

## **Vegan diet for adults with overweight or obesity**

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## Vegan diet for adults with overweight or obesity (Protocol)

Nugent SJ, Rogerson D, Ranchordas MK, Broom DR

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[Intervention Protocol]

# Vegan diet for adults with overweight or obesity

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## ABSTRACT

### Objectives

This is a protocol for a Cochrane Review (intervention). The objectives are as follows:

To assess the effects of a vegan diet for overweight and obese adults.

## BACKGROUND

### Description of the condition

Overweight and obesity are defined as a body mass index (BMI) greater than or equal to 25 kg/m<sup>2</sup> and 30 kg/m<sup>2</sup> respectively, calculated as body weight in kilograms divided by height in metres squared (WHO 2014). In 2016, 1.9 billion adults worldwide were overweight. Of those classed as overweight, 650 million were obese, meaning that globally, 39% of adults were overweight and 13% were obese (WHO 2016). The National Health Survey for England found that, in 2016, 28.7% of adults in England were obese and 35.6% were overweight, meaning 64.3% of the UK population were either obese or overweight (Conolly 2017). Of those people classed as overweight in the UK, men represented a higher proportion than women (40% and 31% respectively), whereas of those people classed as obese, men represented a lower proportion than women (27% and 30% respectively) (Conolly 2017).

Being overweight or obese is considered a risk factor for many other diseases such as cardiovascular disease, diabetes, hypertension and metabolic syndrome (Mandviwala 2016), with obesity contributing to premature mortality worldwide (Preston 2011). Weight gain occurs when more calories from food, drinks or both are consumed above what is needed (WHO 2016). As a result, it is ever more important on a global level to investigate possible interventions which could act as a treatment for overweight and obesity.

A meta-analysis which included 26 observational studies found that an increase in mortality was observed in those who were obese, but not in those who were overweight (McGee 200). In a meta-analysis that included 97 studies, grade II and grade III obesity were shown to increase all-cause mortality, but grade I obesity showed no increase in mortality, with grades I, II and III obesity defined as a BMI of 30 to less than 35, 35 to less than 40, and more than 40, respectively (Flegal 2013). Overweight resulted in significantly lower all-cause mortality in comparison to all grades of obesity, suggesting that the health effects of overweight and obesity are complex (Flegal 2013).

Further, a study which included Korean adults found that optimal BMI ranges differ depending on sex and age, with women having lower optimal BMI especially at younger ages (Yi 2015). Optimal BMI also increased with age for both males and females, and those below BMI guidelines when adjusted for optimal age-sex ranges had greater risk of all-cause mortality than those with grade I obesity. These studies suggest that being overweight might protect against mortality risk. However, observational studies such as these do not elucidate the cause of such phenomena, and obesity is thought to be a complex condition.

Corsi 2019 found that risk factors for obesity were unevenly distributed across the population when wealth, education and caste were assessed. Broady 2015 found that proximity to healthy food outlets had an effect on obesity levels: those within a half-mile radius had reduced levels of obesity, suggesting that proximity to fast food outlets might be a causative factor in the aetiology of the condition. Indeed, socioeconomic factors are now thought to be important in the development of populations-level obesity. To highlight, Hoebel 2019 found that higher socioeconomic groups

in Germany had a lower likelihood of obesity compared to lower socioeconomic groups.

Studies investigating cardiovascular fitness in relation to mortality risk have shown that people classed as 'normal weight' but unfit had double the risk of mortality than those classed as 'normal weight' and fit, whereas overweight people had similar mortality risk to normal weight people (Barry 2014; Lavie 2016). These studies suggest that those with higher cardiovascular fitness have a reduced mortality risk independent of BMI (Barry 2014). Gaesser 2015 suggests that cardiovascular fitness is a more powerful predictor of mortality than BMI or adiposity, suggesting that strategies to increase cardiovascular fitness might be important in disease prevention. Interventions designed to increase the fitness of adolescents could also reduce the risk of cardiovascular disease in middle age, and cerebrovascular function in later life (Ross 2015; Yau 2017), suggesting that these effects exist across the lifespan.

In summary, overweight and obesity are complex conditions with physical and environmental underpinnings. While the effect of obesity on health does not appear to be clear-cut, overweight and obesity are thought to be important risk factors for diseases such as cardiovascular disease, diabetes and hypertension. Treatment strategies to reduce overweight and obesity are therefore important for public health.

### Description of the intervention

A vegan diet is defined as a diet which excludes animal products (Philips 2005). Observational data obtained from 33 Danish vegans highlighted that males consumed an average 11,710 kJ, 86.7 g, 331.9 g, and 75.5 g per day in total energy, fat, carbohydrate and protein respectively, and females consumed an average 8645 kJ, 65.1 g, 221.7 g and 59.1 g per day in total energy, fat, carbohydrate and protein respectively (Kristensen 2015).

Vegan diets are becoming more popular (Rogerson 2017). However, prevalence is difficult to determine at the time of writing. A survey commissioned by the Vegan Society, and organised by the UK's Food Standards Agency and National Centre for Social Science research showed an estimated 400% increase in people following vegan diets between 2014 and 2019 in the UK (Vegan Society 2020). This would account for an estimated total of 600,000 people in the UK during that period (NICE 2014). Globally, similar increases in people interested in a vegan diet has been observed. Between 2004 and 2020 the number of people searching for 'vegan' on the Internet has increased: the top five countries for such searches are Australia, New Zealand, the UK, Canada and the US, in descending order (Google Trends 2020). Whilst global statistics on population-level participation in a vegan diet are not easily accessible, emerging data have revealed that interest in veganism is high. A recent study by Kamiński 2020 found that the term 'veganism' attracted the largest search interest globally between 2004 and 2020, in proportion to mean relative search volume of the Mediterranean diet.

Motivations for adopting a vegan diet appear to be broad, ranging from animal welfare, environmental awareness and personal health factors associated with consuming plant-based diets (Janssen 2016).

High levels of saturated fat intake (30% to 65% of total daily energy intake) and higher sugar intake are thought to be characteristic

of a 'Western diet' which has been linked with obesity and poor health (Noble 2017). A Western diet can be characterised by a high consumption of processed red meat, other fat- and sugar-containing foods, refined grains and a reduced consumption of fruit and vegetables (Statovci 2017). A Mediterranean diet has received much attention in the literature, due in part to being linked to improvements in health status and reductions in mortality and risk of cardiovascular disease (Sofi 2014), perhaps as a result of its ingredients. The Mediterranean diet is rich in plant-based foods (vegetables, fruit, bread, nuts, seeds, cereals and beans) and olive oil (the primary fat source), and contains moderate amounts of dairy (Sofi 2016). The Mediterranean diet contains low amounts of meat and fish, particularly when compared to a Western diet. However, it is unclear whether the effects of a Mediterranean diet are a result of its promotion of plant-based foods and olive oil, or its restricted consumption of animal products.

According to Clarys 2014, people who follow a vegan diet consume fewer total calories per day than people who follow an omnivorous diet, consuming an average of 2383 kcal versus 2985 kcal per day respectively. According to Le 2014, people who follow a vegan diet have a lower BMI compared to those who follow an omnivorous diet: 23.1 kg/m<sup>2</sup> versus 26.2 kg/m<sup>2</sup> on average respectively. These observational studies suggest that consuming a vegan diet could lead to reduced BMI when compared to an omnivorous diet. Indeed, a recent narrative review of studies highlighted the potential of a vegan diet to induce weight loss (Medawar 2019), perhaps due to its ability to promote satiety (Klementova 2019), which reduces food consumption.

Given the growing trend towards veganism observed in the general population, and given that global levels of obesity have approximately trebled in four decades (NCD 2016), a Cochrane Review of this emerging area of research, investigating the potential of a vegan diet as an intervention for overweight and obese people, is prudent and timely. Eichelmann 2016, Hagen 2009 and Medawar 2019 have published reviews of vegan diets, and Barnard 2015 has published a review focusing on vegetarian diets. However, to date, there have been no systematic reviews or meta-analyses on studies using randomised controlled trials (RCTs) of vegan diet for obese and overweight people.

### Adverse effects of the intervention

Woo 2014 reported an increased risk of vitamin B<sub>12</sub> deficiency in people consuming a vegan diet, which can lead to impaired endothelial function. Vitamin B<sub>12</sub> deficiency can potentially lead to a host of neurological disorders such as myelopathy, paraesthesia, proprioception loss, ataxia, spasticity, hyporeflexia, sensory loss and autonomic dysfunction (Hunt 2014). Other micronutrient deficiencies associated with veganism, such as vitamin D (Crowe 2011), calcium (Davey 2003), iodine (Krajčovičová-Kudláčková 2003), iron and zinc (Hunt 2002), have been identified in the literature.

### How the intervention might work

The consumption of a vegan diet has been shown to lead to weight loss when consumed as part of a calorie-controlled diet (Slavin 2007). Weight loss has, therefore, been observed in studies investigating empirically the effects of vegan diets. Barnard 2005, Jakše 2017, Le 2014 and Mishra 2013 observed weight loss in their research, and suggested that plant-based diets might have

the potential to assist weight management if used for such purposes. Turner-McGrievy 2015 also found a 7.5% mean decrease in body mass in participants following a vegan diet without energy restriction, suggesting that this diet could have weight-loss benefits when administered clinically. Their work agrees with the findings of Klementova 2019, which highlighted that vegan meals might have appetite-reducing qualities which could lead to weight loss. These effects appear to have been reflected in observational data: a much-cited landmark study by Davey 2003 showed that people who follow vegan diets consume fewer calories per day and have lower BMI than those following an omnivorous diet. Weight losses greater than 5% of body mass are deemed clinically meaningful according to the National Institute of Health and Care Excellence (NICE 2014), suggesting that the weight loss effects observed in some studies is important.

A potential rationale for these effects might be due to a vegan diet promoting the consumption of higher fibre, reduced calorie-density food, leading to an increase in satiety and lower energy intakes long term. This hypothesis has been partially confirmed recently: Klementova 2019 observed increased concentrations of gut peptide hormones secretion following the consumption of a vegan meal compared to a calorie-matched processed-meat based meal. The authors observed increases in the satiety hormones glucagon-like peptide-1, peptide YY, pancreatic poly-peptide and amylin, and suggested that these changes could explain the effects observed. Vegan diets might therefore possess inherent properties that favour reduced energy intake when compared to omnivorous diets, which would explain the lower energy intakes and reduced BMIs of vegans in observational data that reported weight loss benefits.

### Why it is important to do this review

Given the extent of the worldwide prevalence of overweight and obesity, the increasing popularity of a vegan diet, and the data in the literature which show the reduced daily intake of calories, increased satiety and reduction in risk of all-cause mortality that appear to be associated with vegan diets, it seems timely to conduct a systematic review and meta-analysis to investigate the weight-loss effects of a vegan diet. To the authors' knowledge, to date, there are no similar published Cochrane Reviews or existing systematic reviews and meta-analyses of RCTs investigating a vegan diet for overweight and obese people.

## OBJECTIVES

To assess the effects of a vegan diet for overweight and obese adults.

## METHODS

### Criteria for considering studies for this review

#### Types of studies

We will include randomised controlled trials (RCTs).

#### Types of participants

Participants will be adults classed as overweight or obese.

### Diagnostic criteria for overweight and obese adults

Participants will be adults (18 years of age and older) with a BMI between 25 kg/m<sup>2</sup> and 29.9kg/m<sup>2</sup> classed as overweight, and those with a BMI of 30 kg/m<sup>2</sup> or greater classed as obese.

### Types of interventions

We plan to investigate the following comparisons of intervention versus control or comparator.

#### Intervention

Vegan diet

#### Comparison

Non-vegan diet.

A vegan diet is defined as a diet which excludes all animal products (Philips 2005). Any diet which does not meet this criterion is therefore a non-vegan diet, and will be accepted as a comparison.

Concomitant interventions will have to be identical in both the intervention and comparator groups to establish fair comparisons. If a study includes multiple arms, we will include any arm that meets the inclusion criteria for this review.

#### Minimum duration of intervention

The minimum duration of intervention will be four weeks.

#### Minimum duration of follow-up

The follow-up period after the intervention has taken place will be a minimum of four weeks plus any other follow-up period.

We will define any follow-up period going beyond the original time frame for the primary outcome measure as specified in the power calculation of the trial's protocol as an extended follow-up period (also called 'open-label extension study') (Buch 2011; Megan 2012).

#### Summary of specific exclusion criteria

We will exclude the following studies.

- Studies that combine a vegan diet with other weight loss interventions such as surgery, exercise or pharmacological interventions.
- Studies that have not used a control or comparator group.
- Studies in children or adolescents.

### Types of outcome measures

We will not exclude a study if it failed to report one or several of our primary or secondary outcome measures. If none of our primary or secondary outcomes is reported in the study, we will not include the study but provide some basic information in the 'Characteristics of studies awaiting classification' table.

We will extract the following outcomes, using the methods and time points specified below.

#### Primary outcomes

- Body mass
- Health-related quality of life
- Adverse events

### Secondary outcomes

- All-cause mortality
- Lean body mass
- Body fat
- Waist circumference
- Satiety
- Hunger
- Blood lipid profile
- Blood pressure

#### Method of outcome measurement

- Body mass measured in absolute changes in kg
- Health-related quality of life: measured by validated instruments, e.g. EQ-5D (EuroQol - 5 Dimension, a descriptive instrument used to assess health-related quality of life) or SF-36 scores (36 Item Short Form Health Survey, another widely used instrument used to evaluate health-related quality of life).
- Adverse events such as vitamin B<sub>12</sub> deficiency.
- All-cause mortality: defined as death from any cause.
- Lean body mass: defined as percentage of total body mass.
- Body fat: measured as a percentage of total body mass.
- Waist circumference: measured in centimetres, immediately above the iliac crest (ACSM 2017).
- Satiety: measured using subjective rating methods, or measurements of satiety-related hormones such as peptide YY and GLP-1.
- Hunger: measured using subjective rating methods, or measurements of the hunger-related hormone ghrelin.
- Blood lipid profile: measured by standard blood lipid analysis including plasma total cholesterol, high-density lipoprotein (HD-L) and low-density lipoprotein (LD-L) cholesterol, and triglycerides.
- Blood pressure, i.e. resting systolic and diastolic blood pressure measured in mmHg.

#### Timing of outcome measurement

- For all-cause mortality and adverse events: any time after participants were randomised to the intervention or comparator groups.
- For all other outcome measures: at various time points after the minimum intervention period at baseline, short-term, medium-term and long-term time frames (12 weeks, 12 months and more than 12 months, respectively).

### Search methods for identification of studies

#### Electronic searches

We will search the following sources from the inception of each database to the date of search and will place no restrictions on the language of publication.

- Cochrane Central Register of Controlled Trials (CENTRAL) via the Cochrane Register of Studies Online (CRSO)
- MEDLINE (Ovid MEDLINE ALL 1946 to daily update)
- ClinicalTrials.gov ([www.clinicaltrials.gov](http://www.clinicaltrials.gov))
- World Health Organization International Clinical Trials Registry Platform (ICTRP) ([www.who.int/trialsearch/](http://www.who.int/trialsearch/))

- LILACS (Latin American and Caribbean Health Science Information database)
- Core Collection (Web of Science)

We will not include Embase in our search, as RCTs indexed in Embase are now prospectively added to CENTRAL via a highly sensitive screening process (Cochrane 2020). For detailed search strategies, see [Appendix 1](#).

### Searching other resources

We will try to identify other potentially eligible studies or ancillary publications by searching the reference lists of included studies, systematic reviews, meta-analyses, and health technology assessment reports. We will also contact the authors of included studies to obtain additional information on the retrieved studies and establish whether we may have missed further studies.

We will not use abstracts or conference proceedings for data extraction unless full data are available from study authors because these information sources do not fulfil the CONSORT requirements of "an evidence-based, minimum set of recommendations for reporting randomized trials" (CONSORT 2018; Scherer 2007). We will present information on abstracts or conference proceedings in the 'Characteristics of studies awaiting classification' table.

## Data collection and analysis

### Selection of studies

Two review authors (SN, DR) will independently screen the abstract, title, or both, of every record retrieved by the literature searches. We will obtain the full text of all potentially relevant records. We will resolve disagreements through consensus or by recourse to a third review author (MR). If we cannot resolve a disagreement, we will categorise the study as 'awaiting classification' and will contact the study authors for clarification. We will present an adapted PRISMA flow diagram to show the process of study selection (Liberati 2009). We will list all articles excluded after full-text assessment in a 'Characteristics of excluded studies' table and will provide the reasons for exclusion.

### Data extraction and management

For studies that fulfil our inclusion criteria, two review authors (SN, DR) will independently extract key information on participants, interventions and comparators. We will describe interventions according to the 'template for intervention description and replication' (TIDieR) checklist (Hoffmann 2014; Hoffmann 2017).

We will report data on efficacy outcomes and adverse events using standardised data extraction sheets from the Cochrane Metabolic and Endocrine Disorders (CMED) Group. We will resolve disagreements by discussion or, if required, by consultation with a third review author (MR).

We will provide information including the study identifier for potentially relevant ongoing trials in the 'Characteristics of ongoing trials' table and in a joint appendix entitled 'Matrix of trial endpoint (publications and trial documents)'. We will attempt to find the protocol for each included trial and will report in a joint appendix the primary, secondary and other outcomes from these protocols, alongside the data from the study publications.

We will email the authors of all included studies to enquire whether they would be willing to answer questions regarding their studies. We will present the results of this survey in an appendix. We will thereafter seek relevant missing information on the study from the primary study author(s), if required.

### Dealing with duplicate and companion publications

In the event of duplicate publications, companion documents or multiple reports of a primary study, we will maximise the information yield by collating all available data, and we will use the most complete data set aggregated across all known publications. We will list duplicate publications, companion documents, multiple reports of a primary study and trial documents of included trials (such as trial registry information) as secondary references under the study ID of the included study. Furthermore, we will list duplicate publications, companion documents, multiple reports of a study and trial documents of excluded trials (such as trial registry information) as secondary references under the study ID of the excluded study.

### Data from clinical trials registers

If data from included trials are available as study results in clinical trials registers, such as [ClinicalTrials.gov](http://ClinicalTrials.gov) or similar sources, we will make full use of this information and extract the data. If there is also a full publication of the study, we will collate and critically appraise all available data. If an included study is marked as completed in a clinical trial register but no additional information (study results, publication or both) is available, we will add this trial to the 'Characteristics of studies awaiting classification' table.

### Assessment of risk of bias in included studies

Two review authors (SN, DR) will independently assess the risk of bias for each included study. We will resolve disagreements by consensus or by consulting a third review author (MR). In the case of disagreement, we will consult the remainder of the review author team and make a judgement based on consensus. If adequate information is unavailable from the study publications, study protocols or other sources, we will contact the study authors for more detail to request missing data on 'Risk of bias' items.

We will use the Cochrane 'Risk of bias' assessment tool to assign assessments of low, high, or unclear risk of bias (for details, see [Appendix 2](#); [Appendix 3](#)) (Higgins 2019b). We will evaluate individual bias items as described in the *Cochrane Handbook for Systematic Reviews of Interventions*, according to the criteria and associated categorisations contained therein (Higgins 2019b).

### Summary assessment of risk of bias

We will present a 'Risk of bias' graph and a 'Risk of bias' summary figure. We will distinguish between self-reported and investigator-assessed and adjudicated outcome measures.

We will consider the following self-reported outcomes.

- Body mass
- Health-related quality of life
- Adverse events
- Satiety
- Hunger
- Blood pressure



We will consider the following outcomes to be investigator-assessed.

- All-cause mortality
- Lean body mass
- Body fat
- Waist circumference
- Blood lipid profile

#### **Risk of bias for a study across outcomes**

Some risk of bias domains, such as selection bias (sequence generation and allocation sequence concealment), affect the risk of bias across all outcome measures in a study. In case of high risk of selection bias, we will mark all endpoints investigated in the associated study as being at high risk. Otherwise, we will not perform a summary assessment of the risk of bias across all outcomes for a study.

#### **Risk of bias for an outcome within a study and across domains**

We will assess the risk of bias for an outcome measure by including all entries relevant to that outcome (i.e. both study-level entries and outcome-specific entries). We consider low risk of bias to denote a low risk of bias for all key domains, unclear risk to denote an unclear risk of bias for one or more key domains and high risk to denote a high risk of bias for one or more key domains.

#### **Risk of bias for an outcome across study and across domains**

To facilitate our assessment of the certainty of evidence for key outcomes, we will assess risk of bias across studies and domains for the outcomes included in the 'Summary of findings' table. We will define the evidence as being at low risk of bias when most information comes from studies at low risk of bias, unclear risk of bias when most information comes from studies at low or unclear risk of bias, and high risk of bias when a sufficient proportion of information comes from studies at high risk of bias.

#### **Measures of treatment effect**

When at least two included studies are available for a comparison of a given outcome, we will try to express dichotomous data as a risk ratio (RR) or an odds ratio (OR) with 95% confidence intervals (CIs). For continuous outcomes measured on the same scale (e.g. weight loss in kg) we will estimate the intervention effect using the mean difference (MD) with 95% CIs. For continuous outcomes that measure the same underlying concept (e.g. health-related quality of life) but use different measurement scales, we will calculate the standardised mean difference (SMD). We will express time-to-event data as a hazard ratio (HR) with 95% CIs.

#### **Unit of analysis issues**

We will take into account the level at which randomisation occurred, such as cross-over trials, cluster-randomised trials, and multiple observations for the same outcome. If more than one comparison from the same study is eligible for inclusion in the same meta-analysis, we will either combine groups to create a single pairwise comparison, or we will appropriately reduce the sample size so that the same participants do not contribute data to the meta-analysis more than once (splitting the 'shared' group into two or more groups). Although the latter approach offers a solution for adjusting the precision of the comparison, it does not account for

correlation arising from inclusion of the same set of participants in multiple comparisons (Higgins 2019a).

We will attempt to re-analyse cluster-RCTs that have not appropriately adjusted for potential clustering of participants in their analyses. Variance of the intervention effects will be inflated by a design effect. Calculation of a design effect involves estimation of an intracluster correlation coefficient (ICC). We will obtain estimates of ICCs by contacting study authors, or by imputing ICC values using either estimates from other included studies that report ICCs or external estimates from empirical research (e.g. Bell 2013). We plan to examine the impact of clustering by performing sensitivity analyses.

#### **Dealing with missing data**

If possible, we will obtain missing data from the authors of included studies. We will carefully evaluate important numerical data such as screened, randomly assigned participants, as well as intention-to-treat, as-treated and per-protocol populations. We will investigate attrition rates (e.g. dropouts, losses to follow-up and withdrawals), and we will critically appraise issues concerning missing data and use of imputation methods (e.g. last observation carried forward).

For studies in which the standard deviation (SD) of the outcome is not available at follow-up or we cannot recreate it, we will standardise by the mean of the pooled baseline SD from studies that reported this information. Where included studies do not report means and SDs for outcomes, and we do not receive requested information from study authors, we will impute these values by estimating the mean and the variance from the median, the range and the size of the sample (Hozo 2005). We will investigate the impact of imputation on meta-analyses by performing sensitivity analyses, and we will report for every outcome which studies had imputed SDs.

#### **Assessment of heterogeneity**

In the event of clinical or methodological heterogeneity, we will not report study results as the pooled effect estimate in a meta-analysis.

We will identify heterogeneity (inconsistency) by visually inspecting the forest plots and by using a standard Chi<sup>2</sup> test with a significance level of  $\alpha = 0.1$  (Deeks 2019). In view of the low power of this test, we will also consider the I<sup>2</sup> statistic — which quantifies inconsistency across studies — to assess the impact of heterogeneity on the meta-analysis (Higgins 2002; Higgins 2003). When we identify heterogeneity, we will attempt to determine possible reasons for this by examining individual characteristics of the study and subgroups.

#### **Assessment of reporting biases**

If we include 10 or more studies that investigate a particular outcome, we will use funnel plots to assess small-study effects. Several explanations may account for funnel plot asymmetry, including true heterogeneity of effect with respect to study size, poor methodological design (and hence bias of small studies), and selective non-reporting (Kirkham 2010). Therefore we will interpret the results carefully (Sterne 2011).

## Data synthesis

We plan to undertake (or display) a meta-analysis only if we judge the participants, interventions, comparisons and outcomes to be sufficiently similar to ensure a result that is clinically meaningful. Unless good evidence shows homogeneous effects across studies of different methodological quality, we will primarily summarise data that are low risk of bias data using a random-effects model (Wood 2008). We will interpret random-effects meta-analyses with due consideration for the whole distribution of effects and will present a prediction interval (Borenstein 2017a; Borenstein 2017b; Higgins 2009). A prediction interval requires at least three studies to be calculated and specifies a predicted range for the true treatment effect in an individual trial (Riley 2011). For rare events such as event rates below 1%, we will use the Peto odds ratio method, provided there is no substantial imbalance between intervention and comparator group sizes, and intervention effects are not exceptionally large. In addition, we will perform statistical analyses according to the statistical guidelines presented in the *Cochrane Handbook for Systematic Reviews of Interventions* (Deeks 2019).

## Subgroup analysis and investigation of heterogeneity

We expect the following characteristics to introduce clinical heterogeneity, and we plan to carry out subgroup analyses for these, including investigation of interactions (Altman 2003).

- Male versus female
- 18 to 64 years versus 65 years and older
- Overweight versus obese
- Duration of intervention, depending on data

## Sensitivity analysis

We plan to perform sensitivity analyses to explore the influence of the following factors (when applicable) on effect sizes by restricting analysis to the following.

- Published studies
- Effect of risk of bias, as specified in the [Assessment of risk of bias in included studies](#) section
- Very long or large studies, to establish the extent to which they dominate the results

We will use the following filters, if applicable: diagnostic criteria, imputation used, language of publication (English versus other languages), source of funding (industry versus other), or country (depending on data).

We will also test the robustness of results by repeating analyses using different measures of effect size (i.e. RR, OR, etc.) and different statistical models (fixed-effect and random-effects models).

## Summary of findings and assessment of the certainty of the evidence

### Certainty of the evidence

We will present the overall certainty of evidence for each outcome specified below, according to the GRADE approach, which takes

into account issues related to internal validity (risk of bias, inconsistency, imprecision, publication bias) and external validity (such as directness of results). Two review authors (SN, DR) will independently rate the certainty of evidence for each outcome. We will resolve differences in assessment by discussion or by consultation with a third review author (MR).

We will include an appendix entitled 'Checklist to aid consistency and reproducibility of GRADE assessments', to help with standardisation of the 'Summary of findings' tables (Meader 2014). Alternatively, we will use the GRADEpro GDT software and will present evidence profile tables as an appendix (GRADEproGDT 2015). We will present results for outcomes as described in the [Types of outcome measures](#) section. If meta-analysis is not possible, we will present the results in a narrative format in the 'Summary of findings' table. We will justify all decisions to downgrade the certainty of the evidence by using footnotes, and we will make comments to aid the reader's understanding of the Cochrane Review when necessary.

### 'Summary of findings' table

We will present a summary of the evidence in a 'Summary of findings' table. This will provide key information about the best estimate of the magnitude of effect, in relative terms and as absolute differences for each relevant comparison of alternative management strategies; the numbers of participants and studies addressing each important outcome; and a rating of overall confidence in effect estimates for each outcome. We will create the 'Summary of findings' table using the methods described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Schünemann 2019), along with Review Manager 5 software (RevMan 2020).

The Intervention presented in the 'Summary of findings' table will be vegan diet. The comparator will be a non-vegan diet.

We will report the following outcomes, listed according to priority.

- Body mass
- Health-related quality of life
- Adverse events
- All-cause mortality
- Blood pressure

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## APPENDICES

### Appendix 1. Search strategies

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**MEDLINE (Ovid)**


---

1. Diet, Vegetarian/
  2. Diet, Vegan/
  3. vegan\*.tw.
  4. veganism.tw.
  5. vegetarian\*.tw.
- 

**Vegan diet for adults with overweight or obesity (Protocol)**

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(Continued)

6. plant-based.tw.
7. or/1-6
8. exp Obesity/
9. Overweight/
10. Weight Loss/
11. overweight.tw.
12. obes\*.tw.
13. weight loss.tw.
14. ((reduc\* or lose) adj5 weight).tw.
15. (body mass index adj5 (25 or 30)).tw.
16. or/8-15
17. 7 and 16

[Cochrane Handbook 2019 RCT filter - sensitivity maximizing version, without "drug therapy.fs"]

18. randomized controlled trial.pt.
19. controlled clinical trial.pt.
20. randomi?ed.ab.
21. placebo.ab.
22. randomly.ab.
23. trial.ab.
24. groups.ab.
25. or/18-24
26. exp animals/ not humans/
27. 25 not 26
28. 17 and 27

---

**CENTRAL (Cochrane Register of Studies Online)**

---

1. MESH DESCRIPTOR Diet, Vegetarian
2. MESH DESCRIPTOR Diet, Vegan
3. vegan\*:TI,AB,KY
4. veganism:TI,AB,KY
5. vegetarian\*:TI,AB,KY
6. plant-based:TI,AB,KY
7. #1 OR #2 OR #3 OR #4 OR #5 OR #6
8. MESH DESCRIPTOR Obesity EXPLODE ALL TREES
9. MESH DESCRIPTOR Overweight

---

**Vegan diet for adults with overweight or obesity (Protocol)**

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(Continued)

10. MESH DESCRIPTOR Weight Loss
11. overweight:TI,AB,KY
12. obes\*:TI,AB,KY
13. weight loss:TI,AB,KY
14. ((reduc\* or lose) ADJ5 weight):TI,AB,KY
15. (body mass index ADJ5 (25 or 30)):TI,AB,KY
16. #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15
17. #7 AND #16

---

### LILACS

(vegan\$ OR vegetarian\$ OR "plant based") AND (overweight OR obes\$ OR "weight loss" OR "weight reduction" OR sobrepes\$ OR peso) + Filter "Controlled Clinical Trial"

---

### Web of Science

1. TI=(vegan\* OR veganism OR vegetarian\* OR "plant based") OR AB=(vegan\* OR veganism OR vegetarian\* OR "plant based")
2. TI=(overweight OR obes\* OR "weight loss" OR ((reduc\* or lose) NEAR/5 weight) OR (body mass index NEAR/5 (25 or 30))) OR AB=(overweight OR obes\* OR "weight loss" OR ((reduc\* or lose) NEAR/5 weight) OR (body mass index NEAR/5 (25 or 30)))
3. TI=(random\* OR placebo OR trial OR groups) OR AB=(random\* OR placebo OR trial OR groups)
4. #1 AND #2 AND #3

---

### ClinicalTrials.gov (Advanced search)

**Conditions:** overweight OR obese OR obesity OR "weight loss" OR "weight reduction"

**Interventions:** vegan OR vegans OR veganism OR vegetarian OR vegetarians OR "plant based"

---

### WHO ICTRP (Standard search)

vegan\* AND overweight\* OR  
 vegan\* AND obes\* OR  
 vegan\* AND weight\* OR  
 vegetarian\* AND overweight\* OR  
 vegetarian\* AND obes\* OR  
 vegetarian\* AND weight\* OR  
 plant AND based AND overweight\* OR  
 plant AND based AND obes\* OR  
 plant AND based AND weight\*

---

## Appendix 2. 'Risk of bias' assessment



## 'Risk of bias' domains

### Random sequence generation (selection bias due to inadequate generation of a randomised sequence)

For each included trial, we will describe the method used to generate the allocation sequence in sufficient detail to allow an assessment of whether it should produce comparable groups.

- Low risk of bias: trial authors achieved sequence generation using computer-generated random numbers or a random numbers table. Drawing of lots, tossing a coin, shuffling cards or envelopes, and throwing dice are adequate if an independent person performed this who was not otherwise involved in the trial. We will consider the use of the minimisation technique as equivalent to being random.
- Unclear risk of bias: insufficient information about the sequence generation process.
- High risk of bias: the sequence generation method was non-random or quasi-random (e.g. sequence generated by odd or even date of birth; sequence generated by some rule based on date (or day) of admission; sequence generated by some rule based on hospital or clinic record number; allocation by judgment of the clinician; allocation by preference of the participant; allocation based on the results of a laboratory test or a series of tests; or allocation by availability of the intervention).

### Allocation concealment (selection bias due to inadequate concealment of allocation prior to assignment)

We will describe for each included trial the method used to conceal allocation to interventions prior to assignment and we will assess whether intervention allocation could have been foreseen in advance of or during recruitment or changed after assignment.

- Low risk of bias: central allocation (including telephone, interactive voice-recorder, internet-based and pharmacy-controlled randomisation); sequentially numbered drug containers of identical appearance; sequentially numbered, opaque, sealed envelopes.
- Unclear risk of bias: insufficient information about the allocation concealment.
- High risk of bias: used an open random allocation schedule (e.g. a list of random numbers); assignment envelopes used without appropriate safeguards; alternation or rotation; date of birth; case record number; any other explicitly unconcealed procedure.

We will also evaluate trial baseline data to incorporate assessment of baseline imbalance into the 'Risk of bias' judgement for selection bias (Corbett 2014). Chance imbalances may also affect judgements on the risk of attrition bias. In the case of unadjusted analyses, we will distinguish between trials that we rate as being at low risk of bias on the basis of both randomisation methods and baseline similarity, and trials that we judge as being at low risk of bias on the basis of baseline similarity alone (Corbett 2014). We will reclassify judgements of unclear, low, or high risk of selection bias as specified in Appendix 3.

### Blinding of participants and study personnel (performance bias due to knowledge of the allocated interventions by participants and personnel during the trial)

We will evaluate the risk of detection bias separately for each outcome (Hróbjartsson 2013). We will note whether endpoints were self-reported, investigator-assessed, or adjudicated outcome measures (see below).

- Low risk of bias: blinding of participants and key study personnel was ensured, and it was unlikely that the blinding could have been broken; no blinding or incomplete blinding, but we judge that the outcome is unlikely to have been influenced by lack of blinding.
- Unclear risk of bias: insufficient information about the blinding of participants and study personnel; the trial does not address this outcome.
- High risk of bias: no blinding or incomplete blinding, and the outcome is likely to have been influenced by lack of blinding; blinding of trial participants and key personnel attempted, but likely that the blinding could have been broken, and the outcome is likely to be influenced by lack of blinding.

### Blinding of outcome assessment (detection bias due to knowledge of the allocated interventions by outcome assessment)

We will evaluate the risk of detection bias separately for each outcome (Hróbjartsson 2013). We will note whether endpoints were self-reported, investigator-assessed, or adjudicated outcome measures (see below).

- Low risk of bias: blinding of outcome assessment is ensured, and it is unlikely that the blinding could have been broken; no blinding of outcome assessment, but we judge that the outcome measurement is unlikely to have been influenced by lack of blinding.
- Unclear risk of bias: insufficient information about the blinding of outcome assessors; the trial did not address this outcome.
- High risk of bias: no blinding of outcome assessment, and the outcome measurement was likely to have been influenced by lack of blinding; blinding of outcome assessment, but likely that the blinding could have been broken, and the outcome measurement was likely to be influenced by lack of blinding.

### Incomplete outcome data (attrition bias due to quantity, nature or handling of incomplete outcome data)

(Continued)

For each included trial or each outcome, or both, we will describe the completeness of data, including attrition and exclusions from the analyses. We will state whether the trial reported attrition and exclusions, and we will report the number of participants included in the analysis at each stage (compared with the number of randomised participants per intervention/comparator groups). We will also note if the trial reported the reasons for attrition or exclusion, and whether missing data were balanced across groups or were related to outcomes. We will consider the implications of missing outcome data per outcome such as high dropout rates (e.g. above 15%) or disparate attrition rates (e.g. difference of 10% or more between trial arms).

- Low risk of bias: no missing outcome data; reasons for missing outcome data unlikely to be related to true outcome (for survival data, censoring unlikely to introduce bias); missing outcome data balanced in numbers across intervention groups, with similar reasons for missing data across groups; for dichotomous outcome data, the proportion of missing outcomes compared with observed event risk was not enough to have a clinically relevant impact on the intervention effect estimate; for continuous outcome data, plausible effect size (mean difference or standardised mean difference) among missing outcomes was not enough to have a clinically relevant impact on observed effect size; appropriate methods, such as multiple imputation, were used to handle missing data.
- Unclear risk of bias: insufficient information to assess whether missing data in combination with the method used to handle missing data was likely to induce bias; the trial did not address this outcome.
- High risk of bias: reason for missing outcome data was likely to be related to true outcome, with either imbalance in numbers or reasons for missing data across intervention groups; for dichotomous outcome data, the proportion of missing outcomes compared with observed event risk enough to induce clinically relevant bias in the intervention effect estimate; for continuous outcome data, plausible effect size (mean difference or standardised mean difference) among missing outcomes enough to induce clinically relevant bias in observed effect size; 'as-treated' or similar analysis done with substantial departure of the intervention received from that assigned at randomisation; potentially inappropriate application of simple imputation.

#### Selective reporting (reporting bias due to selective outcome reporting)

We will assess outcome reporting bias by integrating the results of the appendix 'Matrix of trial endpoints (publications and trial documents)' (Boutron 2014; Jones 2015; Mathieu 2009), with those of the appendix 'High risk of outcome reporting bias according to the Outcome Reporting Bias In Trials (ORBIT) classification' (Kirkham 2010). This analysis will form the basis for the judgement of selective reporting.

- Low risk of bias: the trial protocol was available and all the trial's prespecified (primary and secondary) outcomes that were of interest to this review were reported in the prespecified way; the study protocol was unavailable, but it was clear that the published reports included all expected outcomes (ORBIT classification).
- Unclear risk of bias: insufficient information about selective reporting.
- High risk of bias: not all the trial's prespecified primary outcomes were reported; one or more primary outcomes were reported using measurements, analysis methods, or subsets of the data (e.g. subscales) that were not prespecified; one or more reported primary outcomes were not prespecified (unless clear justification for their reporting was provided, such as an unexpected adverse effect); one or more outcomes of interest in the Cochrane Review were reported incompletely so that we cannot enter them into a meta-analysis; the trial report failed to include results for a key outcome that we would expect to have been reported for such a trial (ORBIT classification).

#### Other bias

- Low risk of bias: the trial appears to be free from other sources of bias.
- Unclear risk of bias: information was insufficient to assess whether an important risk of bias existed; insufficient rationale or evidence that an identified problem introduced bias.
- High risk of bias: the trial had a potential source of bias related to the specific trial design used; the trial was claimed to be fraudulent; or the trial had some other serious problem.

### Appendix 3. Selection bias decisions

#### Selection bias decisions for trials that reported unadjusted analyses: comparison of results obtained using method details alone versus results obtained using method details and trial baseline information<sup>a</sup>

Reported randomisation and allocation	'Risk of bias' judgement using	Information gained from study characteristics data	'Risk of bias' using baseline information
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(Continued)

Allocation concealment methods	Blinding methods reporting	Baseline imbalances	Overall risk of bias and methods reporting
Unclear methods	Unclear risk	Baseline imbalances present for important prognostic variable(s)	<b>High risk</b>
		Groups appear similar at baseline for all important prognostic variables	<b>Low risk</b>
		Limited or no baseline details	Unclear risk
Would generate a truly random sample, with robust allocation concealment	Low risk	Baseline imbalances present for important prognostic variable(s)	<b>Unclear risk<sup>b</sup></b>
		Groups appear similar at baseline for all important prognostic variables	Low risk
		Limited baseline details, showing balance in some important prognostic variables <sup>c</sup>	Low risk
		No baseline details	<b>Unclear risk</b>
Sequence is not truly randomised or allocation concealment is inadequate	High risk	Baseline imbalances present for important prognostic variable(s)	High risk
		Groups appear similar at baseline for all important prognostic variables	<b>Low risk</b>
		Limited baseline details, showing balance in some important prognostic variables <sup>c</sup>	<b>Unclear risk</b>
		No baseline details	High risk

<sup>a</sup>Taken from [Corbett 2014](#); judgements highlighted in bold indicate situations in which the addition of baseline assessments would change the judgement about risk of selection bias compared with using methods reporting alone.

<sup>b</sup>Imbalance was identified that appears likely to be due to chance.

<sup>c</sup>Details for the remaining important prognostic variables are not reported.

## HISTORY

Protocol first published: Issue 12, 2020

## CONTRIBUTIONS OF AUTHORS

All review authors contributed to, read and approved the final protocol draft.

## DECLARATIONS OF INTEREST

Shane J Nugent (SJN): the lead author owns a nutrition company (SJN Nutrition) which educates clients about general nutrition, and also offers advice and guidance. The work undertaken by the company will not conflict with the proposed review.

David Rogerson (DR): DR published an opinion piece for 'The Conversation' discussing vegan diets for sport performance: "The high-performance vegan athlete - new research shows it is possible"

Mayur K Ranchordas (MR): none known.

David R Broom (DB): none known.

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- No source of external funding to declare, UK

There are no sources of external funding to declare.

## NOTES

We have based parts of the [Methods](#), as well as [Appendix 1](#), [Appendix 2](#), and Appendix 3 of this Cochrane Protocol, on a standard template established by the CMED Group.