Total red meat intake of ≥0.5 servings/d does not negatively influence cardiovascular disease risk factors: a systemically searched meta-analysis of randomized controlled trials[1,2]

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ABSTRACT

Background: Observational associations between red meat intake and cardiovascular disease (CVD) are inconsistent. There are limited comprehensive analyses of randomized controlled trials (RCTs) that investigate the effects of red meat consumption on CVD risk factors.

Objective: The purpose of this systematically searched meta-analysis was to assess the effects of consuming ≥0.5 or <0.5 servings of total red meat/d on CVD risk factors [blood total cholesterol (TC), LDL cholesterol, HDL cholesterol, triglycerides, ratio of TC to HDL cholesterol (TC:HDL), and systolic and diastolic blood pressures (SBP and DBP, respectively)]. We hypothesized that the consumption of ≥0.5 servings of total red meat/d would have a negative effect on these CVD risk factors.

Design: Two researchers independently screened 945 studies from PubMed, Cochrane Library, and Scopus databases and extracted data from 24 qualified RCTs. Inclusion criteria were *1*) RCT, *2*) subjects aged ≥19 y, *3*) consumption of ≥0.5 or <0.5 total red meat servings/d [35 g (1.25 ounces)], and *4*) reporting ≥1 CVD risk factor. We performed an adjusted 2-factor nested ANOVA mixed-effects model procedure on the postintervention values of TC, LDL cholesterol, HDL cholesterol, TC:HDL cholesterol, triglycerides, SBP, and DBP; calculated overall effect sizes of change values; and used a repeated-measures ANOVA to assess pre- to postintervention changes.

Results: Red meat intake did not affect lipid-lipoprotein profiles or blood pressure values postintervention ($P > 0.05$) or changes over time [weighted mean difference (95% CI): −0.01 mmol/L (−0.08, 0.06 mmol/L), 0.02 mmol/L (−0.05, 0.08 mmol/L), 0.03 mmol/L (−0.01, 0.07 mmol/L), and 0.04 mmol/L (−0.02, 0.10 mmol/L); −0.08 mm Hg (−0.26, 0.11 mm Hg); and −1.0 mm Hg (−2.4, 0.78 mm Hg) and 0.1 mm Hg (−1.2, 1.5 mm Hg) for TC, LDL cholesterol, HDL cholesterol, triglycerides, TC:HDL cholesterol, SBP, and DBP, respectively]. Among all subjects, TC, LDL cholesterol, HDL cholesterol, TC:HDL cholesterol, triglycerides, and DBP, but not SBP, decreased over time ($P < 0.05$).

Conclusions: The results from this systematically searched meta-analysis of RCTs support the idea that the consumption of ≥0.5 servings of total red meat/d does not influence blood lipids and lipoproteins or blood pressures. *Am J Clin Nutr* 2017;105:57–69.

Keywords: dietary guidance, blood lipids, blood lipoproteins, blood pressure, animal flesh, meat products, diet, meat

INTRODUCTION

The effects of red meat consumption on cardiovascular disease (CVD)[3] are inconsistent throughout the literature. CVD has been the leading cause of death in the United States since the 1950s and is currently attributable to 610,000 US deaths each year (1). Historically, epidemiologic cohort data support associations between high red meat intake and CVD-related events (2, 3) and mortality (4–6). This notion is currently being challenged due to data collection methods that group red meat with processed meat and/or inconsistent nomenclature and classification of red meat throughout the literature (7, 8). Regardless of contradicting evidence, an observational study design is unable to show causality such as with a randomized controlled trial (RCT). There is a paucity of literature that systematically and comprehensively assesses the effects of total red meat consumption amounts on CVD risk with data from RCTs (9).

The purpose of this meta-analysis was to systematically search the literature to assess the effects of total red meat consumption on indexes of CVD risk. The search included studies with an RCT design that measured blood lipids, lipoproteins, and/or blood pressures. We hypothesized that the consumption of ≥0.5 servings of red meat/d (or ∼3.5 servings/wk) would negatively affect blood lipids, lipoproteins, and blood pressures. Our hypothesis was based on a current prospective cohort analysis that estimated that 8.6% and 12.2% of CVD-related deaths in men and women, respectively, would be preventable if participants consumed <0.5 servings of total red meat/d (5).

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[2] Supplemental Tables 1 and 2 are available from the "Online Supporting Material" link in the online posting of the article and from the same link in the online table of contents at http://ajcn.nutrition.org.

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[3] Abbreviations used: CVD, cardiovascular disease; DASH, Dietary Approaches to Stop Hypertension; DBP, diastolic blood pressure; DGA, Dietary Guidelines for Americans; RCT, randomized controlled trial; SBP, systolic blood pressure; TC, total cholesterol; TC:HDL, ratio of total cholesterol to HDL cholesterol.

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TABLE 1
Description of PICOS criteria for a systematically searched meta-analysis assessing the effects of consuming ≥0.5 or <0.5 servings of total red meat/d on blood lipids, lipoproteins, and blood pressures[1]

Variable	Description
Population	Adults aged ≥19 y
Intervention	Groups who consumed ≥0.5 servings (35 g or 1.25 ounces) of total red meat/d
Comparator	Groups who consumed <0.5 servings of total red meat/d
Outcome	Changes in modifiable traditional cardiovascular disease risk factors, specifically blood lipids, lipoproteins, and blood pressures
Study design	Randomized controlled trials
Research question	What is the effect of consuming ≥0.5 servings of total red meat/d on blood lipids, lipoproteins, and blood pressure in adults?

[1] PICOS, Population, Intervention, Comparator Outcome, Study design.

METHODS

Search strategy and data extraction

We followed the same systematic search protocol as the 2015 Dietary Guidelines Advisory Committee from the Nutrition Evidence Library (10). The PICOS (Population, Intervention, Comparator, Outcome, Study design) criteria used to define our research question are listed in **Table 1**. Inclusion criteria consisted of the following: *1*) use of an RCT study design, *2*) subjects aged ≥19 y, *3*) an intervention group or phase with consumption of ≥0.5 servings of total red meat/d compared with a control group or phase with consumption of <0.5 servings of total red meat/d, and *4*) reporting of ≥1 CVD risk factor as a dependent variable [i.e., blood total cholesterol (TC), LDL cholesterol, HDL cholesterol, TC-to-HDL-cholesterol ratio (TC:HDL), triglycerides, systolic blood pressure (SBP), and diastolic blood pressure (DBP)]. Our meta-analysis followed the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines (11).

The original search took place in May 2015 but was updated in May 2016. We identified studies via a computerized search of 3 databases: *1*) PubMed (http://www.ncbi.nlm.nih.gov/pubmed), *2*) Cochrane Library (http://www.cochranelibrary.com), and *3*) Scopus (http://www.scopus.com). We reviewed reference lists of the identified studies and found 10 additional potential studies. Search terms and results are identified in **Table 2**. All of the database searches were completed independently by the primary author (LEO) and the secondary author (JEK). A research librarian assisted both reviewers (see Acknowledgments) in database and search term selection to optimize the search process and to reduce the chance of bias.

We excluded 865 of 945 studies from our search for the following reasons: *1*) the study design was not an RCT, *2*) the population was <19 y of age or pregnant, *3*) the control and intervention diets did not differ in total red meat consumption amounts, or *4*) the researchers did not report the dependent variables of interest (see **Figure 1**). The primary and secondary authors independently read 80 potentially eligible studies to further assess inclusion criteria and to avoid selection bias. We contacted corresponding authors when clarification or unpublished data were needed. We excluded 56 of the 80 studies from the analysis for the following reasons: *1*) we were unable to determine the amount of red meat consumed, *2*) the control and intervention diets did not meet our requirements of ≥0.5 or <0.5 servings/d or ≥3.5 or <3.5 servings/wk of total red meat, or *3*) we were unable to obtain the dependent variables of interest in a usable data format. The primary and secondary authors independently extracted data from the final 24 studies including the following: *1*) author name, *2*) publication year, *3*) population size and description, *4*) intervention duration, *5*) protein source comparison consumed by the control group, and *6*) the amount of total red meat intake, dietary patterns, method of diet administration, assessment of dietary compliance, and pre- and postintervention values and net changes in blood TC, LDL cholesterol, HDL

TABLE 2
Search terms and results for a systematically searched meta-analysis assessing the effects of consuming ≥0.5 or <0.5 servings of total red meat/d on blood lipids, lipoproteins, and blood pressures[1]

Source	Search terms	Filters	Results yielded
PubMed database	("Meat"[MESH] OR "Meat Products"[MESH] OR "red meat" OR "beef" OR "pork") AND ("hypertension"[MESH] OR "Cholesterol, LDL"[MESH] OR "Cholesterol, HDL"[MESH] OR "Blood Pressure"[MESH] OR "lipoproteins"[MESH])	Humans, aged ≥19 y, English	332
Scopus database	Meat AND (blood pressure OR lipoprotein)	English, human, humans, source type journals, limit to article and conference paper; exclude physical sciences, social sciences, humanities, agriculture, immunology, chemistry, environmental sciences, neuroscience, chemical engineering, engineering, computer science, psychology, arts and humanities, mathematics, veterinary and multidisciplinary	426
Cochrane Central database	Meat AND (blood pressure OR lipoprotein)	Trials	177
Reference lists of identified studies	N/A	N/A	10
Total	—	—	945

[1] MESH, Medical Subject Heading; N/A, not applicable.

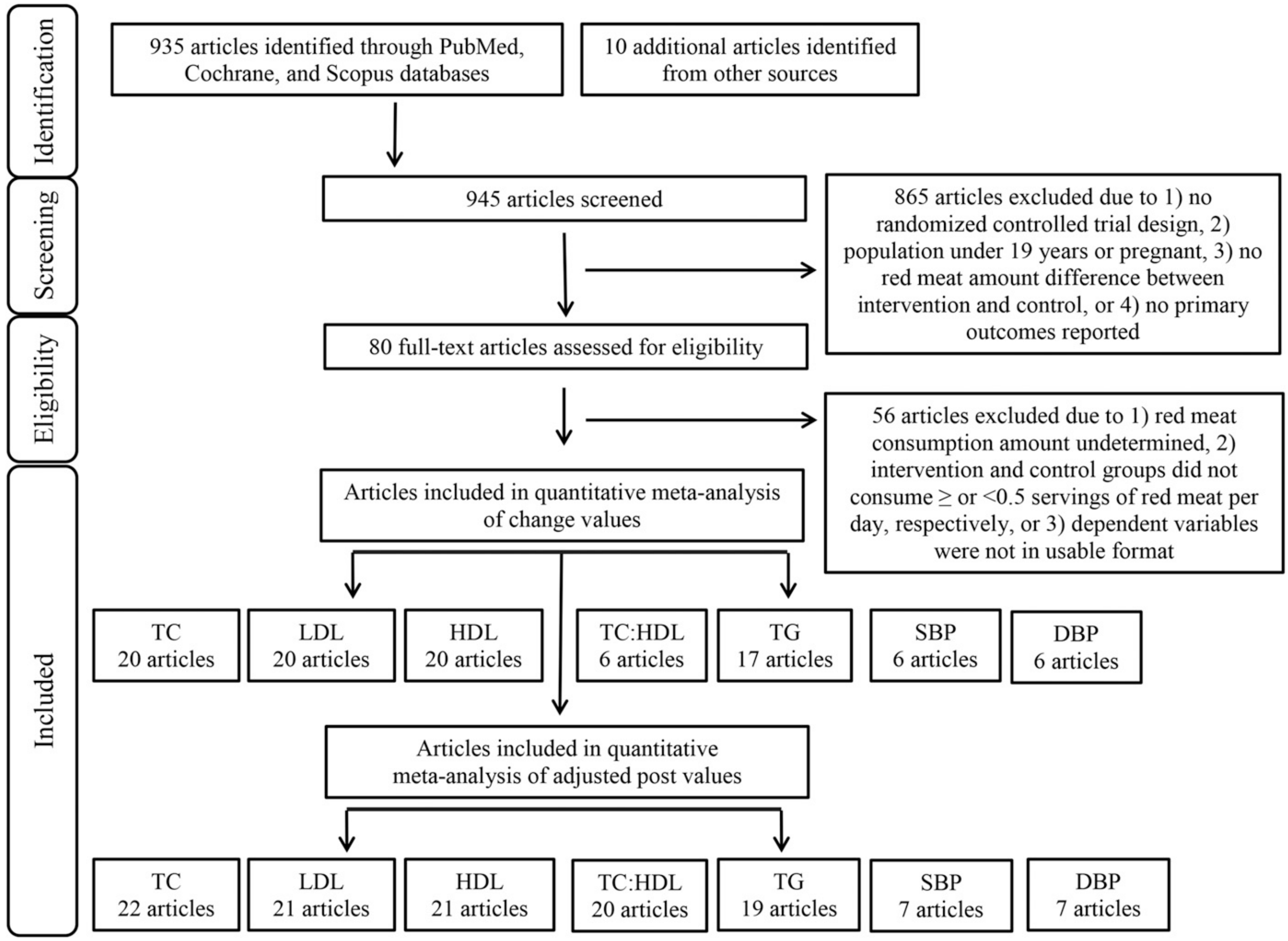

FIGURE 1 PRISMA flowchart. DBP, diastolic blood pressure; PRISMA, Preferred Reporting Items for Systematic Review and Meta-Analyses; SBP, systolic blood pressure; TC, total cholesterol; TG, triglycerides.

cholesterol, TC:HDL, triglycerides, SBP, and DBP for both the control and intervention groups.

Definitions

For this meta-analysis, we used the 2015–2020 Dietary Guidelines for Americans (DGA) glossary definition of red meat (or "meat") and processed meat: "all forms of beef, pork, lamb, veal, goat, and non-bird games (e.g. venison, bison, elk)" and "preserved by smoking, curing, salting, and/or the addition of chemical preservatives," respectively (12). Unprocessed meat refers to meat that is preserved by refrigeration or freezing only (13). However, all meat available for purchase is processed to an extent (e.g., slaughtering and packaging) so the term "minimally processed" will be used in this meta-analysis to further describe the red meat consumed by research subjects. Blood TC, LDL cholesterol, HDL cholesterol, TC:HDL, triglycerides, SBP, and DBP are common modifiable biomarkers of CVD risk regularly assessed by physicians and therefore are the dependent variables assessed in this meta-analysis.

Calculations, bias assessment, and statistical analyses

We obtained or calculated the amount of red meat consumed by each group from the dietary data available in the study and contacted authors for clarification or raw data when needed. According to the American Heart Association, a serving size of cooked meat is 2–3 ounces (14); therefore, we considered 1 serving and 0.5 servings of red meat to be equivalent to 2.5 and 1.25 ounces, respectively. With the use of ProNutra software version 3.3 (Viocare, Inc.), we calculated that 1.25 ounces of red meat was equivalent to 35 g. The cutoff of 0.5 servings/d is supported by a 2012 prospective cohort analysis that estimated that 8.6% and 12.2% of CVD-related deaths in men and women, respectively, were preventable if subjects consumed <0.5 servings of total red meat/d (5).

We converted all blood lipid and lipoprotein data to mmol/L [TC, LDL-cholesterol, and HDL-cholesterol conversion: mg/dL ÷ 38.67; triglycerides conversion: mg/dL ÷ 88.57 (15)]. We extracted pre- and postintervention means, SDs, change values, and SDs of the change values from the studies when available. If not available, we calculated values, when appropriate, either from raw data obtained from the researchers or from information that was provided in the study and calculated change-value SDs by using a correlation factor representative of the change-value SDs that were available from the other studies (16). We evaluated the risk of selection, performance, and detection biases by using the modified Cochrane risk-of-bias assessment tool (17).

When discussing "studies" throughout this meta-analysis, we are referring to the entirety of each publication. Some studies contained >1 intervention or control group or phase. In this case, these interventions are presented separately and treated as independent trials to account for within-study differences (18). Crossover trials were included in this meta-analysis; the present results and figures show crossover trial means and SDs incorporated into the data set as if they were parallel designs (19). This approach uses a correlational factor of 0 for all trial SDs. We recognize that this approach is conservative and causes crossover studies to be underweighted; therefore, we conducted secondary analyses to approximate a paired analysis for each variable by imputing missing SDs with the use of a correlational factor of 0.99 for all crossover design studies (20).

With the use of SAS version 9.4 (SAS Institute), we performed a repeated-measures ANOVA to assess pre- to postintervention changes in TC, LDL cholesterol, HDL cholesterol, TC:HDL, triglycerides, SBP, and DBP. We performed a 2-factor, nested ANOVA mixed-effects model procedure on the postintervention values of each dependent variable after adjustment for baseline values, age, sex, BMI, length of intervention, and whether energy restriction was or was not included in the protocol (21). These results are reported as adjusted least-squares means. We analyzed the change values by using STATA/IC 14 (StataCorp) and calculated the overall effect size by using the metaan function (intervention group or phase change value minus control group or phase change value). We used a random-effects model when heterogeneity was indicated by a significant chi-square test; otherwise, a fixed-effects model was used (22, 23). These results are reported as weighted mean differences and 95% CIs. Studies in **Figures 2–8** are organized in descending order from smallest to largest amounts of total red meat consumed per day by the intervention group or phase. Significance was set at $P < 0.05$. A statistical consultant approved all calculations and analyses (see Acknowledgments).

We performed traditional sensitivity analyses by removing 1 study or trial at a time and reconducting the analyses. We performed additional sensitivity analyses by removing clusters of

	≥0.5 servings of red meat/day			<0.5 servings of red meat/day					
Study	mean (mmol/L)	SD	n	mean (mmol/L)	SD	n	weight (%)	mean difference (mmol/L), random effects	[95% CI]
Grieger, 2014 (24)	-0.10	0.74	37	0.10	0.40	43	3.70	-0.20	[-0.47, 0.07]
Aadland, 2015 (25)	-0.38	0.70	19	-0.37	0.54	20	2.23	-0.01	[-0.40, 0.38]
Nowson, 2009 (26)	0.34	1.00	46	0.38	1.25	49	1.78	-0.05	[-0.50, 0.40]
Liao, 2007 (27)	-0.47	0.22	15	-0.61	0.16	15	7.07	0.15	[0.01, 0.29]
Sayer, 2015 (28)	-0.68	0.41	19	-0.36	0.38	19	4.06	-0.33	[-0.58, -0.07]
Mahon, 2007 CHICK (29)	-0.59	0.87	14	-0.49	1.54	15	0.51	-0.10	[-1.00, 0.80]
Mahon, 2007 CARB (29)	-0.59	0.87	14	-1.14	2.91	14	0.17	0.54	[-1.05, 2.13]
Mahon, 2007 CON (29)	-0.59	0.87	14	-0.16	2.10	11	0.25	-0.44	[-1.75, 0.87]
Flynn, 1981 F1 (30)	-0.13	0.86	31	-0.03	1.05	31	1.66	-0.10	[-0.57, 0.37]
Flynn, 1981 F2 (30)	-0.03	0.68	24	0.18	0.69	24	2.23	-0.21	[-0.60, 0.18]
Flynn, 1981 M1 (30)	-0.10	0.51	38	-0.16	0.77	38	3.39	0.05	[-0.24, 0.34]
Flynn, 1981 M2 (30)	-0.10	0.74	36	0.21	0.68	36	2.85	-0.31	[-0.64, 0.02]
Flynn, 1982 F1 BEEF (31)	-0.10	1.06	12	-0.13	1.09	12	0.56	0.03	[-0.83, 0.89]
Flynn, 1982 F1 PORK (31)	-0.21	0.49	12	-0.13	1.09	12	0.90	-0.08	[-0.75, 0.59]
Flynn, 1982 F2 BEEF (31)	0.13	0.76	17	0.26	0.76	17	1.45	-0.13	[-0.64, 0.38]
Flynn, 1982 F2 PORK (31)	-0.34	0.62	17	0.26	0.76	17	1.66	-0.60	[-1.06, -0.12]
Flynn, 1982 M1 BEEF (31)	-0.18	0.53	21	0.03	0.62	21	2.62	-0.21	[-0.56, 0.14]
Flynn, 1982 M1 PORK (31)	-0.03	0.38	21	0.03	0.62	21	3.10	-0.05	[-0.36, 0.26]
Flynn, 1982 M2 BEEF (31)	-0.16	0.77	26	0.13	0.76	26	2.07	-0.28	[-0.69, 0.13]
Flynn, 1982 M2 PORK (31)	-0.13	0.65	26	0.13	0.76	26	2.23	-0.26	[-0.65, 0.13]
de Mello, 2006 CHICK (32)	0.03	0.68	17	-0.26	0.57	17	1.92	0.29	[-0.14, 0.72]
de Mello, 2006 LVLP (32)	0.03	0.68	17	-0.28	0.56	17	2.07	0.31	[-0.10, 0.72]
Ashton, 2000 (33)	-0.14	0.58	42	-0.37	0.61	42	4.06	0.23	[-0.03, 0.49]
Davidson, 1999 (34)	-0.08	0.27	89	-0.13	0.31	102	8.89	0.05	[-0.03, 0.13]
Wolmarans, 1999 (35)	-0.29	0.63	39	-0.45	0.55	39	4.06	0.16	[-0.10, 0.42]
O'Brien, 1980 HC G1 (36)	0.44	0.87	15	0.00	0.57	15	1.36	0.44	[-0.09, 0.97]
O'Brien, 1980 LC G1 (36)	-0.13	0.81	15	-0.08	0.57	15	1.45	-0.05	[-0.56, 0.46]
O'Brien, 1980 HC G2 (36)	0.41	0.43	14	0.49	0.31	14	3.70	-0.08	[-0.35, 0.19]
O'Brien, 1980 LC G2 (36)	-0.18	0.28	14	-0.47	0.30	14	4.89	0.28	[0.06, 0.50]
Foerster, 2014 (37)	-0.10	0.49	20	0.00	0.58	20	2.85	-0.10	[-0.43, 0.23]
Hodgson, 2006 (38)	-0.10	0.52	29	-0.10	0.47	31	4.06	0.00	[-0.26, 0.26]
Gascon, 1996 (39)	-0.34	0.39	14	-0.14	0.44	14	3.10	-0.20	[-0.51, 0.11]
Wolmarans, 1991 (40)	0.12	0.73	28	-0.14	0.66	28	2.41	0.26	[-0.11, 0.63]
Haub, 2005 (41)	0.30	0.30	11	-0.06	0.70	10	1.66	0.36	[-0.11, 0.83]
Beauchesne-Rondeau, 2003 F (42)	-0.50	0.52	18	-0.30	0.52	18	2.85	-0.20	[-0.53, 0.13]
Beauchesne-Rondeau, 2003 P (42)	-0.50	0.52	18	-0.50	0.52	18	2.85	0.00	[-0.33, 0.33]
Sinclair, 1987 SF (43)	-1.05	0.82	10	-1.03	0.44	10	1.20	-0.02	[-0.59, 0.55]
Sinclair, 1987 TF (43)	-1.05	0.82	10	-0.89	0.52	11	1.13	-0.16	[-0.75, 0.43]
Sinclair, 1987 VEG (43)	-1.05	0.82	10	-1.10	0.49	7	1.01	0.05	[-0.58, 0.68]
						Overall	**100.00**	**-0.01**	**[-0.08, 0.06]**

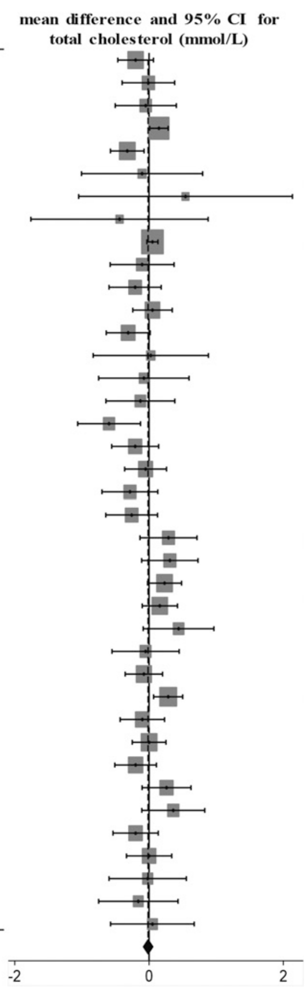

FIGURE 2 Random-effects model meta-analysis for changes in total blood cholesterol concentrations from randomized controlled trials comparing ≥0.5 or <0.5 servings of total red meat/d. Heterogeneity: $\tau^2 = 0.011$, $\chi^2 = 1.48$, df = 38 ($P = 0.028$), $I^2 = 32\%$. Data are shown in descending order from smallest to largest amounts of red meat consumed by the intervention group or phase. CARB, carbohydrate control diet; CHICK, chicken control diet; CON, habitual control diet; F, lean fish control diet; F1, first female group; F1 BEEF, first female group consuming beef diet; F1 PORK, first female group consuming pork diet; F2, second female group; F2 BEEF, second female group consuming beef diet; F2 PORK, second female group consuming pork diet; HC G1, first group consuming high-cholesterol diet; HC G2, second group consuming high-cholesterol diet; LC G1, first group consuming low-cholesterol diet; LC G2, second group consuming low-cholesterol diet; LVLP, lactovegetarian low-protein control diet; M1, first male group; M1 BEEF, first male group consuming beef diet; M1 PORK, first male group consuming pork diet; M2, second male group; M2 BEEF, second male group consuming beef diet; M2 PORK, second male group consuming pork diet; P, poultry control diet; SF, southern fish control diet; TF, tropical fish control diet; VEG, vegetarian control diet.

studies containing design features that had the potential to confound results, including weight-loss diets (27, 29), heart-healthy diets (25, 26, 28, 34, 35, 39, 42, 43), diseased populations [hypertensive (26, 28, 38), hypercholesterolemic (34, 35, 42), and/or diabetic (32)], studies that resulted in significant weight loss (25, 27–29, 35), inclusion of processed meat (45), studies that did not specify the degree of meat processing (24, 25, 27, 32, 36, 40, 43, 46, 47), and studies that used different amounts of protein intake in the control and intervention group or phase (29, 32, 38, 43). We also performed post hoc analyses by dividing the studies into specific quantities of red meat consumption [1.0–1.9 servings of red meat/d (24–29), 2.0–2.9 servings of red meat/d (30–37), or ≥3.0 servings of red meat/d (38–43)] and re-conducted the analyses in STATA.

RESULTS

Study features and subject characteristics

Twenty-four studies were included in the statistical analyses (see Figure 1); some contained >1 control group or phase (29–32, 36, 42, 43) and are reported as separate studies. Details of each study are shown in **Table 3**. The median total red meat servings per day in the control and intervention groups were 0 servings/d (range: 0–0.4 servings/d or 0–30 g/d) and 2 servings/d (or 140 g/d; range 1.0–7.1 servings/d or 68–500 g), respectively. Two of the selected studies included a weight-loss diet (27, 29), 8 studies included a heart-healthy dietary pattern (25, 26, 28, 34, 35, 39, 42, 43), the subjects self-selected their diet similar to their habitual intake in 9 studies (24, 30, 31, 36–38, 46, 40, 41), and 5

	≥0.5 servings of red meat/day			<0.5 servings of red meat/day					
Study	mean (mmol/L)	SD	n	mean (mmol/L)	SD	n	weight (%)	mean difference (mmol/L), random effects	[95% CI]
Grieger, 2014 (24)	-0.10	0.58	37	0.20	0.63	43	3.63	-0.30	[-0.57, -0.03]
Aadland, 2015 (25)	-0.26	0.61	19	-0.22	0.49	20	2.49	-0.04	[-0.39, 0.31]
Nowson, 2009 (26)	0.28	0.75	46	0.30	1.15	49	2.10	-0.01	[-0.40, 0.38]
Liao, 2007 (27)	-0.23	0.18	15	-0.40	0.04	15	9.21	0.17	[0.07, 0.27]
Sayer, 2015 (28)	-0.46	0.23	19	-0.32	0.64	19	2.99	-0.14	[-0.45, 0.17]
Mahon, 2007 CHICK (29)	-0.44	0.49	14	-0.41	1.35	15	0.70	-0.03	[-0.76, 0.70]
Mahon, 2007 CARB (29)	-0.44	0.49	14	-0.52	1.67	14	0.45	0.08	[-0.84, 1.00]
Mahon, 2007 CON (29)	-0.44	0.49	14	-0.26	1.42	11	0.48	-0.18	[-1.06, 0.70]
Flynn, 1981 F1 (30)	0.18	1.74	31	-0.14	1.97	31	0.45	0.32	[-0.60, 1.24]
Flynn, 1981 F2 (30)	0.00	1.38	24	0.28	1.40	24	0.61	-0.28	[-1.06, 0.50]
Flynn, 1981 M1 (30)	-0.01	0.93	38	-0.09	1.25	38	1.44	0.08	[-0.41, 0.57]
Flynn, 1981 M2 (30)	0.02	1.39	36	0.29	1.18	36	1.04	-0.27	[-0.86, 0.32]
Flynn, 1982 F1 BEEF (31)	0.14	1.48	12	-0.13	1.84	12	0.22	0.27	[-1.06, 1.60]
Flynn, 1982 F1 PORK (31)	-0.41	0.82	12	-0.13	1.84	12	0.30	-0.28	[-1.42, 0.86]
Flynn, 1982 F2 BEEF (31)	0.07	1.48	17	0.34	1.53	17	0.37	-0.27	[-1.29, 0.75]
Flynn, 1982 F2 PORK (31)	-0.44	1.23	17	0.34	1.53	17	0.43	-0.78	[-1.72, 0.16]
Flynn, 1982 M1 BEEF (31)	-0.07	0.95	21	0.17	1.14	21	0.92	-0.24	[-0.87, 0.39]
Flynn, 1982 M1 PORK (31)	-0.12	0.69	21	0.17	1.14	21	1.10	-0.29	[-0.86, 0.28]
Flynn, 1982 M2 BEEF (31)	0.06	1.46	26	0.22	1.32	26	0.64	-0.17	[-0.93, 0.59]
Flynn, 1982 M2 PORK (31)	-0.24	1.15	26	0.22	1.32	26	0.82	-0.47	[-1.14, 0.20]
de Mello, 2006 CHICK (32)	0.47	0.91	17	0.22	0.87	17	0.98	0.25	[-0.36, 0.86]
de Mello, 2006 LVLP (32)	0.47	0.91	17	0.13	0.84	17	1.04	0.34	[-0.25, 0.93]
Ashton, 2000 (33)	-0.12	0.84	42	-0.20	0.85	42	2.49	0.08	[-0.27, 0.43]
Davidson, 1999 (34)	-0.08	0.41	89	-0.13	0.44	102	8.38	0.05	[-0.07, 0.17]
Wolmarans, 1999 (35)	0.12	0.86	39	-0.17	0.80	39	2.29	0.29	[-0.08, 0.66]
O'Brien, 1980 HC G1 (36)	0.05	0.07	15	0.08	0.08	15	10.76	-0.03	[-0.09, 0.03]
O'Brien, 1980 LC G1 (36)	0.08	0.07	15	-0.10	0.08	15	10.76	0.18	[0.12, 0.24]
O'Brien, 1980 HC G2 (36)	0.03	0.09	14	0.08	0.12	14	10.02	-0.05	[-0.13, 0.03]
O'Brien, 1980 LC G2 (36)	-0.05	0.10	14	0.00	0.12	14	10.02	-0.05	[-0.13, 0.03]
Hodgson, 2006 (38)	0.00	0.72	29	-0.20	0.72	31	2.29	0.20	[-0.17, 0.57]
Gascon, 1996 (39)	-0.26	0.46	14	-0.06	0.45	14	2.73	-0.20	[-0.53, 0.13]
Wolmarans, 1991 (40)	0.12	0.86	28	-0.17	0.80	28	1.79	0.29	[-0.14, 0.72]
Haub, 2005 (41)	0.30	0.48	11	-0.08	0.76	10	1.18	0.38	[-0.17, 0.93]
Wiebe, 1984 (44)	-0.36	0.72	8	-0.36	0.70	8	0.78	0.00	[-0.69, 0.69]
Beauchesne-Rondeau, 2003 F (42)	-0.30	0.71	18	-0.20	0.81	18	1.44	-0.10	[-0.59, 0.39]
Beauchesne-Rondeau, 2003 P (42)	-0.30	0.71	18	-0.40	0.71	18	1.54	0.10	[-0.37, 0.57]
Sinclair, 1987 SF (43)	-0.58	1.29	8	-0.67	0.57	10	0.41	0.09	[-0.87, 1.05]
Sinclair, 1987 TF (43)	-0.58	1.29	8	-0.56	0.62	8	0.38	-0.02	[-1.00, 0.98]
Sinclair, 1987 VEG (43)	-0.58	1.29	8	-0.53	0.68	7	0.37	-0.05	[-1.07, 0.97]
Overall							**100.00**	**0.02**	**[-0.05, 0.08]**

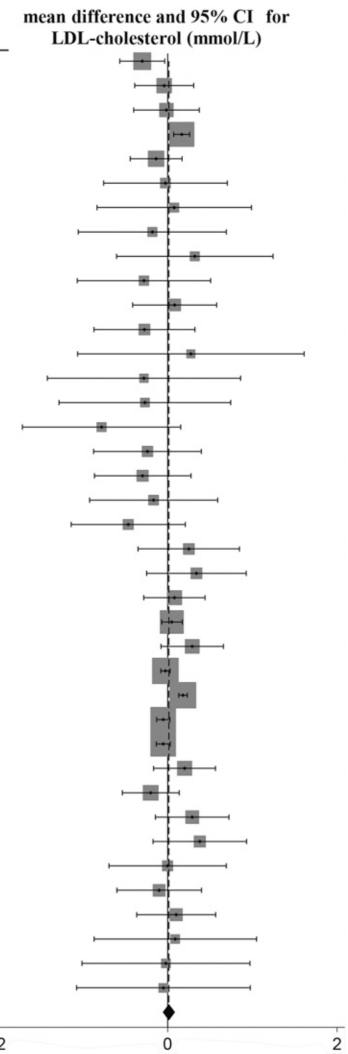

FIGURE 3 Random-effects model meta-analysis for changes in blood LDL-cholesterol concentrations from randomized controlled trials comparing ≥0.5 or <0.5 servings of total red meat/d. Heterogeneity: $\tau^2 = 0.011$, $\chi^2 = 6.62$, df = 38 ($P = 0.001$), $I^2 = 85\%$. Data are shown in descending order from smallest to largest amounts of red meat consumed by the intervention group or phase. CARB, carbohydrate control diet; CHICK, chicken control diet; CON, habitual control diet; F, lean fish control diet; F1, first female group; F1 BEEF, first female group consuming beef diet; F1 PORK, first female group consuming pork diet; F2, second female group; F2 BEEF, second female group consuming beef diet; F2 PORK, second female group consuming pork diet; HC G1, first group consuming high-cholesterol diet; HC G2, second group consuming high-cholesterol diet; LC G1, first group consuming low-cholesterol diet; LC G2, second group consuming low-cholesterol diet; LVLP, lactovegetarian low-protein control diet; M1, first male group; M1 BEEF, first male group consuming beef diet; M1 PORK, first male group consuming pork diet; M2, second male group; M2 BEEF, second male group consuming beef diet; M2 PORK, second male group consuming pork diet; P, poultry control diet; SF, southern fish control diet; TF, tropical fish control diet; VEG, vegetarian control diet.

Study	≥0.5 servings of red meat/day mean (mmol/L)	SD	n	<0.5 servings of red meat/day mean (mmol/L)	SD	n	weight (%)	mean difference (mmol/L), random effects	[95% CI]
Grieger, 2014 (24)	0.10	0.94	37.00	0.10	1.01	43.00	0.75	0.00	[-0.43, 0.43]
Aadland, 2015 (25)	0.03	0.52	46.00	-0.02	0.50	49.00	2.10	0.06	[-0.14, 0.26]
Nowson, 2009 (26)	-0.24	0.22	19.00	-0.09	0.18	20.00	3.02	-0.15	[-0.27, -0.03]
Liao, 2007 (27)	-0.05	0.02	15.00	-0.02	0.09	15.00	3.86	-0.03	[-0.07, 0.01]
Sayer, 2015 (28)	-0.16	0.02	19.00	-0.08	0.01	19.00	3.96	-0.08	[-0.10, -0.06]
Mahon, 2007 CHICK (29)	-0.05	0.08	14.00	0.00	0.17	15.00	3.26	-0.05	[-0.15, 0.05]
Mahon, 2007 CARB (29)	-0.05	0.08	14.00	-0.31	0.19	14.00	3.02	0.26	[0.14, 0.38]
Mahon, 2007 CON (29)	-0.05	0.08	14.00	0.08	0.15	11.00	3.26	-0.13	[-0.23, -0.03]
Flynn, 1981 F1 (30)	-0.18	0.30	31.00	0.00	0.32	31.00	2.54	-0.18	[-0.34, -0.02]
Flynn, 1981 F2 (30)	0.05	0.41	24.00	-0.23	0.36	24.00	1.91	0.28	[0.06, 0.50]
Flynn, 1981 M1 (30)	-0.16	0.15	38.00	0.00	0.19	38.00	3.49	-0.16	[-0.24, -0.08]
Flynn, 1981 M2 (30)	-0.05	0.20	36.00	-0.08	0.17	36.00	3.49	0.03	[-0.05, 0.11]
Flynn, 1982 F1 BEEF (31)	-0.21	0.21	12.00	0.00	0.19	12.00	2.54	-0.21	[-0.37, -0.05]
Flynn, 1982 F1 PORK (31)	0.18	0.17	12.00	0.00	0.19	12.00	2.77	0.18	[0.04, 0.32]
Flynn, 1982 F2 BEEF (31)	0.13	0.40	17.00	-0.28	0.37	17.00	1.59	0.41	[0.16, 0.67]
Flynn, 1982 F2 PORK (31)	0.10	0.40	17.00	-0.28	0.37	17.00	1.59	0.39	[0.14, 0.65]
Flynn, 1982 M1 BEEF (31)	-0.16	0.16	21.00	-0.08	0.22	21.00	3.02	-0.08	[-0.20, 0.04]
Flynn, 1982 M1 PORK (31)	0.10	0.10	21.00	-0.08	0.22	21.00	3.26	0.18	[0.08, 0.27]
Flynn, 1982 M2 BEEF (31)	-0.08	0.20	26.00	-0.10	0.15	26.00	3.26	0.03	[-0.07, 0.13]
Flynn, 1982 M2 PORK (31)	0.08	0.19	26.00	-0.10	0.15	26.00	3.26	0.18	[0.08, 0.28]
de Mello, 2006 CHICK (32)	-0.03	0.34	17.00	-0.03	0.32	17.00	1.91	0.00	[-0.22, 0.22]
de Mello, 2006 LVLP (32)	-0.03	0.34	17.00	-0.03	0.30	17.00	1.91	0.00	[-0.22, 0.22]
Ashton, 2000 (33)	0.07	0.53	42.00	-0.01	0.48	42.00	1.91	0.08	[-0.14, 0.30]
Davidson, 1999 (34)	0.03	0.44	89.00	0.02	0.47	102.00	2.77	0.01	[-0.13, 0.15]
Wolmarans, 1999 (35)	0.00	0.13	39.00	-0.03	0.14	39.00	3.70	0.03	[-0.03, 0.09]
O'Brien, 1980 HC G1 (36)	0.05	0.07	15.00	0.08	0.08	15.00	3.70	-0.03	[-0.09, 0.03]
O'Brien, 1980 LC G1 (36)	0.08	0.07	15.00	-0.10	0.08	15.00	3.70	0.18	[0.12, 0.24]
O'Brien, 1980 HC G2 (36)	0.03	0.09	14.00	0.08	0.12	14.00	3.49	-0.05	[-0.13, 0.03]
O'Brien, 1980 LC G2 (36)	-0.05	0.10	14.00	0.00	0.12	14.00	3.49	-0.05	[-0.13, 0.03]
Hodgson, 2006 (38)	-0.01	0.67	29.00	-0.02	0.65	31.00	1.11	0.01	[-0.32, 0.34]
Gascon, 1996 (39)	-0.09	0.35	14.00	-0.06	0.46	14.00	1.21	-0.03	[-0.34, 0.28]
Wolmarans, 1991 (40)	-0.01	0.54	28.00	0.09	0.53	28.00	1.45	-0.10	[-0.37, 0.17]
Haub, 2005 (41)	0.08	0.10	11.00	-0.10	0.10	10.00	3.49	0.18	[0.10, 0.26]
Wiebe, 1984 (44)	-0.13	0.11	8.00	-0.28	0.09	8.00	3.26	0.16	[0.06, 0.26]
Beauchesne-Rondeau, 2003 F (42)	-0.01	0.23	18.00	0.02	0.30	18.00	2.31	-0.03	[-0.21, 0.15]
Beauchesne-Rondeau, 2003 P (42)	-0.01	0.23	18.00	0.05	0.26	18.00	2.54	-0.06	[-0.22, 0.10]
Sinclair, 1987 SF (43)	-0.29	0.33	8.00	-0.33	0.52	10.00	0.87	0.04	[-0.35, 0.43]
Sinclair, 1987 TF (43)	-0.29	0.33	8.00	-0.32	0.73	8.00	0.50	0.03	[-0.52, 0.58]
Sinclair, 1987 VEG (43)	-0.29	0.33	8.00	-0.46	0.51	7.00	0.69	0.17	[-0.28, 0.62]
Overall							**100.00**	**0.03**	**[-0.01, 0.07]**

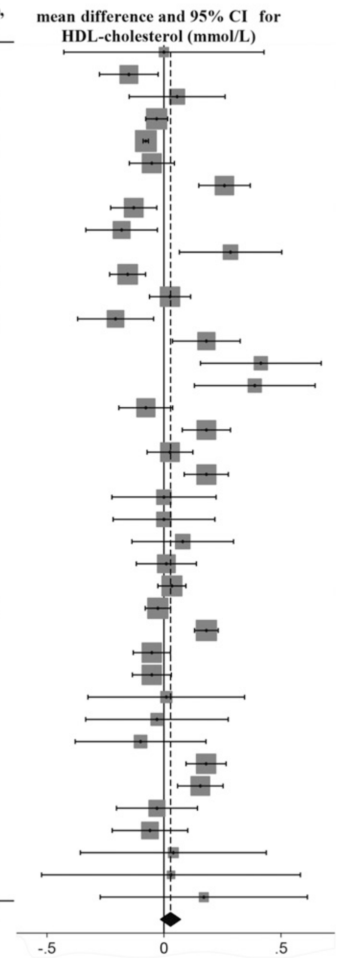

FIGURE 4 Random-effects model meta-analysis for changes in blood HDL-cholesterol concentrations from randomized controlled trials comparing ≥0.5 or <0.5 servings of total red meat/d. Heterogeneity: $\tau^2 = 0.011$, $\chi^2 = 6.62$, df = 38 ($P = 0.001$), $I^2 = 85\%$. Data are shown in descending order from smallest to largest amounts of red meat consumed by the intervention group or phase. CARB, carbohydrate control diet; CHICK, chicken control diet; CON, habitual control diet; F, lean fish control diet; F1, first female group; F1 BEEF, first female group consuming beef diet; F1 PORK, first female group consuming pork diet; F2, second female group; F2 BEEF, second female group consuming beef diet; F2 PORK, second female group consuming pork diet; HC G1, first group consuming high-cholesterol diet; HC G2, second group consuming high-cholesterol diet; LC G1, first group consuming low-cholesterol diet; LC G2, second group consuming low-cholesterol diet; LVLP, lactovegetarian low-protein control diet; M1, first male group; M1 BEEF, first male group consuming beef diet; M1 PORK, first male group consuming pork diet; M2, second male group; M2 BEEF, second male group consuming beef diet; M2 PORK, second male group consuming pork diet; P, poultry control diet; SF, southern fish control diet; TF, tropical fish control diet; VEG, vegetarian control diet.

of the selected studies were unclear about the diet other than the predominant protein source (32, 33, 44, 45, 47). Only minimally processed meats were consumed in 15 studies (25, 26, 28, 29, 30, 31, 33–35, 37–39, 41, 42, 44), highly processed meats were consumed in 1 study (45), and the extent of meat processing was unclear in the remaining 8 studies (24, 27, 32, 36, 40, 43, 46, 47). Intervention lengths varied from 2 to 32 wk.

Quality and bias of selected studies

Due to clear reporting of randomization methods, we deemed 5 studies at low risk of selection bias (24, 25, 29, 38, 46). Researchers disclosed allocation concealment methods in 2 studies (24, 25), but the rest were unclear about allocation methods. Three studies were at low risk of performance bias [2 investigator-blinded studies (34, 38) and 1 double-blind study (45)] but the rest did not report blinding. Detection bias was unclear in all of the studies except for 3 that were blinded for outcome assessment (25, 34, 38) (see **Supplemental Table 1**). In 16 articles, the researchers provided food to the subjects (mainly protein-rich foods) (24, 26–29, 31, 33, 37–45), but the rest did not provide food or did not specify if they provided food to the subjects. Researchers assessed dietary compliance in numerous ways, which are shown in Table 3, including dietary counseling, interviews, or questionnaires (24–27, 33–35, 37, 39, 41, 43, 46); food records, logs, or menus (26, 28–32, 34–36, 38, 40, 43, 46); and/or urinary markers such as urinary 3-methyl histidine (45), urinary electrolyte excretion (26), and 24-h urinary urea nitrogen output (28, 32). Most studies showed the use of >1 of these methods of dietary compliance.

Results of statistical analyses

There was a decrease from pre- to postintervention values of TC, LDL cholesterol, HDL cholesterol, TC:HDL, triglycerides,

Study	≥0.5 servings of red meat/day mean (mmol/L)	SD	n	<0.5 servings of red meat/day mean (mmol/L)	SD	n	weight (%)	mean difference (mmol/L), random effects [95% CI]	
Aadland, 2015 (25)	0.24	0.39	19	-0.1	0.4	20	10.48	0.34	[0.06, 0.60]
Sayer, 2015 (28)	-0.11	0.48	19	-0.06	0.37	19	10.14	-0.50	[-0.32, 0.22]
Mahon, 2007 CHICK (29)	-0.50	0.10	14	-0.30	0.30	15	12.03	-0.20	[-0.36, -0.04]
Mahon, 2007 CARB (29)	-0.50	0.10	14	0.10	0.30	14	12.03	-0.60	[-0.76, -0.44]
Mahon, 2007 CON (29)	-0.50	0.10	14	-0.30	0.20	11	12.29	-0.20	[-0.34, -0.06]
Davidson, 1999 (34)	-0.20	0.25	89	-0.20	0.26	102	12.90	0.00	[-0.08, 0.08]
Haub, 2005 (41)	-0.07	0.40	11	0.33	0.60	10	7.55	-0.40	[-0.83, 0.03]
Beauchesne-Rondeau, 2003 F (42)	-0.40	0.29	18	-0.49	0.31	18	11.45	0.09	[-0.11, 0.29
Beauchesne-Rondeau, 2003 P (42)	-0.40	0.29	18	-0.71	0.37	18	11.13	0.31	[0.09, 0.53]
Overall							**100.00**	**-0.08**	**[-0.26, 0.11]**

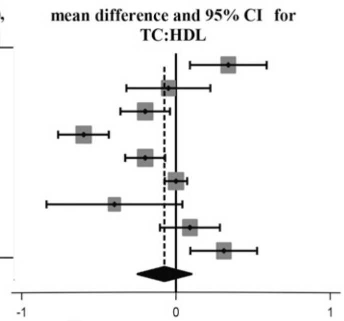

FIGURE 5 Random-effects model meta-analysis for changes in blood TC:HDL from randomized controlled trials comparing ≥0.5 or <0.5 servings of total red meat/d. Heterogeneity: $\tau^2 = 0.064$, $\chi^2 = 9.93$, df = 8 ($P = 0.001$), $I^2 = 90\%$. Data are shown in descending order from smallest to largest amounts of red meat consumed by the intervention group or phase. CARB, carbohydrate control diet; CHICK, chicken control diet; CON, habitual control diet; F, lean fish control diet; P, poultry control diet; TC:HDL, ratio of total cholesterol to HDL cholesterol.

and DBP but not SBP in both groups (repeated-measures ANOVA). The results showed no differences in postintervention values between the groups who consumed ≥0.5 or <0.5 servings of total red meat/d for any of the dependent variables (2-factor nested ANOVA mixed-effects model; $P > 0.05$ for all variables; see **Table 4**). Our analysis of the change values suggested no difference in responses over time between the groups who consumed ≥0.5 or <0.5 servings of total red meat/d in TC, LDL cholesterol, HDL cholesterol, TC:HDL, triglycerides, SBP, or DBP (fixed- or random-effects model; see Figures 2–8). There was no indication that consumption of progressively higher red meat amounts influenced these CVD risk factors (see Figures

Study	≥0.5 servings of red meat/day mean (mmol/L)	SD	n	<0.5 servings of red meat/day mean (mmol/L)	SD	n	weight (%)	mean difference (mmol/L), random effects [95% CI]	
Grieger, 2014 (24)	-0.10	0.48	37	-0.10	0.51	43	3.64	0.00	[-0.22, 0.22]
Aadland, 2015 (25)	0.01	0.45	46	0.09	0.55	49	3.92	-0.08	[-0.28, 0.12]
Nowson, 2009 (26)	0.10	0.20	19	-0.17	0.27	20	4.84	0.29	[0.15, 0.43]
Liao, 2007 (27)	-0.25	0.13	15	-0.11	0.13	15	5.43	-0.14	[-0.24, -0.04]
Sayer, 2015 (28)	-0.11	0.19	19	-0.11	0.13	19	5.43	0.01	[-0.09, 0.11]
Mahon, 2007 CHICK (29)	-0.28	0.26	14	-0.26	0.32	15	3.64	-0.02	[-0.24, 0.20]
Mahon, 2007 CARB (29)	-0.11	0.61	14	-0.26	0.32	14	2.14	0.15	[-0.20, 0.50]
Mahon, 2007 CON (29)	-0.02	0.43	14	-0.26	0.32	11	2.68	0.24	[-0.05, 0.53]
Flynn, 1981 F1 (30)	-0.27	1.44	31	0.26	1.33	31	0.76	-0.53	[-1.22, 0.16]
Flynn, 1981 F2 (30)	-0.17	0.44	24	0.29	1.09	24	1.42	-0.46	[-0.93, 0.01]
Flynn, 1981 M1 (30)	0.14	0.18	38	-0.14	0.17	38	5.69	0.27	[0.19, 0.34]
Flynn, 1981 M2 (30)	-0.16	0.67	36	-0.02	0.67	36	2.49	-0.14	[-0.45, 0.17]
Flynn, 1982 F1 BEEF (31)	-0.09	0.45	12	0.00	0.51	12	1.86	-0.09	[-0.48, 0.30]
Flynn, 1982 F1 PORK (31)	0.05	0.15	12	0.00	0.51	12	2.68	0.05	[-0.24, 0.34]
Flynn, 1982 F2 BEEF (31)	-0.16	0.51	17	0.44	1.36	17	0.76	-0.60	[-1.29, 0.09]
Flynn, 1982 F2 PORK (31)	0.00	0.15	17	0.44	1.36	17	0.84	-0.44	[-1.09, 0.21]
Flynn, 1982 M1 BEEF (31)	0.09	0.19	21	-0.15	0.19	21	5.14	0.24	[0.12, 0.36]
Flynn, 1982 M1 PORK (31)	-0.01	0.13	21	-0.15	0.19	21	5.43	0.14	[0.04, 0.24]
Flynn, 1982 M2 BEEF (31)	-0.29	0.90	26	0.02	0.14	26	2.14	-0.32	[-0.67, 0.03]
Flynn, 1982 M2 PORK (31)	0.08	0.13	26	0.02	0.14	26	5.69	0.06	[-0.02, 0.14]
Ashton, 2000 (33)	-0.19	0.96	42	-0.34	0.96	42	1.73	0.15	[-0.26, 0.56]
Davidson, 1999 (34)	-0.03	0.59	89	-0.03	0.52	102	4.53	0.00	[-0.16, 0.16]
Wolmarans, 1999 (35)	0.03	0.39	39	-0.08	0.32	39	4.53	0.11	[-0.05, 0.27]
Foerster, 2014 (37)	0.10	0.60	20	0.20	0.72	20	1.73	-0.10	[-0.51, 0.31]
Hodgson, 2006 (38)	-0.05	0.95	29	0.01	0.64	31	1.73	-0.06	[-0.47, 0.35]
Gascon, 1996 (39)	-0.01	0.21	14	-0.09	0.17	14	4.84	0.08	[-0.06, 0.22]
Haub, 2005 (41)	-0.16	0.50	11	0.27	0.60	10	1.42	-0.43	[-0.90, 0.04]
Beauchesne-Rondeau, 2003 F (42)	-0.30	0.33	18	-0.30	0.33	18	3.64	0.00	[-0.22, 0.22]
Beauchesne-Rondeau, 2003 P (42)	-0.30	0.33	18	-0.40	0.33	18	3.64	0.10	[-0.12, 0.32]
Sinclair, 1987 SF (43)	0.31	0.59	10	0.04	0.10	10	1.99	0.27	[-0.10, 0.64]
Sinclair, 1987 TF (43)	0.31	0.59	10	0.07	0.25	11	1.86	0.24	[-0.15, 0.63]
Sinclair, 1987 VEG (43)	0.31	0.59	10	0.19	0.25	7	1.73	0.12	[-0.29, 0.53]
Overall							**100.00**	**0.04**	**[-0.02, 0.10]**

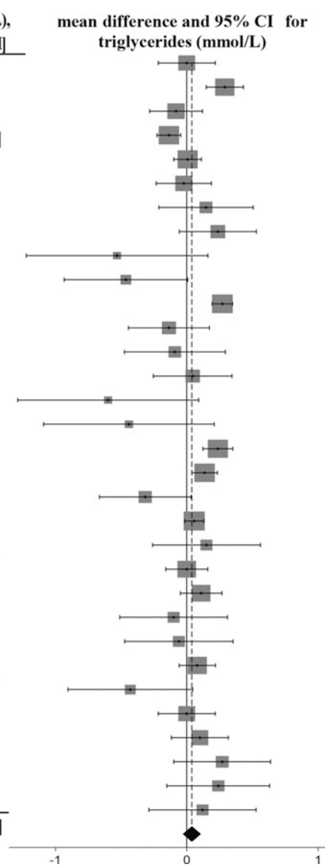

FIGURE 6 Random-effects model meta-analysis for changes in blood triglyceride concentrations from randomized controlled trials comparing ≥0.5 or <0.5 servings of total red meat/d. Heterogeneity: $\tau^2 = 0.017$, $\chi^2 = 3.16$, df = 31 ($P = 0.001$), $I^2 = 68\%$. Data are shown in descending order from smallest to largest amounts of red meat consumed by the intervention group or phase. CARB, carbohydrate control diet; CHICK, chicken control diet; CON, habitual control diet; F, lean fish control diet; F1, first female group; F1 BEEF, first female group consuming beef diet; F1 PORK, first female group consuming pork diet; F2, second female group; F2 BEEF, second female group consuming beef diet; F2 PORK, second female group consuming pork diet; M1, first male group; M1 BEEF, first male group consuming beef diet; M1 PORK, first male group consuming pork diet; M2, second male group; M2 BEEF, second male group consuming beef diet; M2 PORK, second male group consuming pork diet; P, poultry control diet; SF, southern fish control diet; TF, tropical fish control diet; VEG, vegetarian control diet.

	≥0.5 servings of red meat/day			<0.5 servings of red meat/day					
Study	mean (mm Hg)	SD	n	mean (mm Hg)	SD	n	weight (%)	mean difference (mmol/L), fixed effects	[95% CI]
Grieger, 2014 (24)	0.0	13.3	37.0	-2.0	14.3	43.0	8.9	2.0	[-4.1, 8.0]
Nowson, 2009 (26)	-5.6	8.8	46.0	-2.7	7.0	49.0	31.6	-2.9	[-6.1, 0.32]
Liao, 2007 (27)	1.6	11.7	15.0	2.9	6.1	15.0	7.3	-1.3	[-8.0, 5.4]
Sayer, 2015 (28)	-8.0	8.9	19.0	-6.2	7.4	19.0	12.1	-1.8	[-7.0, 3.0]
Wolmarans, 1999 (35)	0.4	6.8	39.0	-1.2	8.6	39.0	27.5	1.7	[-1.8, 5.1]
Hodgson, 2006 (38)	-1.9	9.8	29.0	1.6	10.3	31.0	12.6	-3.5	[-8.6, 1.6]
Overall							**100.0**	**-1.0**	**[-2.4, 0.8]**

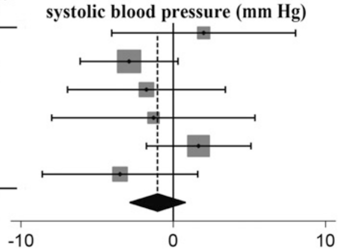

FIGURE 7 Fixed-effects model meta-analysis for changes in systolic blood pressure from randomized controlled trials comparing ≥0.5 or <0.5 servings of total red meat/d. Heterogeneity: $\tau^2 = 0.662$, $\chi^2 = 4.42$, df = 5 ($P = 0.346$), $I^2 = 11\%$. Data are shown in descending order from smallest to largest amounts of red meat consumed by the intervention group or phase.

2–8; the amount of red meat consumed progressively increases from top to bottom of each figure). Results from imputing SDs of crossover designs with 0.99 as the correlational factor did not differ from the original results with the use of 0 as the correlational factor.

More than 99% of the traditional sensitivity analyses showed no significant change in results. No cluster sensitivity analyses significantly changed results when we removed studies that included weight-loss diets, heart-healthy diets, significant weight loss, diseased populations, consumption of processed red meats or no specification of the degree of meat processing, and studies that used different amounts of protein intake in the control and intervention group/phase. Post hoc analyses of red meat consumption amounts showed no differences in change values between the control and intervention group, whether consuming 1.0–1.9, 2.0–2.9, or ≥3.0 servings of red meat/d, with the exception that HDL cholesterol was higher when ≥3.0 servings of red meat/d was consumed (weighted mean difference: 0.10; 95% CI: 0.05, 0.16). (See **Supplemental Table 2** for results of all sensitivity analyses.)

DISCUSSION

To the best of our knowledge, this is the first systematically searched meta-analysis to assess the consumption of ≥0.5 servings of total red meat/d on blood lipids, lipoproteins, and blood pressures by using data from RCTs. This serving size is consistent with the dietary patterns recommended by the 2010–2015 DGA and the Scientific Report of the 2015 Dietary Guidelines Advisory Committee. Our results indicate that the consumption of ≥0.5 servings of total red meat/d does not influence these clinically relevant and commonly measured modifiable CVD risk factors. These results do not support our hypothesis, which was based on a 2012 observational cohort study that estimated that the consumption of ≥0.5 servings of total red meat/d would increase CVD mortality (5). Our results align with a previous meta-analysis of 8 studies, which concluded that changes in blood lipids and lipoproteins did not differ when lean, unprocessed beef was consumed compared with poultry or fish (9). Our meta-analysis of 24 studies is more generalizable because it was inclusive of a variety of red meat types and also assessed blood pressure. It is important to emphasize that our conclusions do not support a cardioprotective effect of higher red meat consumption, such as is shown with fatty fish (48), but that the consumption of ≥0.5 servings of total red meat/d does not affect changes in blood lipids, lipoproteins, and blood pressures.

Although the median daily total red meat intake in the intervention group or phase was 2 servings, almost double what the average American consumes [∼1.2 servings/d (49)], the range was large (1.0–7.1 servings/d). There is no visual threshold of total red meat consumption that indicates an apparent negative effect on blood lipids, lipoproteins, and blood pressures, as shown by the nondescript dispersal of the data in Figures 2–8. Although we used the cutoff of 0.5 servings of total red meat/d (5), we performed post hoc analyses to test if the studies with lower red meat consumption were washing out the effects of higher red meat consumption. The highest category of red meat consumption (>3 servings of red meat/d) showed no negative effects on blood lipid and lipoprotein concentrations and blood pressures and resulted in higher HDL concentrations. Because substituting protein for carbohydrate and adopting a "heart healthy" diet are shown to improve blood lipid and lipoprotein

	≥0.5 servings of red meat/day			<0.5 servings of red meat/day					
Study	mean (mm Hg)	SD	n	mean (mm Hg)	SD	n	weight (%)	mean difference (mmol/L), fixed effects	[95% CI]
Grieger, 2014 (24)	37.0	-1.0	37.0	-1.0	11.0	43.0	15.5	0.0	[-3.8, 3.8]
Nowson, 2009 (26)	46.0	-4.1	46.0	-2.9	4.9	49.0	25.3	-1.2	[-3.4, 1.0]
Liao, 2007 (27)	15.0	-5.0	15.0	-0.2	8.5	15.0	6.7	-4.8	[-11.6, 2.0]
Sayer, 2015 (28)	19.0	-4.9	19.0	-6.0	5.0	19.0	18.0	1.1	[-2.2, 4.4]
Wolmarans, 1999 (35)	39.0	2.2	39.0	-1.2	6.9	39.0	20.9	3.4	[0.5, 6.2]
Hodgson, 2006 (38)	29.0	-0.9	29.0	0.8	7.6	31.0	13.6	-1.7	[-5.9, 2.5]
Overall							**100.0**	**0.1**	**[-1.2, 1.5]**

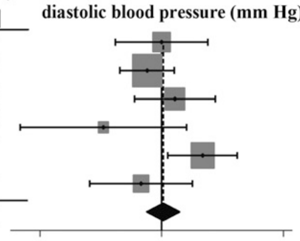

FIGURE 8 Fixed-effects model meta-analysis for changes in diastolic blood pressure from randomized controlled trials comparing ≥0.5 or <0.5 servings of total red meat/d. Heterogeneity: $\tau^2 = 0.662$, $\chi^2 = 4.42$, df = 5 ($P = 0.097$), $I^2 = 46\%$. Data are shown in descending order from smallest to largest amounts of red meat consumed by the intervention group or phase.

TABLE 3
Study design of randomized controlled trials assessing the effects of consuming ≥0.5 or <0.5 servings of total red meat/d on blood lipids, lipoproteins, and blood pressures[1]

First author, year (ref)	Total red meat servings in intervention (g/d); type of red meat; degree of meat processing	Total red meat servings in control (g/d); comparison protein source	Dietary pattern; diet administration method; dietary compliance assessment	Intervention length in weeks; study design	Population size and description; mean age in years; mean BMI in kg/m^2
Grieger, 2014 (24)	1.0 (68); beef, lamb, ham, pork; N/A	0; fatty fish	Habitual diet; protein source and some other foods provided; verbal motivation and interviews every 2 wk	8; 2-arm parallel	80 generally healthy men and women; 69.6; 26.4
Prescott, 1988 (45)	1.0 (72); meat supplement containing sausage, beef, lamb, pork; processed	0; nonmeat supplement	N/A; 2 meals/d and protein source provided; urinary 3-methyl histidine	12; 2-arm parallel	64 generally healthy men and women; N/A; N/A
Aadland, 2015 (25)	1.1 (77); pork and lean beef; minimally processed	0; lean seafood (cod, pollock, saithe, and scallops)	Norwegian nutritional recommendations; some food provided; daily oral questionnaire and regular weigh-ins	20; 2-phase crossover	20 generally healthy men and women; 50.6; 25.6
Nowson, 2009 (26)	1.2 (86); raw lean beef, lamb, veal, or combination; minimally processed	≤0.4 (28.6); combination control	DASH; protein source and some other food provided with dietary counseling; 24-h urinary electrolyte excretion and food records	14; 2-arm parallel	95 normal-hypertensive postmenopausal women; 59.2; 29.6
Liao, 2007 (27)	1.5 (105); N/A; N/A	0; soy	Weight-loss diet (1200 kcal); partial food provided for soy group but none for intervention group with dietary counseling and education; N/A	8; 2-arm parallel	30 generally healthy men and women; 33.4; 29.8
Navas-Carretero, 2009 (46)	1.6 (113); red meat; N/A	0.3 (22.3); oily fish	Habitual diet; daily 24-h dietary recalls and monthly 72-h detailed intake report; daily menu forms and weekly interviews	8; 2-phase crossover	25 iron-deficient women; 18–30; 22.1
Sayer, 2015 (28)	1.7 (121); pork tenderloin, uncured ham, beef tenderloin; minimally processed	0.2 (10.7); chicken or fish	DASH; protein source provided; daily food logs and 24-h urinary urea nitrogen	6; 2-phase crossover	19 prehypertensive or hypertensive men and women; 61; 31.2
Mahon, 2007 (29)	1.7 (121); cooked beef tenderloin; minimally processed	0; chicken, carbohydrate, or habitual control	Weight-loss diet (1250 kcal); protein source provided with dietary counseling, written instructions, menus, and shopping lists; biweekly dietary counseling sessions	9; 4-arm parallel	43 generally healthy postmenopausal women; 58; 29.6
Flynn, 1981 (30)	2.0 (140); raw beef; minimally processed	0; fish or poultry	Habitual diet; protein source provided; daily food logs and 4-d food records	12; 2-phase crossover	129 generally healthy men and women; N/A; N/A
Flynn, 1982 (31)	2.0 (140); raw beef or pork; minimally processed	0; fish or poultry	Habitual diet; protein source provided; 4-d food records	12; 2-phase crossover	76 generally healthy men and women; N/A; N/A
de Mello, 2006 (32)	2.0 (141); beef; N/A	0; chicken or lactoovo low-protein	N/A; no food provided; 2-d weighed food records and 24-h urinary urea nitrogen output	4; 2-phase crossover	17 men with type 2 diabetes and macroalbuminuria; 59; 26.2
Ashton, 2000 (33)	2.1 (150); lean, raw red meat; minimally processed	0; tofu	N/A; tofu provided, dietary counseling for meat selection; N/A	4; 2-phase crossover	42 generally healthy men; 45.8; 26.2
Davidson, 1999 (34)	2.2 (159); lean beef, veal, pork, or lamb; minimally processed	21.9; lean white meat (poultry and fish)	National Cholesterol Education Program Step I diet; no food provided, dietary counseling; food logs	32; 2-arm parallel	165 hypercholesterolemic men and women; 55.8; 27.3

(Continued)

TABLE 3 (*Continued*)

First author, year (ref)	Total red meat servings in intervention (g/d); type of red meat; degree of meat processing	Total red meat servings in control (g/d); comparison protein source	Dietary pattern; diet administration method; dietary compliance assessment	Intervention length in weeks; study design	Population size and description; mean age in years; mean BMI in kg/m^2
Wolmarans, 1999 (35)	2.4 (165); lean beef and lean mutton; minimally processed	0; chicken or fish	Prudent; pre and post 7-d weighed food records; postquestionnaires to assess compliance	6; 2-phase crossover	39 hypercholesterolemic men and women; 33.4; 24.4
O'Brien, 1980 (36)	2.4 (170); beef, pork, or lamb; N/A	0; fish or poultry with varying dietary cholesterol prescriptions	Varying cholesterol prescriptions but otherwise habitual diet; N/A; diet records	6; 4-phase crossover	29 generally healthy men; 43; N/A
Horrocks, 1999 (47)	2.9 (200); pork; N/A	0; chicken	N/A; N/A; N/A	4; 2-phase crossover	20 generally healthy women; N/A; N/A
Foerster, 2014 (37)	2.9 (200); fresh pork cutlet and beef steak; minimally processed	<0.4 (30); whole-grain products	Habitual diet; protein sources provided; regular check-ins with research staff	10; 2-phase crossover	20 generally healthy men and women; 40.1; 24.4
Hodgson, 2006 (38)	3.1 (215); lean, raw red meat; minimally processed	0; plant protein	Habitual diet; protein source provided with dietary counseling; pre and post 3-d weighed food diary	8; 2-arm parallel	60 hypertensive men and women; 58.7; 27.7
Gascon, 1996 (39)	3.3 (230); lean beef, pork, veal; minimally processed	0; lean white fish	American Heart Association prudent diet; partial meals provided; verbal interview every 2 d	∼4 (1 menstrual cycle); 2-phase crossover	14 generally healthy women; 22.4; 22
Wolmarans, 1991 (40)	3.5 (246); beef and mutton; N/A	0; fatty fish	Habitual diet; N/A ; pre and post 7-d dietary records	6; 2-phase crossover	28 generally healthy men and women; 33.8; N/A
Haub, 2005 (41)	3.5 (248); cube steak, ground beef, beef tips; minimally processed	0; plant protein	Habitual diet; protein source provided; routine interviews to assess compliance	12; 2-arm parallel	21 generally healthy men; 65.0; 28.2
Wiebe, 1984 (44)	3.6 (250); frozen beef patties; minimally processed	0; plant protein	Controlled but not specified; food provided; N/A	3; 2-phase crossover	8 generally healthy men; 20.9, 21.7
Beauchesne-Rondeau, 2003 (42)	5.4 (380); lean ground beef, exterior round, sirloin top; minimally processed	0; lean fish or poultry	American Heart Association diet; partial food provided; N/A	3; 3-phase crossover	17 hypercholesterolemic men; 50.1; 26.5
Sinclair, 1987 (43)	7.1 (500); kangaroo; N/A	0; southern fatty fish, tropical fatty fish, or plant protein	Low-fat (<7% of total energy); protein source provided with dietary counseling; daily food records	2; 4-phase crossover	13 generally healthy men and women; 31.3; 21.2

[1] DASH, Dietary Approaches to Stop Hypertension; lactoovo, lacto-ovovegetarian; N/A, not applicable; post, postintervention; pre, preintervention.

TABLE 4
Analysis of postintervention values of consuming ≥0.5 or <0.5 servings of total red meat/d in randomized controlled trials[1]

Dependent variable[2]	Number of studies included	≥0.5 servings of total red meat/d	<0.5 servings of total red meat/d	*P*
Total cholesterol, mmol/L	22	4.93 ± 0.11	4.88 ± 0.10	0.57
LDL cholesterol, mmol/L	21	3.18 ± 0.08	3.13 ± 0.07	0.52
HDL cholesterol, mmol/L	21	1.30 ± 0.04	1.27 ± 0.03	0.41
Triglycerides, mmol/L	20	1.23 ± 0.05	1.21 ± 0.05	0.83
TC:HDL	19	3.93± 0.07	3.98 ± 0.07	0.46
Systolic blood pressure, mm Hg	7	121± 10	122 ± 11	0.51
Diastolic blood pressure, mm Hg	7	64 ± 4	63 ± 5	0.55

[1] Unless otherwise indicated, values are least-squares means ± SEs adjusted for baseline values, age, sex, BMI, length of intervention, and whether energy restriction was or was not included in the protocol. A 2-factor nested ANOVA showed no differences between post values of consuming ≥0.5 or <0.5 servings of total red meat/d. Total cholesterol, LDL-cholesterol, and HDL-cholesterol conversion: mmol/L × 38.67 = mg/dL; triglyceride conversion: mmol/L × 88.57 = mg/dL. TC:HDL, ratio of total cholesterol to HDL cholesterol.

[2] A repeated-measures ANOVA showed that all dependent variables changed over time except for systolic blood pressure ($P < 0.05$).

concentrations and blood pressure (50–53), we performed cluster sensitivity analyses to assess studies without these characteristics. This did not influence our conclusion that consuming ≥0.5 servings of red meat/d does not affect changes in blood lipid and lipoprotein concentrations and blood pressures. Therefore, this meta-analysis compared protein sources rather than macronutrient compositions within the context of a variety of diets.

The Mediterranean-style and the DASH (Dietary Approaches to Stop Hypertension) dietary patterns are "heart healthy" diets that include <0.5 servings of red meat/d. The Mediterranean-style dietary pattern is predominantly modeled on observational cohort studies (54–57) and 1 large-scale RCT (58) that indicate a lower incidence of CVD-related events, mortality, and lower CVD risk with the consumption of this dietary pattern. However, these studies reported red meat consumption of >0.5 servings of red meat/d [range: ∼2–3.5 servings/1000 kcal; see Figure D1.59 in the Scientific Report of the 2015 Dietary Guidelines Advisory Committee (59) for a graphic summary of these studies, with the exception of our reference 57]. Therefore, it is unclear what studies are supportive of this recommendation for red meat in the context of a Mediterranean-style diet. The DASH diet, by design, limits red meat consumption to <0.5 servings/d (60). However, current RCTs showed that the DASH diet has equivalent effectiveness to reduce blood lipids, lipoproteins, and blood pressures when it contains >0.5 servings of red meat/d [1.6 or 2.2 servings of beef (61, 62) or 1.7 servings of pork (28) daily]. Collectively, these studies suggest that the consumption of >0.5 servings of red meat/d in the context of these recommended dietary patterns does not hinder improvements in CVD risk factors.

The conflicting literature creates ambiguous conclusions in dietary guidance pertaining to red meat consumption amounts. The Scientific Report of the 2015 Dietary Guidelines Advisory Committee concluded that "lean meats" can be incorporated into a healthy diet in relatively small amounts, but there is no specificity to the type or amount of lean meat. Communication to the general public from the 2015–2020 DGA combines red meat with the "meat, eggs, and poultry" recommendation rather than its own food group (12), as done in previous DGAs (63). Dietary recommendations based on the 2010–2015 DGA, with support from the 2015 Advisory Report, suggest that red meat consumption should be limited to ∼0.5–0.7 servings/d or ∼3.5–5 servings/wk (59, 63); this varies because the serving size range is 2–3 ounces. The Dietary Guidelines Advisory Committee search process has strict criteria that limit the inclusion of data from available RCTs (64), so this conclusion is based predominantly on epidemiologic associations (63). This restricts the conclusions to be mainly based on associative conclusions of morbidity and mortality rather than cause and effect of disease risk, both of which need to be considered in determining dietary guidance and public policy.

A strength of this systematically searched meta-analysis is the use of RCT designs, which allows our conclusions to be based on the principle of causation. These RCTs assessed the effects of consumption of total red meat on CVD risk factors for relatively short periods of time (2–32 wk). In contrast, epidemiologic studies have assessed the association between total red meat consumption and CVD-related morbidity and mortality that typically require years or decades of follow-up and are not suitable to determine causality. Thus, results from RCTs support that the consumption of red meat does not influence CVD risk factors, whereas epidemiologic studies support that the consumption of red meat is associated with higher incidences of CVD-related morbidity and mortality. Future efforts and research by academic, industry, and government leaders are needed to improve the scientific foundation and communication to the public about the effects of red meat on diet quality and human health by including evidence from both types of study designs.

Another strength of this meta-analysis is the high external validity because we did not restrict our search to certain dietary patterns, populations, or types of red meat (65). Although this created heterogeneity among data within each blood lipid and lipoprotein variable (indicated by the I^2 scores; see Figures 2–6), the extensive sensitivity analyses did not affect overall findings when potential modifiers were excluded. Data from other CVD risk factors, such as endothelial cell function and inflammation, were not collected for this meta-analysis. These factors can progress to CVD when traditional risk factors are unchanged (66) and therefore may be a limitation of this analysis. We did not exclude studies based on the criteria used by the Dietary Guidelines Advisory Committee (64) and recognize that a meta-analysis is only as strong as the empirical evidence included. We raise concern about the unclear bias reporting, which was common in the studies included in this meta-analysis, and urge researchers to comprehensively report study design characteristics. We are also aware that there are other potential human and environmental health risks associated with higher red meat intake, which are beyond the scope of this review, and include but are not limited to cancer (67) and environmental sustainability (68, 69).

In conclusion, the results from this systematically searched meta-analysis of RCTs support that the consumption of ≥0.5 compared with <0.5 servings of total red meat/d does not influence blood lipids, lipoproteins, and/or blood pressures, which are clinically relevant CVD risk factors. These results are generalizable across a variety of populations, dietary patterns, and types of red meat. These results are inconsistent with much of the observational evidence related to red meat consumption and CVD, which prompts the need for future research to reconcile the apparent disconnect between RCT and observation-based conclusions.

Vicki J Killion, an associate professor of Library Science from Purdue's Health and Life Sciences Library Division, assisted LEO and JEK with database and search term selection. Ningning Chen, a statistical consultant from Purdue's Department of Statistics, assisted LEO and JEK with the analyses. Jia Lia, a PhD student from Purdue's Department of Nutrition Science, assisted with calculations.

The authors' responsibilities were as follows—LEO, JEK, and WWC: designed the research; LEO and JEK: conducted the research; LEO: analyzed the data; and LEO and WWC: wrote the manuscript and have primary responsibility for the final content. During the time this manuscript was being developed and written, WWC received research support from American Egg Board–Egg Nutrition Center, Beef Checkoff, Coca-Cola Foundation, National Dairy Council, National Institutes of Health, Pork Checkoff, and USDA and had a consulting arrangement with Coca-Cola Company. None of these organizations provided support to conduct this meta-analysis. WWC also served on the 2015 Dietary Guidelines Advisory Committee and was a member of the Advisory Council on Nutrition and Healthy Food Choices, Foundation for Food and Agriculture Research. JEK received support from the American Egg Board–Egg Nutrition Center. LEO reported no conflicts of interest.

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