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CLINICAL GUIDELINE

Unprocessed Red Meat and Processed Meat Consumption: Dietary Guideline Recommendations From the NutriRECS Consortium

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Description: Dietary guideline recommendations require consideration of the certainty in the evidence, the magnitude of potential benefits and harms, and explicit consideration of people's values and preferences. A set of recommendations on red meat and processed meat consumption was developed on the basis of 5 de novo systematic reviews that considered all of these issues.

Methods: The recommendations were developed by using the Nutritional Recommendations (NutriRECS) guideline development process, which includes rigorous systematic review methodology, and GRADE methods to rate the certainty of evidence for each outcome and to move from evidence to recommendations. A panel of 14 members, including 3 community members, from 7 countries voted on the final recommendations. Strict criteria limited the conflicts of interest among panel members. Considerations of environmental impact or animal welfare did not bear on the recommendations. Four systematic reviews addressed the health effects associated with red meat and processed meat consumption, and 1 systematic review addressed people's health-related values and preferences regarding meat consumption.

Recommendations: The panel suggests that adults continue current unprocessed red meat consumption (weak recommendation, low-certainty evidence). Similarly, the panel suggests adults continue current processed meat consumption (weak recommendation, low-certainty evidence).

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Contemporary dietary guidelines recommend limiting consumption of unprocessed red meat and processed meat. For example, the 2015–2020 Dietary Guidelines for Americans recommend limiting red meat intake, including processed meat, to approximately 1 weekly serving (1). Similarly, United Kingdom dietary guidelines endorse limiting the intake of both red and processed meat to 70 g/d (2), and the World Cancer Research Fund/American Institute for Cancer Research recommend limiting red meat consumption to moderate amounts and consuming very little processed meat (3). The World Health Organization International Agency for Research on Cancer has indicated that consumption of red meat is "probably carcinogenic" to humans, whereas processed meat is considered "carcinogenic" to humans (4).

These recommendations are, however, primarily based on observational studies that are at high risk for confounding and thus are limited in establishing causal inferences, nor do they report the absolute magnitude of any possible effects. Furthermore, the organizations that produce guidelines did not conduct or access rigorous systematic reviews of the evidence, were limited in addressing conflicts of interest, and did not explicitly address population values and preferences, raising questions regarding adherence to guideline standards for trustworthiness (5–9).

A potential solution to the limitations of contemporary nutrition guidelines is for an independent group with clinical and nutritional content expertise and skilled in the methodology of systematic reviews and practice guidelines, methods that include careful management of conflicts of interest, to produce trustworthy recommendations based on the values and preferences of guideline users. We developed the Nutritional Recommendations (NutriRECS) (7) international consortium to produce rigorous evidence-based nutritional recommendations adhering to trustworthiness standards (10–12).

To support our recommendations, we performed 4 parallel systematic reviews that focused both on randomized trials and observational studies addressing the possible impact of unprocessed red meat and processed meat consumption on cardiometabolic and cancer outcomes (13–16), and a fifth systematic review addressing people's health-related values and preferences related to meat consumption (17). On the basis of these reviews, we developed recommendations for unprocessed red meat and processed meat consumption specific to health outcomes.

METHODS

Guideline Development Process

We developed our recommendations by following the NutriRECS guideline development process (7),

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which includes use of GRADE (Grading of Recommendations, Assessment, Development and Evaluation) methodology (18–20). To inform our guideline recommendations, systematic reviews were conducted on the basis of a priori methods (21, 22).

Guideline Team Structure

This work involved 3 teams:

1. A core NutriRECS leadership team was responsible for supervision and coordination of the project and for drafting of the research questions, guideline protocol, and manuscripts.

2. A guideline panel included experts in health research methodology, nutritional epidemiology, dietetics, basic and translational research, family medicine, and general internal medicine. The panel included 3 members from outside the medical and health care communities. Panelists resided in high-income countries (Canada, England, Germany, New Zealand, Poland, Spain, and the United States).

3. A literature review team drafted the protocols for the systematic reviews, completed the literature search and eligibility review, abstracted data and conducted data analysis, and produced narrative and tabular summaries of the results.

Framework for Panel Construction and Guideline Recommendations

The core leadership team applied safeguards against competing interests (7). After generating a list of potential panel members without perceived vested interests, we contacted prospective candidates from North America, Western Europe, and New Zealand. Those who expressed interest completed a detailed form enumerating potential financial or intellectual conflicts during the previous 3 years. If important competing issues were identified (1 interested individual had financial conflicts), the potential panelist was not invited to participate. The **Appendix Table** (available at Annals .org) shows a summary of the authors' conflict of interest forms; a full list of competing interests is available upon request from Dr. Johnston.

Before our initial guideline panel meeting, the methods editor and panel chair contacted panelists, shared the draft questions, and received and incorporated feedback. At the initial meeting, the guideline panel discussed the scope of the project and agreed on the research questions and subgroups of interest. The panel focused on health outcomes thought to be associated with consumption of unprocessed red meat and processed meat and chose not to consider animal welfare and environmental issues related to meat consumption in making recommendations. The panel chose to exclusively focus on health outcomes because environmental and animal welfare concerns are very different issues that are challenging to integrate with health concerns, are possibly more societal than personal issues, and vary greatly in the extent to which people find them a priority. Finally, to consider these issues rigorously would require systematic reviews that we were not resourced to undertake.

The panel also chose to make separate recommendations for unprocessed red meat and processed meat, given the potential for differential health effects and differing values and preferences of members of the public with regard to consumption of unprocessed meat versus processed meat.

Target Audience for Recommendations

The target audience for our guidance statement was individuals who consume unprocessed red meat or processed meat as part of their diet. The panel took the perspective of individual decision making rather than a public health perspective.

Key Principles for PICO Questions and Study Eligibility Criteria

Each NutriRECS project addresses a single nutrition question or topic, in this case guidance regarding the potential harms, benefits, and health-related values and preferences related to consuming unprocessed red meat and processed meat. We conducted a series of systematic reviews to inform our recommendations, addressing the following questions: 1) Among adults, what is the effect of diets and dietary patterns lower in red or processed meat versus diets higher in red or processed meat intake on the risk for outcomes important to community members? and 2) What are their health-related values and preferences for red and processed meat consumption?

The panel considered all-cause mortality, major cardiometabolic outcomes (cardiovascular mortality, stroke, myocardial infarction, and diabetes), cancer incidence and mortality (gastrointestinal, prostate, and gynecologic cancer), quality of life, and willingness to change unprocessed red or processed meat consumption as "critically important" for developing recommendations. "Important" outcomes included surrogate outcomes (weight, body mass index, blood lipids, blood pressure, hemoglobin, anemia) and reasons for eating unprocessed red meat and processed meat.

Methods for Systematic Reviews

In consultation with an expert librarian, we searched the major literature databases to identify all relevant studies on harms, benefits, and health-related values and preferences regarding unprocessed red meat and processed meat. Each database was searched from inception until July 2018 without restrictions on language or date of publication, with MEDLINE searched through to April 2019 (see the systematic reviews in this issue [13–17]).

For harms and benefits, we included any randomized trial, as well as cohort studies including 1000 or more adults, that assessed diets with varying quantities of unprocessed red meat (for example, as servings or times/wk, or g/d) or processed meat (meat preserved by smoking, curing, salting, or addition of preservatives) (23) for a duration of 6 months or more. Studies in which more than 20% of the sample was pregnant or had cancer or a chronic health condition, other than cardiometabolic disease, were excluded. The review articles report our methods for screening, data abstraction, risk of bias assessment, and data analysis (13–17).

Panelists considered 3 servings per week as a realistic reduction in meat consumption (for example, moving from 7 to 4 servings, or 4 to 1 serving) on the basis of the average intake of 2 to 4 servings per week in North America and Western Europe (24–28). We therefore framed the evidence regarding the potential reduced risks associated with a decrease of 3 servings per week of both unprocessed red meat and processed meat.

We used GRADEpro software to formulate GRADE summary of findings tables for each PICO (population, intervention, control, and outcomes) question (29). The overall certainty of evidence was evaluated by using the GRADE approach (18). For estimates of risk with current levels of meat consumption, we used population estimates from the Emerging Risk Factors Collaboration study for cardiometabolic outcomes (30) and population estimates from GLOBOCAN for cancer outcomes (31). Using these resources, we based our estimates for cardiometabolic mortality and incidence outcomes on an average of 10.8 years of follow-up, whereas for cancer mortality and incidence, our estimates are for the overall lifetime risk.

Complementing existing GRADE standards and to determine whether we should rate up for a dose–response effect, we assessed the plausibility of a causal relationship between meat and adverse health outcomes by contrasting results from 2 bodies of evidence (7, 22): cohort studies specifically addressing red meat and processed meat intake, and cohort studies addressing dietary patterns associated with varying red meat and processed meat consumption. We hypothesized that if red meat and processed meat were indeed causally related to adverse health outcomes, we would find stronger associations in studies that specifically addressed red meat and processed meat intake versus studies addressing dietary patterns (7).

To address health-related values and preferences regarding red meat and processed meat, we included qualitative (such as interviews and focus groups) and quantitative (such as cross-sectional surveys) studies conducted in adults. We independently screened studies, abstracted data, and assessed risk of bias (17). We then synthesized the data into narrative themes and tabulated summaries, and again assessed the certainty of evidence by using the GRADE approach (18, 32).

To assist our 3 public panel members without health science backgrounds, the method's editor conducted electronic meetings with them before the guideline panel meetings to explain the systematic review results and the GRADE approach for assessing the certainty of evidence and for moving from evidence to recommendations. During the guideline panel meetings, the leads of each of the systematic reviews shared the summary data and certainty of evidence for each of our outcomes with the guideline panel, and the panel chair answered any questions as necessary.

Moving From Evidence to Recommendations

Before our final guideline panel meeting, we asked each panelist to complete a GRADE Evidence to Decision (EtD) framework. The purpose of EtD frameworks is to help panelists use the evidence summaries in a structured and transparent way to develop the final recommendations. In doing so, the panelists considered evidence summaries for health effects, values, and preferences as well as cost, acceptability, and feasibility of a recommendation to decrease meat consumption (33). During the final meeting, the panel reviewed the results of the EtD survey and considered the implications of those judgments for their recommendations.

RESULTS

Recommendation for Unprocessed Red Meat

For adults 18 years of age or older, we suggest continuing current unprocessed red meat consumption (weak recommendation, low-certainty evidence). Eleven of 14 panelists voted for continuation of current unprocessed red meat consumption, whereas 3 voted for a weak recommendation to reduce red meat consumption.

Recommendation for Processed Meat

For adults 18 years of age or older, we suggest continuing current processed meat consumption (weak recommendation, low-certainty evidence). Again, 11 of 14 panel members voted for a continuation of current processed meat consumption, and 3 voted for a weak recommendation to reduce processed meat consumption.

Evidence Summary for Harms and Benefits of Unprocessed Red Meat Consumption

For our review of randomized trials on harms and benefits (12 unique trials enrolling 54 000 participants), we found low- to very low-certainty evidence that diets lower in unprocessed red meat may have little or no effect on the risk for major cardiometabolic outcomes and cancer mortality and incidence (15). Dose–response meta-analysis results from 23 cohort studies with 1.4 million participants provided low- to very low-certainty evidence that decreasing unprocessed red meat intake may result in a very small reduction in the risk for major cardiovascular outcomes (cardiovascular disease, stroke, and myocardial infarction) and type 2 diabetes (range, 1 fewer to 6 fewer events per 1000 persons with a decrease of 3 servings/wk), with no statistically significant differences in 2 additional outcomes (all-cause mortality and cardiovascular mortality) (16). Dose–response meta-analysis results from 17 cohorts with 2.2 million participants provided low-certainty evidence that decreasing unprocessed red meat intake may result in a very small reduction of overall lifetime cancer mortality (7 fewer events per 1000 persons with a decrease of 3 servings/wk), with no statistically significant differences for 8 additional cancer outcomes (prostate cancer mortality and the incidence of overall, breast, colorectal, esophageal, gastric, pancreatic, and prostate cancer) (13). Similar to studies directly addressing red meat, cohort studies assessing dietary patterns (70 cohort studies with just over 6 million participants) provided mostly uncertain evidence for the risk for adverse cardiometabolic and cancer outcomes. Although statistically significant, low- to very low-certainty evidence indicates that adherence to dietary

Table 1. Causal Inference Assessment Based on Summary of Evidence for Statistically Significant Effects for Red Meat, Processed Meat, and Dietary Patterns

Outcome	Unprocessed Red Meat		Processed Meat		Dietary Patterns	
	Risk Difference	Certainty of Evidence	Risk Difference	Certainty of Evidence	Risk Difference	Certainty of Evidence
Cardiovascular mortality*†	4 fewer per 1000 persons (from 5 fewer to 4 fewer) over 10.8 y	Very low	4 fewer per 1000 persons (from 7 fewer to 1 fewer) over 10.8 y	Very low	6 fewer per 1000 persons (from 9 fewer to 2 fewer) over 10.8 y	Very low
Type 2 diabetes*†	6 fewer per 1000 persons (from 7 fewer to 4 fewer) over 10.8 y	Low	12 fewer per 1000 persons (from 16 fewer to 9 fewer) over 10.8 y	Very low	14 fewer per 1000 persons (from 18 fewer to 8 fewer) over 10.8 y	Very low
Overall cancer mortality†‡	7 fewer per 1000 persons (from 9 fewer to 6 fewer) over lifetime	Low	8 fewer per 1000 persons (from 12 fewer to 6 fewer) over lifetime	Low	12 fewer per 1000 persons (from 18 fewer to 4 fewer) over lifetime	Very low

* Based on reference 16.
† Based on reference 14.
‡ Based on reference 13.

patterns lower in red or processed meat is associated with a very small absolute risk reduction in 9 major cardiometabolic and cancer outcomes (range, 1 fewer to 18 fewer events per 1000 persons), with no statistically significant differences for 21 additional outcomes observed (14). The tables in the Supplement (available at Annals .org) show the GRADE summary of findings for all systematic reviews on the harms and benefits associated with red and processed meat.

We summarize people's attitudes on eating meat below in a section on values and preferences. In short, omnivores enjoy eating meat and consider it an essential component of a healthy diet. There is also evidence of possible health benefits of omnivorous versus vegetarian diets on such outcomes as muscle development and anemia (34, 35), but we did not systematically review this literature.

Evidence Summary for Harms and Benefits for Processed Meat

No randomized trials differed by a gradient of 1 serving/wk for our target outcomes (15). With respect to cohorts addressing adverse cardiometabolic outcomes (10 cohort studies with 778 000 participants providing dose–response meta-analysis), we found low- to very low-certainty evidence that decreased intake of processed meat was associated with a very small reduced risk for major morbid cardiometabolic outcomes, including all-cause mortality, cardiovascular mortality, stroke, myocardial infarction, and type 2 diabetes (range, 1 fewer to 12 fewer events per 1000 persons with a decrease of 3 servings/wk), with no statistically significant difference in 1 additional outcome (cardiovascular disease) (16). For cohort studies addressing adverse cancer outcomes (31 cohorts with 3.5 million participants providing data for our dose–response analysis), we also found low- to very low-certainty evidence that a decreased intake of processed meat was associated with a very small absolute risk reduction in overall lifetime cancer mortality; prostate cancer mortality; and the incidence of esophageal, colorectal, and breast cancer (range, 1 fewer to 8 fewer events per 1000 persons with a decrease of 3 servings/wk), with no statistically significant differences in incidence or mortality for 12 additional cancer outcomes (colorectal, gastric, and pancreatic cancer mortality; overall, endometrial, gastric, hepatic, small intestinal, oral, ovarian, pancreatic, and prostate cancer incidence) (13). For cohort studies assessing dietary patterns (70 cohort studies with over 6 million participants), although statistically significant we found low- to very low-certainty evidence that adherence to dietary patterns lower in red or processed meat was associated with a very small absolute risk reduction in 9 major cardiometabolic and cancer outcomes (range, 1 fewer to 18 fewer events per 1000 persons), with no statistically significant differences for 21 additional outcomes observed (14). Again, we assessed the risk for adverse cardiometabolic outcomes on the basis of an average of 10.8 years follow-up, and adverse cancer outcomes over a lifetime.

In our assessment of causal inferences on unprocessed red meat and processed meat and adverse health outcomes, we found that the absolute effect estimates for red meat and processed meat intake (13, 16) were smaller than those from dietary pattern estimates (14), indicating that meat consumption is unlikely to be a causal factor of adverse health outcomes (Table 1). We anticipated that if unprocessed red meat or processed meat was indeed a causal factor in raising the risk for adverse outcomes, the observed association between unprocessed red and processed meat and adverse outcomes would be greater in studies directly addressing the lowest versus highest intake of unprocessed red or processed meat versus studies in which meat was only one component of a dietary pattern (7, 22). Using our findings, in our assessment of the certainty of evidence, we did not rate up for dose-response, given the potential for residual confounding (36). The tables in the Supplement (available at Annals .org) show the GRADE summary of findings.

Evidence Summary of Health-Related Values and Preferences for Meat

Our systematic review on health-related values and preferences yielded 54 articles from Australia, Canada,

Europe, and the United States, including 41 quantitative and 13 qualitative studies (17). Omnivores reported enjoying eating meat, considered meat an essential component of a healthy diet, and often felt they had limited culinary skills to prepare satisfactory meals without meat. Participants tended to be unwilling to change their meat consumption. The certainty of evidence was low for "reasons for meat consumption" and low for "willingness to reduce meat consumption" in the face of undesirable health effects, owing to issues of risk of bias (for example, unvalidated surveys), imprecision (small number of participants in qualitative studies), and indirectness (failure to specifically ask about the health benefits that would motivate a reduction in red or processed meat consumption) (Table 2).

Rationale for Recommendations for Red Meat and Processed Meat

The rationale for our recommendation to continue rather than reduce consumption of unprocessed red meat or processed meat is based on the following factors. First, the certainty of evidence for the potential adverse health outcomes associated with meat consumption was low to very low (13–16), supported by the similar effect estimates for red meat and processed meat consumption from dietary pattern studies as from studies directly addressing red meat and processed meat intake (13, 14, 16). Second, there was a very small and often trivial absolute risk reduction based on a realistic decrease of 3 servings of red or processed meat per week. Third, if the very small exposure effect is true, given peoples' attachment to their meat-based diet (17), the associated risk reduction is not likely to provide sufficient motivation to reduce consumption of red meat or processed meat in fully informed individuals, and the weak, rather than strong, recommendation is based on the large variability in peoples' values and preferences related to meat (17). Finally, the panel focused exclusively on health outcomes associated with meat and did not consider animal welfare and environmental issues. Taken together, these observations warrant a weak recommendation to continue current levels of red meat and processed meat consumption.

Table 2. Summary of Findings for Health-related Values and Preferences*

Outcomes	Studies (Participants), *n (n)*	Certainty of Evidence	Plain-Language Summary
Reasons for meat consumption	38 quantitative studies (62 963)	Low (rated down for risk of bias and indirectness)	Most omnivores were highly attached to their meat. Men had a more positive attitude than women toward meat consumption. Elderly omnivores were generally concerned about health with respect to their food choices. All vegetarians/low meat consumers reported health as one of the main reasons for not eating meat.
	10 qualitative studies (419)	Low (rated down for risk of bias, indirectness, and imprecision)	Most omnivores are highly attached to their meat consumption. Elderly omnivores believed that aging is associated with a decline in food intake. For many vegetarians, health concerns were the primary motivation to stop eating meat.
Willingness to change meat consumption in the face of undesirable health effects	5 quantitative studies (8983)	Low (rated down for risk of bias and indirectness)	Most omnivores reported low willingness to reduce meat consumption. In general, participants reported an overall mistrust related to the given information. Many participants believed that the presence of additives used in the production process was the real health problem rather than red meat consumption itself. Many participants already reduced their meat consumption in the past and did not plan any further changes.
	4 qualitative studies (616)	Low (rated down for risk of bias, indirectness, and imprecision)	Most omnivores reported low willingness to reduce meat consumption. Omnivores were concerned with reducing meat consumption because they perceived meat as an important component of a healthy diet, they enjoyed eating meat, and they believed they needed protein and the enjoyment of eating meat. Some omnivores believed they only ate small quantities of meat and did not need to reduce it (more often this referred to reducing red meat than all types of meat), and some believed they already reduced their meat consumption in the past. Some omnivores believed that the consequences of meat consumption were trivial compared with other behaviors (e.g., smoking tobacco). Some omnivores did not trust the available scientific information.

* Based on reference 17.

Other Considerations

The panel judged that although for some people in some circumstances, issues of cost, acceptability, feasibility, and equity may be relevant, these issues were not major considerations in making their judgments. Considerations of animal welfare, and particularly of environmental impact, will certainly be important to some individuals; the latter might be of particular importance from a societal perspective (37–41). The panel, at the outset, decided that issues of animal welfare and potential environmental impact were outside the scope of this guideline.

DISCUSSION

We developed recommendations for unprocessed red meat and processed meat by following the NutriRECS guideline development process, which adheres to the Institute of Medicine and GRADE working group standards. On the basis of 4 systematic reviews assessing the harms and benefits associated with red meat and processed meat consumption and 1 systematic review assessing people's health-related values and preferences on meat consumption, we suggest that individuals continue their current consumption of both unprocessed red meat and processed meat (both weak recommendations, low-certainty evidence).

Our weak recommendation that people continue their current meat consumption highlights both the uncertainty associated with possible harmful effects and the very small magnitude of effect, even if the best estimates represent true causation, which we believe to be implausible. Despite our findings from our assessment of intake studies versus dietary pattern studies suggesting that unprocessed red meat and processed meat are unlikely to be causal factors for adverse health outcomes (13, 14, 16), this does not preclude the possibility that meat has a very small causal effect. Taken together with other potential causal factors (for example, such preservatives as sodium, nitrates, and nitrites) (42) among dietary patterns with very small effects, this may explain the larger reductions among dietary patterns high in red meat and processed meat (14). The guideline panel's assessment was based on the available evidence regarding values and preferences suggesting that the majority of individuals, when faced with a very small and uncertain absolute risk reduction in cardiometabolic and cancer outcomes, would choose to continue their current meat consumption. People considering a decrease in their meat consumption should be aware of this evidence.

Our analysis has several strengths. We conducted 5 separate rigorous systematic reviews addressing both evidence from randomized trials and observational studies regarding the impact of unprocessed red meat and processed meat on cardiovascular and cancer outcomes (13–16), and community values and preferences regarding red meat and processed meat consumption (17). By using the GRADE approach, our reviews explicitly addressed the uncertainty of the underlying evidence. We present results focusing on absolute estimates of effects associated with realistic decreases in meat consumption of 3 servings per week (**Tables 4** through **7** in the **Supplement**), and these estimates informed our recommendations. Our panel included nutrition content experts, methodologists, health care practitioners, and members of the public, and we minimized conflicts of interest by prescreening panel members for financial, intellectual, and personal conflicts of interest and providing a full account of potential competing interests.

Our guideline also has limitations. We considered issues of animal welfare and potential environmental impact to be outside the scope of our recommendations. These guidelines may therefore be of limited relevance to individuals for whom these issues are of major importance. Related to this, we took an individual rather than a societal perspective. Decision makers considering broader environmental issues may reasonably consider evidence regarding the possible contribution of meat consumption to global warming and suggest policies limiting meat consumption on that basis.

Regarding the uncertainty of the evidence, randomized trials were limited by the small differences in meat consumption between the intervention and control groups, whereas observational studies were limited in the accuracy of dietary measurement and possible residual confounding related both to aspects of diet other than red meat and processed meat consumption and nondietary confounders, making decisions regarding meat consumption particularly value- and preference-dependent. With respect to our review on dietary patterns, studies did not typically report data separately for red and processed meat. Moreover, although all dietary patterns discriminated between participants with low and high red and processed meat intake, other food and nutrient characteristics of dietary patterns varied widely across studies (14). Evidence was also limited in that we found information insufficient to conduct planned subgroup analyses regarding the method of meat preparation (for example, grilling versus boiling) in terms of possible carcinogenic compounds from grilling, such as polycyclic aromatic hydrocarbons and heterocyclic amines (43). Finally, our panel was not unanimous in its recommendation: Three of the 14 panel members favored a weak recommendation in favor of decreasing red meat consumption.

As noted in our introduction, other dietary guidelines and position statements suggest limiting consumption of red and processed meat because of the reported association with cancer (1, 2, 44–46). There are 3 major explanations for the discrepancy between these guidelines and ours. First, other guidelines have not used the GRADE approach for rating certainty of evidence that highlight the low or very low certainty of evidence to support the potential causal nature of the association between meat consumption and health outcomes. As a result, we are less convinced of meat consumption as a cause of cancer. Because of the likelihood of residual confounding (that is, confounding that exists after adjustment for known prognostic factors)

the GRADE approach we used for assessing causation considers that, in the absence of a large effect or a compelling dose–response gradient, observational studies provide only low- or very low-certainty evidence for causation (47, 48). Second, even if one assumes causation, other guidelines have not calculated, or if calculated have not highlighted, the very small magnitude of the absolute adverse effects over long periods associated with meat consumption. Third, other guidelines have paid little or no attention to the reasons people eat meat, and the extent to which they would choose to reduce meat consumption given small and uncertain health benefits. Indeed, no prior dietary guideline has attended with care to evidence bearing on values and preferences, and in particular has not conducted a systematic review addressing the issue.

Nutritional guidelines are challenging because each potential source of evidence has substantial limitations. Randomized trials are limited by sample size, duration of follow-up, and the difficulties participants have in adhering to prescribed diets. These limitations make showing an intervention effect very challenging. Observational studies are limited in the inevitable residual confounding (unmeasured differences in prognosis that remain after adjusted analyses). These limitations in randomized trials and observational studies are evident in studies addressing meat consumption and health outcomes. Studies focusing on intermediate outcomes (such as cholesterol and triglyceride levels) have additional limitations, in that changes in biomarkers often fail to deliver the anticipated benefits in patient-important health outcomes. Therefore, our reviews focused only on those outcomes important to patients. Nutritional recommendations must, therefore, acknowledge the low-certainty evidence and avoid strong "just do it" recommendations that can, as evidenced by the many low-fat recommendations worldwide (9, 12, 49), be very misleading.

In terms of how to interpret our weak recommendation, it indicates that the panel believed that for the majority of individuals, the desirable effects (a potential lowered risk for cancer and cardiometabolic outcomes) associated with reducing meat consumption probably do not outweigh the undesirable effects (impact on quality of life, burden of modifying cultural and personal meal preparation and eating habits). The weak recommendation reflects the panel's awareness that values and preferences differ widely, and that as a result, a minority of fully informed individuals will choose to reduce meat consumption.

Our studies have implications for future research. Generating higher-certainty evidence regarding the impact of red meat and processed meat on health outcomes would be, were it possible, both desirable and important. It may not, however, be possible. Randomized trials will always face challenges with participants complying with diets that differ sufficiently in meat consumption, adhering to these diets for very long periods, and being available for follow-up over these long periods (12). These challenges are all the more formidable because results of observational studies may well represent the upper boundary of causal effects of meat consumption on adverse health outcomes, and the estimated effects are very small. Observational studies will continue to be limited by challenges of accurate measurement of diet, the precise and accurate measurement of known confounders (50), and the likelihood of residual confounding after adjusted analyses (13, 14, 16).

This assessment may be excessively pessimistic; indeed, we hope that is the case. What is certain is that generating higher-quality evidence regarding the magnitude of any causal effect of meat consumption on health outcomes will test the ingenuity and imagination of health science investigators.

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Reproducible Research Statement: *Study protocol:* Available at PROSPERO (www.crd.york.ac.uk/prospero/) (CRD 42017074074). *Statistical code and data set:* Available upon request from Dr. Johnston (e-mail, bjohnston@dal.ca).

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Appendix Table. Summary of Panelists' Potential Conflicts of Interest

Panel Member	Role	Financial Conflicts	Intellectual Conflicts	Other Relevant Disclosures
Pablo Alonso-Coello	Voting panel member; methodologist	No	No	Consumes 3 to 4 servings of both red or processed meat per week
Malgorzata Bala	Voting panel member; methodologist	No	No	Consumes 0.5 serving of both red or processed meat per week
Carlos Brotons	Voting panel member; primary care physician	No	No	Consumes 1 to 2 servings of both red or processed meat per week
Faiz Bhatia	Voting panel member; nonmedical public-partner	No	No	Consumes 2 to 3 servings of both red or processed meat per week; does not eat pork
Russell de Souza	Voting panel member; nutrition epidemiologist	No	No	Consumes 3 to 4 servings of red or processed meat per week
Susan Fairweather-Taitt	Voting panel member; human nutritionist	No	No	Consumes 2 to 3 servings of red meat per week and 1 to 2 servings of processed meat per month
Gordon Guyatt	Chair of panel; voting panel member; general internist; methodologist	No	No	Pescatarian; does not consume red or processed meat
Bradley Johnston	Guideline methods editor; voting panel member; methodologist	No	No	Consumes 1 to 2 servings of both red or processed meat per week
Catherine Marshall	Voting panel member; nonmedical public-partner; guideline consultant	No	No	Consumes 3 to 4 servings of both red or processed meat per week
Joerg Meerpohl	Voting panel member; pediatrician; methodologist	No	No	Consumes 3 to 5 servings of both red or processed meat per week
Chirag Patel	Voting panel member; bioinformatician	No	No	Consumes 0.5 serving of both red or processed meat per week
Patrick Stover	Voting panel member; basic nutrition scientist	No	No	Consumes 2 to 3 servings of both red or processed meat per week
Grzegorz Wójcik	Voting panel member; nonmedical public-partner	No	No	Consumes 3 to 4 servings of both red or processed meat per week
Dena Zeraatkar	Voting panel member; PhD student; methodologist	No	No	Consumes 6 to 7 servings of red meat per week