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Effects of Vegetarian Diets on Blood Lipids: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

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Background—Vegetarian diets exclude all animal flesh and are being widely adopted by an increasing number of people; however, effects on blood lipid concentrations remain unclear. This meta-analysis aimed to quantitatively assess the overall effects of vegetarian diets on blood lipids.

Methods and Results—We searched PubMed, Scopus, Embase, ISI Web of Knowledge, and the Cochrane Library through March 2015. Studies were included if they described the effectiveness of vegetarian diets on blood lipids (total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, and triglyceride). Weighted mean effect sizes were calculated for net changes by using a random-effects model. We performed subgroup and univariate meta-regression analyses to explore sources of heterogeneity. Eleven trials were included in the meta-analysis. Vegetarian diets significantly lowered blood concentrations of total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, and non–high-density lipoprotein cholesterol, and the pooled estimated changes were −0.36 mmol/L (95% CI −0.55 to −0.17; $P<0.001$), −0.34 mmol/L (95% CI −0.57 to −0.11; $P<0.001$), −0.10 mmol/L (95% CI −0.14 to −0.06; $P<0.001$), and −0.30 mmol/L (95% CI −0.50 to −0.10; $P=0.04$), respectively. Vegetarian diets did not significantly affect blood triglyceride concentrations, with a pooled estimated mean difference of 0.04 mmol/L (95% CI −0.05 to 0.13; $P=0.40$).

Conclusions—This systematic review and meta-analysis provides evidence that vegetarian diets effectively lower blood concentrations of total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, and non–high-density lipoprotein cholesterol. Such diets could be a useful nonpharmaceutical means of managing dyslipidemia, especially hypercholesterolemia. (*J Am Heart Assoc*. 2015;4:e002408 doi: 10.1161/JAHA.115.002408)

Key Words: cholesterol • diet • lipoprotein lipids • triglyceride • vegetarian

D yslipidemia is a primary risk factor for the development of cardiovascular diseases, such as heart disease, stroke, and coronary artery disease.[1,2] Cardiovascular diseases and associated mortality are strongly related to elevated blood concentrations of total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), and triglyceride (TG).[3,4] Although lipid-lowering drugs like statins and fibrates are effective in reducing TC, LDL-C, and TG concentrations,[5–7]

major health organizations have maintained that modification of dietary and lifestyle patterns is the essential approach to prevention and management of dyslipidemia and cardiovascular diseases.[8,9]

In recent years, adopting a vegetarian diet has become increasingly popular. Vegetarian diets exclude all animal flesh. Varieties of vegetarianism include vegan, raw vegan, ovovegetarian, lactovegetarian, lacto-ovovegetarian, and pescovegetarian. Each type of vegetarianism excludes or includes certain foods.[10] Compared with an omnivorous diet, a vegetarian diet is rich in fiber, magnesium, Fe^{3+}, folic acid, vitamins C and E, omega-6 polyunsaturated fatty acids, phytochemicals, and antioxidants but low in cholesterol; total fat and saturated fatty acids; sodium; Fe^{2+}; zinc, vitamins A, B_{12}, and D[11]; and especially omega-3 polyunsaturated fatty acids. A recent meta-analysis of 7 clinical trials and 32 observational studies showed that consumption of vegetarian diets was associated with lower blood pressure.[12] An earlier meta-analysis of 7 prospective studies that included 124 706 participants reported 29% lower mortality from ischemic heart disease (relative risk 0.71, 95% CI 0.56 to 0.87), 16% lower

mortality from circulatory diseases (relative risk 0.84, 95% CI 0.54 to 1.14), and 12% lower mortality from cerebrovascular disease (relative risk 0.88, 95% CI 0.70 to 1.06) with vegetarian diets.[13]

Regarding the effects of vegetarian diets on blood lipid concentrations, several cross-sectional studies showed that vegetarians have significantly lower concentrations of TC, LDL-C, and TG compared with omnivores.[14,15] Nevertheless, data from randomized controlled trials (RCTs) evaluating the effects of vegetarian diets on blood lipid concentrations have generated mixed findings, especially regarding high-density lipoprotein cholesterol (HDL-C) and TG. Some trials[16,17] have indicated that vegetarian diets could lower HDL-C and increase TG concentrations compared with omnivorous diets; however, no such effects were observed in other trials.[18,19] To the best of our knowledge, these results have not been systematically evaluated; therefore, we conducted a meta-analysis of the published RCTs to comprehensively assess the overall effects of vegetarian diets on blood lipids (TC, LDL-C, HDL-C, and TG). The aim of the present study was to ascertain the extent to which a vegetarian diet alters blood lipids.

Methods

This systematic review and meta-analysis followed the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement.[20]

Literature Search

Relevant articles were identified by searching PubMed, Scopus, Embase, ISI Web of Knowledge, and the Cochrane Library databases from their starting dates through March 2015. The structured search strategies used the following format of keywords: *(vegetarian diet OR vegan diet OR vegetarianism OR vegetarian) AND (blood lipids OR total cholesterol OR low density lipoprotein cholesterol OR high density lipoprotein cholesterol OR cholesterol OR triglyceride OR triacylglycerol)*. Reference lists of original studies or reviews were also checked for additional publications. Because the present study is a systematic review and meta-analysis, institutional review board approval was not required for this project.

Eligibility Criteria

Studies that met the PICOS criteria (participants, interventions, comparators, outcomes, study design) were included. "Participants" were studies conducted in adult humans aged ≥18 years. Interventions comprised a vegetarian diet (intervention diet) including vegan, omitting all animal products;

ovovegetarian, omitting all animal products but eggs; lactovegetarian, omitting all animal products but dairy products; or lacto-ovovegetarian, omitting all animal products but including eggs and dairy products. Comparators comprised an omnivorous diet (control diet) containing meats and dairy products and plant-derived foods. Outcomes were baseline and end point values for blood lipids (TC, LDL-C, HDL-C, or TG) or their difference and the SD or SEM or 95% CI of each group. Study design comprised RCTs of either parallel or crossover design.

Study Selection

The title and abstract of each study identified in the search was screened to determine the study's eligibility for full review. The full-text report was retrieved if the study investigated or potentially investigated the effects of vegetarian diets on blood lipid concentrations. Studies that compared vegan and ovo-, lacto-, or lacto-ovovegetarian diets and studies that were cross-sectional, cohort, case–control, animal test, nonoriginal research (reviews, editorials, or commentaries), unpublished, or duplicated were excluded. Only human studies published in English were included.

Data Extraction and Risk-of-Bias Assessment

Data extraction was conducted independently by 2 researchers, and any discrepancies were resolved by discussion. Study characteristics were extracted including author, publication year, country, study design, sample size, population information (sex, age, body mass index [BMI; calculated as weight in kilograms divided by height in square meters], health status, and lipid-lowering medication use), dietary data (type of diet and duration of consumption), and outcome analysis. In each trial, the mean and SD of blood lipid concentrations at baseline and end point in both intervention and control groups were extracted. For studies that had multiple time points for the same participants, only the last end point was used for analysis. In crossover studies, it was recommended to extract paired *t* test data that evaluated the value of "measurement on intervention" minus "measurement on control" separately for each participant[21]; however, because these data were rarely provided, we resorted to using mean and SD separately for intervention and control. This step provided a conservative estimate of effect and reduced the power of crossover studies to show real effects of intervention.[22] If SDs were not reported directly, we calculated them from SEM or 95% CI. Change-from-baseline SD was also estimated using the equation listed in the Cochrane Handbook.[21] Extracted data were converted to international units. For TC, LDL-C, and HDL-C, 1 mg/dL was converted to 0.0259 mmol/L; for TG, 1 mg/dL was converted to 0.0113 mmol/L.

Risk of bias across studies was assessed using the Cochrane Collaboration's risk of bias tool,[21] which rates 7 domains (random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting and other threats to validity [eg, contamination of intervention and carryover effect in crossover trials]) as having low, high, or unclear risk of bias.

Data Synthesis and Statistical Analysis

A random-effects model described by DerSimonian and Laird was used because it takes into account both within- and between-study variability.[23] Heterogeneity between studies was assessed by the Cochrane Q test and I^2 statistic. An I^2 value of 25%, 50%, and 75% represented low, moderate, and high degrees of heterogeneity, respectively. To explore sources of heterogeneity, subgroup and univariate meta-regression analyses were carried out focused on population information: continent (Oceania, Europe, or North America), age (<50 or ≥50 years), BMI (18.5 to 25, 25 to 30, or ≥30), health status (healthy or with high cardiovascular disease risk and lipid-lowering medication use [some or none]), intervention type (lactovegetarian, lacto-ovovegetarian, or vegan) and duration (<3 or ≥3 months), study design (parallel or crossover), outcome analysis (per protocol or intention to treat), and publication year (before 2000 or 2000 or later). To determine whether any single trial exerted undue influence on the overall results, sensitivity analysis was conducted in which each study was removed and the effect size recalculated. Furthermore, publication bias was assessed using Begg's rank correlation test and Egger's linear regression test. All statistical analyses were performed using Stata/SE 12.0 for windows (StataCorp). Except as otherwise specified, $P<0.05$ was considered significant.
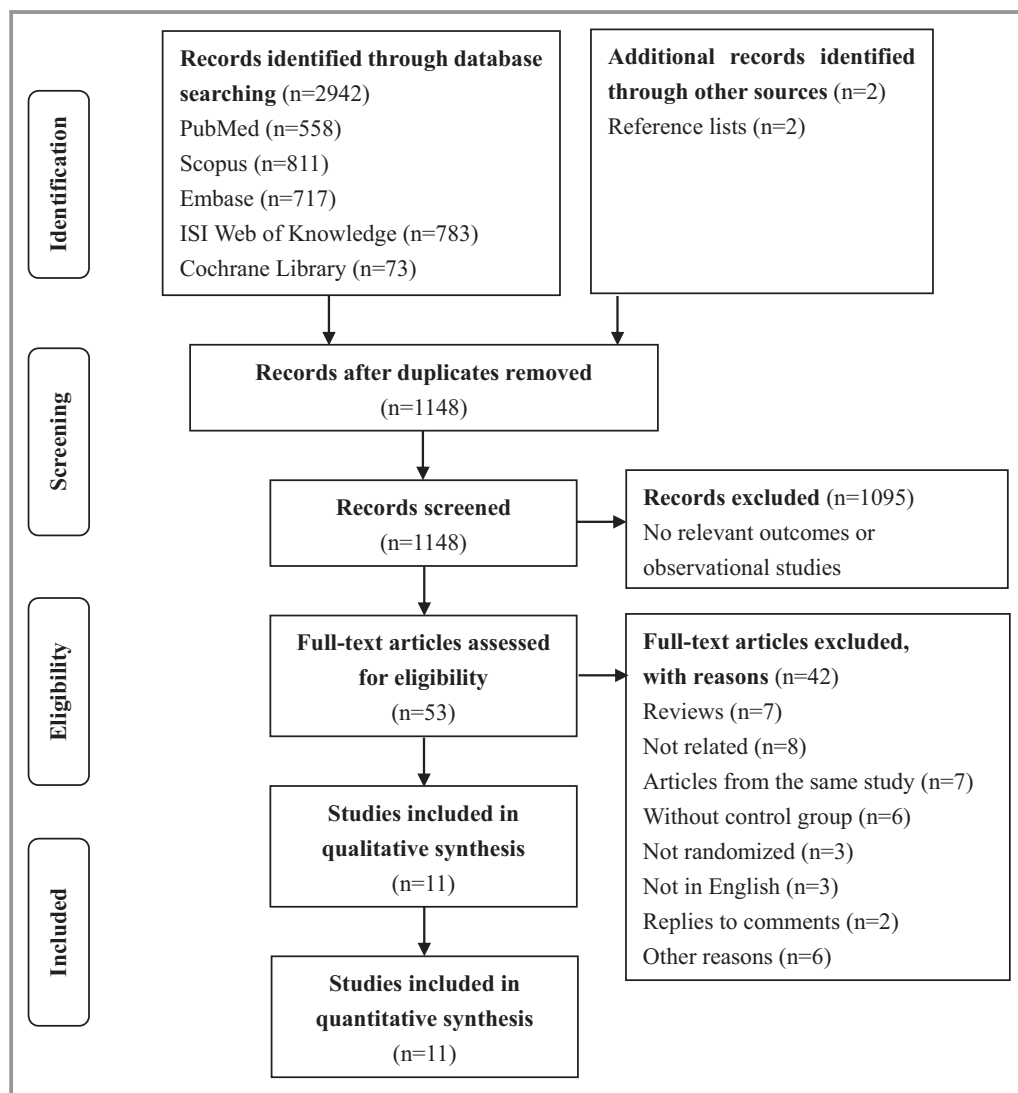

Figure 1. Flow diagram of selection of relevant articles.

Results

Results of the Study Selection

Detailed processes of study selection are shown in Figure 1. Our search strategy retrieved 2944 unique citations: 558 from PubMed, 811 from Scopus, 717 from Embase, 783 from ISI Web of Knowledge, 73 from the Cochrane Library, and 2 from hand searching the reference lists. Of these, 2891 citations were excluded after screening titles and abstracts, leaving 53 articles for full-text review. After reviewing full text, 42 articles were excluded because they did not meet the study inclusion criteria (eg, studies without randomization, studies with nonrelated outcomes, articles from the same study, reviews, replies to comments). Ultimately, 11 studies were included in quantitative synthesis.[16–19,24–30]

Study Characteristics

Characteristics of the 11 selected studies are shown in Tables 1 and 2. Six studies were conducted in North America (all in the United States[16,17,19,24,27,28]), 4 were conducted in Europe (2 in Finland[18,26] and 1 each in Sweden[29] and the Czech Republic[30]), and 1 was conducted in Oceania (Australia[25]). The sample sizes ranged from 11 to 291, with a total of 832 participants. One study involved men only,[25] 1 study involved women only,[16] and the other 9 studies included both men and women. Mean BMI of participants varied from 24.0 to 35.0, and mean age at baseline ranged from 28.0 to 56.2 years. Five trials were performed in participants with higher cardiovascular risk factors such as overweight[17,28] or type 2 diabetes.[19,27,30] Several participants in 3 studies used lipid-lowering medication.[19,27,30] Among these 11 studies, 7 included a vegan diet,[16–19,26,27,29]

Table 1. Characteristics of Studies Included in the Meta-Analysis: Participants, Interventions, and Comparators

Study	Country	No. (F/M)	Mean BMI, kg/m²	Mean Age, Year	Healthy Status	Lipid-Lowering Medication (E/C)	Intervention	Control*
Cooper et al, 1982[24]	US	15 (5/10)	NR	28.0	Healthy subjects	None	Lactovegetarian	Omnivorous
Kestin et al, 1989[25]	Australia	26 (0/26)	25.5	44.0	NR	None	Lacto-ovovegetarian	Omnivorous
Ling et al, 1992[26]	Finland	18 (14/4)	26.6	42.8	Healthy participants and patients for unrelated conditions	NR	Vegan	Omnivorous
Nicholson et al, 1999[27]	US	11 (5/6)	NR	54.3	With NIDDM	4 (3/1)	Vegan	Omnivorous
Barnard et al, 2000[16]	US	35 (35/0)	25.5	36.1	Healthy premenopausal women	None	Vegan	Omnivorous
Agren et al, 2001[18]	Finland	29 (28/1)	24.3	50.8	With rheumatoid arthritis	None	Vegan	Omnivorous
Burke et al, 2007[28]	US	176 (153/23)	34.0	44.0	Overweight and obese adults	None	Lacto-ovovegetarian	Omnivorous
Elkan et al, 2008[29]	Sweden	58 (52/6)	24.0	50.3	With rheumatoid arthritis	None	Vegan	Omnivorous
Barnard et al, 2009[19]	US	99 (60/39)	34.9	55.6	With type 2 diabetes	54 (27/27)	Vegan	Omnivorous
Kahleova et al, 2011[30]	Czech	74 (39/35)	35.0	56.2	With type 2 diabetes	38 (22/16)	Lactovegetarian	Omnivorous
Mishra et al, 2013[17]	US	291 (241/50)	35.0	45.2	With BMI ≥25 and/or a previous diagnosis of type 2 diabetes	NR	Vegan	Omnivorous

BMI indicates body mass index; E/C, experiment diet group/control diet group; F, female; M, male; NR, not reported.
*All control diets adopted in these studies were defined as an omnivorous diet because they contained meat and dairy products and plant-derived foods.

Table 2. Characteristics of Studies Included in the Meta-Analysis: Outcomes and Study Design

Study	Baseline TC, mmol/L (E/C)	Baseline LDL-C, mmol/L (E/C)	Baseline HDL-C, mmol/L (E/C)	Baseline TG, mmol/L (E/C)	Duration	Outcome Analysis	Design
Cooper et al, 1982[24]	4.1	—	—	0.7	3 weeks	PP	CO
Kestin et al, 1989[25]	6.1	4.1	1.5	1.3	6 weeks	PP	CO
Ling et al, 1992[26]	(5.6/5.5)	(3.7/3.6)	(1.3/1.3)	(1.3/1.0)	4 weeks	PP	PL
Nicholson et al, 1999[27]	(5.3/5.6)	—	(1.2/1.1)	(2.1/2.3)	12 weeks	PP	PL
Barnard et al, 2000[16]	4.2	2.5	1.3	0.9	2 months	PP	CO
Agren et al, 2001[18]	(4.6/5.2)	(3.0/3.5)	(1.2/1.2)	(1.0/1.0)	3 months	PP	PL
Burke et al, 2007[28]	(5.3/5.3)	—	—	(1.5/1.5)	18 months	ITT	PL
Elkan et al, 2008[29]	—	—	(1.4/1.3)	(1.1/1.1)	12 months	PP	PL
Barnard et al, 2009[19]	(4.8/5.2)	(2.7/3.0)	(1.4/1.3)	(1.7/1.8)	74 weeks	ITT	PL
Kahleova et al, 2011[30]	(4.4/4.2)	(2.5/2.6)	(1.1/1.1)	(2.1/2.1)	12 weeks	ITT	PL
Mishra et al, 2013[17]	(4.8/4.9)	(2.8/2.8)	(1.4/1.5)	(1.4/1.4)	18 weeks	ITT	PL

CO indicates crossover; E/C, experiment diet group/control diet group; HDL-C, high-density lipoprotein cholesterol; ITT, intention to treat; LDL-C, low-density lipoprotein cholesterol; PL, parallel; PP, per protocol; TC, total cholesterol; TG, triglyceride.

2 included a lacto-ovovegetarian diet,[25,28] and 2 included a lactovegetarian diet.[24,30] The average duration of intervention was 24 weeks (ranging from 3 weeks to 18 months). Five trials lasted >3 months,[17–19,28,29] whereas 2 trials lasted <1 month,[24,26] and the remaining trials fell in between. Seven studies adopted per-protocol analysis,[16,18,24–27,29] and 4 used intention-to-treat analysis.[17,19,28,30] Eight trials used a parallel design,[17–19,26–30] and the other 3 trials used a crossover design.[16,24,25]

Risk of Bias

All studies stated that participants were randomly assigned, but only 5 studies specified the randomization process, such as using a computer-generated random number list,[16] a random number table,[17,19] or a minimization procedure.[28,29] None of the 11 studies mentioned allocation concealment, and none of the participants in any of the trials were blinded. Blinding of outcome assessment was not mentioned in any of the studies. Only 4 studies were analyzed on an intention-to-treat basis.[17,19,28,30] In 3 studies, not all of the concentrations listed in the methods were reported.[24,27,28] Carryover effect in the 3 crossover trials may introduce bias, although this was not mentioned[16,24,25] (Table S1).

Effects of Vegetarian Diets on Blood Lipid Concentrations

A total of 10 studies reported data on TC concentrations. Vegetarian diets significantly affect TC concentrations, and the pooled estimated change in TC concentrations was −0.36 mmol/L (95% CI −0.55 to −0.17; $P<0.001$) (Figure 2). Moderate to high heterogeneity was detected ($I^2=53.5\%$). Seven studies reported data on LDL-C concentrations. Vegetarian diets caused significant reduction in LDL-C concentrations, and the pooled estimated effect was −0.34 mmol/L (95% CI −0.57 to −0.11; $P<0.001$) (Figure 2). High heterogeneity was found ($I^2=72.4\%$). Nine studies reported results on HDL-C concentrations. Vegetarian diets also lowered HDL-C concentrations, and the pooled estimated mean difference was −0.10 mmol/L (95% CI −0.14 to −0.06; $P<0.001$) (Figure 3). No heterogeneity was shown for HDL-C ($I^2=0\%$). The mean change in TG concentrations was calculated in 11 trials. Vegetarian diets did not cause a significant change in TG concentration, and the pooled estimated effect was 0.04 mmol/L (95% CI −0.05 to 0.13; $P=0.40$) (Figure 3). Low heterogeneity was observed ($I^2=19.9\%$). Because non–HDL-C (the difference between TC and HDL-C) was also an important target for cardiovascular
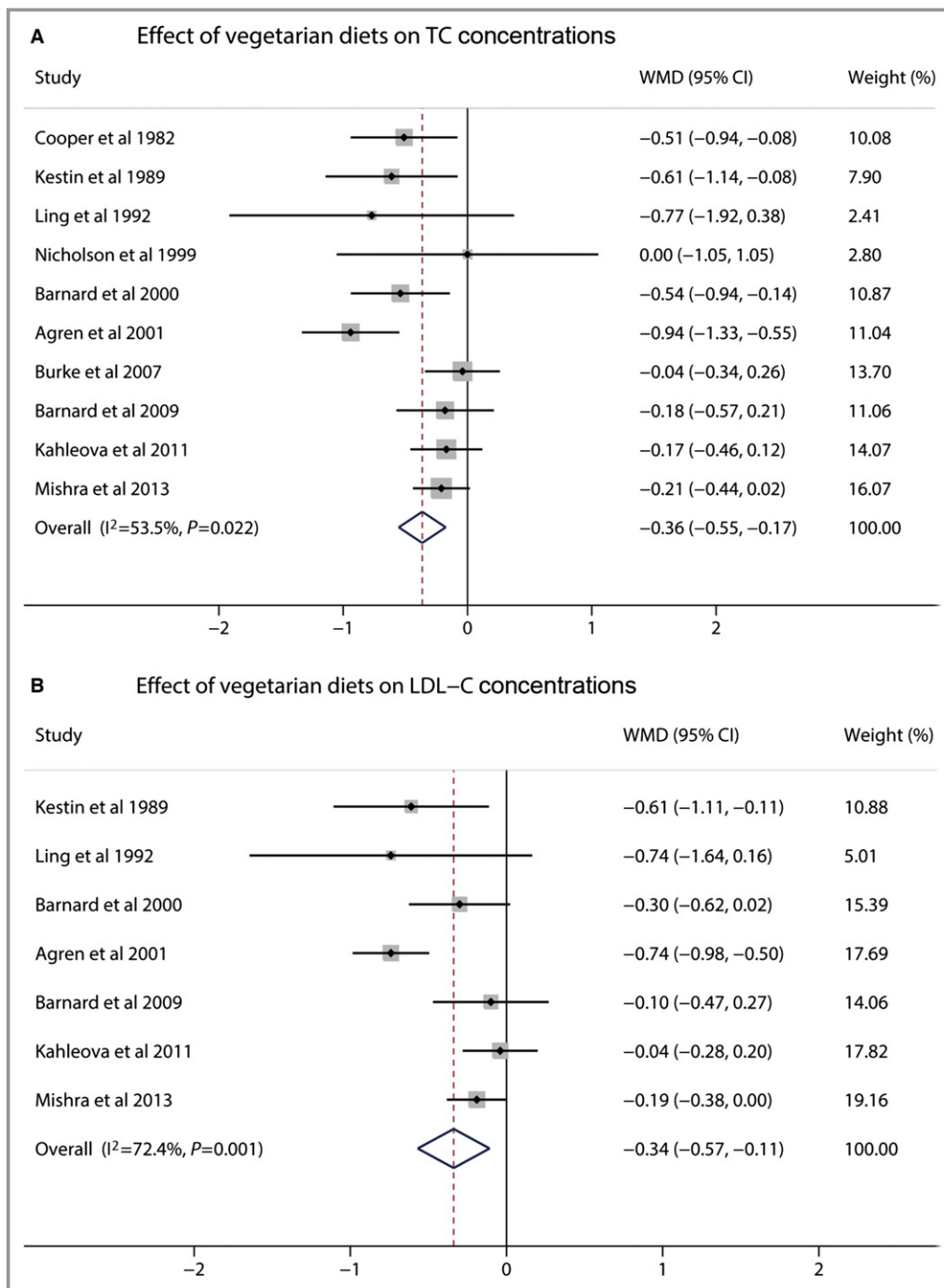
Figure 2. Effects of vegetarian diets on (A) TC and (B) LDL-C concentrations. The meta-analysis used the WMD in the random-effects model. Horizontal lines denote 95% CI. A diamond represents the overall estimated effect. LDL-C indicates low-density lipoprotein cholesterol; TC, total cholesterol; WMD, weighted mean difference.

disease risk set by the Canadian Cardiovascular Society in 2012,[31] it was calculated from 8 studies, and a meta-analysis of the effect of vegetarian diets was performed. Vegetarian diets significantly decreased non–HDL-C concentrations by −0.30 mmol/L (95% CI −0.50 to −0.10; *P*=0.04) (Figure 4). Moderate to high heterogeneity was found (I^2=54.8%).

Subgroup and Meta–Regression Analyses

Subgroup analyses showed that the effect of vegetarian diets on lowering TC concentrations was greater in participants with BMI ranging from 18.5 to 25 (−0.94 mmol/L, 95% CI −1.33 to −0.55) and from
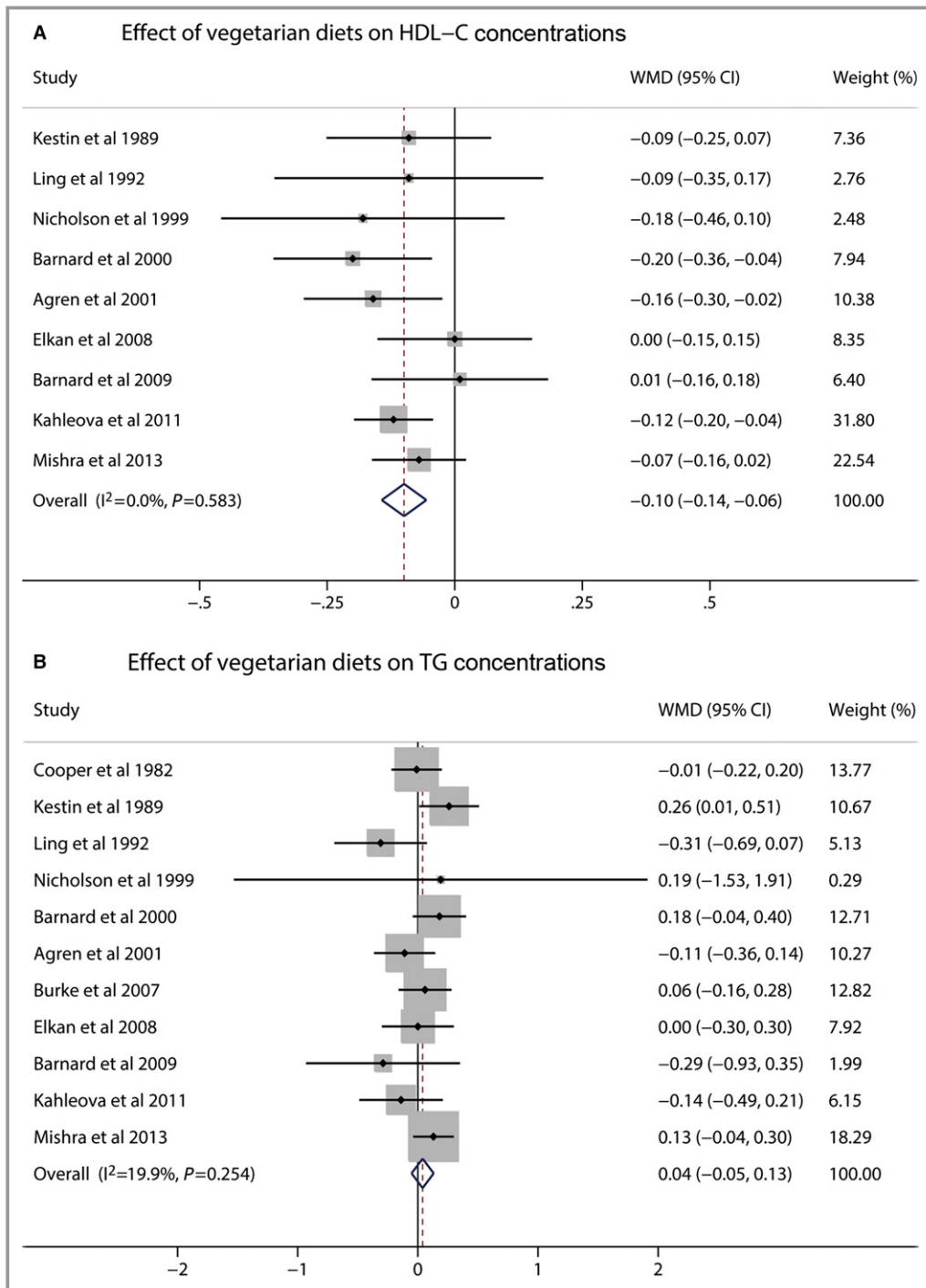
Figure 3. Effects of vegetarian diets on (A) HDL–C and (B) TG concentrations. The meta-analysis used the WMD in the random–effects model. Horizontal lines denote 95% CI. A diamond represents the overall estimated effect. HDL–C indicates high-density lipoprotein cholesterol; TG, triglyceride; WMD, weighted mean difference.

25 to 30 (−0.58 mmol/L, 95% CI −0.89 to −0.27) rather than those >30 (−0.16 mmol/L, 95% CI −0.30, −0.01) (Table 3). A greater lowering effect on TC concentrations was observed in trials analyzed on a per-protocol basis (−0.64 mmol/L, 95% CI −0.85 to −0.43) compared with an intention-to-treat basis (−0.16 mmol/L, 95% CI −0.30 to −0.01) (Table 3). Similarly, a greater reduction in LDL-C concentrations was observed in trials conducted in participants with BMI ranging from 18.5 to 25 and from 25 to 30 or analyzed on a per-protocol basis (Table 3).
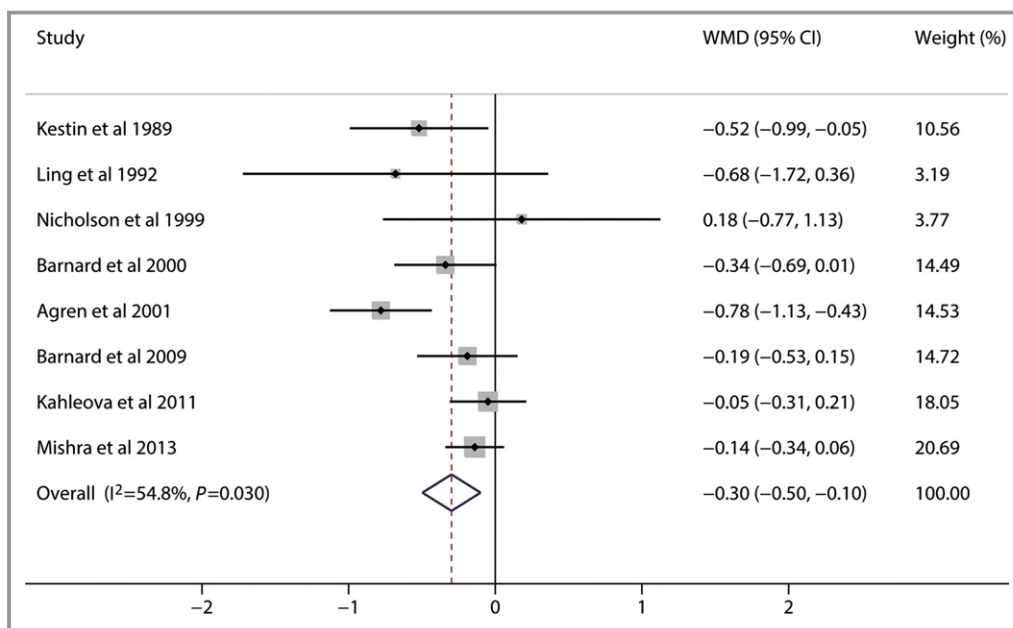
Figure 4. Effects of vegetarian diets on non–high-density lipoprotein cholesterol concentrations. The meta-analysis used the WMD in the random-effects model. Horizontal lines denote 95% CI. A diamond represents the overall estimated effect. WMD, weighted mean difference.

Meta-regressions for BMI (meta-regression P=0.01 in TC analysis and P=0.02 in LDL-C analysis) and outcome analysis (meta-regression P=0.01 in TC analysis and P=0.02 in LDL-C analysis) were significant, suggesting that these 2 factors may be substantial sources of heterogeneity present in TC and LDL-C analyses.

Subgroup and meta–regression analyses did not show any statistically significant differences in the effect of vegetarian diets on HDL-C and TG concentrations between subgroups stratified by population information (continent, age, BMI, health status, and lipid-lowering medication use), intervention information (type and duration), study design, outcome analysis, and publication year (Table 4). For non–HDL-C, subgroup and meta–regression analyses indicated that reduction was greater in trials conducted in participants with lower BMI or analyzed on a per-protocol analysis, which could partly explain the heterogeneity, as for TC and LDL-C (Table 5).

Sensitivity Analysis and Publication Bias

Sensitivity analysis showed that the pooled estimate of the effects of vegetarian diets on TC, LDL-C, HDL-C, TG, and non–HDL-C concentrations did not vary substantially with the exclusion of any 1 study (Figures S1 through S5). Results from Begg's rank correlation test and Egger's linear regression test suggested that no obvious publication bias was detected in the meta-analysis of TC, LDL-C, HDL-C, TG, or non–HDL-C (Table 6).

Discussion

The objective of the present study was to examine the effects of vegetarian diets on blood lipid concentrations. This meta-analysis of 11 RCTs suggests that vegetarian diets had a significant lowering effect on the concentrations of blood TC, LDL-C, HDL-C, and non–HDL-C; however, no remarkable effect was detected on TG concentrations.

Although a large number of cross-sectional studies[14,15] have shown that concentrations of TC, LDL-C, and TG were much lower in vegetarians than in omnivores, a few studies[32,33] have found no such relationships with HDL-C and TG concentrations. A meta-analysis of 12 observational studies with a total of 4177 participants revealed no evidence showing that HDL-C concentrations differed in vegetarians and omnivores.[34] Another meta-analysis of 12 observational studies with 1300 participants indicated that vegetarian diets were effective in lowering TG concentrations.[35] Although this phenomenon was obvious in developing countries, it was nonsignificant in developed countries. Likewise, results from RCTs in humans were not necessarily consistent, particularly those results on HDL-C and TG. Our meta-analysis was performed based on this inconsistent evidence to assess the overall effect of vegetarian diets on blood lipid concentrations.

Subgroup and meta–regression analyses indicated that the lowering effects of vegetarian diets on TC, LDL-C, and non–HDL-C concentrations were less evident in obese participants (BMI ≥30). Obesity is associated with an increased rate of

Table 3. Subgroup and Meta-Regression Analyses for TC and LDL-C Concentrations

Subgroup Factors	TC				LDL-C			
	No. of Trials	Pooled Effect (95% CI) mmol/L	I^2 (%)	P Value*	No. of Trials	Pooled Effect (95% CI) mmol/L	I^2 (%)	P Value*	P Value†
Overall analyses	10	−0.36 (−0.55 to −0.17)	53.5	0.02		7	−0.34 (−0.57 to −0.11)	72.4	<0.001	
Overall analyses‡	10	−0.32 (−0.43 to −0.20)	53.5	0.02		7	−0.30 (−0.41 to −0.19)	72.4	<0.001	
Continent					0.24					0.39
Oceania	1	−0.61 (−1.14 to −0.08)	—	—		1	−0.61 (−1.11 to −0.11)	—	—	
Europe	3	−0.58 (−1.20 to 0.04)	79.8	0.01		3	−0.46 (−1.04 to 0.11)	87.9	<0.001	
North America	6	−0.25 (−0.40 to −0.09)	13.0	0.33		3	−0.20 (−0.35 to −0.05)	0.0	0.72	
Age, y					0.96					0.79
<50	6	−0.33 (−0.53 to −0.13)	35.1	0.17		4	−0.30 (−0.48 to −0.11)	15.1	0.32	
≥50	4	−0.37 (−0.80 to 0.05)	73.5	0.01		3	−0.30 (−0.78 to 0.18)	88.8	<0.001	
BMI, kg/m²					0.01					0.01
18.5 to 25	1	−0.94 (−1.33 to −0.55)	—	—		1	−0.74 (−0.68 to −0.16)	—	—	
25 to 30	3	−0.58 (−0.89 to −0.27)	0	0.92		3	−0.42 (−0.68 to −0.16)	0	0.46	
≥30	4	−0.16 (−0.30 to −0.01)	0	0.85		3	−0.13 (−0.27 to 0.01)	0	0.62	
Health status					0.08					0.44
Healthy	2	−0.53 (−0.82 to −0.23)	0	0.92		1	−0.30 (−0.62 to 0.02)	—	—	
High CVD risk	5	−0.15 (−0.30 to −0.01)	0	0.93		3	−0.13 (−0.27 to 0.01)	0.0	0.62	
Lipid-lowering medication					0.20					0.19
Some	3	−0.17 (−0.39 to 0.06)	0	0.95		2	−0.06 (−0.26 to 0.14)	0	0.79	
None	5	−0.51 (−0.84 to −0.18)	70.9	0.01		2	−0.40 (−0.68 to −0.11)	4.6	0.31	
Intervention					0.59					0.23
Lactovegetarian	2	−0.30 (−0.63 to 0.02)	39.6	0.20		1	−0.04 (−0.28 to 0.20)	—	—	
Lacto-ovovegetarian	2	−0.28 (−0.83 to 0.27)	70.1	0.07		1	−0.61 (−1.11 to −0.11)	—	—	
Vegan	6	−0.44 (−0.73 to −0.14)	60.1	0.03		5	−0.37 (−0.65 to −0.09)	73.3	0.01	
Duration, months					0.64					0.92
<3	6	−0.38 (−0.57 to −0.19)	0	0.46		4	−0.30 (−0.59 to −0.01)	50.2	0.11	
≥3	4	−0.33 (−0.67 to 0.02)	78.5	0.003		3	−0.35 (−075 to 0.05)	85.9	0.001	
Design					0.26					0.68
Crossover	3	−0.55 (−0.80 to −0.29)	0	0.96		2	−0.40 (−0.68 to −0.11)	4.6	0.31	
Parallel	7	−0.29 (−0.53 to −0.05)	60.8	0.02		5	−0.31 (−0.61 to −0.01)	80.1	<0.001	
Analysis					0.01					0.02
PP	6	−0.64 (−0.85 to −0.43)	0	0.50		4	−0.57 (−0.82 to −0.33)	35.3	0.20	
ITT	4	−0.16 (−0.30 to −0.01)	0	0.85		3	−0.13 (−0.27 to 0.01)	0	0.62	
Publication year					0.45					0.29
Before 2000	4	−0.52 (−0.83 to −0.21)	0	0.74		2	−0.64 (−1.08 to −0.20)	0	0.80	
2000 or later	6	−0.32 (−0.56 to −0.09)	69.0	0.01		5	−0.28 (−0.54 to −0.02)	79.1	<0.001	

BMI indicates body mass index; CVD, cardiovascular disease; ITT, intention to treat; LDL-C, low-density lipoprotein cholesterol; PP, per protocol; TC, total cholesterol.

*P for heterogeneity

†P for meta–regression analysis.

‡Results from fixed-effect analysis.

Table 4. Subgroup and Meta–Regression Analyses for HDL–C and TG Concentrations

Subgroup Factors	HDL-C					TG				
	No. of Trials	Pooled Effect (95% CI) mmol/L	I^2 (%)	P Value*	P Value[†]	No. of Trials	Pooled Effect (95% CI) mmol/L	I^2 (%)	P Value*	P Value[†]
Overall analyses	9	−0.10 (−0.14 to −0.06)	0	0.58		11	0.04 (−0.05 to 0.13)	19.9	0.25	
Overall analyses[‡]	9	−0.10 (−0.14 to −0.06)	0	0.58		11	0.05 (−0.03 to 0.13)	19.9	0.25	
Continent					0.72					0.09
Oceania	1	−0.09 (−0.25 to 0.07)	—	—		1	0.26 (0.01 to 0.51)	—	—	
Europe	4	−0.11 (−0.17 to −0.05)	0	0.45		4	−0.12 (−0.27 to 0.04)	0	0.67	
North America	4	−0.09 (−0.18 to −0.01)	21.0	0.28		6	0.08 (−0.01 to 0.18)	0	0.68	
Age, y					0.97					0.08
<50	4	−0.10 (−0.17 to −0.03)	0	0.57		6	0.09 (−0.03 to 0.20)	35.4	0.17	
≥50	5	−0.10 (−0.16 to −0.03)	12.1	0.34		5	−0.09 (−0.26 to 0.07)	0	0.92	
BMI, kg/m²					0.82					0.72
18.5 to 25	2	−0.08 (−0.24 to 0.07)	57.9	0.12		2	−0.06 (−0.26 to 0.13)	0	0.58	
25 to 30	3	−0.14 (−0.24 to −0.04)	0	0.58		3	0.08 (−0.20 to 0.36)	68.1	0.04	
≥30	3	−0.09 (−0.14 to −0.03)	1.6	0.36		4	0.06 (−0.07 to 0.18)	2.6	0.38	
Health status					0.29					0.33
Healthy	1	−0.20 (−0.36 to −0.04)	—	—		2	0.08 (−0.10 to 0.27)	33.0	0.22	
High CVD risk	4	−0.09 (−0.15 to −0.04)	0	0.49		5	0.06 (−0.06 to 0.18)	0	0.54	
Lipid-lowering medication					0.99					0.20
Some	3	−0.10 (−0.18 to −0.03)	5.6	0.35		3	−0.16 (−0.46 to 0.14)	0	0.85	
None	3	−0.10 (−0.21 to 0.02)	38.9	0.20		6	0.07 (−0.04 to 0.17)	15.0	0.32	
Intervention					0.76					0.85
Lactovegetarian	1	−0.12 (−0.20 to −0.04)	—	—		2	−0.04 (−0.22 to 0.13)	0	0.53	
Lacto-ovovegetarian	1	−0.09 (−0.25 to 0.07)	—	—		2	0.15 (−0.04 to 0.35)	28.2	0.24	
Vegan	7	−0.09 (−0.15 to −0.03)	2.8	0.40		7	0.02 (−0.12 to 0.15)	27.2	0.22	
Duration, months					0.20					0.81
<3	5	−0.13 (−0.19 to −0.07)	0	0.86		6	0.04 (−0.13 to 0.21)	43.7	0.11	
≥3	4	−0.07 (−0.13 to 0.00)	9.6	0.34		5	0.04 (−0.07 to 0.15)	0	0.47	
Design					0.39					0.17
Parallel	7	−0.09 (−0.14 to −0.04)	0	0.57		8	0.00 (−0.10 to 0.10)	3.0	0.41	
Crossover	2	−0.15 (−0.26 to −0.04)	0	0.34		3	0.13 (−0.03 to 0.29)	32.4	0.23	
Analysis					0.54					0.99
PP	6	−0.12 (−0.19 to −0.05)	0	0.53		7	0.03 (−0.10 to 0.17)	35.9	0.15	
ITT	3	−0.09 (−0.14 to −0.03)	1.6	0.36		4	0.06 (−0.07 to 0.18)	2.6	0.38	
Publication year					0.89					0.98
Before 2000	3	−0.11 (−0.23 to 0.02)	0	0.85		4	0.02 (−0.24 to 0.27)	53.3	0.09	
2000 or later	6	−0.10 (−0.15 to −0.04)	19.7	0.28		7	0.05 (−0.04 to 0.15)	0.7	0.42	

BMI indicates body mass index; CVD, cardiovascular disease; HDL-C, high-density lipoprotein cholesterol; ITT, intention to treat; PP, per protocol; TG, triglyceride.
*P for heterogeneity.
[†]P for meta–regression analysis.
[‡]Results from fixed-effect analysis.

Table 5. Subgroup and Meta–Regression Analyses for Non–HDL-C Concentrations

Subgroup Factors	Non-HDL-C				
	No. of Trials	Pooled Effect (95% CI) mmol/L	I^2 (%)	P Value*	P Value†
Overall analyses	8	−0.30 (−0.50 to −0.10)	54.8	0.03	
Overall analyses‡	8	−0.25 (−0.37 to −0.13)	54.8	0.03	
Continent					0.35
Oceania	1	−0.52 (−0.99 to −0.05)	—	—	
Europe	3	−0.46 (−1.05 to 0.14)	82.4	0.003	
North America	4	−0.18 (−0.33 to −0.03)	0	0.68	
Age, y					0.83
<50	4	−0.26 (−0.44 to −0.08)	9.8	0.34	
≥50	4	−0.27 (−0.66 to 0.12)	75.3	0.01	
BMI, kg/m²					0.01
18.5 to 25	1	−0.78 (−1.13 to −0.43)	—	—	
25 to 30	3	−0.42 (−0.69 to −0.15)	0	0.74	
≥30	4	−0.12 (−0.26 to 0.02)	0	0.79	
Health status					0.32
Healthy	1	−0.34 (−0.69 to 0.01)	—	—	
High CVD risk	4	−0.11 (−0.26 to 0.03)	0	0.84	
Lipid-lowering medication					0.08
Some	3	−0.09 (−0.29 to 0.11)	0	0.69	
None	3	−0.55 (−0.83 to −0.28)	35.5	0.21	
Intervention					0.47
Lactovegetarian	1	−0.05 (−0.31 to 0.21)	—	—	
Lacto-ovovegetarian	1	−0.52 (−0.99 to −0.05)	—	—	
Vegan	6	−0.33 (−0.58 to −0.08)	57.4	0.04	
Duration, months					0.72
<3	5	−0.24 (−0.47 to −0.01)	21.4	0.28	
≥3	3	−0.35 (−0.74 to 0.03)	80.3	0.01	
Design					0.56
Crossover	2	−0.40 (−0.68 to −0.12)	0	0.55	
Parallel	6	−0.26 (−0.52 to −0.01)	63.6	0.02	
Analysis					0.02
PP	5	−0.51 (−0.77 to −0.25)	25.7	0.25	
ITT	3	−0.12 (−0.26 to 0.02)	0	0.79	
Publication year					0.70
Before 2000	3	−0.42 (−0.81 to −0.03)	0	0.38	
2000 or later	5	−0.28 (−0.51 to −0.05)	68.5	0.01	

BMI indicates body mass index; CVD, cardiovascular disease; HDL-C, high-density lipoprotein cholesterol; ITT, intention to treat; PP, per protocol.
*P for heterogeneity.
†P for meta–regression analysis.
‡Results from fixed-effect analysis.

cholesterol synthesis.[36] Leptin, a hormone secreted by adipocytes, could promote hepatic cholesterol clearance[37]; however, most obese subjects always experience leptin resistance, and its effects might be diminished or lacking in the obese state.[38] Consequently, the lowering effect of vegetarian diets on TC, LDL-C, and non–HDL-C concentrations

Table 6. Results of Publication Bias Test

	No. of Trials	Pooled Effect (95% CI) mmol/L	*P* for Begg's Test	*P* for Egger's Test
TC	10	−0.36 (−0.55 to −0.17)	0.28	0.27
LDL-C	7	−0.34 (−0.57 to −0.11)	0.37	0.54
HDL-C	9	−0.10 (−0.14 to −0.06)	1.00	0.93
TG	11	0.04 (−0.05 to 0.13)	0.35	0.16
Non-HDL-C	8	−0.30 (−0.50 to −0.10)	0.27	0.42

HDL-C indicates high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TC, total cholesterol; TG, triglyceride.

could be attenuated in obese participants. Subgroup and meta-regression analyses also showed that reduction in TC, LDL-C, and non–HDL-C concentrations was greater in trials that adopted per-protocol analysis compared with those that adopted intention-to-treat analysis. This result is consistent with the idea that, on average, per-protocol analysis tends to provide higher estimates of effect than the intention-to-treat analysis.[39] A per-protocol analysis is performed in which participants are included only if they received the intended intervention in line with the protocol, whereas an intention-to-treat analysis includes all randomized participants.[21] Losses do not retain the intervention effect, and missing data in trials will lead to systematic differences between the approaches.[39]

Studies have shown that a 1-mmol/L reduction in TC and LDL-C levels results in a 26.6% to 29.5% decrease for any cardiovascular disease–related event.[40] The average reductions of TC and LDL-C concentrations following a vegetarian diet intervention included in this meta-analysis were 0.36 and 0.34 mmol/L, respectively, which would correspond to a decrease in cardiovascular disease risk of about 9.0% to 10.6%. Vegetarian diets may reduce blood cholesterol concentrations through several mechanisms. Vegetarian diets are low in cholesterol, total fat, and saturated fatty acids,[11] leading to less absorption and conversion to blood cholesterol.[41] Moreover, vegetarian diets provide a high intake of dietary fiber and many health-promoting phytochemicals including phytosterols, phenolics, carotenoids, flavonoids, indoles, saponins, and sulfides, derived primarily from fruits, vegetables, whole grains, legumes, nuts, and various soy products.[42] These phytochemicals can exert substantial influence on cholesterol levels via multiple mechanisms. Phytosterols reduce intestinal cholesterol absorption by competing with cholesterol for a place in the mixed micelles.[43] Phenolics inhibit the oxidation of LDL-C, improving cardiovascular health.[44] Flavonoids and saponins disrupt the cholesterol micelle solubility, leading to potential reduction in cholesterol absorption.[45] Sulfides or organosulfur compounds decrease blood lipids, especially TC and non–HDL-C, like LDL-C, by inhibiting the biosynthesis of cholesterol.[46]

Like other cholesterol subfractions (eg, non–HDL-C), blood HDL-C concentrations were also decreased after the vegetarian diet intervention. A reduction in the apolipoprotein A-I
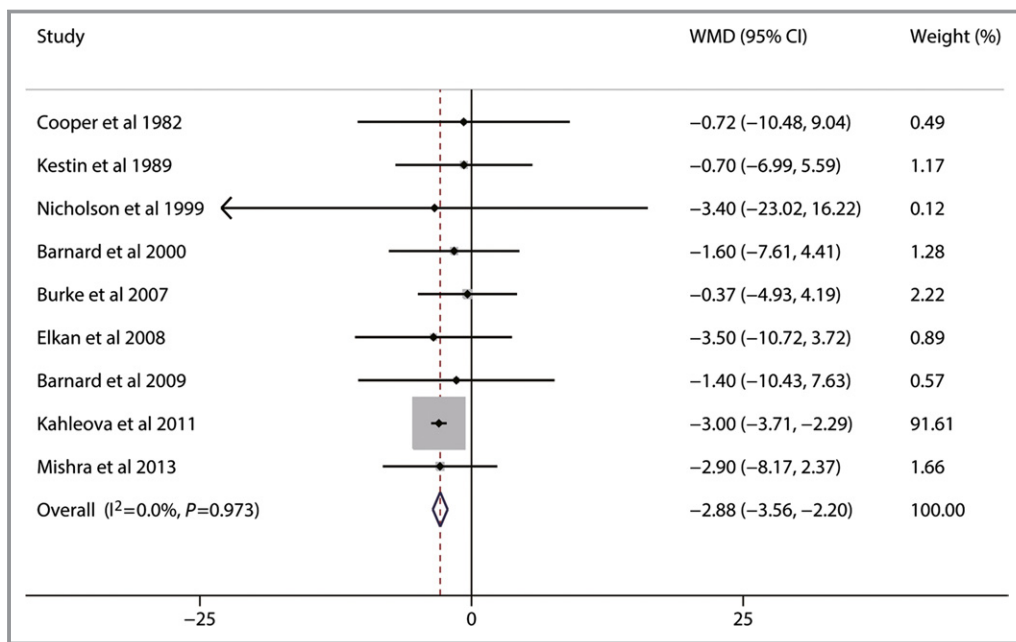

Figure 5. Effects of vegetarian diets on weight loss. The meta-analysis used the WMD in the random-effects model. Horizontal lines denote 95% CI. A diamond represents the overall estimated effect. WMD, weighted mean difference.

production rate appears to explain the decrease in HDL–C concentrations.[47] HDL–C is inversely associated with risk of coronary heart disease.[48] Despite lowering of HDL–C in observational studies or RCTs, vegetarian diets are not associated with poor cardiovascular health.[49] As for TG, the pooled estimated change in TG concentrations was not significant. Considering that all studies were conducted in developed countries, this result was consistent with a previous meta-analysis.[35] The mechanisms for the effect of vegetarian diets on TG still need to be studied.

This study has several strengths. First, as far as we are aware, this is the first meta-analysis of RCTs to examine the effects of vegetarian diets on blood lipid concentrations. Second, the considerably large number of pooled participants provided sufficient statistical power to detect the treatment effects. In addition, results from both random- and fixed-effects models were similar (Tables 3 through 5), indicating that our findings were stable. Third, to avoid double counting of participants, if a study had multiple time points for the same participants, only the last end point was used for calculation of the pooled effect. Finally, the results were unlikely to be affected by publication bias. Both Begg's rank correlation test and Egger's linear regression test suggested no significant asymmetry for the overall effects estimation of TC, LDL-C, HDL-C, TG, and non–HDL-C.

Although the present meta-analysis may provide some useful information, several potential limitations of this meta-analysis should be considered. First, dietary intervention studies typically cannot be double blinded.[2] Lack of blinding could cause bias by affecting the actual outcomes of the participants in the trial.[21] Although objective outcomes like blood lipid concentrations may not be influenced, subjective behaviors of participants across different groups (eg, dropout rate) could be affected. Second, moderate to high heterogeneity was present for the TC, LDL-C, and non–HDL-C analyses and was only partly explained by subgroup and meta–regression analyses. Although moderate to high heterogeneity still remained in some subgroups, the pooled weighted mean effect sizes showed consistent lowering effects of vegetarian diets on TC, LDL-C, and non–HDL-C concentrations. Third, this meta-analysis suggested vegetarian diets could reduce blood TC, LDL-C, and HDL-C concentrations. Only a few studies provided data on the effect of vegetarian diets on the ratio of TC (or LDL-C) to HDL-C. Given that reductions of TC (or LDL-C) and HDL-C have different impacts on CVD risk, it was difficult to ascertain which impact was larger. Nevertheless, vegetarian diets have not been found to be associated with poor cardiovascular health.[49] Fourth, greater weight reduction in the vegetarian groups was found compared with omnivorous groups (−2.88 kg, 95% CI −3.56 to −2.20, $P < 0.001$) (Figure 5). Weight reduction was

significantly associated with decrease of TC and LDL-C[50]; therefore, some of the effect of the change in TC and LDL-C in this meta-analysis could be a consequence of weight loss. Fifth, our analysis covers a long time span of 30 years, with the oldest study performed in 1982 and the latest trial conducted in 2013. The time of study may be an important confounder because lifestyles changed and medical sciences advanced considerably; however, no significant difference was found between studies published before 2000 and those published in and after 2000 in subgroup and univariate meta–regression analyses. Finally, studies that examined the effects of vegetarian diets on serum lipid concentrations and on plasma lipid concentrations were both included in this meta-analysis to guarantee a considerable number of participants. The commonly recommended anticoagulant for plasma is disodium ethylenediaminetetraacetate. Its use may produce a shift of water from red blood cells to plasma and thus dilutes the plasma and lowers the concentration of lipids.[51] Comparing final values may introduced bias due to the difference between plasma lipids and serum lipids. This meta-analysis was analyzed based on changes from baseline to minimize this bias.

In conclusion, vegetarian diets could effectively lower blood concentrations of TC, LDL-C, HDL-C, and non–HDL-C. These findings have important public health implications with regard to the management of dyslipidemia, especially hypercholesterolemia, via dietary intervention. Further well-designed RCTs that are designed to evaluate the effects of specific vegetarian diets on blood lipids are required, and additional studies with detailed population information should be performed to clarify the possible mechanism.

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