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Association between plant-based diets and plasma lipids: a systematic review and meta-analysis

Yoko Yokohama

Susan Levin

Neal Barnard
George Washington University

Lead Article

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Yoko Yokoyama, Susan M. Levin, and Neal D. Barnard

Context: *Although a recent meta-analysis of randomized controlled trials showed that adoption of a vegetarian diet reduces plasma lipids, the association between vegetarian diets and long-term effects on plasma lipids has not been subjected to meta-analysis.* ***Objective:*** *The aim was to conduct a systematic review and meta-analysis of observational studies and clinical trials that have examined associations between plant-based diets and plasma lipids.* ***Data Sources:*** *MEDLINE, Web of Science, and the Cochrane Central Register of Controlled Trials were searched for articles published in English until June 2015.* ***Study Selection:*** *The literature was searched for controlled trials and observational studies that investigated the effects of at least 4 weeks of a vegetarian diet on plasma lipids.* ***Data Extraction:*** *Two reviewers independently extracted the study methodology and sample size, the baseline characteristics of the study population, and the concentrations and variance measures of plasma lipids. Mean differences in concentrations of plasma lipids between vegetarian and comparison diet groups were calculated. Data were pooled using a random-effects model.* ***Results:*** *Of the 8385 studies identified, 30 observational studies and 19 clinical trials met the inclusion criteria ($N = 1484$; mean age, 48.6 years). Consumption of vegetarian diets was associated with lower mean concentrations of total cholesterol (−29.2 and −12.5 mg/dL, $P < 0.001$), low-density lipoprotein cholesterol (−22.9 and −12.2 mg/dL, $P < 0.001$), and high-density lipoprotein cholesterol (−3.6 and −3.4 mg/dL, $P < 0.001$), compared with consumption of omnivorous diets in observational studies and clinical trials, respectively. Triglyceride differences were −6.5 ($P = 0.092$) in observational studies and 5.8 mg/dL ($P = 0.090$) in intervention trials.* ***Conclusions:*** *Plant-based diets are associated with decreased total cholesterol, low-density lipoprotein cholesterol, and high-density lipoprotein cholesterol, but not with decreased triglycerides.* ***Systematic Review Registration:*** *PROSPERO number CRD42015023783. Available at: https://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42015023783.*

INTRODUCTION

Elevated blood concentrations of low-density lipoprotein cholesterol (LDL-C) are associated with increased risk of coronary heart disease. Although lowering LDL-C concentrations can reduce cardiovascular morbidity and mortality, hyperlipidemia is underdiagnosed and undertreated.[1] A 10% increase in the prevalence of

Affiliation: *Y. Yokoyama* is with the Graduate School of Media and Governance, Keio University, Fujisawa, Kanagawa, Japan. *S.M. Levin* and *N.D. Barnard* are with the Physicians Committee for Responsible Medicine, Washington, DC, USA. *N.D. Barnard* is with School of Medicine and Health Sciences, George Washington University, School of Medicine and Health Sciences, Washington, DC, USA.

Correspondence: *Y. Yokoyama*, Keio University, 5322 Endo, Fujisawa, Kanagawa, 252-0882, Japan. Email: yyokoyama-kyt@umin.ac.jp.

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treatment for hyperlipidemia could prevent an estimated 8000 deaths per year.[2] It has been further estimated that even modest steps, such as those proposed by the National Cholesterol Education Program Adult Treatment Panel 3 primary prevention guidelines, could prevent approximately 20 000 heart attacks and 10 000 deaths due to coronary heart disease and save almost $3 billion in heart disease-related medical costs per year.[3] Although LDL-C has been the primary lipoprotein of concern, total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), and triglycerides also play roles in heart disease risk, with TC, LDL-C, and triglycerides positively associated with risk and HDL-C possibly playing a protective role.[4] Here, "plasma lipids" refers to the group of lipids including TC, LDL-C, HDL-C, and triglycerides.

Modifiable factors, including diet, weight, and exercise, may play significant roles in developing hyperlipidemia.[5] Vegetarian diets are defined as diets that exclude meats; some vegetarian diets include dairy products and eggs. Vegetarian diets usually emphasize the consumption of fruits, vegetables, beans, and grains. Previous reviews have suggested that vegetarian diets are associated with lower plasma lipid concentrations.[6,7] Although a recent meta-analysis of randomized controlled trials showed that adoption of a vegetarian diet reduces plasma lipids, long-term effects of vegetarian diets were not studied. To the best of knowledge, the association between vegetarian diets and long-term effects on plasma lipids has not been subjected to meta-analysis. Therefore, a meta-analysis of studies that have examined vegetarian diets' relationship on plasma lipid concentrations was performed.

METHODS

Data sources and search strategy

The search strategy is shown in Table S1 in the Supporting Information online. The electronic databases MEDLINE, Web of Science, and the Cochrane Central Register of Controlled Trials were searched for English-language articles published from 1946 to June 2015, from 1900 to June 2015, and from 1966 to June 2015, respectively, and containing one or more of the keywords for vegetarian diets ("plant-based diet" or "diet, vegetarian" or "vegetarian diets" or "vegetarianism" or "diets vegan" or "vegan diets") and for plasma lipids ("hyperlipidemia" or "cholesterol" or "low-density lipoprotein" or "high-density lipoprotein" or "triglyceride"). The reference lists of the retrieved articles were then reviewed to identify additional articles. This review was registered with the PROSPERO register of systematic reviews (registration no. CRD42015023783) and was conducted in accordance with PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines.

Study selection

Two reviewers (Y.Y. and S.M.L.) separately searched and retrieved abstracts for articles that met the following inclusion criteria: (1) participants aged over 20 years; (2) an intervention or exposure consisting of a vegetarian diet, defined as a diet that included meat less than once per month; a semivegetarian diet, defined as a diet that included meat more than once per month, but less than once per week; a vegan diet, defined as a diet that excluded all animal products; or a vegetarian diet that included some animal products as defined by the terms "lacto" (dairy products), "ovo" (eggs), or "pesco" (fish); (3) the collection of sufficient data to allow calculation of mean differences in total or LDL-C between participants who consumed a vegetarian diet and those who consumed a control diet; and (4) the use of a controlled trial or observational study design. The following exclusion criteria were applied: (1) article not an original paper; (2) lack of a comparison diet; (3) lack of continuous lipid data; (4) use of a duplicate sample; (5) small sample size ($<$ 10); (6) animal studies; (7) trial duration of $<$ 4 weeks; (8) article not in English; and (9) for observational studies, failure to adjust for sex and age. The PICOS (Participants, Intervention, Comparators, Outcomes, Study Design) criteria are shown in Table 1.[10–39]

Data extraction and quality assessment

For each study, the following information was extracted: study methodology and sample size; baseline characteristics of the study population, including mean age, sex (proportion of men), use of antihyperlipidemic drugs, body mass index (BMI); diets examined and duration of their consumption; concentrations and variance measures of plasma lipids, including those measured in response to dietary interventions in clinical trials; adjustment factors for observational studies, and Jadad score for clinical trials.

Data synthesis and analysis

Mean differences in concentrations of plasma lipids (TC, LDL-C, HDL-C, triglycerides) between vegetarian and comparison diet groups were calculated. For intervention trials, the pooled standard error for the net difference in lipid concentrations was used or, when it was not given, estimated using the method of

Table 1 **PICOS criteria for inclusion and exclusion of studies**

Parameter	Criteria
Population	Adult humans, without regard to sex, race, or ethnicity
Intervention or exposure	Vegetarian or vegan diets
Comparator	Basis for comparison was preintervention total cholesterol, LDL-C, HDL-C, and triglyceride concentrations in the intervention group or the corresponding changes in an untreated comparison group, if available
Outcome	Primary outcomes: changes in LDL-C Secondary outcomes: changes in HDL-C, total cholesterol, triglycerides
Study design	Controlled trial or observational study design

Abbreviations: HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol.

Follmann et al,[8] assuming a correlation of 0.50 between the baseline and final plasma lipids values (parallel design) or between the intervention and the control period (crossover design) plasma lipid values. For studies comparing more than one exposure group or treatment arm, data were extracted from groups eating the fewest animal products, as this was deemed the best means of assessing the effects of vegetarian diets.

Using a random-effects model, which assigns a weight to each study on the basis of the study's inverse variance, estimates of differences in plasma lipids associated with consumption of vegetarian diets were combined. Using the study as the unit of analysis, estimates were obtained for observational studies and controlled trials separately. Estimates of plasma lipid differences were presented as means and 95%CIs. Statistical significance was set to 2-sided P values < 0.05. Although triglyceride concentrations typically do not follow a normal distribution, inverse variances were calculated from original data because a previous simulation study showed that results were consistent across a range of underlying effect size distributions.[9]

Analyses stratified by type of vegetarian diet, country, sample size, age, sex, BMI, duration of diet, antihyperlipidemic medication use, and baseline lipid status were conducted separately for controlled trials and observational studies. A sensitivity analysis to assess the impact of each study on the combined effect was conducted by performing a 1-study removed analysis. To assess heterogeneity, calculations of I^2 and meta-regression were done with subgroups, using the study as the unit of analysis.

To identify publication bias, funnel plots were created and examined, and to assess the relationship between sample size and effect size, Egger's test was performed. The "trim and fill" method, which determines where missing studies are likely to appear, was used to adjust for publication bias. These analyses were done separately for controlled trials and observational studies and were conducted for the main outcomes of TC and LDL-C. All analyses were performed using Comprehensive Meta-Analysis, version 2 software (BioStat, Englewood, NJ, USA).

RESULTS

Search results

The search strategy led to the retrieval of 8385 studies, of which 30 observational studies[10–39] and 19 clinical trials[40–58] met the inclusion criteria (Figure 1).

Study characteristics and quality

Observational studies. The 30 observational studies (Table 2[40–58]) included 10 143 participants (median sample size, 74.5; range, 13–3424) with a mean age of 40.6 years (range, 23.8–71.8 years). Each of the 30 observational studies used a cross-sectional design. In 23 of these studies, participants had been following vegetarian diets for more than 1 year.[10–12,14–19,22–24,26–36,38] Eight studies focused on vegan diets,[11,23,24,29,32,33,35,38] 12 on lacto-ovo-vegetarian diets,[15,17,19,21,25–28,30,31,37,39] and 10 on mixed diet types (vegan, lacto, lacto-ovo, pesco, and/or semivegetarian).[10,12–14,16,18,20,22,34,36] The matched or adjusted factors in each study are shown in Table 2.

Clinical trials. Nineteen clinical trials were identified (Table 3). These trials included a total of 1484 participants (median sample size = 58; range, 11–291) with a mean age of 48.6 years (range, 21–65 years). All were open (nonmasked) trials. The mean duration was 25.5 weeks. Eighteen were randomized controlled trials.[40–50,52–58] Vegan diets were examined in 9,[41,45–47,49,51–54] lacto-vegetarian diets in 2,[40,48] and lacto-ovo-vegetarian diets in 8.[42–44,50,55–58] Fourteen studies used a parallel design,[41–43,46,48–55,57,58] while 5 used a crossover design.[40,44,45,47,56] Baseline plasma lipid concentrations for each trial are shown in Table 3.

Pooled effects of vegetarian diets on plasma lipids. In the observational studies, consumption of vegetarian diets was associated with lower mean concentrations of TC (−29.2 mg/dL; 95%CI, −34.6, −23.8; $P < 0.001$; $I^2 = 81.4$; P for heterogeneity < 0.001); LDL-C (−22.9 mg/dL; 95%CI, −27.9, −17.9; $P < 0.001$; $I^2 = 83.3$; P for heterogeneity < 0.001); HDL-C (−3.6 mg/dL; 95%CI, −4.7, −2.5; $P < 0.001$; $I^2 = 49.7$;

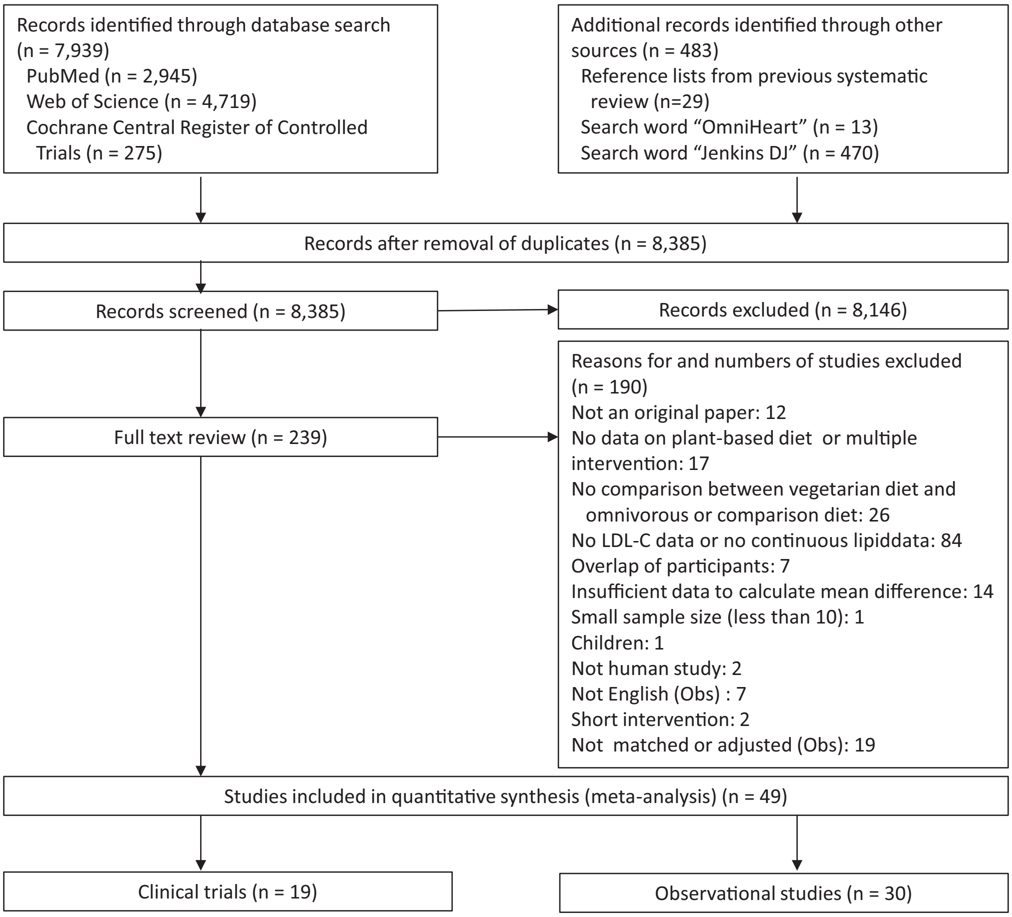


Figure 1 **Flow diagram of the literature search process.** *Abbreviations*: LDL-C, low-density lipoprotein cholesterol; Obs, observational study.

P for heterogeneity < 0.001); and triglycerides (−6.5 mg/dL; 95%CI, −14.0, 1.1; $P = 0.092$; $I^2 = 83.0$; P for heterogeneity < 0.001) compared with consumption of omnivorous diets (Figure 2A–D).

In the clinical trials, consumption of vegetarian diets was associated with a mean reduction in TC (−12.5 mg/dL; 95%CI, −17.8, −7.2; $P < 0.001$; $I^2 = 54.8$; P for heterogeneity $= 0.003$); LDL-C (−12.2 mg/dL; 95%CI, −17.7, −6.7; $P < 0.001$; $I^2 = 79.2$; P for heterogeneity < 0.001); and HDL-C (−3.4 mg/dL; 95%CI, −4.3, −2.5; $P < 0.001$; $I^2 = 8.5$; P for heterogeneity $= 0.354$) and a nonsignificant increase in triglyceride concentration (5.8 mg/dL; 95%CI, −0.9, 12.6; $P = 0.090$; $I^2 = 22.5$; P for heterogeneity $= 0.182$), compared with consumption of omnivorous diets (Figure 3A–D).

Subgroup analysis and meta-regression. Pooled changes in plasma lipids associated with consumption of vegetarian diets in planned strata for observational studies and clinical trials are summarized in Tables S2 and S3 in the Supporting Information online.

In observational studies, heterogeneity was statistically significant for TC, LDL-C, HDL-C, and triglycerides. Subgroup analysis in observational studies revealed that vegetarian effect size for TC and LDL-C was statistically larger with vegan than with lacto-ovo vegetarian diets; in studies conducted in North or South America; and in younger age groups ($<$ 50 vs $>$ 50 years). Moreover, LDL-C concentrations were lower in studies with smaller sample sizes ($<$ 100). Meta-regression in observational studies also revealed that younger age was associated with lower values for TC (0.44, $P < 0.001$) and LDL-C (0.31, $P = 0.002$). In addition, TC and LDL-C in vegetarian groups were lower in studies with smaller sample sizes (slope 0.006, $P < 0.001$ for TC; slope 0.006, $P < 0.001$ for LDL-C), larger percentages of male participants (slope −0.14, $P < 0.001$; slope −0.11, $P < 0.001$), and lower overall mean plasma lipids for all participants, vegetarian and nonvegetarian (slope 0.41, $P < 0.001$ for TC; slope 0.30, $P < 0.001$ for LDL-C).

In clinical trials, the reductions of TC and LDL-C were greater in the BMI subgroup 18.5 to 25 kg/m^2 than in other subgroups. Meta-regression also revealed that smaller BMI was associated with larger TC (slope 1.49, $P < 0.001$) or LDL-C (slope 1.02, $P < 0.001$) reductions with vegetarian diets. Participants who did not use

Table 2 **Study design and population characteristics of observational studies of plant-based diets and plasma lipids**

Reference, country	Study design	Matched factors	*N*	Mean age (y)	Percent male	Mean BMI (kg/m^2) or mean weight (kg)	Mean baseline plasma lipids (mg/dL)				Percent using medication	Duration of vegetarian diets	Exposure	Control	Comorbidities
							TC	LDL-C	HDL-C	TG					
Sacks et al (1975),[10] USA	CS	Age, sex	230	44.0	62.9	65.5 kg	155.0	95.5	46.0	72.5	Strongly discouraged using medication	38 mo	Pesco	Omnivorous	
Burslem et al (1978),[11] USA	CS	Age, sex	134	27.3	37.0	NR	161.6	103.3	45.9	85.4	0	5.2 y	Vegan	Omnivorous	No metabolic diseases
Male, 20–30 y	CS	Age, sex	45	20–30	100	NR	161.7	103.3	43.8	90.1	0	5.2 y	Vegan	Omnivorous	No metabolic diseases
Female, 20–30 y	CS	Age, sex	56	20–30	0.0	NR	156.4	99.9	47.0	81.4	0	5.2 y	Vegan	Omnivorous	No metabolic diseases
Male, 30–40 y	CS	Age, sex	15	30–40	100	NR	164.5	102.3	43.3	94.3	0	5.2 y	Vegan	Omnivorous	No metabolic diseases
Female, 30–40 y	CS	Age, sex	18	30–40	0.0	NR	175.1	114.8	50.1	78.3	0	5.2 y	Vegan	Omnivorous	No metabolic diseases
Huijbregts et al (1980),[39] the Netherlands	CS	Age, sex, weight	14	18–26	100	69.9 kg	176.9	106.5	55.3	100.1	NR	NR	Lacto-ovo	Omnivorous	Healthy
Nestel et al (1981),[37] Australia	CS	Age, sex, weight	13	28.5	100	63.9 kg	163.1	103.6	41.8	100.4	NR	NR	Lacto-ovo	Omnivorous	NR
Knuiman & West (1982),[23] the Netherlands	CS	Age, sex	27	33.8	100	23.0	172.3	98.1	42.9	NR	NR	4 y	Vegan	Omnivorous	NR
Liebman & Bazzarre (1983),[21] USA	CS	Age, sex, height, weight, exercise level, alcohol consumption, smoking	54	30.7	100	23.3	187.0	120.0	43.7	85.3	0	> 6 mo	Lacto-ovo	Omnivorous	No hyperlipidemia, CHD, angina, hypertension, or diabetes
Roshanai & Sanders (1984),[24] UK	CS	Age, sex	47	NR	48.9	22.0	151.6	87.1	52.9	58.3	NR	NR	Vegan	Omnivorous	NR
Male			23	NR	100	23.0	159.2	96.1	51.2	60.1					
Female			24	NR	0.0	21.0	144.2	78.5	54.5	56.7					
Fisher et al (1986),[12] USA	CS	Age, sex	50	20–47	44.0	NR	156.5	105.3	45.5	96.0	NR	Vegan 9 y; lacto-ovo 7.7 y	Vegan/lacto-ovo	Omnivorous	NR
Nieman et al (1989),[30] USA	CS	Age, sex, religion	37	71.8	0.0	23.3	229.1	139.5	64.6	123.5	0	47 y	Lacto-ovo	Omnivorous (low fat)	No stroke, hypertension, diabetes, cancer, or CHD
Sanders & Roshanai (1992),[29] UK	CS	Age, sex	40	32.3	50.0	21.9	157.0	90.4	54.4	61.3	0	12 y	Vegan	Omnivorous	Healthy (not receiving any treatment)
Male			20	32.5	100	22.7	160.3	96.5	51.2	62.4					
Female			20	32.0	0.0	21.2	153.7	84.3	57.6	60.2					
Krajcovicova-Kudlackova et al (1994),[34] Slovakia	CS	Age, sex, geographical region	109	23.8	50.5	21.7	183.0	111.9	51.3	99.9	NR	Males 2.4 y; females 2.8 y	Lacto-ovo/lacto	Omnivorous	Healthy
Male			55	24.0	100	22.6	185.5	114.4	50.8	102.6					
Female			54	23.6	0.0	20.7	180.3	109.4	51.8	97.2					

(continued)

Table 2 **Continued**

Reference, country	Study design	Matched factors	*N*	Mean age (y)	Percent male	Mean BMI (kg/m^2) or mean weight (kg)	Mean baseline plasma lipids (mg/dL)				Percent using medication	Duration of vegetarian diets	Exposure	Control	Comorbidities
							TC	LDL-C	HDL-C	TG					
Harman & Parnell (1998),[13] New Zealand	CS	Age, sex	47	42.8	48.9	24.9	196.1	127.4	49.4	99.5	NR	NR	Lacto/vegan	Omnivorous	NR
Male			23	44.7	100	25.2	197.0	129.3	46.4	106.3					
Female			24	41.0	0.0	24.7	195.3	125.7	52.2	93.0					
Li et al (1999),[25] Australia	CS	Sex	74	25.3	0.0	22.5	166.0	91.9	59.9	84.0	NR	> 6 mo	Lacto-ovo	Omnivorous	Healthy
Richter et al (1999),[28] Germany	CS	Age, sex	95	36.4	37.5	NR	200.5	124.9	51.8	109.9	NR	> 2 y	Lacto-ovo	Omnivorous	No diabetes, gout, hypo- or hyper-thyreosis, or disease of liver and kidney
Male			37	42.0	100	NR	205.0	129.9	46.4	130.5					
Female			58	33.0	0.0	NR	197.7	121.7	55.2	96.8					
Lee et al (2000),[15] Hong Kong	CS	Age, sex, BMI	193	40.0	36.8	23.7	183.2	113.6	49.6	95.2	NR	> 1 y	Lacto-ovo	Omnivorous	Healthy
Lu et al (2000),[16] Taiwan	CS	Age, sex	109	38.6	48.6	21.5	171.9	109.4	50.7	83.6	NR	> 2 y	Vegan/lacto	Omnivorous	No liver disease, diabetes, or hypertension
Male			53	38.0	100	21.9	169.0	113.1	43.4	88.6					
Female			56	39.2	0.0	21.2	171.5	103.9	56.7	77.3					
Lin et al (2001),[27] Taiwan	CS	Age, sex	40	57.5	50.0	24.0	164.0	118.0	47.0	97.0	0	> 1 y	Lacto-ovo	Omnivorous	No hypertension, diabetes, hyper-lipoproteinemia, or overt vascular disease
Goff et al (2005),[35] UK	CS	Age, sex, BMI	46	35.5	46.9	23.1	153.7	88.1	49.3	79.4	0	> 3 y	Vegan	Omnivorous	No diabetes, CHD, or metabolic disorder
Fu et al (2008),[17] Taiwan	CS	Age, sex	70	55.1	0.0	23.3	188.8	123.8	49.9	78.1	0	> 2 y (mean, 7.9 y)	Lacto-ovo	Omnivorous	Healthy
Teixeira et al (2007),[14] Brazil	CS	Age, sex, ethnicity, socioeconomic class	201	47.0	47.8	25.3	207.7	136.0	45.5	141.7	NR	> 5 y (mean, 19 y)	Lacto-ovo/vegan/pesco/ lacto	Omnivorous	
Karabudak et al (2008),[36] Turkey	CS	Age, sex, BMI	52	28.2	0.0	21.7	164.3	88.9	54.1	88.6	0	> 2 y	Semi-/lacto-ovo/lacto	Omnivorous	Healthy
Chen et al (2011),[31] Taiwan	CS	Sex	363	51.9	0.0	23.1	187.0	122.5	59.0	90.5	0	> 1 y	Lacto-ovo	Omnivorous	No diabetes, dyslipidemia, hypertension, cerebrovascular disease, chronic gingivitis, connective tissue disease, coronary artery disease, or fever
Fernandes Dourado et al (2011),[26] Brazil	CS	Age, sex	87	40.0	58.6	24.3	191.4	125.0	41.6	127.3	0	> 1 y (mean, 16 y)	Lacto-ovo	Omnivorous	No temporary or permanent physical impairments or chronic disease in those who took medications that might influence the lipid profile

(continued)

Table 2 **Continued**

Reference, country	Study design	Matched factors	*N*	Mean age (y)	Percent male	Mean BMI (kg/m^2) or mean weight (kg)	Mean baseline plasma lipids (mg/dL)				Percent using medication	Duration of vegetarian diets	Exposure	Control	Comorbidities
							TC	LDL-C	HDL-C	TG					
Yang et al (2011),[19] China	CS	Age, sex	300	33.3	100	23.9	177.2	108.8	45.1	109.6	NR	> 1 y (mean, 10.4 y)	Lacto-ovo	Omnivorous	No renal disease, cancer, diabetes, heart disease, or hypertension
Kim et al (2012),[18] Korea	CS	Age, sex	75	49.2	50.7	22.6	181.5	109.1	48.7	123.8	0	> 15 y (mean, 24.6 y)	Vegan/lacto-ovo	Omnivorous	Healthy
Gojda et al (2013),[38] Czech Republic	CS	Age, sex, BMI, ethnicity, physical activity, energy intake	21	28.4	57.1	22.7	147.8	77.5	58.5	60.5	0	> 3 y (mean, 8.05 y)	Vegan	Omnivorous	Healthy
Jung et al (2013),[20] Korea	CS	Age, sex	296	52.9	53.4	24.1	207.0	131.7	55.2	141.6	NR	NR	Vegan/lacto/ovo/lacto-ovo	Omnivorous	Metabolic syndrome (vegetarian, 30.4%, control, 17.6%)
Chiang et al (2013),[22] Taiwan	CS	Age, sex	706	56.4	0.0	23.3	189.9	123.7	57.2	107.2	0.4	>1 y	Lacto-ovo/lacto/ovo/vegan	Omnivorous	No systemic diseases such as cancer, heart failure, uremia, and liver cirrhosis or acute illness such as acute myocardial infarction
Huang et al (2014),[32] Taiwan	CS	Sex, pre- or post-menopausal	3424	43.2	0.0	NR	184.5	114.6	59.2	111.9	0	> 1 y	Vegan	Omnivorous	NR
Jian et al (2015),[33] Taiwan	CS	Sex	3189	43.4	100	NR	181.5	116.2	51.5	141.8	0	> 1 y	Vegan	Omnivorous	NR

Abbreviations: BMI, body mass index; CHD, coronary heart disease; CS, cross-sectional; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; NR, not reported; TC, total cholesterol; TG, triglycerides.

Table 3 **Study design and population characteristics of clinical trials of plant-based diets and plasma lipids**

Reference, country	Study design and duration	Jadad score	*N*	Mean age (y)	Percent male	Mean BMI (kg/m^2)	Mean baseline plasma lipids (mg/dL)				Medication use	Intervention diet	Control diet	Comorbidities
							TC	LDL-C	HDL-C	TG				
Kestin et al (1989),[44] Australia	RCT (CO), 6 wk	2	26	44.0	100	25.5	234.7	157.8	56.5	113.4	None	Lacto-ovo	Omnivorous	Not on hyperlipoproteinemia or hypertension medication
Ling et al (1992),[54] Finland	RCT (PL), 4 wk	2	18	42.8	22.2	26.6	213.3	141.5	50.1	102.3	NR	Vegan	Omnivorous	2 coronary heart disease, 1 obesity, 1 hypertension
Ornish et al (1998),[42] USA	RCT (PL), 48 wk	3	35	59.3	91.4	27.1	234.9	153.5	45.3	225.9	None	Ornish (low-fat lacto-ovo)	Omnivorous	Coronary heart disease
Nicholson et al (1999),[53] USA	RCT (PL), 12 wk	2	11	54.3	54.5	NR	207.6	NR	44.0	193.2	36.4 %	Low-fat vegan	Omnivorous	Non–insulin-dependent diabetes mellitus
Barnard et al (2000),[45] USA	RCT (CO), 8 wk	3	35	36.1	0	25.5	163.0	97.0	49.0	81.0	None	Low-fat vegan	Omnivorous	Healthy premenopausal women
Agren et al (2001),[46] Finland	RCT (PL), 12 wk	2	29	50.8	3.4	24.3	190.3	126.8	45.5	89.7	None	Vegan	Omnivorous	Rheumatoid arthritis
Dansinger et al (2005),[58] USA	RCT (PL), 48 wk	3	80	49.0	50.0	35.0	217.5	139.0	46.0	164.0	Mean of 2.4 medications per person	Ornish (low-fat lacto-ovo)	Calorie restriction	Presence of at least 1 of the metabolic cardiac risk factors
Gardner et al (2005),[43] USA	RCT (PL), 4 wk	3	120	48.5	50.0	26.5	224.3	148.9	48.3	128.5	None	Lacto-ovo	Omnivorous (low-fat)	No heart disease or diabetes
de Mello et al (2006),[40] Brazil	RCT (CO), 4 wk	2	17	59.0	82.4	26.2	206.5	132.3	45.2	139.1	None	Lacto (low-protein)	Omnivorous	T2D
Aldana et al (2007),[55] USA	RCT (PL), 48 wk	2	93	61.6	56.3	31.0	170.2	95.4	43.4	157.1	Yes, unknown percentage	Ornish (low-fat lacto-ovo)	Omnivorous	Coronary heart disease
Burke et al (2007),[50] USA	RCT (PL), 72 wk	2	176	44.0	13.1	34.0	204.0	NR	NR	134.0	None	Lacto-ovo (calorie- and fat-restricted)	Omnivorous (calorie- and fat-restricted)	Overweight and obese
Gardner et al (2007),[57] USA	RCT (PL), 48 wk	2	155	41.0	0.0	31.5	NR	107.4	50.5	118.5	None	Ornish (low-fat lacto-ovo)	Calorie restriction	Overweight in premenopause
Elkan et al (2008),[41] Sweden	RCT (PL), 12 wk	2	58	50.3	10.3	24.0	191.7	118.1	52.3	97.4	None	Vegan	Omnivorous	Rheumatoid arthritis
Barnard et al (2009),[49] USA	RCT (PL), 74 wk	3	99	55.6	39.4	34.9	193.0	111.1	51.0	153.2	54.5 %	Low-fat vegan	ADA diet	T2D

(continued)

Table 3 **Continued**

Reference, country	Study design and duration	Jadad score	*N*	Mean age (y)	Percent male	Mean BMI (kg/m^2)	Mean baseline plasma lipids (mg/dL)				Medication use	Intervention diet	Control diet	Comorbidities
							TC	LDL-C	HDL-C	TG				
Miller et al (2009),[56] USA	RCT (CO), 4 wk	2	18	30.6	50.0	22.6	184.9	107.2	62.2	78.1	None	Ornish (low-fat lacto-ovo)	Mediterranean South Beach	Healthy (no history of metabolic, hepatic, renal, or systemic disease)
Ferdowsian et al (2010),[51] USA	CT (PL), 22 wk	1	107	21–65	17.7	NR	186.5	105.4	51.8	147.2	Yes, unknown percentage	Low-fat vegan	Omnivorous	BMI $\geq$ 25 and/or T2D
Kahleova et al (2013),[48] Czech Republic	RCT (PL), 24 wk	2	74	56.2	47.3	35.1	166.3	98.8	41.8	186.0	51.4 %	Lacto	EASD diet	T2D
Mishra et al (2013),[52] USA	RCT (PL), 18 wk	3	291	45.2	17.2	35.0	187.6	108.2	55.2	121.4	NR	Low-fat vegan	Omnivorous	BMI $\geq$ 25 and/or T2D
Bunner et al (2014),[47] USA	RCT (CO), 16 wk	3	42	45.7	7.1	27.6	187.1	106.0	61.5	96.1	NR	Low-fat vegan	Omnivorous	Migraine

Abbreviations: ADA, American Diabetes Association; BMI, body mass index; CT, clinical trial; CO, crossover; EASD, European Association for the Study of Diabetes; NR, not reported; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; PL, parallel; RCT, randomized controlled trial; TC, total cholesterol; TG, triglycerides; T2D, type 2 diabetes.

lipid-lowering medication showed larger reductions in TC and LDL-C than participants who used them. Vegan diets were associated with larger LDL-C reductions than lacto-ovo vegetarian diets. Smaller sample size was associated with greater LDL-C reductions in the subgroup analysis and greater reductions of both TC and LDL-C in meta-regression analysis (slope 0.03, $P = 0.050$; and slope 0.03, $P = 0.015$, respectively).

Sensitivity analysis. In the 1-study removed analysis, results were largely unchanged, with plasma lipid differences between vegetarian and comparison groups ranging from −30.0 to −28.0 mg/dL for TC and from −23.74 to −21.96 mg/dL for LDL-C in observational studies ($P < 0.001$ in all cases) and from −13.5 to −10.4 mg/dL for TC and from −13.2 to −9.2 mg/dL for LDL-C in clinical trials (all results were $P < 0.001$).

Publication bias. Funnel plot outcomes revealed that larger trials reporting large reductions in TC were possibly overrepresented in observational studies. A few studies showing a smaller effect size were absent in the middle right side (see Figure S1A in the Supporting Information online). Egger's test could not confirm this impression ($P = 0.133$). Trim-and-fill method outcomes suggested that 7 studies were missing, and their addition would have changed the overall effect on TC to −23.8 mg/dL (95%CI, −29.6, −18.0).

Funnel plot outcomes for the clinical trials suggested that smaller trials that reported large reductions in TC were overrepresented (see Figure S1B in the Supporting Information online). If publication bias did not exist, study results would be symmetrically displayed about the mean effect size; studies showing smaller lipid reductions were missing in the bottom right side. Egger's test could not confirm this impression ($P = 0.069$). Trim-and-fill method outcomes suggested that 4 trials might have been missing, and their addition would have changed the overall effect on TC from −12.5 mg/dL to −8.57 mg/dL (95%CI, −14.79, −2.35).

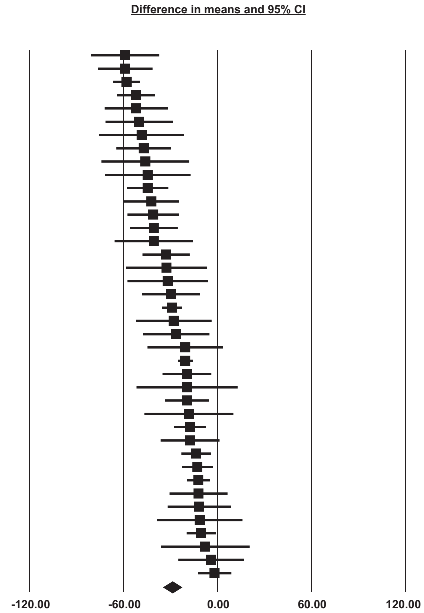
DISCUSSION

This meta-analysis of 30 observational studies and 19 controlled trials shows that, compared with consumption of omnivorous diets, consumption of vegetarian diets is associated with lower TC, LDL-C, and HDL-C concentrations but not with differences in triglyceride concentrations. The meta-analysis shows overall differences in TC of −29.2 mg/dL in observational studies and −12.5 mg/dL in clinical trials and differences in LDL-C of −22.9 mg/dL in observational studies and −12.2 mg/dL in clinical trials. High-density lipoprotein

A

Study name	Subgroup within study	Comparison	Outcome	Difference in means	Lower limit	Upper limit
Burslem et al., 1978 (11), 30-40 yr male	Vegan	Omnivorous	TC	-59.00	-81.09	-36.91
Burslem et al., 1978 (11), 20-30 yr male	Vegan	Omnivorous	TC	-59.00	-76.67	-41.33
Sacks et al., 1975 (10)	Pesco	Omnivorous	TC	-58.00	-66.71	-49.29
Teixeira et al., 2007 (14)	Lacto-ovo/ Vegan/ Pesco/ Lacto	Omnivorous	TC	-52.00	-64.38	-39.62
Lu et al., 2000 (16), female	Vegan/Lacto	Omnivorous	TC	-51.82	-72.22	-31.42
Nestel et al., 1981 (37)	Lacto-ovo	Omnivorous	TC	-50.00	-71.72	-28.28
Sanders & Roshanai, 1992 (29) , male	Vegan	Omnivorous	TC	-48.34	-75.68	-21.00
Fernandes Dourado et al., 2011 (26)	Lacto-ovo	Omnivorous	TC	-47.05	-64.79	-29.31
Burslem et al., 1978 (11), 30-40 yr female	Vegan	Omnivorous	TC	-46.00	-74.26	-17.74
Knuiman & West, 1982 (23)	Vegan	Omnivorous	TC	-44.47	-72.04	-16.91
Krajcovicova-Kudlackova et al., 1994 (34), female	Lacto-ovo/Lacto	Omnivorous	TC	-44.47	-57.82	-31.12
Lu et al., 2000, male (16)	Vegan/Lacto	Omnivorous	TC	-42.15	-60.00	-24.30
Burslem et al., 1978 (11), 20-30 yr female	Vegan	Omnivorous	TC	-41.00	-57.66	-24.34
Krajcovicova-Kudlackova et al., 1994 (34), male	Lacto-ovo/Lacto	Omnivorous	TC	-40.60	-56.07	-25.14
Roshanai & Sanders, 1984 (24), male	Vegan	Omnivorous	TC	-40.60	-65.90	-15.31
Fisher et al., 1986 (12)	Vegan/Lacto-ovo	Omnivorous	TC	-32.80	-48.05	-17.55
Nieman et al., 1989 (30)	Lacto-ovo	Omnivorous (low fat)	TC	-32.48	-58.66	-6.31
Richter et al., 1999 (28), male	Lacto-ovo	Omnivorous	TC	-31.71	-57.66	-5.76
Fu et al., 2008 (17)	Lacto-ovo	Omnivorous	TC	-29.60	-48.45	-10.75
Yang et al., 2011 (19)	Lacto-ovo	Omnivorous	TC	-29.00	-35.52	-22.48
Gojda et al., 2013 (38)	Vegan	Omnivorous	TC	-27.84	-52.26	-3.42
Richter et al., 1999 (28), female	Lacto-ovo	Omnivorous	TC	-26.30	-47.77	-4.82
Huijbregts et al., 1980 (39)	Lacto-ovo	Omnivorous	TC	-20.50	-44.89	3.90
Chiang et al., 2013 (22)	Lacto-ovo/lacto/Ovo/Vegan	Omnivorous	TC	-20.50	-25.44	-15.55
Kim et al., 2012 (18)	Vegan/Lacto-ovo	Omnivorous	TC	-19.44	-35.21	-3.67
Harman & Parnell, 1998 (13), female	Lacto/Vegan	Omnivorous	TC	-19.34	-51.86	13.19
Li et al., 1999 (25)	Lacto-ovo	Omnivorous	TC	-19.34	-33.54	-5.13
Sanders & Roshanai, 1992 (29), female	Vegan	Omnivorous	TC	-18.17	-46.83	10.48
Jian et al., 2015 (33)	Vegan	Omnivorous	TC	-17.50	-28.06	-6.94
Goff et al. 2005 (35)	Vegan	Omnivorous	TC	-17.40	-36.41	1.60
Huang et al., 2014 (32), postmenopausal	Vegan	Omnivorous	TC	-13.50	-23.20	-3.80
Lee et al., 2000 (15)	Lacto-ovo	Omnivorous	TC	-12.76	-22.82	-2.70
Chen et al., 2011 (31)	Lacto-ovo	Omnivorous	TC	-12.11	-19.64	-4.58
Liebman & Bazzarre, 1983 (21)	Lacto-ovo	Omnivorous	TC	-12.00	-30.71	6.71
Karabudak et al., 2008 (36)	Semi/ Lacto-ovo/ Lacto	Omnivorous	TC	-11.60	-31.99	8.79
Roshanai & Sanders, 1984 (24), female	Vegan	Omnivorous	TC	-11.21	-38.68	16.25
Jung et al., 2013 (20)	Vegan/Lacto/Ovo/Lacto-ovo	Omnivorous	TC	-10.30	-19.85	-0.75
Harman & Parnell, 1998 (13), male	Lacto/Vegan	Omnivorous	TC	-7.73	-36.23	20.76
Lin et al., 2001 (27)	Lacto-ovo	Omnivorous	TC	-4.00	-25.11	17.11
Huang et al., 2014 (32), premenopausal	Vegan	Omnivorous	TC	-1.80	-12.73	9.13
				-29.19	-34.57	-23.80

Statistics for each study

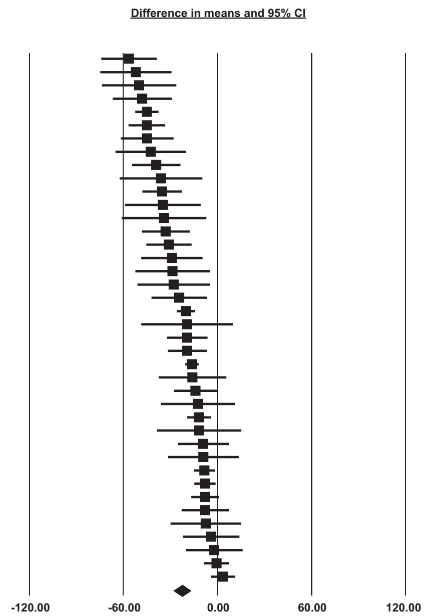


Meta Analysis

B

Study name	Subgroup within study	Comparison	Outcome	Difference in means	Lower limit	Upper limit
Fernandes Dourado et al., 2011 (26)	Lacto-ovo	Omnivorous	LDL	-56.390	-74.306	-38.474
Burslem et al., 1978 (11), 30-40 yr male	Vegan	Omnivorous	LDL	-52.000	-74.929	-29.071
Sanders & Roshanai, 1992 (29) , male	Vegan	Omnivorous	LDL	-49.884	-73.827	-25.941
Lu et al., 2000 (16), female	Vegan/Lacto	Omnivorous	LDL	-47.951	-67.020	-28.882
Sacks et al., 1975 (10)	Pesco	Omnivorous	LDL	-45.000	-52.606	-37.394
Teixeira et al., 2007 (14)	Lacto-ovo/ Vegan/ Pesco/ Lacto	Omnivorous	LDL	-45.000	-56.884	-33.116
Lu et al., 2000, male (16)	Vegan/Lacto	Omnivorous	LDL	-44.857	-61.912	-27.802
Roshanai & Sanders, 1984 (24), male	Vegan	Omnivorous	LDL	-42.537	-65.214	-19.860
Burslem et al., 1978 (11), 20-30 yr male	Vegan	Omnivorous	LDL	-39.000	-54.672	-23.328
Nestel et al., 1981 (37)	Lacto-ovo	Omnivorous	LDL	-36.000	-62.641	-9.359
Krajcovicova-Kudlackova et al., 1994 (34), female	Lacto-ovo/Lacto	Omnivorous	LDL	-35.190	-48.070	-22.309
Knuiman & West, 1982 (23)	Vegan	Omnivorous	LDL	-34.803	-59.145	-10.461
Burslem et al., 1978 (11), 30-40 yr female	Vegan	Omnivorous	LDL	-34.000	-61.204	-6.796
Burslem et al., 1978 (11), 20-30 yr female	Vegan	Omnivorous	LDL	-33.000	-48.443	-17.557
Krajcovicova-Kudlackova et al., 1994 (34), male	Lacto-ovo/Lacto	Omnivorous	LDL	-30.936	-45.517	-16.355
Richter et al., 1999 (28), female	Lacto-ovo	Omnivorous	LDL	-29.003	-48.792	-9.213
Nieman et al., 1989 (30)	Lacto-ovo	Omnivorous (low fat)	LDL	-28.616	-52.489	-4.743
Richter et al., 1999 (28), male	Lacto-ovo	Omnivorous	LDL	-27.842	-51.245	-4.439
Fu et al., 2008 (17)	Lacto-ovo	Omnivorous	LDL	-24.300	-42.204	-6.396
Yang et al., 2011 (19)	Lacto-ovo	Omnivorous	LDL	-20.108	-26.063	-14.154
Harman & Parnell, 1998 (13), female	Lacto/Vegan	Omnivorous	LDL	-19.335	-48.770	10.100
Kim et al., 2012 (18)	Vegan/Lacto-ovo	Omnivorous	LDL	-19.240	-32.396	-6.084
Fisher et al., 1986 (12)	Vegan/Lacto-ovo	Omnivorous	LDL	-19.200	-31.898	-6.502
Chiang et al., 2013 (22)	Lacto-ovo/lacto/Ovo/Vegan	Omnivorous	LDL	-16.241	-20.671	-11.811
Gojda et al., 2013 (38)	Vegan	Omnivorous	LDL	-15.855	-37.686	5.977
Li et al., 1999 (25)	Lacto-ovo	Omnivorous	LDL	-13.921	-27.872	0.030
Sanders & Roshanai, 1992 (29), female	Vegan	Omnivorous	LDL	-12.374	-36.280	11.531
Jian et al., 2015 (33)	Vegan	Omnivorous	LDL	-11.800	-19.653	-3.947
Harman & Parnell, 1998 (13), male	Lacto/Vegan	Omnivorous	LDL	-11.601	-38.685	15.483
Liebman & Bazzarre, 1983 (21)	Lacto-ovo	Omnivorous	LDL	-9.000	-25.471	7.471
Huijbregts et al., 1980 (39)	Lacto-ovo	Omnivorous	LDL	-8.894	-31.641	13.852
Chen et al., 2011 (31)	Lacto-ovo	Omnivorous	LDL	-8.260	-15.177	-1.343
Huang et al., 2014 (32), postmenopausal	Vegan	Omnivorous	LDL	-7.900	-14.890	-0.910
Lee et al., 2000 (15)	Lacto-ovo	Omnivorous	LDL	-7.734	-16.816	1.348
Karabudak et al., 2008 (36)	Semi/ Lacto-ovo/ Lacto	Omnivorous	LDL	-7.734	-23.033	7.565
Roshanai & Sanders, 1984 (24), female	Vegan	Omnivorous	LDL	-7.347	-30.085	15.390
Lin et al., 2001 (27)	Lacto-ovo	Omnivorous	LDL	-4.000	-22.287	14.287
Goff et al. 2005 (35)	Vegan	Omnivorous	LDL	-1.934	-20.247	16.380
Jung et al., 2013 (20)	Vegan/Lacto/Ovo/Lacto-ovo	Omnivorous	LDL	-0.500	-8.555	7.555
Huang et al., 2014 (32), premenopausal	Vegan	Omnivorous	LDL	3.600	-4.348	11.548
				-22.927	-27.923	-17.931

Statistics for each study



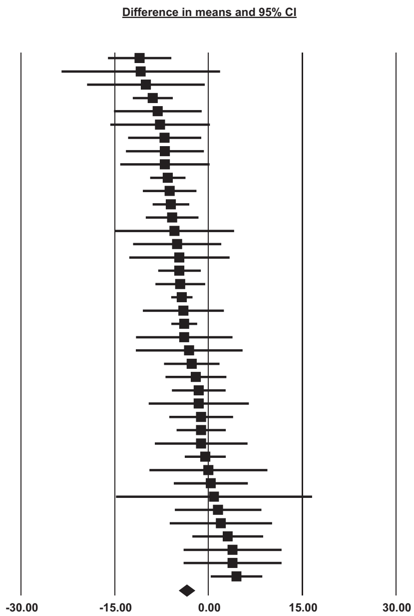
Meta Analysis

Figure 2 **Pooled plasma lipid responses to vegetarian diets in observational studies.** Effects on (**A**) TC (total cholesterol), (**B**) LDL-C (low-density lipoprotein cholesterol),

C

Study name	Subgroup within study	Comparison	Outcome	Difference in means	Lower limit	Upper limit
Burslem et al., 1978 (11), 20-30 yr male	Vegan	Omnivorous	HDL	-11.000	-16.117	-5.883
Gojda et al., 2013 (38)	Vegan	Omnivorous	HDL	-10.828	-23.561	1.906
Burslem et al., 1978 (11), 30-40 yr female	Vegan	Omnivorous	HDL	-10.000	-19.459	-0.541
Jung et al., 2013 (20)	Vegan/Lacto/Ovo/Lacto-ovo	Omnivorous	HDL	-8.900	-12.151	-5.649
Fisher et al., 1986 (12)	Vegan/Lacto-ovo	Omnivorous	HDL	-8.100	-15.168	-1.032
Karabudak et al., 2008 (36)	Semi/ Lacto-ovo/ Lacto	Omnivorous	HDL	-7.734	-15.747	0.279
Burslem et al., 1978 (11), 20-30 yr female	Vegan	Omnivorous	HDL	-7.000	-12.900	-1.100
Huijbregts et al., 1980 (39)	Lacto-ovo	Omnivorous	HDL	-6.961	-13.250	-0.671
Lu et al., 2000 (16), female	Vegan/Lacto	Omnivorous	HDL	-6.961	-14.165	0.244
Chen et al., 2011 (31)	Lacto-ovo	Omnivorous	HDL	-6.500	-9.374	-3.626
Huang et al., 2014 (32), premenopausal	Vegan	Omnivorous	HDL	-6.200	-10.542	-1.858
Sacks et al., 1975 (10)	Pesco	Omnivorous	HDL	-6.000	-8.975	-3.025
Jian et al., 2015 (33)	Vegan	Omnivorous	HDL	-5.800	-10.069	-1.531
Nieman et al., 1989 (30)	Lacto-ovo	Omnivorous (low fat)	HDL	-5.414	-14.984	4.156
Burslem et al., 1978 (11), 30-40 yr male	Vegan	Omnivorous	HDL	-5.000	-12.095	2.095
Li et al., 1999 (25)	Lacto-ovo	Omnivorous	HDL	-4.640	-12.712	3.432
Lee et al., 2000 (15)	Lacto-ovo	Omnivorous	HDL	-4.640	-8.091	-1.189
Huang et al., 2014 (32), postmenopausal	Vegan	Omnivorous	HDL	-4.500	-8.538	-0.462
Yang et al., 2011 (19)	Lacto-ovo	Omnivorous	HDL	-4.254	-6.005	-2.502
Nestel et al., 1981 (37)	Lacto-ovo	Omnivorous	HDL	-4.000	-10.534	2.534
Chiang et al., 2013 (22)	Lacto-ovo/lacto/Ovo/Vegan	Omnivorous	HDL	-3.867	-5.981	-1.753
Goff et al. 2005 (35)	Vegan	Omnivorous	HDL	-3.867	-11.642	3.908
Sanders & Roshanai, 1992 (29), female	Vegan	Omnivorous	HDL	-3.094	-11.668	5.481
Kim et al., 2012 (18)	Vegan/Lacto-ovo	Omnivorous	HDL	-2.660	-7.151	1.831
Liebman & Bazzarre, 1983 (21)	Lacto-ovo	Omnivorous	HDL	-2.000	-6.914	2.914
Krajcovicova-Kudlackova et al., 1994 (34), female	Lacto-ovo/Lacto	Omnivorous	HDL	-1.547	-5.893	2.800
Roshanai & Sanders, 1984 (24), female	Vegan	Omnivorous	HDL	-1.547	-9.604	6.510
Lu et al., 2000, male (16)	Vegan/Lacto	Omnivorous	HDL	-1.160	-6.311	3.991
Krajcovicova-Kudlackova et al., 1994 (34), male	Lacto-ovo/Lacto	Omnivorous	HDL	-1.160	-5.148	2.828
Sanders & Roshanai, 1992 (29) , male	Vegan	Omnivorous	HDL	-1.160	-8.625	6.305
Teixeira et al., 2007 (14)	Lacto-ovo/ Vegan/ Pesco/ Lacto	Omnivorous	HDL	-0.500	-3.836	2.836
Harman & Parnell, 1998 (13), male	Lacto/Vegan	Omnivorous	HDL	0.000	-9.491	9.491
Roshanai & Sanders, 1984 (24), male	Vegan	Omnivorous	HDL	0.387	-5.575	6.349
Fu et al., 2008 (17)	Lacto-ovo	Omnivorous	HDL	0.900	-14.835	16.635
Richter et al., 1999 (28), male	Lacto-ovo	Omnivorous	HDL	1.547	-5.431	8.524
Lin et al., 2001 (27)	Lacto-ovo	Omnivorous	HDL	2.000	-6.234	10.234
Richter et al., 1999 (28), female	Lacto-ovo	Omnivorous	HDL	3.094	-2.622	8.809
Knuiman & West, 1982 (23)	Vegan	Omnivorous	HDL	3.867	-4.029	11.763
Harman & Parnell, 1998 (13), female	Lacto/Vegan	Omnivorous	HDL	3.867	-4.022	11.756
Fernandes Dourado et al., 2011 (26)	Lacto-ovo	Omnivorous	HDL	4.500	0.329	8.671
				-3.590	-4.728	-2.452

Statistics for each study

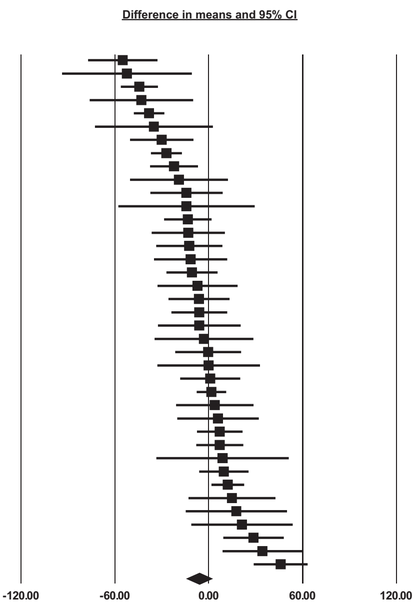


Meta Analysis

D

Study name	Subgroup within study	Comparison	Outcome	Difference in means	Lower limit	Upper limit
Goff et al. 2005 (35)	Vegan	Omnivorous	TG	-54.913	-77.295	-32.531
Richter et al., 1999 (28), male	Lacto-ovo	Omnivorous	TG	-52.256	-93.921	-10.592
Krajcovicova-Kudlackova et al., 1994 (34), male	Lacto-ovo/Lacto	Omnivorous	TG	-44.285	-56.371	-32.199
Teixeira et al., 2007 (14)	Lacto-ovo/ Vegan/ Pesco/ Lacto	Omnivorous	TG	-43.000	-76.243	-9.757
Krajcovicova-Kudlackova et al., 1994 (34), female	Lacto-ovo/Lacto	Omnivorous	TG	-38.085	-48.040	-28.130
Burslem et al., 1978 (11), 30-40 yr male	Vegan	Omnivorous	TG	-35.000	-72.938	2.938
Fu et al., 2008 (17)	Lacto-ovo	Omnivorous	TG	-30.000	-50.463	-9.537
Sacks et al., 1975 (10)	Pesco	Omnivorous	TG	-27.000	-37.094	-16.906
Yang et al., 2011 (19)	Lacto-ovo	Omnivorous	TG	-22.143	-37.678	-6.607
Liebman & Bazzarre, 1983 (21)	Lacto-ovo	Omnivorous	TG	-19.000	-50.506	12.506
Richter et al., 1999 (28), female	Lacto-ovo	Omnivorous	TG	-14.171	-37.489	9.147
Sanders & Roshanai, 1992 (29), female	Vegan	Omnivorous	TG	-14.171	-57.923	29.580
Lu et al., 2000 (16), female	Vegan/Lacto	Omnivorous	TG	-13.286	-28.668	2.097
Burslem et al., 1978 (11), 20-30 yr male	Vegan	Omnivorous	TG	-13.000	-36.589	10.589
Huijbregts et al., 1980 (39)	Lacto-ovo	Omnivorous	TG	-12.400	-33.754	8.955
Roshanai & Sanders, 1984 (24), female	Vegan	Omnivorous	TG	-11.514	-35.125	12.097
Li et al., 1999 (25)	Lacto-ovo	Omnivorous	TG	-10.628	-27.170	5.913
Lu et al., 2000, male (16)	Vegan/Lacto	Omnivorous	TG	-7.086	-32.892	18.721
Gojda et al., 2013 (38)	Vegan	Omnivorous	TG	-6.200	-25.921	13.521
Burslem et al., 1978 (11), 20-30 yr female	Vegan	Omnivorous	TG	-6.000	-24.056	12.056
Lin et al., 2001 (27)	Lacto-ovo	Omnivorous	TG	-6.000	-32.622	20.622
Nestel et al., 1981 (37)	Lacto-ovo	Omnivorous	TG	-3.000	-34.772	28.772
Huang et al., 2014 (32), postmenopausal	Vegan	Omnivorous	TG	-0.300	-21.542	20.942
Harman & Parnell, 1998 (13), male	Lacto/Vegan	Omnivorous	TG	0.000	-32.980	32.980
Jung et al., 2013 (20)	Vegan/Lacto/Ovo/Lacto-ovo	Omnivorous	TG	1.000	-18.420	20.420
Chiang et al., 2013 (22)	Lacto-ovo/lacto/Ovo/Vegan	Omnivorous	TG	1.771	-7.839	11.382
Fisher et al., 1986 (12)	Vegan/Lacto-ovo	Omnivorous	TG	3.900	-21.047	28.847
Burslem et al., 1978 (11), 30-40 yr female	Vegan	Omnivorous	TG	6.000	-20.268	32.268
Roshanai & Sanders, 1984 (24), male	Vegan	Omnivorous	TG	7.086	-7.655	21.826
Lee et al., 2000 (15)	Lacto-ovo	Omnivorous	TG	7.086	-8.168	22.340
Nieman et al., 1989 (30)	Lacto-ovo	Omnivorous (low fat)	TG	8.857	-33.670	51.384
Sanders & Roshanai, 1992 (29) , male	Vegan	Omnivorous	TG	9.743	-6.262	25.747
Chen et al., 2011 (31)	Lacto-ovo	Omnivorous	TG	12.250	1.609	22.891
Jian et al., 2015 (33)	Vegan	Omnivorous	TG	14.900	-13.126	42.926
Karabudak et al., 2008 (36)	Semi/ Lacto-ovo/ Lacto	Omnivorous	TG	17.714	-14.857	50.285
Kim et al., 2012 (18)	Vegan/Lacto-ovo	Omnivorous	TG	21.290	-11.337	53.917
Huang et al., 2014 (32), premenopausal	Vegan	Omnivorous	TG	28.700	9.188	48.212
Fernandes Dourado et al., 2011 (26)	Lacto-ovo	Omnivorous	TG	34.390	8.648	60.132
Harman & Parnell, 1998 (13), female	Lacto/Vegan	Omnivorous	TG	46.033	28.637	63.429
				-6.485	-14.034	1.063

Statistics for each study

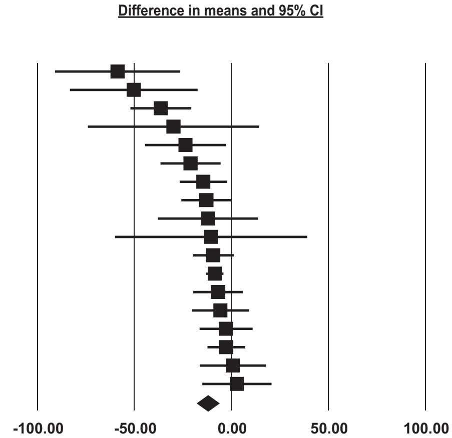


Meta Analysis

Figure 2 (Continued) (**C**) HDL-C (high-density lipoprotein cholesterol), and (**D**) triglycerides are depicted as squares; error bars indicate 95%CIs. Meta-analysis yielded pooled estimates of TC (−29.2 mg/dL; 95%CI, −34.6, −23.8; $P < 0.001$); LDL (−22.9 mg/dL; 95%CI, −27.9, −17.9; $P < 0.001$); HDL-C (−3.6 mg/dL; 95%CI, −4.7, −2.5; $P < 0.001$); and triglycerides (−6.5 mg/dL; 95%CI, −14.0, 1.1; $P = 0.092$), which are depicted as black diamonds. Vegan diets were defined as those that omitted all animal products; vegetarian diets may include some animal products, as indicated by the terms lacto (dairy products), ovo (eggs), and pesco (fish). Reference numbers of studies are shown in parentheses.

A

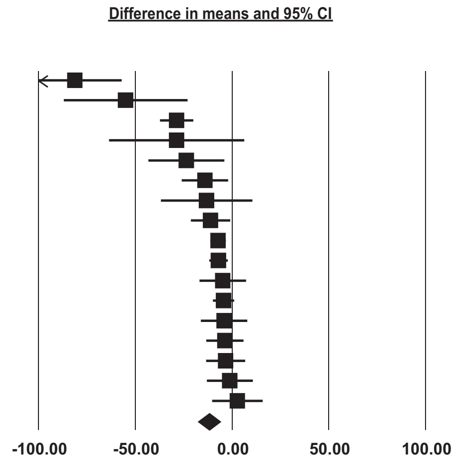
Study name	Subgroup within study	Comparison	Outcome	Difference in means	Lower limit	Upper limit
Ornish et al., 1998 (42)	Lacto-ovo	Omnivorous	TC	-58.600	-91.054	-26.146
Elkan et al., 2008 (41)	Vegan	Omnivorous	TC	-50.271	-83.332	-17.210
Agren et al., 2001 (46)	Vegan	Omnivorous	TC	-36.350	-52.186	-20.514
Ling et al., 1992 (54)	Vegan	Omnivorous	TC	-29.776	-74.068	14.516
Kestin et al., 1989 (44)	Lacto-ovo	Omnivorous	TC	-23.589	-44.644	-2.534
Barnard et al., 2000 (45)	Vegan	Omnivorous	TC	-21.000	-36.652	-5.348
Bunner et al., 2014 (47)	Vegan	Omnivorous	TC	-14.400	-26.797	-2.003
Miller et al., 2009 (56)	Lacto-ovo	Mediterranean	TC	-12.900	-25.927	0.127
de Mello et al., 2006 (40)	Lacto-ovo	Omnivorous	TC	-11.988	-38.027	14.052
Nicholson et al., 1999 (53)	Vegan	Omnivorous	TC	-10.441	-60.163	39.281
Ferdowsian et al., 2010 (51)	Vegan	Omnivorous	TC	-9.300	-20.025	1.425
Mishra et al., 2013 (52)	Vegan	Omnivorous	TC	-8.500	-13.131	-3.869
Barnard et al., 2009 (49)	Vegan	ADA diet	TC	-6.800	-19.786	6.186
Burke et al., 2007 (50), pref no	Lacto-ovo	Carorie restricted, low fat	TC	-5.600	-20.441	9.241
Kahleova et al., 2013 (48)	Lacto-ovo	EASD diet	TC	-2.707	-16.547	11.133
Dansinger et al., 2005 (58)	Lacto-ovo	Carolie restricted	TC	-2.600	-12.483	7.283
Aldana et al., 2007 (55)	Lacto-ovo	Omnivorous	TC	0.800	-16.357	17.957
Burke et al., 2007 (50), pref yes	Lacto-ovo	Carorie restricted, low fat	TC	2.900	-15.095	20.895
				-12.454	-17.758	-7.150



Meta Analysis

B

Study name	Subgroup within study	Comparison	Outcome	Difference in means	Lower limit	Upper limit
Elkan et al., 2008 (41)	Vegan	Omnivorous	LDL	-81.207	-105.548	-56.866
Ornish et al., 1998 (42)	Lacto-ovo	Omnivorous	LDL	-54.970	-87.107	-22.833
Agren et al., 2001 (46)	Vegan	Omnivorous	LDL	-28.616	-37.403	-19.829
Ling et al., 1992 (54)	Vegan	Omnivorous	LDL	-28.616	-63.682	6.450
Kestin et al., 1989 (44)	Lacto-ovo	Omnivorous	LDL	-23.589	-43.395	-3.782
Barnard et al., 2000 (45)	Vegan	Omnivorous	LDL	-14.000	-26.168	-1.832
de Mello et al., 2006 (40)	Lacto-ovo	Omnivorous	LDL	-13.148	-36.950	10.654
Bunner et al., 2014 (47)	Vegan	Omnivorous	LDL	-11.100	-21.385	-0.815
Mishra et al., 2013 (52)	Vegan	Omnivorous	LDL	-7.200	-11.382	-3.018
Gardner et al., 2005 (43)	Lacto-ovo	Low fat	LDL	-7.000	-11.949	-2.051
Miller et al., 2009 (56)	Lacto-ovo	Mediterranean	LDL	-4.800	-16.996	7.396
Gardner et al., 2007 (57)	Lacto-ovo	National guideline	LDL	-4.400	-10.071	1.271
Barnard et al., 2009 (49)	Vegan	ADA diet	LDL	-4.100	-16.245	8.045
Ferdowsian et al., 2010 (51)	Vegan	Omnivorous	LDL	-3.700	-13.436	6.036
Dansinger et al., 2005 (58)	Lacto-ovo	Carolie restricted	LDL	-3.300	-13.531	6.931
Kahleova et al., 2013 (48)	Lacto-ovo	EASD diet	LDL	-1.160	-13.143	10.822
Aldana et al., 2007 (55)	Lacto-ovo	Omnivorous	LDL	2.760	-10.430	15.950
				-12.188	-17.710	-6.665



Meta Analysis

Figure 3 **Pooled plasma lipid responses to vegetarian diets in clinical trials.** Effects on (**A**) TC (total cholesterol), (**B**) LDL-C (low-density lipoprotein cholesterol),

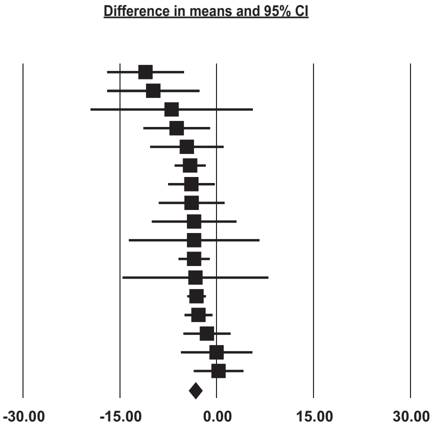
cholesterol was also lower in vegetarian groups than in omnivorous groups, although the degree of difference was relatively modest (−3.6 mg/dL in observational studies and −3.4 mg/dL in clinical trials). Subgroup analysis indicated that younger age (< 50 years), male sex, lower baseline plasma lipids, and lower BMI were associated with greater reductions in TC and LDL-C.

The findings of the current study are consistent with those of previous reviews,[6,7] and the present analysis extends these findings to include a meta-analysis of observational study data. While observational studies present a higher risk of bias compared with clinical trials, they also reflect long-term effects of vegetarian diets on plasma lipids that are not apparent in most clinical trials. Those who have followed vegetarian dietary patterns for longer periods may have healthier body compositions as well as better adherence to a vegetarian diet, both of which may have an effect on blood lipids. In addition, this study presents the raw mean difference for each endpoint, which is useful when the measure is meaningful either inherently or because of widespread use.[59]

For context, a previous meta-analysis showed that, on average, statin use reduced LDL-C concentrations

C

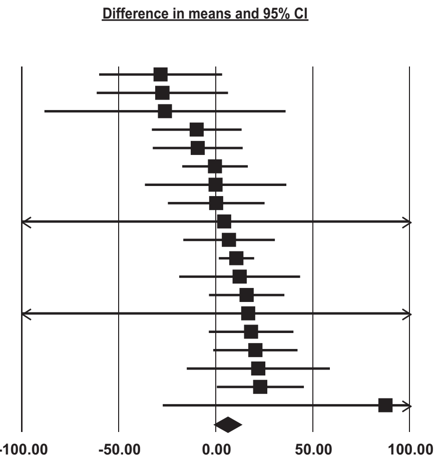
Study name	Subgroup within study	Comparison	Outcome	Difference in means	Lower limit	Upper limit
Barnard et al., 2000 (45)	Vegan	Omnivorous	HDL	-11.000	-17.000	-5.000
Miller et al., 2009 (56)	Lacto-ovo	Mediterranean	HDL	-9.800	-17.007	-2.593
Nicholson et al., 1999 (53)	Vegan	Omnivorous	HDL	-6.961	-19.568	5.647
Agren et al., 2001 (46)	Vegan	Omnivorous	HDL	-6.187	-11.409	-0.965
Bunner et al., 2014 (47)	Vegan	Omnivorous	HDL	-4.600	-10.346	1.146
Ferdowsian et al., 2010 (51)	Vegan	Omnivorous	HDL	-4.100	-6.571	-1.629
Dansinger et al., 2005 (58)	Lacto-ovo	Carolie restricted	HDL	-3.900	-7.570	-0.230
Elkan et al., 2008 (41)	Vegan	Omnivorous	HDL	-3.867	-9.014	1.280
Kestin et al., 1989 (44)	Lacto-ovo	Omnivorous	HDL	-3.480	-10.099	3.138
Ling et al., 1992 (54)	Vegan	Omnivorous	HDL	-3.480	-13.636	6.676
Kahleova et al., 2013 (48)	Lacto-ovo	EASD diet	HDL	-3.480	-5.947	-1.013
Ornish et al., 1998 (42)	Lacto-ovo	Omnivorous	HDL	-3.280	-14.632	8.072
Mishra et al., 2013 (52)	Vegan	Omnivorous	HDL	-3.100	-4.594	-1.606
Gardner et al., 2007 (57)	Lacto-ovo	National guideline	HDL	-2.800	-5.020	-0.580
Aldana et al., 2007 (55)	Lacto-ovo	Omnivorous	HDL	-1.500	-5.214	2.214
de Mello et al., 2006 (40)	Lacto-ovo	Omnivorous	HDL	0.000	-5.573	5.573
Barnard et al., 2009 (49)	Vegan	ADA diet	HDL	0.300	-3.601	4.201
				-3.398	-4.335	-2.462



Meta Analysis

D

Study name	Subgroup within study	Comparison	Outcome	Difference in means	Lower limit	Upper limit
Kahleova et al., 2013 (48)	Lacto-ovo	EASD diet	TG	-28.342	-60.164	3.479
Ling et al., 1992 (54)	Vegan	Omnivorous	TG	-27.457	-61.420	6.506
Barnard et al., 2009 (49)	Vegan	ADA diet	TG	-26.100	-88.413	36.213
Agren et al., 2001 (46)	Vegan	Omnivorous	TG	-9.743	-33.013	13.528
Ferdowsian et al., 2010 (51)	Vegan	Omnivorous	TG	-9.200	-32.528	14.128
Gardner et al., 2007 (57)	Lacto-ovo	National guideline	TG	-0.300	-17.349	16.749
Elkan et al., 2008 (41)	Vegan	Omnivorous	TG	0.000	-36.619	36.619
Burke et al., 2007 (50), pref no	Lacto-ovo	Carorie restricted, low fat	TG	0.300	-24.778	25.378
de Mello et al., 2006 (40)	Lacto-ovo	Omnivorous	TG	4.429	-301.801	310.658
Bunner et al., 2014 (47)	Vegan	Omnivorous	TG	6.900	-16.853	30.653
Mishra et al., 2013 (52)	Vegan	Omnivorous	TG	10.700	1.489	19.911
Burke et al., 2007 (50), pref yes	Lacto-ovo	Carorie restricted, low fat	TG	12.400	-18.911	43.711
Barnard et al., 2000 (45)	Vegan	Omnivorous	TG	16.000	-3.600	35.600
Nicholson et al., 1999 (53)	Vegan	Omnivorous	TG	16.828	-106.031	139.687
Dansinger et al., 2005 (58)	Lacto-ovo	Carolie restricted	TG	18.300	-3.650	40.250
Miller et al., 2009 (56)	Lacto-ovo	Mediterranean	TG	20.500	-1.397	42.397
Aldana et al., 2007 (55)	Lacto-ovo	Omnivorous	TG	22.010	-15.003	59.023
Kestin et al., 1989 (44)	Lacto-ovo	Omnivorous	TG	23.028	0.437	45.619
Ornish et al., 1998 (42)	Lacto-ovo	Omnivorous	TG	87.600	-27.441	202.641
				5.825	-0.919	12.569



Meta Analysis

Figure 3 (Continued) (**C**) HDL-C (high-density lipoprotein cholesterol), and (**D**) triglycerides are depicted as squares; error bars indicate 95%CIs. Meta-analysis yielded pooled estimates of TC (−12.5 mg/dL; 95%CI, −17.8, −7.2; $P < 0.001$); LDL-C (−12.2 mg/dL; 95%CI, −17.7, −6.7; $P < 0.001$); HDL-C (−3.4 mg/dL; 95%CI, −4.3, −2.5; $P < 0.001$); and triglycerides (5.8 mg/dL; 95%CI, −0.9, 12.6; $P = 0.090$), which are depicted as black diamonds. Vegan diets were defined as those that omitted all animal products; vegetarian diets may include some animal products, as indicated by the terms lacto (dairy products) and ovo (eggs). Reference numbers of studies are shown in parentheses.

by 70 mg/dL (1.8 mmol), with considerable variation depending on statin type.[60] The results of the present analysis showed that diet alone reduced LDL-C by 22.9 mg/dL in observational studies and by 12.2 mg/dL in clinical trials. While dietary changes may not be as powerful as statins in reducing plasma lipids, dietary and pharmacologic interventions are not mutually exclusive. They can work together, and, in some cases, dietary practices can obviate the need for medications. Because side effects may interfere with medication compliance and may preclude statin use for certain patients, dietary options have some intrinsic advantages.

Vegetarian diets are typically lower in saturated fatty acids and cholesterol, compared with omnivorous diets. In 3 large cohort studies that included large numbers of vegetarian participants (Adventist Health Study 2 cohort, European Prospective Investigation into Cancer and Nutrition (EPIC)-Oxford study, and UK Women's Study), intakes of saturated fatty acid and cholesterol were lower in vegetarians than in omnivorous participants, with strict vegetarians having the lowest intakes of both.[61] The subgroup analysis in the present study showed that a vegan diet had larger effects on plasma lipids than a lacto-ovo vegetarian diet. The observed effects of plant-based diets on plasma lipids are likely to be, in large part, the result of differences in saturated fatty acid intake and, to a lesser extent, cholesterol intake.[62,63] The role of saturated fat intake in cardiovascular outcomes has been questioned recently, in part due to heterogeneity in meta-analyses.[64] This issue is beyond the scope of the present article, which is limited to the effect of diet on blood lipid concentrations.

The effects of changes in dietary cholesterol on serum cholesterol decline as baseline dietary cholesterol increases.[65] Hopkins's analysis indicated that hepatic cholesterol overload may be the primary basis for the observed weak response to increasing dietary cholesterol in the context of a high baseline concentration.[65] However, according to the subgroup analysis in the present study, a lower baseline plasma lipid concentration was related to a greater reduction of TC and LDL-C in plasma by vegetarian diets in clinical trials.

This meta-regression and subgroup analysis showed that the duration of adherence to a vegetarian diet did not modulate the observed effects of the diet. However, younger age was associated with lower TC and LDL-C, suggesting that an effect of diet duration may play a role. Additionally, the present analysis could not adjust for dietary compliance. Further studies are needed to clarify the relation between the duration of vegetarian diets and its effect on plasma lipids.

In this study, HDL-C concentrations were also significantly lower in the context of vegetarian diets than in omnivorous diets. Although some studies have suggested that HDL-C concentrations are inversely associated with coronary heart disease,[66] recent studies have shown that interventions that increase HDL-C do not reduce the risk of coronary heart disease[67] and that genetic variants that raise HDL-C do not necessarily reduce the risk of coronary heart disease.[68]

Due to their range of health benefits, vegetarian diets are specifically mentioned in the *2015–2020 Dietary Guidelines for Americans*[69] as 1 of 3 noteworthy healthful diet patterns. As demonstrated in this study, improved lipid profiles are among these benefits. Moreover, the range of plant-derived foods is enormous, including simple fruits, vegetables, beans, and whole grains as well as products that are processed and prepared with a variety of additional ingredients. The lipid-lowering effect of a plant-based diet can be maximized by selection of specific foods. In a randomized trial of a so-called portfolio diet that included foods rich in soluble fiber, soy protein, plant sterols, and almonds, an LDL-C reduction of 28.6% was observed in 4 weeks.[70] The strengths of the present meta-analysis include a substantial sample size that lends confidence to these findings and allowed subgroup analyses in specific population groups. In addition, the focus of the meta-analysis on food consumption as opposed to supplements or other artificial interventions makes the findings applicable to the public.

An important limitation is heterogeneity. Meta-regression and subgroup analyses showed that sex, age, baseline plasma lipids, type of vegetarian diets, sample size, and BMI may be key reasons for this heterogeneity. Still, lower TC and LDL-C concentrations were seen in all subgroups. In addition, all observational studies used cross-sectional rather than prospective designs, a limitation that is somewhat alleviated by the inclusion of randomized clinical trials. Lastly, although all observational studies included in this study adjusted for age and sex, some did not adjust for other possible confounders such as BMI or physical activity level. Further studies are needed to explore the possible mechanisms by which vegetarian diets influence plasma lipids. The results of this meta-analysis suggest a strong association between consumption of vegetarian diets and lower plasma lipid concentrations.

CONCLUSION

Consumption of vegetarian diets, particularly vegan diets, is associated with lower levels of plasma lipids, which could offer individuals and healthcare professionals an effective option for reducing the risk of heart disease or other chronic conditions. Although not all clinicians have the training or time to confidently guide patients toward healthful vegetarian diets, registered dietitians can provide the services necessary to assist patients in making this transition.

Acknowledgments

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Declaration of interest. The authors have no relevant interests to declare.

Supporting Information

The following Supporting Information is available through the online version of this article available at the publisher's website.

Table S1 **Search strategy**

Table S2 **Subgroup analysis on plasma total cholesterol and low-density lipoprotein cholesterol for clinical trials**

Table S3 **Subgroup analysis on plasma high-density lipoprotein cholesterol and triglyceride for clinical trials**

Figure S1 **Funnel plot of comparison of weight and differences in mean total cholesterol associated with consumption of vegetarian diets.** Funnel plot of study weights against change in TC in (**A**) observational studies and (**B**) clinical trials. TC results in individual studies are depicted as circles scattered around the pooled TC estimate. The trim-and-fill method indicates that 7 observational studies and 4 trials might have been missing owing to publication bias. After adjustment for putative missing data, the overall differences for TC changed to −23.8 mg/dL (95%CI, −29.6 to −18.0) in observational studies and −8.57 mg/dL (95%CI, −14.79 to −2.35) in clinical trials.

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