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Red and Processed Meat Consumption and Risk for All-Cause Mortality and Cardiometabolic Outcomes

A Systematic Review and Meta-analysis of Cohort Studies

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Background: Dietary guidelines generally recommend limiting intake of red and processed meat. However, the quality of evidence implicating red and processed meat in adverse health outcomes remains unclear.

Purpose: To evaluate the association between red and processed meat consumption and all-cause mortality, cardiometabolic outcomes, quality of life, and satisfaction with diet among adults.

Data Sources: EMBASE (Elsevier), Cochrane Central Register of Controlled Trials (Wiley), Web of Science (Clarivate Analytics), CINAHL (EBSCO), and ProQuest from inception until July 2018 and MEDLINE from inception until April 2019, without language restrictions, as well as bibliographies of relevant articles.

Study Selection: Cohort studies with at least 1000 participants that reported an association between unprocessed red or processed meat intake and outcomes of interest.

Data Extraction: Teams of 2 reviewers independently extracted data and assessed risk of bias. One investigator assessed certainty of evidence, and the senior investigator confirmed the assessments.

Data Synthesis: Of 61 articles reporting on 55 cohorts with more than 4 million participants, none addressed quality of life or satisfaction with diet. Low-certainty evidence was found that a reduction in unprocessed red meat intake of 3 servings per week is associated with a very small reduction in risk for cardiovascular mortality, stroke, myocardial infarction (MI), and type 2 diabetes. Likewise, low-certainty evidence was found that a reduction in processed meat intake of 3 servings per week is associated with a very small decrease in risk for all-cause mortality, cardiovascular mortality, stroke, MI, and type 2 diabetes.

Limitation: Inadequate adjustment for known confounders, residual confounding due to observational design, and recall bias associated with dietary measurement.

Conclusion: The magnitude of association between red and processed meat consumption and all-cause mortality and adverse cardiometabolic outcomes is very small, and the evidence is of low certainty.

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Growing evidence shows an increased risk for cardiometabolic disease associated with the consumption of red and processed meat. Although previous systematic reviews reported positive associations between red meat intake and all-cause mortality (1), cardiovascular mortality (2), and stroke (3) and between processed meat consumption and all-cause mortality (1, 4), cardiovascular mortality (2), stroke (3), coronary heart disease (5), and type 2 diabetes (5), results have not been consistent. One review did not find an association between unprocessed red meat and all-cause mortality (4), and another found no association with cardiovascular disease (5). Although Aune and colleagues (6) reported a relationship between red meat intake and type 2 diabetes, Micha and colleagues (5) did not detect this association in a review published 1 year later.

Methodological limitations in previous reviews included failure to address risk of bias of primary studies (for example, references 3 and 6), lack of evaluation of certainty of evidence (for example, references 2 to 6), and failure to consider the magnitude of observed effect (for example, references 2 to 6). These limitations may have affected the credibility of recommendations issued by governments and authoritative organizations regarding red and processed meats.

As part of NutriRECS (Nutritional Recommendations and accessible Evidence summaries Composed of Systematic reviews), a new initiative to establish trustworthy dietary recommendations that meet internationally accepted standards for guideline development, we developed guidelines addressing red and processed meat consumption (7). To inform these recommendations, we conducted 5 systematic reviews of the evidence (8–11). Here, we present results from a systematic review of cohort studies addressing the association between red and processed meat consumption and all-cause mortality, cardiometabolic outcomes, quality of life, and satisfaction with diet among adults.

See also:

Related articles 711, 721, 732, 742, 756
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METHODS

We registered a protocol for this review at PROSPERO (CRD42017074074) in August 2017.

Data Sources and Search Strategy

An experienced research librarian developed the search strategy, which was used across all supporting reviews except the one addressing public values and preferences (Supplement 1, available at Annals.org). We searched MEDLINE, EMBASE (Elsevier), Cochrane Central Register of Controlled Trials (Wiley), Web of Science (Clarivate Analytics), CINAHL (EBSCO), and ProQuest from inception. We also reviewed reference lists of relevant systematic reviews. The final search of all databases included references up to July 2018, except for the MEDLINE search, which included references up to April 2019.

Study Selection

We included cohort studies in any language that enrolled at least 1000 adults, compared participants consuming different amounts of unprocessed red meat or processed meat, and reported on 1 or more of our outcomes of interest. Red meat and processed meat were defined, respectively, as mammalian meat and white or red meat preserved by smoking, curing, salting, or adding chemical compounds (for example, hot dogs, charcuterie, sausage, ham, and deli meats) (12). We also included studies comparing vegetarians with nonvegetarians for sensitivity analyses. Our outcomes of interest were determined in consultation with our guideline panel–which comprised members of the public, clinicians, epidemiologists, and methodologists–and include all-cause mortality, cardiovascular mortality (or fatal coronary heart disease or fatal myocardial infarction [MI]), cardiovascular disease (or coronary heart disease), stroke, MI, type 2 diabetes, anemia, quality of life, and satisfaction with diet. For studies reporting on ischemic and hemorrhagic stroke separately, we included results only for ischemic stroke in our meta-analyses (13).

Cohorts in which more than 20% of the sample was younger than 18 years, had a noncardiometabolic disease (such as cancer), or was pregnant at baseline were excluded. We also excluded studies in which diet was assessed before adulthood, participants were asked to recall their diet before adulthood, or dietary assessments were completed by proxies, as well as studies that reported on specific components of red meat (such as iron or fat) or specific types of red meat (such as lamb). However, we did include studies reporting on beef–pork combinations because beef and pork account for most red meat intake in most Western populations (14, 15). If we encountered more than 1 eligible article on the same exposure and cohort and addressing the same outcome, we included results only from the study with the longest follow-up. If the follow-up was the same, we chose the study with the most participants.

Pairs of reviewers completed calibration exercises, after which they performed screening independently and in duplicate, with disagreements resolved by discussion or through third-party adjudication by an expert research methodologist. Screening was done in 2 stages: First, the reviewers assessed titles and abstracts; then, for those deemed potentially eligible, they evaluated the full-text articles.

Data Extraction and Quality Assessment

Using standardized, pilot-tested forms, reviewers completed calibration exercises and worked in pairs to independently extract the following information from eligible studies: cohort characteristics (such as cohort name and country), participant characteristics (including age and proportion who were female), diet characteristics (such as frequency and quantity of consumption of unprocessed red meat or processed meat), and outcomes (including absolute and relative effect measures for outcomes of interest and measures of variability). Disagreements between pairs of extractors were resolved through discussion or by third-party adjudication by an expert research methodologist.

Reviewers, working independently and in duplicate, assessed each study's risk of bias by using the CLARITY (Clinical Advances Through Research and Information Translation) risk-of-bias instrument for cohort studies, omitting an item related to co-interventions that was not relevant to our review (16). Disagreements were resolved through discussion or by third-party adjudication. Research methodologists and nutrition researchers were consulted to confirm the appropriateness of the CLARITY instrument and to advise us regarding criteria for evaluating each of its items. The instrument and detailed guidance are presented in Supplement Table 1 (available at Annals.org). Studies rated as high risk of bias on 2 or more of the 7 domains were considered to have a high overall risk of bias. This threshold, although somewhat arbitrary, represents a compromise between excessive stringency and leniency.

Data Synthesis and Analysis

We conducted separate analyses for unprocessed red meat, processed meat, and mixed unprocessed red and processed meat. If an article reported on red meat and did not specify whether it was processed or unprocessed, we assumed that it included both unprocessed and processed red meat. We included such studies in the analysis of mixed unprocessed red and processed meat because most processed meat is typically consumed as red meat (17, 18).

For our primary analyses, we conducted a random-effects dose–response meta-analysis using methods proposed by Greenland and Longnecker (19) and Orsini and colleagues (20). These methods require knowledge of the distribution of events and number of participants or person-years and mean or median quantity of intake across categories of exposure. When results from studies were analyzed across quantiles of intake but person-years or number of participants was not reported within each quantile, we estimated these values by using figures reported for the total population and dividing the total person-years or total number of participants by the number of quantiles. For studies reporting effect estimates stratified by participant characteristics (such as sex), we meta-analyzed across sub-

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groups by using the fixed-effects model. For studies that treated the exposure as a continuous predictor in a logistic regression and did not present categorical analyses, we calculated a regression coefficient based on the relative effect reported and meta-analyzed these regression coefficients with effects from other studies obtained via the estimation method described by Greenland and Longnecker (19). These studies were excluded from the nonlinear analyses. For analyses including 5 or more studies, we tested for nonlinearity by using restricted cubic splines with knots at 10%, 50%, and 90% and a Wald-type test. For analyses in which we observed statistically significant nonlinear associations, we present results from the nonlinear model.

For studies reporting the intake of red meat or processed meat as a range of values, we assigned the midpoint of upper and lower boundaries in each category as the average intake. If the highest or lowest category was open ended, we assumed that the open-ended interval was the same size as the adjacent interval. For studies reporting exposure as number of servings, we assumed that each serving of unprocessed red meat was equal to 120 g; processed meat, 50 g; and mixed unprocessed red and processed meat, 100 g. These serving sizes were selected for comparability with those used in other systematic reviews, as well as to reflect serving sizes used by the U.S. Department of Agriculture and United Kingdom Food Agency (1–3, 21–25). We report results corresponding to the effects of a reduction in unprocessed red or processed meat intake of 3 servings per week.

We used the dosresmeta package in R, version 3.5.1 (R Foundation for Statistical Computing), for our dose–response meta-analyses (26). Further details about these meta-analyses, including sample code, are presented in Supplement 2 (available at Annals.org).

As a secondary analysis, we used the Hartung–Knapp–Sidik–Jonkman approach to calculate pooled relative effects, comparing the lowest category of exposure in each study with the highest one (27, 28). We also present results using a random-effects meta-analysis with the restricted maximum likelihood estimator. In these analyses, we also included studies comparing vegetarians with nonvegetarians. For studies that treated the exposure as a continuous predictor in logistic regression models and did not present categorical analyses, we converted relative effect estimates from the logistic regression model to correspond to a difference in intake of 1 serving per day—which was the difference observed most often between lowest and highest categories of consumption across studies—and used them in our meta-analyses. We used the metafor package in R (version 3.5.1) for these secondary analyses (29).

Because all outcomes of interest were rare (<10% event rate) within included studies for all analyses, we assumed that odds ratios and hazard ratios were similar to estimates of relative risk. We quantified heterogeneity using the I^2 statistic and interpreted the magnitude of heterogeneity according to guidelines from the *Cochrane Handbook for Systematic Reviews of Interventions* (0% to 40%, low; 30% to 60%, moderate; 50% to 90%, substantial; 75% to 100%, considerable) (30). We also visually inspected forest plots for consistency, given that I^2 statistics may be artificially inflated when effect estimates from primary studies are very precise—as was the case in many of our analyses (31). For all meta-analyses with at least 10 studies, we used the Egger test to look for small study effects (32).

We conducted a priori specified meta-regressions to test for differences among studies at higher versus lower risk of bias. For analyses with a statistically significant subgroup effect based on risk of bias, we present results only for studies at lower risk of bias. We had also planned to conduct subgroup analyses on the effects of red versus white processed meat and the effects of red meat consumption in iron-deficient populations, as well as a sensitivity analysis on the robustness of results to incomplete outcome data (33). However, we could not complete these additional analyses because of insufficient information reported in the primary studies.

Certainty of Evidence

One investigator assessed certainty of evidence by using the GRADE (Grading of Recommendations Assessment, Development and Evaluation) approach for each outcome, and the senior investigator confirmed the assessments (34). According to GRADE, observational studies start at low certainty and may be downgraded for risk of bias, inconsistency, indirectness, imprecision, or publication bias and may be upgraded for large effect, if suspected biases work against the observed direction of effect, or for dose–response gradient. To calculate absolute effects presented in summary-of-findings tables, we used population risks from the Emerging Risk Factors Collaboration to calculate risk differences associated with a reduction in red meat intake of 3 servings per week (35). The Emerging Risk Factors Collaboration is a consortium of 102 international cohorts, primarily from North America and western Europe, including mostly middle-aged to older adults who are omnivores.

Role of the Funding Source

This review received no external funding or other support.

RESULTS

Study Selection

Supplement Figure 1 (available at Annals.org) presents study selection details. A total of 62 articles including 56 cohorts proved eligible. One article did not provide sufficient quantitative information for meta-analysis (36). The quantitative analysis included 61 reports of 55 cohorts (4.2 million participants). Thirty-one cohort studies (2.2 million participants) were eligible for inclusion in the dose–response meta-analyses.

Study Characteristics

We found 20 articles (30 cohorts) addressing all-cause mortality; 18 (28 cohorts), cardiovascular mortality; 9 (7 cohorts), cardiovascular disease; 6 (7 cohorts),

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Table 1. Summary of Findings for Unprocessed Red Meat Intake (Reduction of 3 Servings per Week) and Risk for Cardiometabolic Outcomes

Outcome	Studies, *n*	Participants, *n*	Follow-up, *y*	RR (95% CI)	Population Risk per 1000 Persons Over 10.8 y*	Risk Difference per 1000 Persons (95% CI)	GRADE Certainty of Evidence	Plain-Language Summary
All-cause mortality	8	893 436	9–28	0.93 (0.87–1.00)	113	−8 (0 to −15)	Very low due to observational design, imprecision†‡	We are uncertain of the effects of unprocessed red meat on all-cause mortality.
Cardiovascular mortality	7	874 896	9–28	0.90 (0.88–0.91)	41	−4 (−5 to −4)	Very low due to observational design, risk of bias§	We are uncertain of the effects of unprocessed red meat on cardiovascular mortality.
Cardiovascular disease	3	191 803	8–26	0.95 (0.85–1.06)	76	−3 (−11 to 5)	Very low due to observational design, imprecision‖	We are uncertain of the effects of unprocessed red meat on cardiovascular disease.
Stroke (fatal and nonfatal)	6	254 742	12–26	0.94 (0.90–0.98)	19	−1 (0 to −2)	Low due to observational design	Reduction in unprocessed red meat may have little or no effect on stroke.
Fatal stroke	3	671 259	Median, 5.5–15.6	0.94 (0.89–0.99)	1	0	Very low due to observational design, risk of bias¶	We are uncertain of the effects of unprocessed red meat on fatal stroke.
MI (fatal and nonfatal)	1	55 171	Median, 13.6	0.93 (0.87–0.99)	36	−3 (0 to −5)	Very low due to observational design, risk of bias**	We are uncertain of the effects of unprocessed red meat on MI.
Type 2 diabetes††	6	293 869	5–28	0.90 (0.88–0.92)	56	−6 (−7 to −4)	Low due to observational design	Reduction in unprocessed red meat may result in a very small decrease in type 2 diabetes.

GRADE = Grading of Recommendations Assessment, Development and Evaluation; MI = myocardial infarction; RR = relative risk.
* Based on the Emerging Risk Factors Collaboration, which comprises 102 cohorts including 698 782 participants, with a median follow-up of 10.8 y (5th/95th percentile: 2.8–25.6 y). Numbers of events accrued are 78 853, 28 964, 52 765, 13 113, 768, 24 848, and 38 851 for all-cause mortality, cardiovascular mortality, cardiovascular disease, fatal and nonfatal stroke, fatal stroke, fatal and nonfatal MI, and type 2 diabetes, respectively.
† CI around absolute effect includes both appreciable benefit and no appreciable benefit.
‡ I^2 = 96.0%; P for Q test < 0.001. However, the evidence was not downgraded for inconsistency because overlap exists between CIs of most studies.
§ Four of 7 studies are at high risk of bias due to lack of periodic repeated measurement of diet and inadequate adjustment for confounders.
‖ CI around absolute effect includes both appreciable benefit and harm.
¶ Two of 3 studies are at high risk of bias due to assessment of exposure only at baseline for more than 10 y of follow-up and inadequate adjustment for confounders.
** Study at high risk of bias due to assessment of diet only at baseline for >10 y of follow-up and inadequate adjustment for confounders.
†† We found a statistically significant difference between studies at high risk and those at low risk of bias. Here, we report results from studies at low risk.

fatal and nonfatal stroke; 8 (11 cohorts), fatal stroke; 1 (1 cohort), fatal and nonfatal MI; 1 (1 cohort), nonfatal MI; 24 (25 cohorts), type 2 diabetes; and 1 (1 cohort), anemia (**Supplement Table 2**, available at Annals.org). We found no publications reporting on nonfatal stroke, fatal MI, quality of life, or satisfaction with diet.

Eighteen cohorts were from North America (United States and Canada), 21 from Europe, 15 from Asia, and 1 from the Middle East. The number of participants in each cohort ranged from 1757 to 536 969. Participants ranged in age from 17 to 92 years, with most cohorts recruiting those aged 40 to 50 years. Follow-up ranged from 2 to 28 years. Authors of 8 articles disclosed intellectual, financial, or personal conflicts of interest. All studies were funded by governmental bodies, with some receiving additional support from not-for-profit organizations.

Risk of Bias

Supplement Tables 3 through **11** (available at Annals.org) present risk-of-bias assessments. The proportion of studies with high overall risk of bias varied on the basis of outcome: 10 of 31 studies for all-cause mortality, 17 of 22 for cardiovascular mortality, 3 of 8 for cardiovascular disease, 3 of 7 for fatal and nonfatal stroke, 10 of 13 for fatal stroke, 1 of 1 for fatal and nonfatal MI, 0 of 1 for nonfatal MI, 15 of 27 for type 2 diabetes, and 0 of 1 for anemia. The most common limitations in the studies were a lack of periodic repeated evaluation of dietary intake with a measure validated for red and processed meat and inadequate adjustment for potential confounders.

Reduction of 3 Servings per Week of Unprocessed Red Meat

Table 1 presents results of the possible effect of a reduction in unprocessed red meat intake of 3 servings per week. Details are presented in **Supplement Table 12** (available at Annals.org). Results showed a very small apparent effect on cardiovascular mortality, fatal and nonfatal stroke, fatal stroke, fatal and nonfatal MI, and type 2 diabetes, but not all-cause mortality or cardiovascular disease. We found evidence of a subgroup difference between studies at higher and those at lower risk of bias for type 2 diabetes (P < 0.001), so we present results from studies with a lower risk of bias. We did not find evidence of publication bias for type 2 diabetes.

The certainty of evidence was downgraded from low to very low for all-cause mortality and cardiovascular disease because CIs around absolute effect esti-

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mates included appreciable benefit as well as no effect or appreciable harm. The certainty of evidence for cardiovascular mortality, fatal stroke, and fatal and nonfatal MI was downgraded to very low because of the lack of periodic repeated measurement of diet and inadequate adjustment for potential confounders in the primary studies.

Reduction of 3 Servings per Week of Processed Meat

Table 2 presents results of the possible effect of a reduction in processed meat intake of 3 servings per week. Details are presented in Supplement Table 13 (available at Annals.org). Results show a very small apparent effect on all-cause mortality, cardiovascular mortality, fatal and nonfatal stroke, fatal stroke, fatal and nonfatal MI, and type 2 diabetes, but not cardiovascular disease. We found evidence of a nonlinear association between processed meat intake and type 2 diabetes ($P < 0.001$), with a decrease from 3 to 0 servings per week associated with a very small reduced risk for type 2 diabetes (Figure). We found no evidence of publication bias for type 2 diabetes.

The certainty of evidence was downgraded to very low for cardiovascular mortality, fatal stroke, fatal and nonfatal MI, and type 2 diabetes because of a lack of periodic repeated measurement of diet and inadequate adjustment for potential confounders in the primary studies, as well as for type 2 diabetes because of substantial statistical heterogeneity.

Reduction of 3 Servings per Week of Mixed Unprocessed Red and Processed Meat

Supplement Table 14 (available at Annals.org) presents results of the possible effect of a reduction in intake of mixed unprocessed red and processed meat of 3 servings per week. Details are presented in Supplement Table 15 (available at Annals.org). Results show a small to very small apparent effect on all-cause mortality, cardiovascular mortality, cardiovascular disease, fatal and nonfatal stroke, fatal stroke, fatal and nonfatal MI, and type 2 diabetes, but not on nonfatal MI or anemia. We found evidence of a subgroup difference between studies at higher and those at lower risk of bias for all-cause mortality ($P = 0.002$) and type 2 diabetes ($P = 0.027$), so we present results only from studies at lower risk of bias. We found evidence of a nonlinear association between intake of mixed unprocessed red and processed meat and all-cause mortality ($P = 0.037$), with a reduction from 3 to 0 servings per week associated with a small decrease in risk (Supplement Figure 2, available at Annals.org). We found no evidence of publication bias for type 2 diabetes.

The certainty of evidence was downgraded to very low for cardiovascular mortality, fatal stroke, and fatal and nonfatal MI because of a lack of periodic repeated

Table 2. Summary of Findings for Processed Red Meat Intake (Reduction of 3 Servings per Week) and Risk for Cardiometabolic Outcomes

Outcome	Studies, *n*	Participants, *n*	Follow-up, *y*	RR (95% CI)	Population Risk per 1000 Persons Over 10.8 y*	Risk Difference per 1000 Persons (95% CI)	GRADE Certainty of Evidence	Plain-Language Summary
All-cause mortality	8	1 241 900	9–28	0.92 (0.87–0.96)	113	−9 (−15 to −5)	Low due to observational design†	Reduction in processed meat may result in a very small decrease in all-cause mortality.
Cardiovascular mortality	7	1 240 634	9–28	0.90 (0.84–0.97)	41	−4 (−7 to −1)	Very low due to observational design, risk of bias‡§	We are uncertain of the effects of processed meat on cardiovascular mortality.
Cardiovascular disease	3	200 421	8–26	0.97 (0.87–1.09)	76	−2 (−10 to 7)	Low due to observational design‖	Reduction in processed meat may have little or no effect on cardiovascular disease.
Stroke (fatal and nonfatal)	6	254 742	12–26	0.94 (0.90–0.98)	19	−1 (0 to −2)	Low due to observational design	Reduction in processed meat may have little or no effect on stroke.
Fatal stroke	2	571 378	15–16	0.95 (0.92–0.98)	1	0	Very low due to observational design, risk of bias¶	We are uncertain of the effects of processed meat on fatal stroke.
MI (fatal and nonfatal)	1	55 171	Median, 13.6	0.94 (0.91–0.98)	36	−2 (−3 to −1)	Very low due to observational design, risk of bias**	We are uncertain of the effects of processed meat on MI.
Type 2 diabetes	14	669 530	5–28	0.78 (0.72–0.84)††	56	−12 (−16 to −9)	Very low due to observational design, risk of bias, inconsistency‡‡§§	We are uncertain of the effects of processed meat on type 2 diabetes.

GRADE = Grading of Recommendations Assessment, Development and Evaluation; MI = myocardial infarction; RR = relative risk.
* Based on the Emerging Risk Factors Collaboration, which comprises 102 cohorts including 698 782 participants, with a median follow-up of 10.8 y (5th/95th percentile: 2.8–25.6 y). The numbers of events accrued are 78 853, 28 964, 52 765, 13 113, 768, 24 848, and 38 851 for all-cause mortality, cardiovascular mortality, cardiovascular disease, fatal and nonfatal stroke, fatal stroke, fatal and nonfatal MI, and type 2 diabetes, respectively.
† $I^2 = 87.4\%$; P for Q test < 0.001. However, the evidence was not downgraded for inconsistency because overlap exists between CIs of most studies.
‡ Four of 7 studies at high risk of bias, primarily because of a lack of periodic repeated measurement of diet and inadequate adjustment for confounders.
§ $I^2 = 84.9\%$; P for Q test < 0.001. However, the evidence was not downgraded for inconsistency because overlap exists between CIs of most studies.
‖ $I^2 = 59.6\%$; P for Q test = 0.098. However, the evidence was not downgraded for inconsistency because overlap exists between CIs of studies.
¶ Two of 2 studies had high risk of bias due to lack of periodic repeated measurement of diet and inadequate adjustment for confounders.
** Study had high risk of bias due to measurement of diet only at baseline for >10 y of follow-up and inadequate adjustment for confounders.
†† Nonlinear relationship. Effect estimate presented represents reduction in intake from 3 to 0 servings per week.
‡‡ Nine of 14 studies had high risk of bias, primarily due to lack of periodic repeated measurement of diet and inadequate adjustment for confounders.
§§ $I^2 = 54.5\%$; P for Q test < 0.001.

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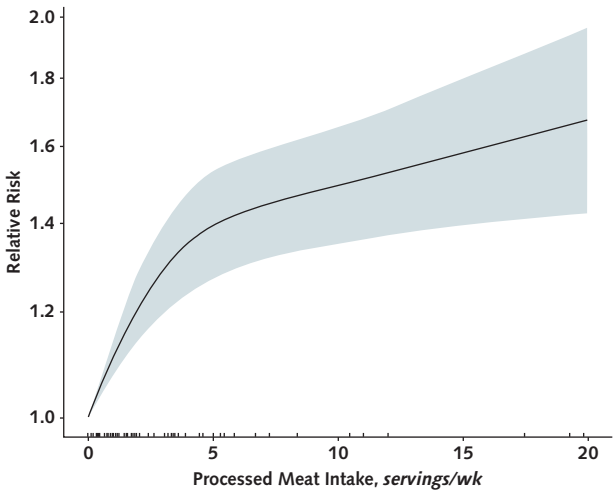
Figure. Nonlinear association between processed meat intake and type 2 diabetes.



The solid black line represents the point estimate, the shaded region represents the 95% CIs, and tick marks represent the positions of the study-specific estimates.

measurement of diet and inadequate adjustment for potential confounders in the primary studies.

Comparison of Extreme Categories of Intake

Results from meta-analyses comparing extreme categories of intake were generally consistent with the findings from our dose–response meta-analyses, although effect sizes typically were smaller than those from dose–response meta-analyses (Supplement Tables 16 to 18, available at Annals.org).

Discussion

We found low- to very-low-certainty evidence that reducing unprocessed red meat intake by 3 servings per week is associated with a very small reduction in risk for cardiovascular mortality, stroke, MI, and type 2 diabetes. Likewise, we found low- to very-low-certainty evidence that a reduction in processed meat intake is associated with a small to very small reduction in risk for all-cause mortality, cardiovascular mortality, stroke, MI, and type 2 diabetes. The magnitude of apparent effect of processed meat consumption on adverse cardiometabolic outcomes was somewhat greater than that observed for unprocessed red meat.

According to the GRADE system, the certainty of evidence may be upgraded if evidence suggests a dose–response relationship between the exposure and the outcomes of interest. Although we found evidence for dose–response relationships, we did not upgrade the certainty of evidence because of the possibility that red and processed meat consumption may be correlated with other dietary components, which may then confound their relationship to health outcomes (37). Support for this concern comes from a parallel systematic review in which we found the magnitude of association between dietary patterns lower versus higher in red and processed meat and adverse cardiometabolic outcomes to be very similar to the estimates found in this review (10). If red meat and processed meat were indeed the primary drivers of the association between diet and adverse cardiometabolic outcomes, we would anticipate stronger associations in our analyses of red and processed meat compared with dietary patterns (7).

Strengths of this review include the prespecification of our methods in the review protocol and the inclusion of a large number of cohorts and participants. We conducted both linear and nonlinear dose–response meta-analyses, which provide the most compelling evidence for the association between red and processed meat consumption and health outcomes, in addition to secondary analyses comparing extreme categories of intake. Results from our dose–response analyses are presented for a realistic reduction of 3 servings per week, which corresponds to the elimination of red and processed meat from the typical North American and western European diet based on the average intake of these foods in these populations (38–40). We assessed risk of bias and, when results differed, based our estimates on studies with lower versus higher risk of bias. Finally, we used the GRADE approach to rate the certainty of evidence.

In evaluating risk of bias of the primary studies, we assessed whether studies adjusted for a set of important potential confounders for each outcome. However, our results are limited by the potential for residual confounding or measurement error in confounders. In addition, studies varied in their choice of adjustment variables. All included studies measured diet via recall-based methods, primarily food-frequency questionnaires, which are subject to measurement error that can both attenuate and overestimate observed associations (41, 42). Although food-frequency questionnaires may provide reliable information on relative intake, substantial error regarding absolute intake may compromise dose–response meta-analyses that rely on these estimates (41). We could not assess the effects of reduced intake of red meat and processed meat on the basis which foods were consumed in their place, and the associated health effects of these alternative food choices may differ.

Half the studies in our review did not report sufficient information to be included in the dose–response meta-analyses (19, 20). Nonetheless, we are more confident in our results from these meta-analyses because they account for differences in gradients of intake across cohorts (43). In secondary analyses comparing extreme categories of intake, studies omitted from dose–response meta-analyses produced smaller effect estimates. The reason may be that studies that could not be included in dose–response meta-analyses had a higher risk of bias and typically measured diet with methods not validated for red and processed meat and did not repeat diet measurements throughout the study; hence, they may have underestimated the association between red and processed meat and adverse cardiometabolic health outcomes.

We could not conduct 3 additional analyses that we had planned—a subgroup analysis on the effects of red versus white processed meat, a subgroup analysis on the effects of red meat intake in iron-deficient populations, and a sensitivity analysis to assess the robust-

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ness of results to loss to follow-up—because the primary studies did not report sufficient information (33). We converted effect estimates reported in grams to servings. Although we used typical serving sizes in our conversions, our estimates may have been unreliable (1–3, 21, 23–25).

Although we found no evidence of publication bias, given the lack of standard registration practices for observational studies, publication bias is possible. In addition, none of the included studies had a priori specified statistical analysis plans (44); therefore, analysts' modeling decisions may have been guided by the possibility of obtaining interesting results.

Previous reviews reported similar positive associations between red and processed meat intake and all-cause mortality, cardiovascular disease, stroke, MI, and type 2 diabetes (1, 3–6). Similar to our work, other reviews reported slightly stronger associations between processed meat versus unprocessed red meat and adverse health outcomes. We believe our review provides the most up-to-date evidence on the topic and adds to the existing literature by using a more rigorous evaluation of risk of bias and by providing an assessment of certainty of evidence. Our results, as well as those of other reviews of observational studies, contrast with findings from randomized trials, which have failed to demonstrate an effect of lower red and processed meat consumption on cardiometabolic outcomes (8).

Current dietary guidelines recommend limiting red and processed meat consumption (25, 45). Our results, however, demonstrate that the evidence implicating red and processed meat in adverse cardiometabolic outcomes is of low quality; thus, considerable uncertainty remains regarding a causal relationship. Moreover, even if a causal relationship exists, the magnitude of association between red and processed meat consumption and cardiometabolic outcomes is very small.

Reducing the consumption of unprocessed red and processed meat may result in a decrease in risk for cardiometabolic disease and mortality. The magnitude of absolute effect, if indeed it exists, is very small, and the certainty of evidence is low. Findings from our review raise questions regarding whether—on the basis of possible adverse effects on cardiometabolic outcomes—the evidence is sufficient to recommend decreasing consumption of red and processed meat.

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Reproducible Research Statement: *Study protocol:* Registered with PROSPERO (CRD42017074074). *Statistical code and data set:* Available from Ms. Zeraatkar (e-mail, dena.zera@gmail.com). For sample code, see **Supplement 2** (available at Annals.org).

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References

1. **Schwingshackl L, Schwedhelm C, Hoffmann G, et al.** Food groups and risk of all-cause mortality: a systematic review and meta-analysis of prospective studies. Am J Clin Nutr. 2017;105:1462-1473. [PMID: 28446499] doi:10.3945/ajcn.117.153148

2. **Abete I, Romaguera D, Vieira AR, et al.** Association between total, processed, red and white meat consumption and all-cause, CVD and IHD mortality: a meta-analysis of cohort studies. Br J Nutr. 2014;112:762-75. [PMID: 24932617] doi:10.1017/S000711451400124X

3. **Chen GC, Lv DB, Pang Z, et al.** Red and processed meat consumption and risk of stroke: a meta-analysis of prospective cohort studies. Eur J Clin Nutr. 2013;67:91-5. [PMID: 23169473] doi:10.1038/ejcn.2012.180

4. **Wang X, Lin X, Ouyang YY, et al.** Red and processed meat consumption and mortality: dose-response meta-analysis of prospective cohort studies. Public Health Nutr. 2016;19:893-905. [PMID: 26143683] doi:10.1017/S1368980015002062

5. **Micha R, Wallace SK, Mozaffarian D.** Red and processed meat consumption and risk of incident coronary heart disease, stroke, and diabetes mellitus: a systematic review and meta-analysis. Circulation. 2010;121:2271-83. [PMID: 20479151] doi:10.1161/CIRCULATIONAHA.109.924977

6. **Aune D, Ursin G, Veierød MB.** Meat consumption and the risk of type 2 diabetes: a systematic review and meta-analysis of cohort studies. Diabetologia. 2009;52:2277-87. [PMID: 19662376] doi:10.1007/s00125-009-1481-x

7. **Johnston BC, Alonso-Coello P, Bala MM, et al.** Methods for trustworthy nutritional recommendations NutriRECS (Nutritional Recommendations and accessible Evidence summaries Composed of Systematic reviews): a protocol. BMC Med Res Methodol. 2018;18:162. [PMID: 30518328] doi:10.1186/s12874-018-0621-8

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8. **Zeraatkar D, Johnston BC, Bartoszko J, et al.** Effect of lower versus higher red meat intake on cardiometabolic and cancer outcomes. A systematic review of randomized trials. Ann Intern Med. 2019;171: 721-31. doi:10.7326/M19-0622
9. **Han MA, Zeraatkar D, Guyatt GH, et al.** Reduction of red and processed meat intake and cancer mortality and incidence. A systematic review and meta-analysis of cohort studies. Ann Intern Med. 2019;171:711-20. doi:10.7326/M19-0699
10. **Vernooij RWM, Zeraatkar D, Han MA, et al.** Patterns of red and processed meat consumption and risk for cardiometabolic and cancer outcomes. A systematic review and meta-analysis of cohort studies. Ann Intern Med. 2019;171:732-41. doi:10.7326/M19-1583
11. **Valli C, Rabassa M, Johnston BC, et al.** Health-related values and preferences regarding meat consumption. A mixed-methods systematic review. Ann Intern Med. 2019;171:742-55. doi:10.7326/M19 -1326
12. **Wiseman M.** The second World Cancer Research Fund/ American Institute for Cancer Research expert report. Food, nutrition, physical activity, and the prevention of cancer: a global perspective. Proc Nutr Soc. 2008;67:253-6. [PMID: 18452640] doi:10 .1017/S002966510800712X
13. **Zhang Y, Tuomilehto J, Jousilahti P, et al.** Lifestyle factors and antihypertensive treatment on the risks of ischemic and hemorrhagic stroke. Hypertension. 2012;60:906-12. [PMID: 22868396] doi:10 .1161/HYPERTENSIONAHA.112.193961
14. **Bentley J.** U.S. per capita availability of red meat, poultry, and fish lowest since 1983. Accessed at www.ers.usda.gov/amber-waves /2017/januaryfebruary/us-per-capita-availability-of-red-meat-poultry -and-fish-lowest-since-1983 on 25 February 2019.
15. **Food and Agriculture Organization of the United Nations.** FAOSTAT. Food and agriculture data. Accessed at www.fao.org /faostat/en on 26 February 2019.
16. **Evidence Partners.** Tool to assess risk of bias in cohort studies. Accessed at www.evidencepartners.com/wp-content/uploads/2014 /02/Tool-to-Assess-Risk-of-Bias-in-Cohort-Studies.doc on 27 February 2019.
17. **IARC Working Group on the Evaluation of Carcinogenic Risk to Humans.** IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Red Meat and Processed Meat. Lyon, France: International Agency for Research on Cancer; 2018.
18. **Inoue-Choi M, Sinha R, Gierach GL, et al.** Red and processed meat, nitrite, and heme iron intakes and postmenopausal breast cancer risk in the NIH-AARP Diet and Health Study. Int J Cancer. 2016; 138:1609-18. [PMID: 26505173] doi:10.1002/ijc.29901
19. **Greenland S, Longnecker MP.** Methods for trend estimation from summarized dose-response data, with applications to meta-analysis. Am J Epidemiol. 1992;135:1301-9. [PMID: 1626547]
20. **Orsini N, Bellocco R, Greenland S.** Generalized least squares for trend estimation of summarized dose–response data. Stata Journal. 2006;6:40-57.
21. **Church S.** Trends in portion sizes in the UK—a preliminary review of published information. London: Food Standards Agency; 2008.
22. **Pan A, Sun Q, Bernstein AM, et al.** Red meat consumption and risk of type 2 diabetes: 3 cohorts of US adults and an updated meta-analysis. Am J Clin Nutr. 2011;94:1088-96. [PMID: 21831992] doi:10 .3945/ajcn.111.018978
23. **Kaluza J, Wolk A, Larsson SC.** Red meat consumption and risk of stroke: a meta-analysis of prospective studies. Stroke. 2012;43:2556-60. [PMID: 22851546]
24. **Larsson SC, Orsini N.** Red meat and processed meat consumption and all-cause mortality: a meta-analysis. Am J Epidemiol. 2014; 179:282-9. [PMID: 24148709] doi:10.1093/aje/kwt261
25. **U.S. Department of Agriculture, U.S. Department of Health and Human Services.** Dietary Guidelines for Americans 2015–2020. New York: Skyhorse; 2015.
26. **Crippa A, Orsini N.** Multivariate dose-response meta-analysis: the dosresmeta R package. Journal of Statistical Software. 2016;72:1-15.
27. **Hartung J, Knapp G.** A refined method for the meta-analysis of controlled clinical trials with binary outcome. Stat Med. 2001;20: 3875-89. [PMID: 11782040]
28. **Sidik K, Jonkman JN.** A simple confidence interval for meta-analysis. Stat Med. 2002;21:3153-9. [PMID: 12375296]
29. **Viechtbauer W.** Metafor: meta-analysis package for R. R package version. Journal of Statistical Software. 2010;363:1-48.
30. **Higgins JPT, Green S, eds.** Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011. Accessed at www.handbook.cochrane .org on 7 August 2019.
31. **Rücker G, Schwarzer G, Carpenter JR, et al.** Undue reliance on I(2) in assessing heterogeneity may mislead. BMC Med Res Methodol. 2008;8:79. [PMID: 19036172] doi:10.1186/1471-2288-8-79
32. **Egger M, Davey Smith G, Schneider M, et al.** Bias in meta-analysis detected by a simple, graphical test. BMJ. 1997;315:629-34. [PMID: 9310563]
33. **Akl EA, Johnston BC, Alonso-Coello P, et al.** Addressing dichotomous data for participants excluded from trial analysis: a guide for systematic reviewers. PLoS One. 2013;8:e57132. [PMID: 23451162] doi:10.1371/journal.pone.0057132
34. **Guyatt GH, Oxman AD, Vist GE, et al; GRADE Working Group.** GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. BMJ. 2008;336:924-6. [PMID: 18436948] doi:10.1136/bmj.39489.470347.AD
35. **Sarwar N, Gao P, Seshasai SR, et al; Emerging Risk Factors Collaboration.** Diabetes mellitus, fasting blood glucose concentration, and risk of vascular disease: a collaborative meta-analysis of 102 prospective studies. Lancet. 2010;375:2215-22. [PMID: 20609967] doi: 10.1016/S0140-6736(10)60484-9
36. **Laguzzi F, Carlsson AC, Gigante B, et al.** Predictive role of dietary habits in relation to incident CVD and all-cause mortality: results from a Swedish cohort of 60-year-old [Abstract]. In: Bols E, Smits L, Weijenberg M, eds. Healthy living: the European Congress of Epidemiology, 2015. Eur J Epidemiol. 2015;30:724-5. Abstract no. O 10.
37. **Johansson I, Nilsson LM, Esberg A, et al.** Dairy intake revisited–associations between dairy intake and lifestyle related cardiometabolic risk factors in a high milk consuming population. Nutr J. 2018;17:110. [PMID: 30466440] doi:10.1186/s12937-018-0418-y
38. **Daniel CR, Cross AJ, Koebnick C, et al.** Trends in meat consumption in the USA. Public Health Nutr. 2011;14:575-83. [PMID: 21070685] doi:10.1017/S1368980010002077
39. **Borrud L, Wilkinson E, Mickle S.** Continuing survey of food intakes by individuals, 1994-96. Accessed at www.cfpub.epa.gov/si/si _public_record_Report.cfm?Lab=OEI&dirEntryID=132556 on 13 August 2019.
40. **Micha R, Khatibzadeh S, Shi P, et al; Global Burden of Diseases Nutrition and Chronic Diseases Expert Group (NutriCoDE).** Global, regional and national consumption of major food groups in 1990 and 2010: a systematic analysis including 266 country-specific nutrition surveys worldwide. BMJ Open. 2015;5:e008705. [PMID: 26408285] doi:10.1136/bmjopen-2015-008705
41. **Archer E, Marlow ML, Lavie CJ.** Controversy and debate: Memory-Based Methods Paper 1: the fatal flaws of food frequency questionnaires and other memory-based dietary assessment methods. J Clin Epidemiol. 2018;104:113-124. [PMID: 30121379] doi:10 .1016/j.jclinepi.2018.08.003
42. **Brakenhoff TB, van Smeden M, Visseren FLJ, et al.** Random measurement error: Why worry? An example of cardiovascular risk factors. PLoS One. 2018;13:e0192298. [PMID: 29425217] doi:10.1371 /journal.pone.0192298
43. **Yu WW, Schmid CH, Lichtenstein AH, et al.** Empirical evaluation of meta-analytic approaches for nutrient and health outcome dose-response data. Res Synth Methods. 2013;4:256-68. [PMID: 25379059]
44. **Thomas L, Peterson ED.** The value of statistical analysis plans in observational research: defining high-quality research from the start. JAMA. 2012;308:773-4. [PMID: 22910753] doi:10.1001/jama.2012 .9502
45. **Bouvard V, Loomis D, Guyton KZ, et al; International Agency for Research on Cancer Monograph Working Group.** Carcinogenicity of consumption of red and processed meat. Lancet Oncol. 2015;16: 1599-600. [PMID: 26514947] doi:10.1016/S1470-2045(15)00444-1

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Correction: Nutritional Recommendations (NutriRECS) on Consumption of Red and Processed Meat

On the author disclosure forms accompanying recent related articles on red and processed meat consumption and health outcomes (1-6), Bradley Johnston did not indicate a grant from Texas A&M AgriLife Research to fund investigator-driven research related to saturated and polyunsaturated fats. This funding is for work in the field of nutrition and the start of funding period was within the 36-month reporting period required in Section 3 of the disclosure form of the International Committee of Medical Journal Editors (ICMJE). Dr. Johnston has updated his disclosure form to include this research funding and also to note funding received from the International Life Science Institute (North America) that ended before the 36-month ICMJE reporting period. The corrected disclosure forms now accompany the articles (1-6).

References

1. **Zeraatkar D, Han MA, Guyatt GH, et al.** Red and processed meat consumption and risk for all-cause mortality and cardiometabolic outcomes. A systematic review and meta-analysis of cohort studies. Ann Intern Med. 2019;171:703-10. [PMID: 31569213] doi:10.7326/M19-0655

2. **Han MA, Zeraatkar D, Guyatt GH, et al.** Reduction of red and processed meat intake and cancer mortality and incidence. A systematic review and meta-analysis of cohort studies. Ann Intern Med. 2019;171:711-20. [PMID: 31569214] doi: 10.7326/M19-0699

3. **Zeraatkar D, Johnston BC, Bartoszko J, et al.** Effect of lower versus higher red meat intake on cardiometabolic and cancer outcomes. A systematic review of randomized trials. Ann Intern Med. 2019;171:721-31. [PMID: 31569236] doi:10.7326/M19-0622

4. **Vernooij RWM, Zeraatkar D, Han MA, et al.** Patterns of red and processed meat consumption and risk for cardiometabolic and cancer outcomes. A systematic review and meta-analysis of cohort studies. Ann Intern Med. 2019;171:732-41. [PMID: 31569217] doi:10.7326/M19-1583

5. **Valli C, Rabassa M, Johnston BC, et al; NutriRECS Working Group**. Health-related values and preferences regarding meat consumption. A mixed-methods systematic review. Ann Intern Med. 2019;171:742-55. [PMID: 31569219] doi: 10.7326/M19-1326

6. **Johnston BC, Zeraatkar D, Han MA, et al.** Unprocessed red meat and processed meat consumption: dietary guideline recommendations from the nutritional recommendations (NutriRECS) consortium. Ann Intern Med. 2019;171:756-64. [PMID: 31569235] doi:10.7326/M19-1621

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