Cardiometabolic risk factors in vegans; A meta-analysis of observational studies

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Abstract

Background
There is increasing evidence that plant based diets are associated with lower cardiovascular risk.

Objective
To evaluate effects of a vegan compared to an omnivorous diet on cardio-metabolic risk factors.

Methods
Meta-analysis of observational studies published between 1960 and June 2018 that reported one or more cardio-metabolic risk factors in vegans and controls eating an omnivorous diet were undertaken. Macro-nutrient intake and cardio-metabolic risk factors were compared by dietary pattern. The Newcastle Ottawa Scale (NOS) was used to assess the quality of each study. The inverse-variance method was used to pool mean differences. Statistical analyses were performed using RevMan software version 5.2 (The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen).

Results
40 studies with 12 619 vegans and 179 630 omnivores were included. From food frequency questionnaires in 28 studies, vegans compared to omnivores consumed less energy (-11%, 95% confidence interval -14 to -8) and less saturated fat (-51%, CI -57 to -45). Compared to controls vegans had a lower body mass index (-1.72 kg/m², CI -2.30 to -1.16), waist circumference (-2.35 cm, CI -3.93 to -0.76), low density lipoprotein cholesterol (-0.49 mmol/L, CI -0.62 to -0.36), triglycerides (-0.14 mmol/L, CI -0.24 to -0.05), fasting blood glucose (-0.23 mmol/L, CI -0.35 to -0.10), and systolic (-2.56 mmHg, CI -4.66 to -0.45) and diastolic blood pressure (-1.33 mmHg, CI -2.67 to -0.02), p < 0.0001 for all. Results were consistent for studies with < and ≥50 vegans, and published before and after 2010. However in several large studies from Taiwan a vegan diet was not associated with favourable cardio-metabolic risk factors compared to the control diets.
Conclusion

In most countries a vegan diet is associated with a more favourable cardio-metabolic profile compared to an omnivorous diet.

Introduction

Dietary habits are an important determinant of health. According to current guidelines, a healthy dietary pattern is high in vegetables, fruit, whole grains, seafood, legumes, and nuts, and includes a modest amount of low- and non-fat dairy products. It is also low in red and processed meat, sugar-sweetened foods and beverages, and refined grains.[1,2] In the randomised Dietary Approach to Adults with systolic Hypertension (DASH) study, this dietary pattern was shown to reduce blood pressure,[3] and insulin resistance.[4] The Mediterranean diet is similar, but includes a higher intake of fruit and lower intake of dairy food.[5] The Mediterranean diet has been associated with reduced cardiovascular events,[6,7] diabetes,[8,9] obesity, lower blood pressure[9] and modest decrease in LDL cholesterol. [10] The 'healthy vegetarian eating pattern'[1] has been associated with lower LDL-cholesterol[11,12] and blood pressure.[13] These diets include at least some dairy food, eggs and processed foods which may contain trans fatty acids and saturated fatty acids that affect lipid levels.[14] More recently the Prospective Urban Rural Epidemiological (PURE) study reported that a diet which included more dairy food and meat is associated with lower all cause and cardiovascular mortality in 138,000 people from lower, middle and high income countries.[15] This large study raises questions on whether and how dairy food and meat consumption may influence mortality risk, including their impact on known cardio-metabolic risk factors.

In contrast to most other dietary patterns, vegans generally strictly adhere to a plant based diet which avoids all animal products. Therefore, vegans provide an opportunity to assess the effects of a strict plant based diet on cardiometabolic risk factors. Cardiometabolic risk factors include increased waist circumference, low high density lipoprotein–cholesterol (HDL-c), high triglycerides, high blood pressure and insulin resistance. These risk factors are associated with increased risk of developing atherosclerotic cardiovascular (CV) disease and diabetes mellitus.[16] A literature review identified a number of studies which have reported these risk factors in vegans compared to omnivores, but most were small and evaluated only some risk factors. Also, studies have been undertaken over many years during which dietary patterns have often changed, and in diverse geographies. This meta-analysis was therefore undertaken to more reliably evaluate effects of a vegan diet on different cardiometabolic risk factors, and to determine whether associations are consistent across diverse populations, and over time.

Methods

Assessment of study eligibility and data extraction

The review was conducted according to Meta-analysis Of Observational Studies in Epidemiology (MOOSE) statement.[17] A protocol was developed and is available as a supplementary document. The search strings used are listed in the protocol (S2 File). Searches were performed of literature published from 1960 through to June 2018 using Medline, PubMed, Science Direct, Embase, Google, reference lists of articles, and proceedings of major meetings for relevant literature. The search terms were ‘vegan’ or ‘vegetarian’ and each of the following: ‘cardiometabolic risk’, ‘cardiovascular’, ‘weight’, ‘glucose’, ‘insulin’, ‘insulin resistance’, ‘blood
pressure’, ‘cholesterol’ and ‘lipids’. It became apparent that some vegan studies were coded under the term ‘vegetarian’, so this was added to the search items.

A search was performed for all observational studies that reported any cardio-metabolic risk factor in healthy adults following a vegan diet longer than 6 months and also reported a control group who ate an omnivorous diet. The definition of ‘vegan’ varied between studies and was noted. Healthy adults were defined as those aged over 18 with no renal disease, diabetes and heart disease, or other significant comorbidities and who are not taking lipid, glucose or blood pressure lowering medication. There was no upper age restriction for participants for the metaanalysis.

Studies needed to include sufficient data to calculate estimates of effect with standard deviations on at least one of the following: body mass index, waist circumference, blood pressure, triglycerides, LDL cholesterol, fasting glucose and insulin resistance. We restricted inclusion to studies of healthy adults who did not have diabetes, hypertension or vascular disease and were not on lipid or glucose lowering medication. Studies were excluded if they included any other intervention or they were commentaries, reviews, were not in English, or were duplicate publications from the same study.

Both (JB, RS) reviewers screened abstracts, titles and when appropriate full text to determine eligibility. For eligible studies data were abstracted by JB in duplicate. Questions arising during data abstraction were resolved by discussion. Through an iterative process, a standard list was used to extract descriptive, methodological and key variables from all eligible studies.

Data extracted included year of publication, the primary aim of the study, population characteristics, funding source, age and gender, whether a food frequency questionnaire was used, how long patients were vegan, estimates of effect and standard deviations. If data was not included in the published report corresponding authors were contacted. [18–20] Studies that present results separately for males and females,[21–27] or pre and post-menopausal women [28] are treated as separate studies. The Newcastle Ottawa Scale (NOS) was used to assess the quality of each study[29]. Using this scale, each study is judged on eight items, categorized into three groups: the selection of the study groups; the comparability of the groups; and how diet pattern was ascertained (objectively or subjectively). Stars are awarded for each quality item and the highest quality studies are awarded up to nine stars. A study is considered of good quality if there are 3 or 4 stars in selection domain AND 1 or 2 stars in comparability domain AND 2 or 3 stars in outcome/exposure domain.

Statistical analysis. The inverse-variance method was used to pool mean differences to yield an overall effect size with 95% confidence intervals. For two studies where standard deviations or confidence intervals were not available despite contacting authors, (Fraser 2015 and Appleby),[12,19] the mean SD of all other studies was used.

For studies that present results of food frequency questionnaires, total energy (kilojoules), carbohydrate, total, saturated, polyunsaturated and mono unsaturated fat and protein intake (grams/day) were calculated. The mathematical weighted mean of each risk factor and for total energy, fat, protein and carbohydrate intake was calculated as follows = \( \frac{\sum (x \times n)}{N} \), where \( x = \) mean of each study \( N = \) total number of participants in metaanalysis and \( n = \) number of participants in the study.

Each meta-analysis was assessed for heterogeneity by a Chi square test and \( I^2 \) statistic. A fixed effects model was used when heterogeneity was not present (\( I^2 = 0 \)) and a random effects model was used when statistical heterogeneity (\( I^2 \geq 1\% \)) was present. The meta-analysis was also repeated using a fixed effects model to assess the effects of small studies on results.[30] A p-value of <0.05 was considered statistically significant. Studies are presented in Forrest plots in order of statistical power.
Sensitivity analysis excluded studies that deviated significantly from the standard error of the total study result, and studies where baseline values differed significantly from the overall average.

Stratified analyses were conducted by size of study (<50 or >50 vegan participants), geography (North America, Europe, Asia and other), and date of publication (<2000, 2000–2010, >2010). Funnel plots were used to evaluate for possible publication bias. However, Asian studies were found to be different across all measures so results are reported separately for Asian and non-Asian cohorts.

The statistical analyses were performed using RevMan software version 5.2 (The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen). Subgroup analysis followed guidelines suggested by Wang. The study was not funded.

Results

Summary of studies included

The study flow chart is presented in Fig 1. Forty studies met inclusion criteria and were included in the meta-analysis with a total of 12,619 vegans and 179,630 omnivores (Table 1). Of these, 7 reported outcomes separately for male and females and one for pre and post-menopausal women, that could not be combined, and are therefore treated as separate studies for a total of 48 studies. In all studies the vegan group had been on a vegan diet longer than 1 year, and all were funded publicly except the study by Li et al. The countries involved in the studies are listed in Table 1 and in Fig 2.

Most studies were of high quality as assessed by the Newcastle-Ottawa Scale (NOS) with a mean 7.1 Standard deviation (SD) 1.3 stars- the domain which consistently had the lowest star rating was for ascertainment of outcome. Most studies did not objectively measure diet and were dependent on self-reported intake. Few studies measured biomarkers such as fatty acids. A few studies scored low on the scale because it was not clear how the vegan or control population was sourced, so possible selection bias could not be assessed.

33 (69%) studies included less than 50 vegans (Table 2) and the majority of these were published before 2010. The three largest studies were the Adventist Health Study 2 (n = 5548 vegans), the EPIC-Oxford studies (n = 739,422, and 2246 vegans respectively), and the MJ Health database study (n = 1913 vegans). All studies included an equivalent or greater number of controls compared to vegans. Eight studies reported separate outcomes for males (n = 987 vegans and 11,735 controls) and females (n = 1577 vegans and 27,498 controls) and are reported separately. All studies were publically funded except Li et al which was funded by the meat industry in Australia. Three studies required contact with authors for further data.

Two authors responded and provided additional measurement such as lipids, weight and BP.

Asian studies contributed the most participants for all cardiometabolic risk factors except BMI. These studies also contributed most participants for the subgroup analysis based on studies published ≥ 2010 and those with > 50 vegans. All Asian studies were from Taiwan. The largest ones derive from two large databases; the Taiwanese Survey on Hypertension, Hyperglycemia, and Hyperlipidemia (TwSHHH) and the MJ screening centre.

Macro-nutrient and energy intake

The definition of vegan for one Asian and all non-Asian studies was avoidance of all animal flesh and by-product. For the other Asian studies, the definition was less...
restrictive being defined as consumption of non-animal based food 3 times a day for 30 days a month. One study [20] reported results that were outside the normal range (for example total protein in each group was 15g per day which is 3 times less than for other studies). Authors for this study were contacted to address these disparities but they did not respond so it is not possible to account for these differences.

Vegan status was supported by food frequency questionnaires in most studies (n = 26, 63%). The mean and proportional difference in intake of major macronutrients by dietary pattern is presented in Fig 3 and Figures A-G in S1 File. Proportional differences for individual studies are presented in Table 3 and subgroup analysis in Table 4. The mean daily energy intake was 11% less for than vegans compared to omnivores (8610KJ versus 7700KJ/day, respectively). Compared to omnivores vegans consumed less total fat (-16.06g, CI -18.98 to -13.13, p < 0.0001), less saturated fat (-14.0g, CI -15.7 to -12.3), less mono-unsaturated fat (-6.6 g, CI -9.56 to -3.7) but more polyunsaturated fat (+4.0g, 2.2 to 5.9) (Table 3). Compared to omnivores, vegans also consumed less protein (-23.1g, CI -24.9 to -21.2) but more carbohydrate (+13.6g, CI 4.3 to 22.9) (p < 0.0001 for all comparisons). (Table 3)
| Trial Country Year published | Population | Vegans Number (% female) | Omnivores Number (% female) | Age in years Mean (SD) | Primary outcome | Risk factors assessed | Definition of vegan cohort | NOS Stars |
|-----------------------------|------------|--------------------------|-----------------------------|------------------------|-----------------|----------------------|---------------------------|----------|
| Agren [36] Finland 1995     | Adults Fins | 8 (87%)                  | 11(91%)                     | 47 (12.1)              | Lipids and phospholipids | BMI                  | Strictly uncooked vegan diet for many years with no animal products or added salt- ‘living diet’. | 7        |
| Appleby [12] United Kingdom 2002 | EPIC– Oxford cohort. | 739 (63%)                  | 4737 (79%)                  | 47 (12.1)              | Blood pressure | BMI Systolic BP Diastolic BP | Identified via FFQ questions as not eating any meat, fish, eggs or dairy products | 7        |
| Benatar [37] New Zealand 2017 | Health New Zealand adults | 25 (76%)                  | 61(74%)                     | 33.5 (8.1)              | Cardiometabolic risk factors | BMI Waist circumference Fasting blood glucose Insulin resistance LDL-cholesterol Triglycerides Systolic BP Diastolic BP | Self-identified vegans recruited via vegan Facebook group. Confirmed with FFQ and fatty acid levels of 17:0 and 15:0. | 8        |
| Bradbury [38] United Kingdom 2014 | EPIC– Oxford cohort. | 422 (NR)                  | 424(NR)                     | 45 (12.0)              | Lipids | BMI LDL-cholesterol | Identified via FFQ questions as not eating any meat, fish, eggs or dairy products | 7        |
| Chiu[39] Taiwan 2016 | MJ Health Screening Centre | 1913 (75%)                  | 40 915 (75%)                 | 48.9 (12.5)              | Metabolic syndrome | BMI Waist circumference Fasting blood glucose LDL-cholesterol Triglycerides Systolic BP Diastolic BP | Identified via FFQ questions as not eating any meat, fish, eggs or dairy products | 8        |
| De Biase[40] Brazil 2005 | Seventh Day Adventists in São Paulo | 18 (45%)                  | 22 (68%) | 34.0 (13.0)              | Lipids | BMI Waist circumference LDL-cholesterol Triglycerides | Self-identified vegans recruited via vegetarian restaurants at Seventh-day Adventist Churches, among Hare-Krishna members, and at spiritualistic centres. | 4        |
| Elorinne [41] Finland 2016 | Healthy Finnish adults 18–50 years | 22 (72%)                  | 19 (58%) | 34.0 (13.0)              | Nutritional status | BMI | Self-identified vegans found via Finnish Vegan Association’s monthly newspaper and via an online discussion forum | 8        |
| Famodu[42] Nigeria 1998 | Seventh-Day Adventist Seminary Institute of West Africa | 8 (0%)                  | 40 (0%) | 47.8 (1.7)              | Blood pressure and lipids | BMI Fasting blood glucose Systolic BP Diastolic BP | Seminary students and lecturers where cafeteria provide the majority of meals–‘habitual vegans’ | 7        |
| Fisher[43] United States America 1986 | Seventh day adventists | 10 (NR)                  | 25 (56%) | 37 (10)              | Lipid and platelet levels | LDL-cholesterol Triglycerides | Identified via FFQ as consuming eggs and dairy products never or infrequently (less than once per week), | 6        |

(Continued)
| Trial Country Year published | Population | Vegans Number (% female) | Omnivores Number (% female) | Age in years Mean (SD) | Primary outcome | Risk factors assessed | Definition of vegan cohort | NOS Stars |
|-----------------------------|------------|--------------------------|-----------------------------|------------------------|----------------|----------------------|-------------------------|-----------|
| Fokkema Males [26] Netherlands 2000 | Healthy Dutch males 20–60 years | 8(0%) | 9 (0%) | 38.5 (3.4) | Polyunsaturated fatty acids | BMI | Self-identified vegans recruited by advertisement in the periodicals of the Dutch Vegan Association and the Groningen University | 8 |
| Fokkema Females [26] Netherlands 2000 | Healthy Dutch females 20–60 years | 4 (100%) | 6 (100%) | 34.2 (12.5) | Polyunsaturated fatty acids | BMI | Self-identified vegans recruited by advertisement in the periodicals of the Dutch Vegan Association and the Groningen University | 8 |
| Fontana[44] United States America 2007 | Sedentary vegans and omnivores | 21(55%) | 21(55%) | 53.1 (11) | Cardiometabolic risk factors | BMI | Assessed for fasting blood glucose, LDL-cholesterol, Triglycerides, Systolic BP and Diastolic BP | 9 |
| Fraser[19] United States America 2015 | Adventist Health Study-2 (AHS-2)- African American cohort | 51 (NR) | 366 (NR) | NR | Cardiometabolic risk factors | BMI | Identified via FFQ within 2–3 years—Vegan defined as those, who eat no animal products | 8 |
| Goff[45] United Kingdom 2004 | Caucasian subjects | 21 (45%) | 25 (50%) | 42.4 (2.8) | Insulin and lipids | BMI | BMI for fasting blood glucose, Insulin resistance LDL-cholesterol, Triglycerides, Systolic BP and Diastolic BP | 9 |
| Gojda[46] Czechoslovakia 2013 | Caucasian subjects | 11 (45%) | 10 (40%) | 28.4 (3.2) | Insulin resistance | BMI | BMI for waist circumference, Fasting blood glucose, Insulin resistance LDL-cholesterol, Triglycerides, Systolic BP and Diastolic BP | 4 |
| Haddad [47] United States America 1999 | Seventh Day Adventist (University students) | 25(60%) | 20(50%) | 34.8 (8.1) | Dietary and nutritional status | BMI | Not clear—suggests vegan identified based on results of 4 day prospective FFQ. | 5 |
| Huang[18] Taiwan 2011 | Elderly Nutrition and Health Survey in Taiwan (1999–2000) | 83 (84%) | 802 (40-5%) | 71.9 (5.7) | Metabolic syndrome | BMI | Identified via FFQ—three vegetarian meals/d and 30 d per month. 1 question asked what type of vegetarian diet—habitual vegans | 8 |

(Continued)
| Trial Country Year published | Population | Vegans Number (%) female | Omnivores Number (%) female | Age in years Mean (SD) | Primary outcome | Risk factors assessed | Definition of vegan cohort | NOS Stars |
|-----------------------------|------------|--------------------------|-----------------------------|------------------------|----------------|----------------------|---------------------------|-----------|
| **Huang** Pre menopausal [28] Taiwan 2014 | Taiwanese Survey on Hypertension, Hyperglycemia, and Hyperlipidemia (TwSHHH) | 36 (100%) | 2285 (100%) | 41.1 (7.2) | Lipids | Waist circumference Fasting blood glucose LDL-cholesterol Triglycerides Systolic BP Diastolic BP | Identified via FFQ—diet excluded egg, milk, meat, poultry, seafood and by-products of animal slaughter for more than 1 year | 8 |
| **Huang** Postmenopausal [28] Taiwan 2014 | Taiwanese Survey on Hypertension, Hyperglycemia, and Hyperlipidemia (TwSHHH) | 63 (100%) | 1040 (100%) | 62.2 (10) | Lipids | Waist circumference Fasting blood glucose LDL-cholesterol Triglycerides Systolic BP Diastolic BP | Identified via FFQ—excluded egg, milk, meat, poultry, seafood and by-products of animal slaughter for more than 1 year | 8 |
| **Jian** Females [33] Taiwan 2014 | Taiwanese Survey on Hypertension, Hyperglycemia, and Hyperlipidemia (TwSHHH) | 99 (100%) | 3325(100%) | 50.2 (13.6) | Lipids and BP | Waist circumference Fasting blood glucose LDL-cholesterol Triglycerides Systolic BP Diastolic BP | Identified via FFQ—excluded egg, milk, meat, poultry, seafood and by-products of animal slaughter for more than 1 year | 8 |
| **Jian** Males [33] Taiwan 2014 | Taiwanese Survey on Hypertension, Hyperglycemia, and Hyperlipidemia (TwSHHH) | 45 (0%) | 3144(0%) | 47.6 (16.3) | Lipids and BP | Waist circumference Fasting blood glucose LDL-cholesterol Triglycerides Systolic BP Diastolic BP | Identified via FFQ—excluded egg, milk, meat, poultry, seafood and by-products of animal slaughter for more than 1 year | 8 |
| **Key** Males [27] United Kingdom 2014 | Oxford Vegetarian Study + EPIC-Oxford cohort | 862 (0%) | 8474 (0%) | 43.8 (14) | Cancer rates | BMI | Identified via FFQ questions as not eating any meat, fish, eggs or dairy products—from GP practices and vegan society | 7 |
| **Key** Females [27] United Kingdom 2014 | Oxford Vegetarian Study + EPIC-Oxford cohort | 1384 (100%) | 24017 (100%) | 43.8 (14) | Cancer rates | BMI | Identified via FFQ questions as not eating any meat, fish, eggs or dairy products—from GP practices and vegan society | 7 |
| **Krajcovickova-Kudlackova** [48] Slovakia 2000 | Healthy Slovaksians | 32 (69%) | 59(63%) | 41.2 (5.8) | Homocysteine and lipids | BMI LDL-cholesterol Triglycerides | Slovak vegetarian society and boarders of the centre of healthy nutrition in Bratislava ‘who only ate plant food’ | 4 |
| **Kritchevsky** [49] United States America 1984 | Seventh-day Adventists | 18 (50%) | 25 (48%) | Not stated | Lipids | LDL-cholesterol Triglycerides | Identified via FFQ—eat no animal products | 6 |

(Continued)
| Trial Country Year published | Population | Vegans Number % female | Omnivores Number % female | Age in years Mean (SD) | Primary outcome | Risk factors assessed | Definition of vegan cohort | NOS Stars |
|----------------------------|------------|-------------------------|---------------------------|------------------------|----------------|-----------------------|---------------------------|--------|
| Kuchta [50] Poland 2016    | Gdansk healthy adults | 21 (57%) | 21 (62%) | 28 (5) | Lipids | BMI LDL-cholesterol Triglycerides Systolic BP Diastolic BP | Identified via FFQ—eat no animal products for at least 10 months-unclear how recruited | 5 |
| Li [35] Australia 1999     | Males from Melbourne | 18 (0%) | 60 (0%) | 34.5 (13.1) | Thrombotic risk factors | BMI LDL-cholesterol Triglycerides Systolic BP Diastolic BP | Self-identified vegans recruited from adverts; vegan was defined as someone who ate no meat and eggs and dairy products less than six times per year on FFQ. | 8 |
| Lin [51] Taiwan 2010       | Buddhist nuns | 102 (100%) | 102 (100%) | 46.6 (16.8) | Renal functions | BMI Fasting blood glucose LDL-cholesterol Triglycerides Systolic BP Diastolic BP | Vegetarian nuns- mainly only eat vegan food but occasionally consume dairy and eggs- habitual vegans | 7 |
| Newby [52] Sweden 2005     | Swedish Mammography Cohort. | 83 (100%) | 54257 (100%) | 53.5 (9.7) | Weight, BMI | BMI | Identified via FFQ zero consumption of meat, fish, eggs, and dairy products, respectively in large mammogram cohort | 9 |
| Orlich [53] United States America 2013 | Adventist Health Study 2 (AHS-2) | 5548 (64%) | 35359 (66%) | 56.3 (13.6) | Mortality | BMI | Identified via FFQ—from churches in the United States and Canada between 2002 and 2007. | 8 |
| Orlov [54] Finland 1994    | Finnish adults | 9 (NR) | 11(NR) | 50(10) | Univalent cation fluxes in human erythrocytes | Systolic BP Diastolic BP | Strictly uncooked vegan diet for many years with no animal products or added salt- ‘living diet’ | 7 |
| Pettersen [55] United States 2012 | Adventist Health Study-2 (non-African American cohort) | 49 (71.4%) | 198 (61.6%) | 62.7 (12.8) | Blood pressure | BMI Systolic BP Diastolic BP | Identified via FFQ—from churches in the United States and Canada between 2002 and 2007. | 8 |
| Roshanai Males [23] United kingdom 1984 | NR | 11(0%) | 12(0%) | NR | Fatty acid intakes | LDL-cholesterol Triglycerides | Self-identified vegans from vegan society | 6 |
| Roshanai Females [23] United kingdom 1984 | NR | 12 (100%) | 12 (100%) | NR | Fatty acid intakes | LDL-cholesterol Triglycerides | Self-identified vegans from vegan society | 6 |
| Sambol [56] Croatia 2009   | Croatian adults | 20 | 50 | 35.5 (3.2) | Bone Density | BMI LDL-cholesterol Triglycerides | Not defined where vegans sourced. | 4 |
| Sanders [57] United Kingdom 1978 | Healthy British adults | 22 (45%) | 22 (45%) | 38 (12) | Phospholipids | BMI LDL-cholesterol Triglycerides | Self-identified vegans from vegan society | 7 |

(Continued)
| Trial Country Year published | Population | Vegans Number (% female) | Omnivores Number (% female) | Age in years Mean (SD) | Primary outcome | Risk factors assessed | Definition of vegan cohort | NOS Stars |
|----------------------------|------------|--------------------------|----------------------------|------------------------|----------------|----------------------|--------------------------|-----------|
| Sanders Males [24] United Kingdom 1987 | Healthy British men | 11 (5%) | 11(0%) | 30 (3.2) | Blood pressure, aldosterone, renin | BMI LDL-cholesterol Triglycerides | Self-identified vegans from vegan society | 7 |
| Sanders Females [24] United Kingdom 1987 | Healthy British women | 11 (100%) | 11 (100%) | 30 (3.2) | Blood pressure, aldosterone, renin | BMI LDL-cholesterol Triglycerides | Self-identified vegans from vegan society | 7 |
| Sanders Males [25] United Kingdom 1992 | Healthy British men | 10 (0%) | 10(0%) | 32 | Platelet phospholipid fatty acid composition and function | BMI LDL-cholesterol Triglycerides | Self-identified vegans from vegan society | 7 |
| Sanders Females [25] United Kingdom 1992 | Healthy British women | 10 (100%) | 10(100%) | 32 | Platelet phospholipid fatty acid composition and function | BMI LDL-cholesterol Triglycerides | Self-identified vegans from vegan society | 7 |
| Schüpbach [58] Switzerland 2015 | Healthy Swiss adults | 53 (60%) | 100(63%) | 30.5 (8.6) | Micronutrient status | BMI | Self-identified vegans using advertisements in schools, restaurants and shops. | 6 |
| Timko[59] United States America 2012 | University students | 35 (86%) | 265 (70%) | 24.89 (12.4) | Dietary restraint and eating disorder symptoms | BMI | Self-identified vegans from psychology department research pools of two urban universities, via flyers distributed to local health food stores, and through the internet | 7 |
| Thomas[60] United Kingdom 1999 | European Prospective Investigation into Nutrition and Cancer | 105 (100%) | 153(100%) | 47.8 (12.8) | Oestradiol and sex hormone-binding globulin | BMI | Self-identified vegans recruited through vegetarian and health food magazines, the Vegetarian Society and the Vegan Society, and word of mouth | 8 |
| Thorogood Males [21] United Kingdom 1990 | Healthy British men | 26(0%) | 26 (0%) | 42.5 (5.7) | Lipids | BMI LDL-cholesterol Triglycerides | Self-identified vegans recruited through the Vegetarian Society, through publicity in national and local media and word of mouth | 8 |
| Thorogood Females [21] United Kingdom 1990 | Healthy British females | 26 (100%) | 26 (100%) | 42.5 (5.7) | Lipids | BMI LDL-cholesterol Triglycerides | Self-identified vegans recruited through the Vegetarian Society, through publicity in national and local media and word of mouth | 8 |
| Toohey Males[34] United States America 1998 | African American Seventh-day Adventist | 14 (0%) | 49 (0%) | 47.5 (12) | Cardiometabolic risk factors | BMI | Identified via FFQ - African American Church members from Washington, DC; Philadelphia, PA; and Baltimore, MD. | 8 |
| Toohey Females[34] United States America 1998 | African American Seventh-day Adventist | 31 (100%) | 94 (100%) | 51.5 (12) | Cardiometabolic risk factors | BMI Waist circumference | Identified via FFQ - African American Church members from Washington, DC; Philadelphia, PA; and Baltimore, MD. | 8 |
| Vinagre[20] Brazil 2013 | Healthy adults | 21(47%) | 29 (41.3%) | 36 (10) | Regulation metabolism of triglyceride rich lipoprotein | BMI LDL-cholesterol Triglycerides | Self-identified vegans from web site for vegetarians | 6 |

Abbreviations: M = Male, F = female, pre-M = premenopausal, Post M = post-menopausal, BMI = body mass index, BP = blood pressure, NR = not reported

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Total energy intake in vegans was 30% from fat (5.8% saturated), 13% protein and 56% carbohydrate. In controls 33% of total energy was from total fat, 11% saturated fat, 17% protein and 51% from carbohydrate. The nutrient intake was similar across studies including the sole study from Asia (Taiwan) that reported results of FFQ. Differences in energy intake between vegans and controls were similar by publication date, geography or size of study (Table 4).

**Cardiometabolic risk factors**

On pre-specified subgroup analysis based on geographic region, there was a statistically significant differences comparing Asian and non-Asian studies for all factors except blood glucose and diastolic blood pressure. For geographic regions excluding Asia there was no difference by year of publication or size of study. Results are therefore reported separately for Asian and non-Asian studies (Figs 3–6). Generally, for all risk factors Asian studies reported smaller or no difference in cardiometabolic risk factors between vegans and omnivores.

**Table 2. Summary of studies included in the meta-analysis.**

| Study Characteristics | Number of studies | Total number of vegans (% of all vegans) | Total number omnivores (% of all vegans) | Non-Asian studies vegans | omnivores | Asian studies vegans | omnivores |
|-----------------------|-------------------|------------------------------------------|------------------------------------------|--------------------------|-----------|----------------------|-----------|
| Total Number of Studies | 48                | 12 619 (100%)                            | 179 630 (100%)                           | 41                       | 10 134    | 129 062              | 7         | 2 485                 | 50 568     |
| Studies < 50 vegans   | 34                | 671 (5%)                                 | 6 637 (4%)                               | 32                       | 635       | 1 208                | 2         | 81                    | 5 429      |
| Studies > 50 vegans   | 14                | 12 619 (95%)                             | 179 630 (96%)                            | 9                        | 9 544     | 127 854              | 5         | 2 404                 | 45 139     |
| Published < 2010      | 29                | 1 920 (15%)                              | 60 238 (34%)                             | 29                       | 1 920     | 60 238               | 0         | 0                     | 0          |
| Published ≥ 2010      | 19                | 10 699 (85%)                             | 119 392 (66%)                            | 12                       | 8 214     | 68 824               | 7         | 2 485                 | 50 568     |

**Cardiometabolic Risk factor evaluated**

- Body mass index: 37 studies, vegans 12 241 (97%), omnivores 169 385 (94%), 34 studies, vegans 9 999, omnivores 12 8611, 3 242, 40 774
- Waist circumference: 10 studies, vegans 2 288 (18%), omnivores 50 571 (28%), 5 studies, vegans 132, omnivores 582, 5 156, 49 989
- Fasting glucose: 13 studies, vegans 2 448 (19%), omnivores 51 798 (29%), 6 studies, vegans 107, omnivores 185, 7 2485, 50 568
- LDL- cholesterol: 31 studies, vegans 3 355 (27%), omnivores 53 393 (30%), 24 studies, vegans 1 014, omnivores 1 780, 7 2485, 50 568
- Triglycerides: 29 studies, vegans 2 731 (22%), omnivores 51 814 (29%), 23 studies, vegans 473, omnivores 1 003, 6 2258, 50 811
- Systolic and diastolic blood pressure: 19 studies, vegans 3 222 (26%), omnivores 53 870 (30%), 12 studies, vegans 881, omnivores 2 257, 7 2485, 50 568

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Fig 3. Macronutrient intake in vegans compared to omnivores.

Table 3. Proportional intake of macronutrients in vegans compared to omnivores.

| Study | Total energy | Total Fat | Saturated fat | MUFA | PUFA | Carbohydrate | Protein |
|-------|--------------|-----------|---------------|-------|-------|--------------|---------|
| Agren [36] | 1.09 | 1.01 | 0.36 | 1.40 | 1.74 | 1.23 | 0.77 |
| Appelbym [12] | 0.88 | 0.91 | 0.47 | NR | 1.00 | 1.09 | 0.80 |
| Appelby F [12] | 0.89 | 0.91 | 0.52 | NR | 1.33 | 1.13 | 0.77 |
| Bradbury M [61] | 0.86 | 0.91 | 0.50 | 0.79 | 1.45 | 1.19 | 0.81 |
| Bradbury F [61] | 0.87 | 0.94 | 0.64 | 0.78 | 1.44 | 1.12 | 0.76 |
| Famodu [42] | 1.05 | 1.00 | 0.47 | NR | 1.27 | 1.05 | 0.75 |
| Fontana [44] | 1.17 | 1.12 | 0.71 | 1.47 | 1.37 | 0.87 | 0.54 |
| Goff [45] | 0.94 | 0.90 | 0.47 | 0.90 | 1.29 | 1.24 | 0.75 |
| Gojda [46] | 1.04 | 0.85 | NR | NR | NR | 1.21 | 0.82 |
| Haddad M [47] | 1.03 | 0.81 | 0.50 | 0.63 | 0.93 | NR | NR |
| Haddad F [47] | 0.86 | 0.74 | 0.50 | 0.74 | 1.31 | NR | NR |
| Huang 2011 [18] | 0.83 | 0.97 | 0.73 | NR | 0.91 | 1.02 | 1.00 |
| Key F [27] | 0.87 | 0.87 | 0.57 | NR | NR | 1.17 | 0.78 |
| Key M [27] | 0.87 | 0.90 | 0.55 | NR | NR | 1.09 | 0.81 |
| Krajcoviová-Kudlácková [48] | 0.77 | 0.92 | 0.46 | 0.83 | 1.15 | NR | NR |
| Kritchevsky M [49] | 0.93 | 0.73 | NR | NR | NR | 1.40 | 0.61 |
| Kritchevsky F [49] | 0.87 | 0.68 | NR | NR | NR | 1.33 | 0.75 |
| Kuchta [50] | 1.06 | 0.95 | NR | NR | NR | 1.32 | 0.64 |
| Li [33] | 0.74 | 0.75 | 0.38 | 0.56 | 1.50 | 1.43 | 0.74 |
| Newby [63] | 0.83 | 0.75 | 0.69 | 0.60 | 0.77 | 1.23 | 0.76 |
| Orlich [53] | 1.01 | NR | NR | NR | NR | NR | NR |
| Orlov [54] | 1.05 | 101.17 | 0.35 | 1.40 | 1.66 | 1.14 | 0.78 |
| Thorogood M [21] | 1.01 | 0.88 | 0.47 | NR | 1.83 | 1.22 | 0.77 |
| Thorogood F [21] | 0.98 | 0.94 | 0.52 | NR | 1.57 | 1.18 | 0.79 |
| Toole V [34] | 0.79 | 0.88 | 0.63 | NR | 1.13 | 0.99 | 0.83 |
| Toohey F [34] | 0.97 | 0.99 | 0.73 | NR | 0.75 | 1.00 | 0.90 |
| Vinagre [20] | 0.77 | 0.76 | 0.38 | 1.01 | 1.36 | 1.21 | 0.91 |
| Total weighted difference | 0.89 | 0.75 | 0.49 | 0.91 | 1.31 | 1.04 | 0.73 |
Body mass index. BMI was reported in 37 studies with 12,241 vegans and 169,385 controls ([Fig 4](https://doi.org/10.1371/journal.pone.0209086.g004) and [Fig H](https://doi.org/10.1371/journal.pone.0209086.g004) in S1 File). The BMI of controls was within the healthy weight range, 24.2 ±1.2 kg/m². There was no difference in BMI for vegans compared to controls in Asia (-0.20 95% CI -1.21 to 0.82, p = 0.70) kg/m², p = 0.92), but for non-Asian studies the difference

### Table 4. Intake of macronutrients in vegans compared to omnivores.

| Study Characteristics | Number of studies | Total energy (MJ) | Total Fat (g/day) | Saturated fat (g/day) | Protein (g/day) | Carbohydrate (g/day) |
|-----------------------|-------------------|-------------------|-------------------|----------------------|----------------|----------------------|
|                       | Mean (SD)         | Mean (SD)         | Mean (SD)         | Mean (SD)            | Mean (SD)      | Mean (SD)            |
| < 50 vegans [20–22,34–36,42,45–50,54] | 18                | -1.04 [1.59, -0.49] | -12.67 [22.18, -3.17] | 0.009                | -12.63 [-13.06, -12.20] | -22.80 [-32.00, -13.59] |
| >50 vegans [12,18,27,53,61,63]       | 8                 | -0.93 [-1.25, -0.60] | -18.00 [-20.84, -15.17] | <0.0001              | -14.05 [-14.27, -13.82] | -24.04 [-25.59, -22.49] |
| North America[34,47,49,53]          | 8                 | -0.79 [-1.34, -0.24] | -11.60 [-24.96, 1.75] | 0.09                 | -5.63 [-7.52, -3.75] | -18.71 [-31.84, -5.59] |
| Europe [12,21,27,36,45,46,48,50,52,54,61] | 14                | -1.11 [-1.28, -0.95] | -14.31 [-16.34, -12.29] | <0.0001              | -14.11 [-14.31, -13.91] | -24.61 [-25.78, -23.44] |
| Asia [18]                          | 1                 | -1.18 [-1.81, -0.56] | -39.68 [-44.06, -35.30] | <0.0001              | -2.90 [-4.26, -1.54] | -10.30 [-13.63, -6.97] |
| Other [20,35,42]                   | 3                 | -1.86 [-3.79, -0.69] | -27.34 [-73.20, 18.52] | 0.24                 | -11.83 [-13.59, -10.07] | <0.0001              |
| Published <2010 [12,20,21,34–36,42,45,47–49,52,54] | 17                | -1.00 [-1.32, -0.69] | -14.86 [-20.05, -9.68] | <0.0001              | -12.59 [-13.02, -12.16] | -23.31 [-27.84, -18.78] |
| Published ≥2010 [18,27,46,50,53,61] | 9                 | -0.99 [-1.50, -0.48] | -17.63 [-21.42, -13.83] | <0.0001              | -14.07 [-14.29, -13.84] | -23.78 [-25.79, -21.78] |
| OVERALL                           | 26                | -0.98 [-1.23, -0.72] | -16.06 [-18.98, -13.13] | <0.0001              | -13.99 [-15.67, -12.31] | -23.08 [-24.93, -21.22] |

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![Fig 4. Body mass index (kg/m²) and waist circumference (cm) in vegans compared to omnivores.](https://doi.org/10.1371/journal.pone.0209086.g004)
was -1.92 kg/m$^2$ (95% CI -2.52 to -1.32, p < 0.0001). There was significant heterogeneity in results ($I^2 = 98\%$) across these subgroups. However there is no suggestion of publication bias from funnel plots (Fig I in S1 File).

**Waist circumference.** Waist circumference was reported in 10 studies with 2,288 vegans and 50,571 controls (Fig 4 and Fig J in S1 File). Weighted mean waist circumference was 77.5 cm for omnivores and 76.2 cm for vegans. There was no difference in waist circumference between vegans and omnivores in studies from Asian. For non-Asian studies waist circumference in vegans was -4.93 cm [-7.70 to -2.16] less than controls, p = 0.0005. However, there were only 132 vegans in the non-Asian cohort and 2,156 vegans in the Asian cohort. There was significant heterogeneity in the difference in waist circumference between vegans and controls between studies ($I^2 = 48\%$), but no evidence to suggest publication bias on the funnel plot (Fig K in S1 File).

**Blood glucose and insulin resistance.** Fasting blood glucose was reported in 13 studies with 2,448 vegans and 51,798 controls (Fig 5 and Fig LI in S1 File). Studies from Asia predominated with 94% of the total vegan population. The mean fasting plasma glucose in controls was 5.2 (0.59) mmol/L. The difference in fasting glucose overall was -0.23 [95% CI -0.35 to -0.10] mmol/L, p = 0.0005. Vegans in both Asian and non-Asian studies had reduced blood sugars and there was no statistical difference between these subgroups (p = 0.10). There was moderate heterogeneity between studies ($I^2 = 48\%$) and some suggestion of publication bias (Fig M in S1 File). Results are unchanged when the study by Vinagre [20] which reports the largest effect on fasting plasma glucose was excluded.

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Fig 5. Fasting blood glucose (mmol/L) in vegans compared to omnivores.
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Fig 6. Low density lipoprotein cholesterol and triglycerides (mmol/L) in vegans compared to omnivores.
https://doi.org/10.1371/journal.pone.0209086.g006
The Homeostatic model assessment—insulin resistance (HOMA-IR) was reported in 3 non-Asian studies with 57 vegans and 92 controls (Fig N in S1 File). The difference in HOMA-IR was -0.04 [95% CI -0.36 to 0.28] using the fixed effects model and there was no heterogeneity between studies (Fig O in S1 File).

**LDL-cholesterol.** LDL-cholesterol was reported in 31 studies with 3,355 vegans and 53,393 controls (Fig 6 and Fig P in S1 File). For all studies the difference in LDL-cholesterol between vegans and controls was -0.49 mmol/L [95% CI -0.62 to -0.36], p<0.0001. The mean LDL-cholesterol was 2.85 (4.9) mmol/L for controls. Asian controls had higher baseline LDL-cholesterol compared to non-Asians but this difference was not statistically significant (p = 0.32). There was no difference between vegans and controls in LDL-cholesterol in Asian studies. However, for non-Asian studies this was -0.60 mmol/L [95% CI -0.74 to -0.47], p<0.0001. There was significant heterogeneity between results (I² = 92%) (Fig Q in S1 File).

Results were similar when the study with the greatest difference (>1.2 mmol/L) [25] was excluded (-0.48 [95% CI -0.61, -0.35]).

**Triglycerides.** Triglycerides were reported in 29 studies with 2,731 vegans and 51,814 controls (Fig 6 and Fig R in S1 File). The mean triglyceride was 1.24 (0.41) mmol/l for omnivores. Vegans had lower triglyceride levels than controls -0.14 mmol/l [95% CI -0.24 to -0.05], p = 0.004. However in studies from Asia, the converse was true with vegans having higher triglycerides than controls (0.15 [95% CI 0.02 to 0.28]; p = 0.02). Asian studies contributed 82% of all vegans in the analysis. There was significant heterogeneity between results (I² = 88%) and some risk of publication bias from funnel plots (Fig S in S1 File).

**Blood pressure.** Blood pressure was reported in 19 studies with 3,222 vegans and 53,870 controls (Fig 7, Figures T-W in S1 File). The mean systolic and diastolic blood pressure for controls was 121.8 (7.8) and 75.2 (3.4) mmHg respectively. There was no difference in blood pressure between vegans and controls in Asian studies, which contributed 82% of the total vegan cohort with blood pressure data. In non-Asians studies systolic (-5.87 mmHg [95% CI -9.19 to -2.56], p = 0.005) and diastolic blood pressure (-3.19 mmHg [-5.90 to -0.48], p = 0.002) were lower in vegans compared to controls.

There was significant heterogeneity between results for both diastolic and systolic blood pressure (I² = 82%). No effect on systolic and diastolic BP was seen when two non-Asian studies [44,54] with effects >15 mmHg were excluded from the analysis (mean difference -1.14 [95% CI -3.03, 0.75] mmHg).

**Subgroup and sensitivity analysis.** In pre-specified subgroup analysis there was no difference in results based on publication date or size of study once the impact of studies from Asia was taken into account. There was no overlap in confidence interval between Asia and Non-Asian studies for all risk factors except for fasting blood glucose and diastolic blood pressure. Results were similar for all sensitivity analysis performed where differences in risk factors differed significantly from the mean values of the whole population, and where studies reported outcomes much larger than the mean change. Results were unchanged within the Asian studies when subgroup analysis was done in restrictive compared to less restrictive definition of vegan.

**Discussion**

In most countries vegans consumed less energy, total fat, saturated fat and protein compared to controls that ate an omnivorous diet. Vegans had a lower body mass index, LDL-cholesterol, blood glucose, triglycerides and blood pressure compared to healthy controls. However in studies from Taiwan, the only Asian country included in the meta-analysis, there was no difference in risk factors in vegans compared to controls with the exception of fasting blood glucose.
glucose, which was slightly lower in vegans and triglycerides that were higher in vegans. These studies were large, contemporary and contributed substantially to the overall estimates, but results for ‘Asian’ and non-Asian studies differed significantly. It is therefore important to consider reasons for this geographic difference, and whether excluding studies from Taiwan provides more reliable estimates of the impact of a vegan diet in other countries.

The lack of difference in risk factors between vegans and omnivores in studies from Taiwan may reflect differences in the diet of vegans and/or controls compared to other populations. [64] Vegans included in the studies from Taiwan may adhere less strictly to a vegan diet. In these studies [18,28,35,39] the definition of vegan was less restrictive and was defined as consumption of non-animal based food 3 times a day, 30 days a month. When a subgroup analysis was done in restrictive compared to less restrictive definition of vegan in Asia, there was no difference in the result. This suggests that other factors may explain difference between Asian and non-Asian studies. For example, the diet pattern for omnivores in Asia may include less animal product than for non-Asian countries, so the differences between omnivores and vegans may be less. Diets across Asia are diverse, but there were no studies from other Asian countries which met inclusion criteria. Based on these observations the subgroup analysis which excludes Asian studies may provide a more reliable estimate of effects of a strictly vegan diet compared to a omnivorous diet in non-Asian countries.

The risk factor with the most evidence is body mass index, and this was consistently lower in vegans compared to controls in diverse geographies outside Asia, in larger and smaller studies, and in studies published over many years. Vegans consumed 980 less kilojoules per day which translated into 11% less energy than controls. Reduced energy intake rather than specific components of diet is the likely major reason for lower BMI and waist circumference in vegans.[65,66]

In non-Asian studies LDL cholesterol was 0.6mmol/l lower in vegans compared to controls based on observations in 1014 vegans from 24 studies. This reduction is consistent with effects of reducing saturated fat intake by 51%, and a 26% increase in PUFA intake compared to controls. [67,68] Avoidance of dairy food and meat [69] which may contain trans fatty acids, may also have a favourable effect on LDL cholesterol. In this study, it was not possible to assess the intake of processed foods that contain trans fatty acids in vegans or controls. Based on

![Fig 7. Systolic and diastolic blood pressure (mmHg) in vegans compared to omnivores.](https://doi.org/10.1371/journal.pone.0209086.g007)
randomised trials of statins, a 0.6mmol/L reduction in LDL-cholesterol would be expected to reduce cardiovascular risk by ~19%. [70]

In non-Asian studies systolic blood pressure was ~ 6mmHg lower in vegans compared to controls. This would be expected to reduce cardiovascular risk by ~12%. [71] This lower blood pressure is similar to that observed in a meta-analysis of vegetarian diets.[72] It is possible lower body mass index is the principal reason for lower blood pressure, triglycerides and glucose for vegans compared to controls. [73–75] We were not able to determine whether features of the vegan eating patterns, [41,76] such as higher fruit and vegetable intake, [3] or low intake of processed foods high in salt [3] contributed to lower blood pressure in vegans.

In non-Asian studies, vegans had -0.39mmol/l lower fasting blood glucose compared to controls. This is also consistent with randomised studies that suggest that the vegan diet improves glycaemic control in people with type 2 diabetes.[77,78] It was not possible to confidently assess the association between the vegan diet and insulin resistance as too few studies have reported this.

For many studies, self-identified vegans were sourced from vegan societies and websites, with omnivores from the broader community. For others, both vegans and omnivores were sourced from religious institutions. This may have impacted on cardiometabolic risk factors in both vegans and omnivores. For example, vegans who belong to vegan societies are more likely to be strictly vegan and to consider themselves as ethical and political vegans. [79] These vegans also are more likely to engage in other health behaviours like exercising more and smoking less which may impact on cardiometabolic risk factors. The difference between vegans and omnivores may therefore be more marked. In contrast where study populations are sourced from religious institutes, the difference between vegans and omnivores in diet and health behaviours may be less. For example, Buddhist nuns are often habitual vegans rather than strictly vegan and their omnivorous counterparts eat a diet that is low in animal products. This may dilute differences between the groups. Differences between Asian vegans and omnivores may also be reduced as the Asian diet is traditionally low in animal products and high in carbohydrates.

A vegan diet has favourable effects on multiple risk factors, which would be expected to reduce CV risk much more than an intervention which influenced only one risk factor. However the size of the CV risk reduction is difficult to quantify.[80] Also it is possible the vegan diet has other effects on health and CV risk by mechanisms such as inflammatory pathways which were not assessed in this meta-analysis. Deficiencies in some nutrients such as vitamin B12, creatine, carnosine, taurine, vitamin D3, heme-iron and the omega-3 fatty acids may also influence cardiovascular health.[76]

**Limitations**

It is possible some associations could be influenced by factors other than diet. Vegans may choose this diet because of perceived health benefits or religious/cultural reasons, and they may have fewer adverse health behaviours including smoking, drinking alcohol and sedentary lifestyle. [81]

Individual participant data was not available and this limits the ability to address a number of questions. We could not reliably evaluate possible gender differences, or associations between energy or saturated fat intake and cardiometabolic risk factors. Food frequency questionnaires are known to be unreliable, [82–84] and we could not assess the quality of the food consumed, including intake of processed food, trans fat and refined sugars. Most included studies were small, but results were similar in smaller and larger studies and by year of
publication. Associations with triglyceride need to be interpreted with caution due to the significant scattered distribution seen in the funnel plot.

Larger cohort studies which evaluate a broad range of risk factors would overcome the limitation of small numbers, and additional studies in diverse populations would provide further information on the effects of a vegan diet compared to other diets. However even large observational studies will be limited by the potential for bias related to the impact of non-diet related factors. Randomised clinical trials which compare introduction of a vegan with omnivorous diet would provide more reliable information on effects on cardio-metabolic risk factors, but have not been undertaken. A limitation is that maintaining a vegan diet for a prolonged time as part of a clinical trial may be difficult for many people.

**Conclusion**

In most countries a vegan diet has less energy and saturated fat compared to omnivorous control diets, and is associated with favourable cardiometabolic risk profile including lower body weight, LDL cholesterol, fasting blood glucose, blood pressure and triglycerides. These observations support other evidence that plant based diets are likely to lower the risk of cardiovascular disease and diabetes. However the improvement in cardiometabolic risk profile is also likely to depend on the comparison diet, and the difference may be less with some Asian compared to western dietary patterns.

**Supporting information**

**S1 File.** Supplementary document containing supplementary figures

- **Figure A:** Total energy intake (Mega joules) in vegans compared to omnivores
- **Figure B:** Total fat intake in grams per day in vegans compared to omnivores
- **Figure C:** Saturated fat intake in grams per day in vegans compared to omnivores
- **Figure D:** Monounsaturated fat intake in grams per day in vegans compared to omnivores
- **Figure E:** Polyunsaturated fat intake in grams per day in vegans compared to omnivores
- **Figure F:** Protein intake in grams per day in vegans compared to omnivores
- **Figure G:** Carbohydrate intake in grams per day in vegans compared to omnivores
- **Figure H:** Body mass index (kg/m2) in vegans compared to omnivores
- **Figure I:** Funnel plot of body mass index (kg/m2) in vegans compared to omnivores
- **Figure J:** Waist circumference (cm) in vegans compared to omnivores
- **Figure K:** Funnel plot waist circumference (cm) in vegans compared to omnivores
- **Figure L:** Fasting blood glucose (mmol/L) in vegans compared to omnivores
- **Figure M:** Fasting blood glucose (mmol/L) in vegans compared to omnivores
- **Figure N:** Insulin resistance as calculated by the homeostasis model (insulin resistance) in vegans compared to omnivores
- **Figure O:** Insulin resistance as calculated by the homeostasis model (insulin resistance) in vegans compared to omnivores
- **Figure P:** Low density lipoprotein cholesterol (mmol/L) level in vegans compared to omnivores
- **Figure Q:** Low density lipoprotein cholesterol (mmol/L) level in vegans compared to omnivores
- **Figure R:** Triglyceride (mmol/L) levels in vegans compared to omnivores
- **Figure S:** Triglyceride (mmol/L) levels in vegans compared to omnivores
- **Figure T:** Systolic blood pressure (mmHg) in vegans compared to omnivores
- **Figure U:** Systolic blood pressure (mmHg) in vegans compared to omnivores
- **Figure V:** Diastolic blood pressure (mmHg) in vegans compared to omnivores
- **Figure W:** Diastolic blood pressure (mmHg) in vegans compared to omnivores.

(DOCX)

**S2 File.** Study protocol.

(DOCX)
S3 File. Prisma 2009 checklist.
(DOCX)

S4 File. Newcastle—Ottawa Quality Assessment Scale (NOS Scale).
(DOCX)

S5 File. MOOSE checklist final.
(DOCX)

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