controlled trial Sri Lanka diabetes aerobic and resistance training study (SL-DARTS). *Diabetes Metab Syndr* 2021;15:77–85.
- 34 Aziz KU, Dennis B, Davis CE, et al. Efficacy of CVD risk factor modification in a lower-middle class community in Pakistan: the Metroville health study. Asia Pac J Public Health 2003;15:30–6.
- 35 Khanal MK, Bhandari P, Dhungana RR, et al. Effectiveness of community-based health education and home support program to reduce blood pressure among patients with uncontrolled hypertension in Nepal: a cluster-randomized trial. *PLoS One* 2021;16:e0258406.
- 36 Sharma AK, Baig VN, Ahuja J, et al. Efficacy of IVRS-based mHealth intervention in reducing cardiovascular risk in metabolic syndrome: a cluster randomized trial. *Diabetes Metab Syndr* 2021;15:102182.
- 37 Chandraratne N, Yamaguchi M, Indrawansa S, et al. The effect of youths as change agents on cardiovascular disease risk factors among adult neighbours: a cluster randomised controlled trial in Sri Lanka. BMC Public Health 2019;19:893.
- 38 Neupane D, McLachlan CS, Mishra SR, et al. Effectiveness of a lifestyle intervention led by female community health volunteers versus usual care in blood pressure reduction (COBIN): an openlabel, cluster-randomised trial. *Lancet Glob Health* 2018;6:e66–73.
- 39 Kaur J, Kaur M, Chakrapani V, et al. Effectiveness of information technology-enabled 'SMART Eating' health promotion intervention: A cluster randomized controlled trial. PLoS One 2020;15:e0225892.
- 40 Kondal D, Jeemon P, Manimunda S, et al. Structured lifestyle modification interventions involving frontline health workers for population-level blood pressure reduction: results of a cluster randomized controlled trial in India (DISHA study). J Am Heart Assoc 2022;11:e023526.
- 41 Valentine Jeffrey PT, Hanah R. How many studies do you need? A primer on stastical power for meta-analysis. *Journal of Educational and Behavioural Statistics* 2010;35:215–47.
- 42 Deeks JJ HJ, Altman DG, edseds. *Chapter 9: Analysing data and undertaking meta-analyses*. Version 5.1.0. The Cochrane Collaboration, 2011.
- 43 Saxena S, Katare C. Evaluation of flaxseed formulation as a potential therapeutic agent in mitigation of dyslipidemia. *Biomed J* 2014;37:386–90.
- 44 Singh RB, Rastogi SS, Singh NK, *et al*. Can guava fruit intake decrease blood pressure and blood lipids? *J Hum Hypertens* 1993;7:33–8.
- 45 Singh RB, Rastogi SS, Singh R, *et al.* Effects of guava intake on serum total and high-density lipoprotein cholesterol levels and on systemic blood pressure. *Am J Cardiol* 1992;70:1287–91.
- 46 Schunemann Holger BJ, Gordon G, Andrew O, eds. GRADE Handbook, 2013.
- 47 Bradley R, Kozura E, Buckle H, *et al.* Description of clinical risk factor changes during naturopathic care for type 2 diabetes. *J Altern Complement Med* 2009;15:633–8.
- 48 Spracklen CN, Smith CJ, Saftlas AF, et al. Maternal hyperlipidemia and the risk of preeclampsia: a meta-analysis. Am J Epidemiol 2014;180:346–58.
- 49 Saiz LC, Gorricho J, Garjón J, et al. Blood pressure targets for the treatment of people with hypertension and cardiovascular disease. *Cochrane Database Syst Rev* 2018;7:CD010315.
- 50 HAPO Study Cooperative Research Group, Metzger BE, Lowe LP, et al. Hyperglycemia and adverse pregnancy outcomes. N Engl J Med 2008;358:1991–2002.
- 51 Blackburn G. Effect of degree of weight loss on health benefits. Obes Res 1995;3 Suppl 2:211s–6.
- 52 Anand SS, Samaan Z, Middleton C, et al. A digital health intervention to lower cardiovascular risk: a randomized clinical trial. JAMA Cardiol 2016;1:601–6.
- 53 Bhardwaj S, Misra A, Gulati S, et al. A randomized controlled trial to evaluate the effects of high Protein Complete (IActo) VEgetaRian (PACER) diet in non-diabetic obese Asian Indians in North India. Heliyon 2017;3:e00472.
- 54 Mohan V, Gayathri R, Jaacks LM, *et al.* Cashew nut consumption increases HDL cholesterol and reduces systolic blood pressure in Asian Indians with type 2 diabetes: a 12-week randomized controlled trial. *J Nutr* 2018;148:63–9.

- 55 Gulati S, Misra A, Pandey RM. Effects of 3 g of soluble fiber from oats on lipid levels of Asian Indians a randomized controlled, parallel arm study. *Lipids Health Dis* 2017;16:71.
- 56 Gulati S, Misra A, Pandey RM, *et al.* Effects of pistachio nuts on body composition, metabolic, inflammatory and oxidative stress parameters in Asian Indians with metabolic syndrome: a 24-wk, randomized control trial. *Nutrition* 2014;30:192–7.
- 57 Gulati S, Misra A, Tiwari R, et al. Effect of high-protein meal replacement on weight and cardiometabolic profile in overweight/ obese Asian Indians in North India. Br J Nutr 2017;117:1531–40.
- 58 Kumar N, Iyer U. Impact of Wheatgrass (Triticum aestivum L.) Supplementation on Atherogenic Lipoproteins and Menopausal Symptoms in Hyperlipidemic South Asian Women - A Randomized Controlled Study. J Diet Suppl 2017;14:503–13.
- 59 Majid M, Younis MA, Naveed AK, et al. Effects of natural honey on blood glucose and lipid profile in young healthy Pakistani males. J Ayub Med Coll Abbottabad 2013;25:44–7.
- 60 Shakil-Ur-Rehman S, Karimi H, Gillani SA. Effects of supervised structured aerobic exercise training program on fasting blood glucose level, plasma insulin level, glycemic control, and insulin resistance in type 2 diabetes mellitus. *Pak J Med Sci* 2017;33:576–80.
- 61 Kandula NR, Dave S, De Chavez PJ, *et al.* Translating a heart disease lifestyle intervention into the community: the South Asian heart lifestyle intervention (SAHELI) study; a randomized control trial. *BMC Public Health* 2015;15:1064.
- 62 Naseem S, Ghazanfar H, Assad S, *et al.* Role of sodium-restricted dietary approaches to control blood pressure in Pakistani hypertensive population. *J Pak Med Assoc* 2016;66:837–42.
- 63 Patnaik L, Joshi A, Sahu T. Mobile phone-based education and counseling to reduce stress among patients with diabetes mellitus attending a tertiary care hospital of India. *Int J Prev Med* 2015;6:37.
- 64 Malve H, Kerkar P, Mishra N, et al. Ldl-Cholesterol lowering activity of a blend of rice bran oil and safflower oil (8:2) in patients with hyperlipidaemia: a proof of concept, double blind, controlled, randomised parallel group study. J Indian Med Assoc 2010;108:785–8.
- 65 Punia S, Singh V, Joshi S, *et al.* Effects of walking in individuals with prehypertension and stage 1 hypertension in India: a randomised controlled trial. *Int J Ther Rehabil* 2022;29:1–10.
- 66 Bhandari B, Narasimhan P, Jayasuriya R, *et al.* Effectiveness and acceptability of a mobile phone text messaging intervention to improve blood pressure control (TEXT4BP) among patients with hypertension in Nepal: a feasibility randomised controlled trial. *Glob Heart* 2022;17:13.
- 67 Bhoite R, Chandrasekaran A, Pratti VL, *et al.* Effect of a high-protein high-fibre nutritional supplement on lipid profile in overweight/ obese adults with type 2 diabetes mellitus: a 24-week randomized controlled trial. *J Nutr Metab* 2021;2021:1–9.
- 68 Pavithran N, Kumar H, Menon AS, et al. The effect of a low Gi diet on truncal fat mass and glycated hemoglobin in South Indians with type 2 Diabetes-A single centre randomized prospective study. *Nutrients* 2020;12:179.
- 69 Pavithran N, Kumar H, Menon AS, et al. South Indian Cuisine with low glycemic index ingredients reduces cardiovascular risk factors in subjects with type 2 diabetes. *Int J Environ Res Public Health* 2020;17:6232.
- 70 Jahan Y, Rahman MM, Faruque ASG, et al. Awareness development and usage of mobile health technology among individuals with hypertension in a rural community of Bangladesh: randomized controlled trial. J Med Internet Res 2020;22:e19137.
- 71 Nigam V, Nambiar VS. Aegle marmelos leaf juice as a complementary therapy to control type 2 diabetes randomised controlled trial in Gujarat, India. *Adv Integr Med* 2019;6:11–22.
  72 Punia S, Kulandaivelan S. Home-Based isometric handgrip training
- 72 Punia S, Kulandaivelan S. Home-Based isometric handgrip training on RBP in hypertensive adults-Partial preliminary findings from RCT. *Physiother Res Int* 2020;25:e1806.
- 73 The Cochrane C. GRADEpro GDT, 2017.
- 74 White C. Suspected research fraud: difficulties of getting at the truth. *BMJ* 2005;331:281–8.
- 75 Santesso N, Glenton C, Dahm P, et al. Grade guidelines 26: informative statements to communicate the findings of systematic reviews of interventions. J Clin Epidemiol 2020;119:126–35.
- 76 Sisti LG, Dajko M, Campanella P, et al. The effect of multifactorial lifestyle interventions on cardiovascular risk factors: a systematic review and meta-analysis of trials conducted in the general population and high risk groups. *Prev Med* 2018;109:82–97.
- 77 Dixit AA, Azar KM, Gardner CD, et al. Incorporation of whole, ancient grains into a modern Asian Indian diet to reduce the burden of chronic disease. *Nutr Rev* 2011;69:479–88.

#### **Open access**

- 78 Kalita S, Khandelwal S, Madan J, et al. Almonds and cardiovascular health: a review. *Nutrients* 2018;10:468.
- 79 Jenkins DJA, Wong JMW, Kendall CWC, et al. The effect of a plantbased low-carbohydrate ("Eco-Atkins") diet on body weight and blood lipid concentrations in hyperlipidemic subjects. Arch Intern Med 2009;169:1046–54.
- 80 Jin Y, Kanaya AM, Kandula NR, et al. Vegetarian diets are associated with selected cardiometabolic risk factors among Middle-Older aged South Asians in the United States. J Nutr 2018;148:1954–60.
- 81 Shridhar K, Dhillon PK, Bowen L, *et al*. The association between a vegetarian diet and cardiovascular disease (CVD) risk factors in India: the Indian migration study. *PLoS One* 2014;9:e110586.
- 82 Rippe JM. Lifestyle strategies for risk factor reduction, prevention, and treatment of cardiovascular disease. *Am J Lifestyle Med* 2019;13:204–12.
- 83 Nystoriak MA, Bhatnagar A. Cardiovascular effects and benefits of exercise. *Front Cardiovasc Med* 2018;5:135–35.
- 84 Gepner Y, Shelef I, Schwarzfuchs D, et al. Effect of distinct lifestyle interventions on mobilization of fat storage pools: central magnetic resonance imaging randomized controlled trial. *Circulation* 2018;137:1143–57.
- 85 Volgman AS, Palaniappan LS, Aggarwal NT, *et al.* Atherosclerotic cardiovascular disease in South Asians in the United States: epidemiology, risk factors, and treatments: a scientific statement from the American heart association. *Circulation* 2018;138:e1–34.

- 86 Cutler DM. Behavioural Health Interventions: What Works and Why? In: Anderson NB, Bulatao RA, Cohen B, eds. *Critical perspectives on racial and ethnic differences in health in late life*. Washington (DC), 2004.
- 87 Stuart-Shor EM, Berra KA, Kamau MW, et al. Behavioral strategies for cardiovascular risk reduction in diverse and underserved racial/ ethnic groups. *Circulation* 2012;125:171–84.
- 88 Soran H, Dent R, Durrington P. Evidence-Based goals in LDL-C reduction. *Clin Res Cardiol* 2017;106:237–48.
- 89 Karmali KN, Lloyd-Jones DM. Global risk assessment to guide blood pressure management in cardiovascular disease prevention. *Hypertension* 2017;69:e2–9.
- 90 Hardy ST, Loehr LR, Butler KR, *et al.* Reducing the blood Pressure-Related burden of cardiovascular disease: impact of achievable improvements in blood pressure prevention and control. *J Am Heart Assoc* 2015;4:e002276.
- 91 Collins R, Reith C, Emberson J, et al. Interpretation of the evidence for the efficacy and safety of statin therapy. Lancet 2016;388:2532–61.
- 92 Lindström J, Peltonen M, Eriksson JG, et al. Improved lifestyle and decreased diabetes risk over 13 years: long-term follow-up of the randomised Finnish Diabetes Prevention Study (DPS). *Diabetologia* 2013;56:284–93.

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