

Non-communicable disease risk associated with red and processed meat consumption—magnitude, certainty, and contextuality of risk?

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Implications

- Mean global intakes per person of red and processed meats are 51 and 17 g/day respectively. Consumption is lowest in South Asia (7 and 3 g/d), and highest in Central Europe/Asia (114 and 54 g/d).
- While some researchers claim that red meat consumption is intrinsically harmful, the evidence does not support this being the case where intakes are below 75 and 20 g/d, respectively.
- Even beyond these intake levels, only small increases in relative risks are reported (<25%), there is little to no effect on absolute risk, and the certainty of evidence remains low to very low based on the best available summary evidence.
- Importantly the relationship is not necessarily causal - when meat consumption is part of healthy dietary

patterns, harmful associations tend to disappear, suggesting that risk is more likely to be contingent on the dietary context rather than meat itself.

Key words: certainty, meat, mortality, noncommunicable diseases, public health, risk

Introduction

Despite being a foundational part of human evolutionary diets and a source of high-quality protein and bioavailable micronutrients in a global context of nutrient insecurity (see elsewhere in this Special Issue; Leroy *et al.*, 2023), the consumption of red and processed meats is nowadays increasingly discouraged by a vocal group of scientists and organizations. The rationale for this is based on a purported association of their intake with an increased risk of obesity and non-communicable diseases, such as myocardial infarction, stroke, diabetes, and particular cancers. As for most foods, one could assume that there may be compelling evidence for optimal intake levels, balancing the potential benefits and harms of meat as a human food. Such an optimum, however, is difficult to estimate, as the evidence is highly contextual and complex, or even conceptually incorrect to begin with.

A first factor complicating the reliable and universal estimation of optimal intake levels has to do with interpersonal variability, based on differences in genetics, sex, age group,

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health status, socio-economic background, etc. For instance, whereas some population groups with relatively higher iron requirements may benefit from more meat, others may be prone to iron accumulation and overload. A second problem is that optimal intake levels are defined by the background diet and the lifestyle of an individual. Assuming that meat would indeed have to be considered as a health *hazard*, as proclaimed by the IARC (Bouvard *et al.*, 2015), despite controversy (Klurfeld, 2018), this still leaves the question of its role in disease *risk*. Appropriate risk assessment requires considering the frequency and amount of meat intake, preparation method, and interactions with other compounds in the diet. There is considerable scientific debate over the certainty of the evidence associating intake with morbidity and mortality based on what has been provided by many nutritional epidemiologists vis-à-vis the absence of long-term randomized trials of red and processed meat intake and clinical health outcomes. All this makes it difficult to establish an upper limit for safe consumption. Whereas some researchers go as far as claiming that *no* amount is harmless, others oppose this assumption (Klurfeld, 2018; Johnston *et al.*, 2019; Leroy and Cofnas, 2020; Stanton *et al.*, 2022).

Taken together, the following issues need to be addressed: 1) what are the methods and limitations of epidemiological research, 2) how can we evaluate the certainty of the underpinning evidence, 3) what can be inferred from the current data with respect to safe or optimal intake levels, 4) what is the role of exposure in the framework of risk assessment, and 5) how can we arrive at a trustworthy message, by contextualizing these findings and relating them to the various benefits of meat (products), including contributions to food culture and nutrient security?

Methods and Limitations of Nutritional Epidemiology

Reporting the absolute magnitude of risk

Patients, members of the public, and health care professionals should rely on the best available evidence to guide their lifestyle and health care decisions. Typically, the standard for making causal connections between an exposure and the risk of desirable (benefits) and undesirable (harms) health outcomes is to conduct robust randomized controlled trials of the putative causal factor and to measure clinical outcome events. For optimal decision-making, clinical trial evidence should then be summarized using high-quality, up-to-date systematic review, and meta-analysis methodology. In the absence of long-term trials of red and processed meats as isolated dietary interventions for health outcomes, dietary guidelines and policies can be informed by high-quality systematic reviews with meta-analysis of the evidence originating from observational studies. Informed decision-making requires knowledge of the magnitude of the potential benefits and adverse health outcomes—ranging from trivial to large—and the corresponding certainty of evidence for all important health outcomes. These outcomes include quality of life, mortality, and major morbidity (e.g., stroke, cancer incidence). Investigators may express the impact

of an intervention or exposure for dichotomous outcomes in either relative terms (i.e., odds ratio, relative risk, or hazard ratio) or in absolute terms (risk difference, also known as absolute risk reduction or increase, or as the number needed to treat or harm). There are upsides, as well as downsides, to the presentation of exposure or treatment effects using either approach (Alonso-Coello *et al.*, 2016).

Exclusive use of relative risk estimates can be highly misleading, since the relative risk typically yields larger, often much larger, treatment/exposure effects than if absolute risk is used. For example, a relative risk of 0.50 equivalent to 50% relative risk reduction can, when based on a low baseline risk, mean an absolute risk reduction of a mere 1%; i.e., from 2% to 1%. This difference not only influences the judgment of lay persons and leads to hyperbolic public discourse (cf. Leroy *et al.*, 2018), but also affects clinicians and policymakers. Relative effect estimates, however, are usually—though not always—similar across populations and subgroups, whereas absolute effect estimates typically vary with the baseline risk. Therefore, expressing a treatment/exposure effect estimate as only an absolute risk is also misleading, because it will under- or overestimate the effect for patients at high or low baseline risk, respectively. As a result, in the context of conducting and using meta-analysis for decision-making, one may need to apply the relative effect estimate to a range of baseline risks typically seen in the population of interest (Guyatt *et al.*, 2013). This may require ascertaining clinically identifiable risk groups and clarifying the period over which the associated baseline risk applies, ideally based on the largest available cohort study or a summary of cohort or controlled studies that best represent one's population of interest, as was done in the recent NutriRECS guideline on red and processed meats (Johnston *et al.*, 2019). To optimize data interpretation, systematic reviews and meta-analyses should always present the estimates of absolute risks in intervention/exposure and control groups, alongside the corresponding relative risks, together with the 95% confidence intervals for all important desirable and undesirable outcomes. Cochrane, the Joanna Briggs Institute, and the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) system all endorse and require this approach to data presentation.

Research methodologies and their limitations

The above-mentioned treatment or exposure effects, which lead to risk estimates, can be obtained from a set of different study designs. The latter are usually categorized as observational studies, e.g., cross-sectional, case-control, and cohort studies, and interventional studies with either humans or animals. It is important to emphasize that observational studies on their own very rarely allow the inference of causal relationships. Causal relationships from observational data should be supported by large exposure effects, e.g., relative risk > 2.0, and additional evidence based on intervention studies, plausible mechanisms, clear dose–response relationships, etc., as also echoed in the Bradford Hill criteria (Hill *et al.*, 2022). For good practice, the certainty of estimates for each target outcome using

the GRADE system should be considered when systematically evaluating a body of evidence (see below). When the certainty is low, authors should avoid causal inferences or strong public health recommendations (Schünemann *et al.*, 2011).

The limitations that are inherent to nutritional epidemiology can be illustrated by the case of the IARC Monograph Working Group evaluation of the carcinogenicity of red and processed meat (Bouvard *et al.*, 2015), and the criticism related to this procedure (Klurfeld, 2018). According to IARC methodology, most weight was given to prospective cohort studies, supported by case-control studies and information from mechanistic studies. It was concluded that red and processed meat consumption was not a hazard for almost all cancers, except for colorectal cancer. The hazard classification of the latter was primarily based on positive associations in 7 of 14 cohort studies on red meat and 12 of 18 cohort studies on processed meat. Importantly, it was also concluded that chance, bias, and confounding could not be ruled out with the same degree of confidence for the data on red meat compared to processed meats. Red and processed meats were nonetheless classified as hazards for colorectal cancer from a precautionary principle, although this was done without further assessment of risk (cf. “Contextuality and risk assessment”).

The focus on observational research by IARC and similar organizations relates to the fact that human intervention studies of a size and follow-up period sufficient to measure people-important health outcomes of noncommunicable diseases are incredibly challenging and costly. Therefore, if data from intervention studies is available, this typically comes from short-term human intervention studies, in which biomarkers are measured as proxies, or from animal studies. In human intervention studies, the effects on biomarkers are small or neutral, and sometimes even benign, for example, in the case of red meat and glycemic control and inflammatory biomarkers (O’Connor *et al.*, 2021) or cardiovascular risk factors (O’Connor *et al.*, 2017; Zeraatkar *et al.*, 2019). Animal studies suffer from an often nonrepresentative dietary context and from problems of extrapolation (issues of indirectness according to GRADE). Because of such limitations, the evidence to confirm a mechanistic link between the (moderate) intake of unprocessed red meat as part of a healthy dietary pattern and colorectal cancer *risk* should be considered insufficient (Turner and Loyd, 2017; Kruger and Zhou, 2018; Johnston *et al.*, 2019; Lescinsky *et al.*, 2022), and similarly so for cardiovascular diseases (Johnston *et al.*, 2019; Mente *et al.*, 2020; Delgado *et al.*, 2021; Lescinsky *et al.*, 2022).

Certainty of evidence and strength of recommendations

In the domain of life sciences, the reliability of evidence varies widely across studies. Making health recommendations, either strong or weak, needs to be based on a common, rigorous, and transparent evaluation of the *certainty* of the evidence for all health outcomes. The current standard in guideline development is the GRADE system. The latter is used by >110

organizations worldwide (e.g., Cochrane, the World Health Organization, and the Centers for Disease Control) and comprehensively and transparently allows for rating the certainty of evidence based on systematic review(s) of the literature. As a common, robust, transparent system, GRADE enables users of the evidence to both reproduce the evidence and agree or disagree with the published outputs. For a given research question, GRADE categorizes certainty using four categories: high, moderate, low, or very low for each target outcome (Table 1). A systematic review of the evidence starts as “high” certainty evidence when it is based on randomized clinical trials and “low” certainty evidence when based on observational studies, e.g., cohort and case-control studies.

Systematic reviews of randomized trials start at high certainty evidence because they offer a high level of control for confounding variables—or outside “third” variables that may affect the results. Yet, reviews of such trials can be rated down for issues of risk of bias, indirectness, inconsistency, imprecision, or risk of publication bias. In contrast, systematic reviews of observational studies are considered low certainty evidence because they are not conducted in a controlled setting, rely largely on self-reporting, and are at high risk of confounding, even after adjusting for prognostic variables. Their certainty can however be rated up if there is a convincing large effect of treatment or exposure that residual confounding alone is unlikely to explain (depending on the direction of effect, this corresponds with a relative risk > 2.0 or < 0.5, both representing a 2-fold risk compared to control; Guyatt *et al.*, 2011), or if there is evidence of a credible dose–response gradient (Zeraatkar and Johnston 2019).

Using GRADE, high or moderate certainty evidence may result in strong “just do it” recommendations if the benefits clearly outweigh harms and burdens (e.g., costs, inconvenience) or vice-versa. Low-certainty evidence leaves uncertainty about the impact of exposure, resulting in weak (conditional) recommendations. The latter call for shared decision-making, wherein potential benefits, harms, and burdens are discussed between decision-makers, such as individual patients, families, and health care providers, so that individuals can make their own value- and preference-sensitive decisions.

While GRADE guidance is based on over 35 published papers, users of the GRADE system may differ in their training

Table 1. Overview of the certainty level as applied in the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) system

Certainty level	Implication
High	Further research is very unlikely to change certainty in the estimate of effect
Moderate	Further research is likely to have an important impact on certainty in the estimate of effect and may change the estimate
Low	Further research is very likely to have an important impact on certainty in the estimate of effect and is likely to change the estimate
Very low	Any estimate of effect is very uncertain

and understanding. One of the great merits of the system is that it requires transparency. That is, footnotes with justifications are required when making decisions on the certainty of evidence for each outcome, and when determining the strength of recommendations. Given the necessity to be transparent with all decisions, different researchers or groups of researchers may arrive at different ratings.

When investigators use the same standards accompanied by transparent decisions on the certainty of evidence and strength of recommendation, such as GRADE, individuals and society are better equipped to make optimally informed decisions. If an individual at cardiovascular risk wants to know the evidence for statins vs. regular exercise vs. reducing meat and the risk of stroke, a common standard supports decision-making. “The most vocal nutritional epidemiologists” (dixit Vernooij *et al.*, 2021), however, claim that an exception should be made for the nutritional sciences, involving grading systems with a higher tolerance for low-certainty evidence (as in the NutriGrade or HEALM system; Qian *et al.*, 2020). The rationale for this claim relates mostly to the fact that randomized trials are difficult and expensive to perform in nutrition science, thus rejecting the premise that standards should be identical and, perhaps more importantly, sufficiently robust across all health fields (Vernooij *et al.*, 2021).

To sum up, for trustworthy patient and population dietary recommendations, a coherent, common, and reliable framework is needed for transparent evaluation of 1) the magnitude of relative and absolute estimates of effect, and (2) the *certainty* of evidence for each important health outcome (Vernooij *et al.*, 2021)

What do the large summary studies say concerning the risks and optimal intakes of red and processed meats?

Using Cochrane and GRADE methods, the NutriRECS Consortium recently reported on four parallel systematic reviews of all relevant randomized trials and cohort studies (Johnston *et al.*, 2019). The consortium reported finding only low- or very low-certainty evidence that diets substantially lower in either red meat or processed meats could have any appreciable impact on the risks of important cardiometabolic outcomes (myocardial infarction, stroke, and type-2 diabetes), and for cancer incidence and mortality. Hence, the panel made a weak recommendation that most “adults should continue their current red and processed meat consumption”, thus encouraging shared decision-making.

Despite these findings and recommendations, some recent publications strongly advocate dramatic reductions and/or exclusion of red and processed meats from the human diet. The EAT-Lancet Commission, for instance, recommended a maximum combined intake of red and processed meats of 14 g/d (Willett *et al.*, 2019), about one 100 g serving per week. The Global Burden of Disease (GBD) 2019 Risk Factors Study and the Lancet Countdown on Health and Climate Change both recently reported that approximately 900,000 annual deaths globally were caused by consumption of unprocessed red meat (Murray *et al.*, 2020; Watts *et al.*, 2021). Stylianou *et al.* (2021)

have claimed that each single serving of a Frankfurter sandwich resulted in 35 min of life lost, and Fadnes *et al.* (2022) estimated that changing from a typical Western diet, which they (incorrectly) claimed included 100 g/d and 50 g/d of unprocessed red meat and processed meats, respectively, to a diet which totally excludes these foods, would increase life expectancy by three years for women and by four years for men.

Modeled analyses and estimates by Murray *et al.* (2020), Watts *et al.* (2021), and others, are dependent on two key assumptions; 1) that the theoretical minimum risk exposure levels (TMREL) or optimal intakes of red and processed meats are zero; and 2) that risk rises sharply even with moderate consumption of red and processed meats. However, these assumptions do not appear to be consistent with the results from the large epidemiology studies that have evaluated the relationships of red and processed meats with total mortality (Figures 1 and 2).

For unprocessed red meat, an intake range of 0 to 25 g/d is not associated with risk in any of the large cohort studies of unselected populations (Figure 1). At higher intake levels, results remain uncertain and variable, being contingent on the study. Two studies, both from North America, reported small increases in relative risk (<15%) at 50 to 75 g/d, while the single global study (the Prospective Urban Rural Epidemiology Study, covering 21 countries from five continents), two European studies, four Asian studies, and one North American study either showed no increased risk at any intake or only demonstrated increased risk at intakes above 75 g/d. For processed meats (Figure 2), increased relative risks were reported in most studies where intake exceeded 40g/d. At lower intakes (10 to 20 g/d), only studies from North America reported relative risks above 1.

The above seems to suggest that there is something different about the risk estimates captured in North American study setups. Typically, North American studies report that the subjects that consumed more meat were also more likely to be current smokers and to have lower education and physical activity levels, a higher body mass index and daily intake of energy, and lower fruit, vegetable, and fiber intakes—hence, residual confounding by these factors is very possible. None of the North American studies adjusted the unprocessed red meat analyses for processed meat, nor vice versa. Surprisingly, no study to date, has adjusted for ultra-processed food intake, despite ultra-processed foods accounting for >50% of the calories in the diets of North Americans (Martínez Steele *et al.*, 2016). Ultra-processed foods are formulations consisting mostly of cheap industrial sources of energy and nutrients, typically with multiple additives, using a series of processes. They contain little if any intact food, are often nutrient-unbalanced, and increasingly associated with diet-related noncommunicable diseases (Monteiro *et al.*, 2018).

Overall, it appears that causality claims related to meat intake need to be closely scrutinized using multiple methods (Hill *et al.*, 2022) and that there is no robust reason to assume a TMREL for unprocessed red meat of zero or even below the range of 50 to 75 g/d, equivalent to 3.5 to 5.25 servings/wk. For processed meats, the TMREL might be at least 10 to 20 g/d (and arguably even 40 g/d), equivalent to 1 to 3 servings/wk. Even if such low TMRELs could be firmly established, then

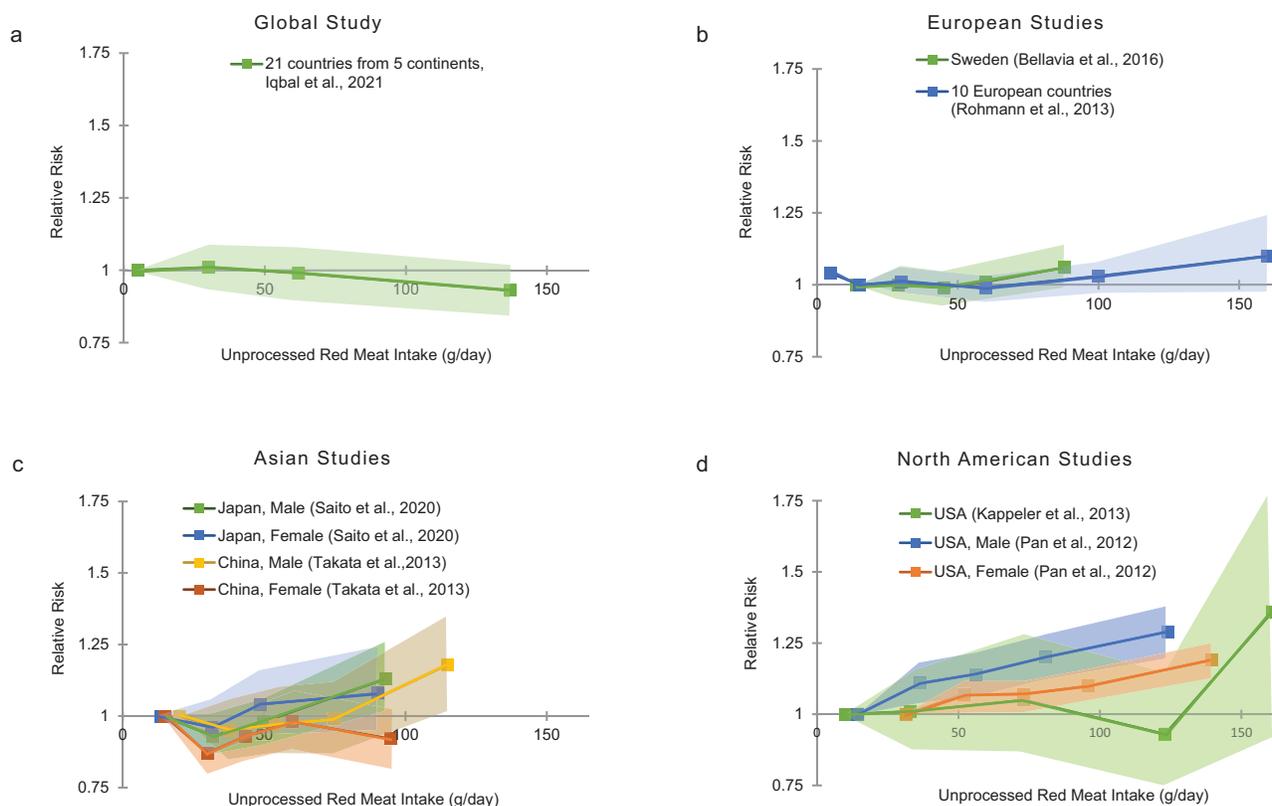


Figure 1. Relative risk estimates for all-cause mortality from all large, published cohort studies of unselected populations (recording at least 2000 deaths) by levels of unprocessed red meat intake. Relative risks and 95% confidence intervals (shaded areas) are plotted on the y-axes, and red meat intake (g/d) on the x-axes. Global, European, Asian, and North American studies are shown in panels a, b, c, and d, respectively. Regional location, gender, first author, and year of publication are indicated for each cohort study. Full reference details are provided in the [Supplementary Material](#).

these risks would still need to be offset against not consuming these foods, in view of increased nutrient deficiencies (as explained elsewhere in this Special Issue; [Leroy et al., 2023](#)). It is encouraging that Professor Christopher Murray, on behalf of the GBD Risk Factors Collaborators, in reply to [Stanton et al. \(2022\)](#), has acknowledged that the “setting of the red meat TMREL to zero in the GBD 2019 analysis was not correct”, and thereby confirmed that the “estimates of attributable deaths for red meat will be reduced in all future GBD analyses” ([Murray, 2022](#)). The joint call from the Academy of Nutrition Sciences and the World Cancer Research Fund ([Gordon-Dseagu et al., 2022](#)) for further clarification, justification, or reconsideration of the TMREL of zero for unprocessed red meat selected by GBD in their latest estimates very likely ensures that correction of the errors in the GBD 2019 analysis will impact many other modeling studies ([Willett et al., 2019](#); [Stylianou et al., 2021](#); [Watts et al., 2021](#); [Fadnes et al., 2022](#)), especially if they currently do assume red and processed meats TMRELs of zero. Indeed, the GBD collaborators eventually published their systematic review of the health effects associated with consumption of unprocessed red meat, thereby concluding that the evidence for any increased risk in disease incidence or mortality is weak, and certainly insufficient to make strong or conclusive recommendations ([Lescinsky et al., 2022](#)). Furthermore, their analysis showed that the 95% uncertainty

interval for the TMREL for unprocessed red meat is very wide, from 0 to 200 g/d.

Revising the TMRELs of red meat and processed meats from 0 g/d to more reasonable yet still uncertain estimates as proposed here (e.g., 50 to 75 g/d and 10 to 20 g/d, respectively; also, to be validated by further research), puts a different perspective on the current consumption levels of these foods. The Global Dietary Database reported that the mean global intake per person of unprocessed red meat and processed meats in 2018 was 51 g/d and 17 g/d, respectively ([Miller et al., 2022](#)). Obviously, there is considerable regional variation in intakes—red and processed meat consumption are lowest in South Asia (7 and 3 g/d, respectively), intermediate in high-income countries including the USA and Western Europe (45 and 30 g/d), and highest in Central/Eastern Europe and Central Asia (114 and 54 g/d). Evidence-based estimates of optimal intakes of meat combined with accurate estimates of consumption patterns are of importance in the identification of populations with both lower and higher than optimal intakes, thereby facilitating the targeting of intervention, surveillance, and policy priorities relevant to both human and planetary health. However, it should be noted that the certainty in “optimal intakes” may remain low given the complexity of diet and lifestyle patterns, our environmental exome, and the limitations of our current methods of measurement, as discussed below.

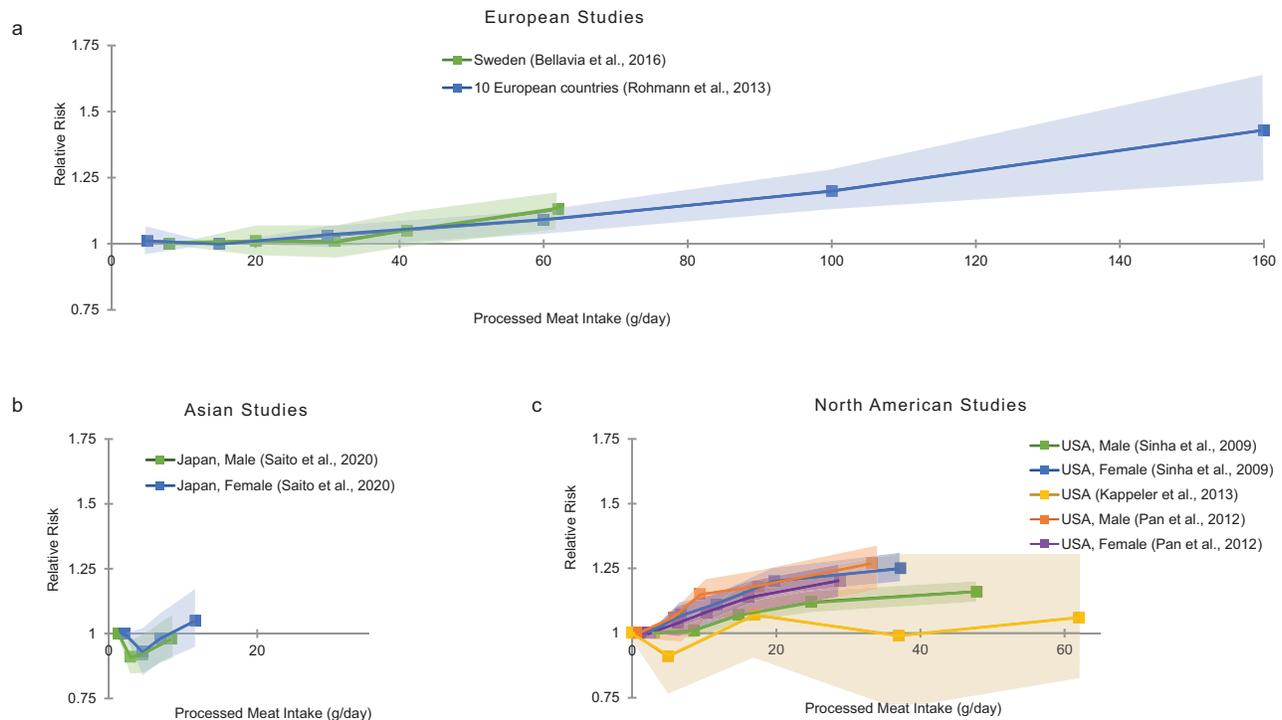


Figure 2. Relative risk estimates for all-cause mortality from all large, published cohort studies of unselected populations (recording at least 2000 deaths) by levels of processed red meat intake. Relative risks and 95% confidence intervals (shaded areas) are plotted on the y-axes, and processed meat intake (g/d) on the x-axes. European, Asian, and North American studies are shown in panels a, b, and c, respectively. Regional location, gender, first author, and year of publication are indicated for each cohort study. Full reference details are provided in the [Supplementary Material](#).

Contextuality and Risk Assessment

Red and processed meats are integral parts of many diets across the world and are typically consumed together with other foods in meals. Consequently, the digestion of meats and the subsequent effects on metabolism are affected by the meal and diet matrix, as well as by host factors and the gut microbiome (Van Hecke *et al.*, 2017). This tripartite is very complex and numerous interactions may occur. Co-consumption of vegetables and fruits, for instance, may be associated with reduced cancer risk estimates upon increased meat consumption, to the point of becoming neutral or potentially protective (e.g., Maximova *et al.*, 2020). Well-known confounding lifestyle factors are usually accounted for in observational studies by including these variables in the statistical models, thereby expecting that the risk estimates will be less biased. Residual confounding, however, is likely in nutritional epidemiology given the complexity of diets and lifestyles, and the limitations of statistical control for these relationships. One may therefore wonder if disease risk assessment of single food groups such as red and/or processed meat makes sense to begin with, and whether nutritional observational studies should not be restricted to dietary patterns (although “pattern” definition and measurement is also challenging). Because relative risks for meat tend to become mostly nonsignificant when controlling for known confounding factors, like those shown for the Women’s Health Initiative study cohorts (Zheng *et al.*, 2022), the higher chronic disease risks

associated with a relatively high meat consumption are arguably related to the overall dietary pattern, not the intake of red or processed meat as such (Johnston *et al.*, 2019; Zeraatkar & Johnston, 2019).

To further illustrate this, the association of heme iron intake with colorectal adenoma risk is likely mediated by the total dietary anti-oxidant capacity (Bastide *et al.*, 2016). This may relate to the fact that one of the main hypotheses for the red meat and colorectal cancer association is the lipid oxidation-promoting effect of heme iron. Dietary antioxidants, e.g., by using herbs and spices in meals, may potentially mitigate this effect, as shown in several types of studies (Van Hecke *et al.*, 2017). Additionally, an inhibitory effect of calcium has been demonstrated (Pierre *et al.*, 2013). In contrast, polyunsaturated fatty acids (abundantly present in vegetable oils) and refined sugars may increase heme iron-induced oxidation during food preparation and digestion (Van Hecke *et al.*, 2017). The formation of harmful oxidation compounds is, thus, the result of a complex dose- and matrix-dependent balance between oxidizable substrates and the activity of reducing compounds, and as such, it is simplistic to classify a single food or food compound as promoting or protecting in this context. This concern is especially valid when the doses of heme iron found in mixed meals for human consumption are compared to the much higher and unrealistic doses used in experimental studies (Turner and Lloyd, 2017).

Similarly, the degree of harmfulness of nitrite curing, a customary practice in meat processing for several reasons, is

likely contextual and its impact on health remains a matter of uncertainty due to gaps and inconsistencies in the evidence (Bedale *et al.*, 2016; Turner and Lloyd, 2007; Crowe *et al.*, 2019). Along the same line, it has become clear that the prevailing hypotheses for potential adverse effects of lean red meat consumption on cardiovascular diseases, i.e., saturated fatty acids, lipid oxidation, trimethylamine-N-oxide, lack support from experimental studies and conflict with the compositional characteristics of some so-called protective or neutral foods (Delgado *et al.*, 2021). This suggests that either long-held views on specific food-disease associations based on early observational studies must be revisited, or that these associations, if deemed to be causal, are a result of complex metabolic interactions that cannot be explained by a single mechanism. The latter further emphasizes that one should be cautious in blaming a single food or food compound for a negative health impact.

Conclusion

Regrettably, the scientific discussion on the potential associations between meat and noncommunicable diseases is often no longer a transparent assessment of the evidence, but is affected by agendas, including vested interests and ideologies (Rubin, 2020). It is nonetheless important to maintain sufficiently high standards of evidence within a coherent framework, to safeguard the robustness of dietary recommendations and policy. To meet this concern, the GRADE approach offers a comprehensive methodology for developing and presenting summaries of evidence, making use of standards that are identical across health fields. A convincing argument for departure from such standards is yet to be presented. Following from the evidence explained in this article, a reduction of meat intake below the current levels of consumption is not sufficiently supported to warrant public policy for health reasons. This especially tends to be the case when study quality improves (e.g., case-control *vs.* cohort studies *vs.* randomized clinical trials *vs.* robust systematic reviews with meta-analysis of all available evidence), when confounding is addressed to a higher degree, when results are presented as absolute estimates of effect and the certainty of evidence for the estimates is based on the GRADE approach, and—more generally—when red and processed meats are integrated in a healthy background diet. Based on the contextuality of the findings, dietary recommendations should focus on healthy meal patterns tailored to individual needs, rather than on specific foods, while noting that red meat (and food derived thereof) is a good source of (micro)nutrients that are not always readily available from other dietary options, in particular, from plant-sourced materials (see elsewhere in this Special Issue; Leroy *et al.*, 2023). Moreover, any health recommendation or dietary guideline arguing for a reduction of meat intake should consider that this may also lead to additional deaths and illnesses from iron-deficiency anemia, sarcopenia, and child and maternal malnutrition.

A more holistic, robust analysis of potential harms and benefits of red and processed meat consumption is required.

This relates to differences in interpersonal vulnerabilities and needs as well as to differences in dietary patterns and processing methods, which necessitate caution in the case of processed meats, if harsh curing, smoking, or heating treatments are used.

Supplementary Data

Supplementary data are available at *Animal Frontiers* online.

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Andrew Mente received his doctoral degree in Epidemiology from the University of Toronto. He is currently an Associate Professor in Health Research Methods at the Population Health Research Institute, McMaster University. His team conducted the largest ever epidemiologic study of sodium intake and blood pressure, cardiovascular disease risk, and mortality in the Prospective Urban Rural Epidemiology (PURE) study, a study of >100,000 individuals from 21 countries on five continents. Recently, Dr. Mente has co-led an investigation on the role of fats and carbohydrates in cardiovascular disease in PURE. He also has conducted numerous large systematic reviews of diet and cardiovascular disease.

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Literature Cited

Alonso-Coello, P., A. Carrasco-Labra, R. Brignardello-Petersen, I. Neumann, E.A. Akl, R.W. Vernooij, B.C. Johnston, X. Sun, M. Briel, J.W. Busse, et al. 2016. Systematic reviews experience major limitations in reporting absolute effects. *J. Clin. Epidemiol.* 72:16–26. doi:[10.1016/j.jclinepi.2015.11.002](https://doi.org/10.1016/j.jclinepi.2015.11.002)

Bastide, N., S. Morois, C. Cadeau, S. Kangas, M. Serafini, G. Gusto, L. Dossus, F.H. Pierre, F. Clavel-Chapelon, and M.-C. Boutron-Ruault. 2016. Heme iron intake, dietary antioxidant capacity, and risk of colorectal adenomas in a large cohort study of French women. *Cancer Epidemiol. Biomarkers Prev.* 25:640–647. doi:[10.1158/1055-9965.epi-15-0724](https://doi.org/10.1158/1055-9965.epi-15-0724)

Bedale, W., J.J. Sindelar, and A.L. Milkowski. 2016. Dietary nitrate and nitrite: benefits, risks, and evolving perceptions. *Meat Sci.* 120:85–92. doi:[10.1016/j.meatsci.2016.03.009](https://doi.org/10.1016/j.meatsci.2016.03.009)

Bouvard, V., D. Loomis, K.Z. Guyton, Y. Grosse, F.E. Ghissassi, L. Benbrahim-Tallaa, N. Guha, H. Mattock, K. Straif, and the IARC Monograph Working Group. 2015. Carcinogenicity of consumption of red and processed meat. *Lancet Oncol.* 16:1600. doi:[10.1016/S1470-2045\(15\)00444-1](https://doi.org/10.1016/S1470-2045(15)00444-1)

Crowe, W., C.T. Elliott, and B.D. Green. 2019. A review of the in vivo evidence investigating the role of nitrite exposure from processed meat consumption in the development of colorectal cancer. *Nutrients* 11:2673. doi:[10.3390/nu11112673](https://doi.org/10.3390/nu11112673)

Delgado, J., D. Ansorena, T. Van Hecke, I. Astiasarán, S. De Smet, and M. Estévez. 2021. Meat lipids, NaCl and carnitine: do they unveil the conundrum of the association between red and processed meat intake and cardiovascular diseases? *Meat Sci.* 171:108278. doi:[10.1016/j.meatsci.2020.108278](https://doi.org/10.1016/j.meatsci.2020.108278)

Fadnes, L.T., J.M. Økland, O.A. Haaland, and K.A. Johansson. 2022. Estimating impact of food choices on life expectancy: a modeling study. *PLoS Med.* 19:e1003889. doi:[10.1371/journal.pmed.1003889](https://doi.org/10.1371/journal.pmed.1003889)

Gordon-Dseagu, V.L.Z., M.J. Wiseman, K. Allen, J. Buttriss, and C. Williams. 2022. Troubling assumptions behind GBD 2019 on the health risks of red meat. *Lancet* 400:427–428. doi:[10.1016/s0140-6736\(22\)01283-1](https://doi.org/10.1016/s0140-6736(22)01283-1)

Guyatt, G.H., A.D. Oxman, N. Santesso, M. Helfand, G. Vist, R. Kunz, J. Brozek, S. Norris, J. Meerpohl, B. Djulbegovic, et al. 2013. GRADE guidelines: 12. Preparing summary of findings tables-binary outcomes. *J. Clin. Epidemiol.* 66:158–172. doi:[10.1016/j.jclinepi.2012.01.012](https://doi.org/10.1016/j.jclinepi.2012.01.012)

Guyatt, G.H., A.D. Oxman, S. Sultan, P. Glasziou, E.A. Akl, P. Alonso-Coello, D. Atkins, R. Kunz, J. Brozek, V. Montori, et al. 2011. GRADE guidelines: 9. Rating up the quality of evidence. *J. Clin. Epidemiol.* 64:1311–1316. doi:[10.1016/j.jclinepi.2011.06.004](https://doi.org/10.1016/j.jclinepi.2011.06.004)

Hill, E.R., L.E. O’Connor, Y. Wang, C.M. Clark, B.S. McGowan, M.R. Forman, and W.W. Campbell. 2022. Red and processed meat intakes and cardiovascular disease and type 2 diabetes mellitus: an umbrella systematic review and assessment of causal relations using Bradford Hill’s criteria. *Crit. Rev. Food Sci. Nutr.* doi:[10.1080/10408398.2022.2123778](https://doi.org/10.1080/10408398.2022.2123778) (in press)

Johnston, B.C., D. Zeraatkar, M.A. Han, R.W.M. Vernooij, C. Valli, R. El Dib, C. Marshall, P.J. Stover, S. Fairweather-Tait, G. Wójcik, et al. 2019. Unprocessed red meat and processed meat consumption: dietary guideline recommendations from the Nutritional Recommendations (NutriRECS) consortium. *Ann. Intern. Med.* 171:756–764. doi:[10.7326/M19-1621](https://doi.org/10.7326/M19-1621)

Klurfeld, D.M. 2018. What is the role of meat in a healthy diet? *Anim. Front.* 8:5–10. doi:[10.1093/af/vfy009](https://doi.org/10.1093/af/vfy009)

Kruger, C., and Y. Zhou. 2018. Red meat and colon cancer: a review of mechanistic evidence for heme in the context of risk assessment methodology. *Food Chem. Toxicol.* 118:131–153. doi:[10.1016/j.fct.2018.04.048](https://doi.org/10.1016/j.fct.2018.04.048)

Leroy, F., M. Brengman, W. Ryckbosch, and P. Scholliers. 2018. Meat in the post-truth era: mass media discourses on health and disease in the attention economy. *Appetite* 125:345–355. doi:[10.1016/j.appet.2018.02.028](https://doi.org/10.1016/j.appet.2018.02.028)

Leroy, F., and N. Cofnas. 2020. Should dietary guidelines recommend low red meat intake? *Crit. Rev. Food Sci. Nutr.* 60:2763–2772. doi:[10.1080/10408398.2019.1657063](https://doi.org/10.1080/10408398.2019.1657063)

Leroy, F., N. Smith, A.T. Adesogan, T. Beal, L. Iannotti, P.J. Moughan, and N. Mann. 2023. The role of meat in the human diet: evolutionary aspects and nutritional value. *Anim. Front.* (in press)

Lescinsky, H., A. Afshin, C. Ashbaugh, C. Bisignano, M. Brauer, G. Ferrara, S.I. Hay, J. He, V. Iannucci, L.B. Marczak, et al. 2022. Health effects associated with consumption of unprocessed red meat: a Burden of Proof study. *Nat. Med.* 28:2075–2082. doi:[10.1038/s41591-022-01968-z](https://doi.org/10.1038/s41591-022-01968-z)

Martínez Steele, E., L.G. Baraldi, M.L.D.C. Louzada, J. Moubarac, D. Mozaffarian, and C.A. Monteiro. 2016. Ultra-processed foods and added sugars in the US diet: evidence from a nationally representative cross-sectional study. *BMJ Open* 6:e009892. doi:[10.1136/bmjopen-2015-009892](https://doi.org/10.1136/bmjopen-2015-009892)

Maximova, K., E.K. Moez, J. Dabravolskaj, A.R. Ferdinands, I. Dinu, G.L. Siou, A. Al Rajabi, and P.J. Veugelaers. 2020. Co-consumption of vegetables and fruit, whole grains, and fiber reduces the cancer risk of red and processed meat in a large prospective cohort of adults from Alberta’s Tomorrow Project. *Nutrients* 12:2265. doi:[10.3390/nu12082265](https://doi.org/10.3390/nu12082265)

Mente, A., M. Dehghan, and S. Yusuf. 2020. Diet and health: the need for new and reliable approaches. *Eur. Heart J.* 41:2641–2644. doi:[10.1093/eurheartj/ehaa317](https://doi.org/10.1093/eurheartj/ehaa317)

Miller, V., J. Reedy, F. Cudhea, J. Zhang, P. Shi, J. Erndt-Marino, J. Coates, R. Micha, P. Webb, and D. Mozaffarian, et al. 2022. Global, regional, and national consumption of animal-source foods between 1990 and 2018: findings from the Global Dietary Database. *Lancet Planet. Health* 6:e243–e256. doi:[10.1016/S2542-5196\(21\)00352-1](https://doi.org/10.1016/S2542-5196(21)00352-1)

Monteiro, C.A., G. Cannon, J.-C. Moubarac, R.B. Levy, M.L.C. Louzada, and P.C. Jaime. 2018. The UN Decade of Nutrition, the NOVA food classification and the trouble with ultra-processing. *Pub. Health Nutr.* 21:5–17. doi:[10.1017/S1368980017000234](https://doi.org/10.1017/S1368980017000234)

Murray, C.J.L.; GBD Risk Factors Collaborators. 2022. 36-fold higher estimate of deaths attributable to red meat intake in GBD 2019: is this reliable? Author’s reply. *Lancet* 399:e27–e28. doi:[10.1016/s0140-6736\(22\)00518-9](https://doi.org/10.1016/s0140-6736(22)00518-9)

Murray, C.J.L., A.Y. Aravkin, P. Zheng, C. Abbafati, K.M. Abbas, M. Abbasi-Kangevari, F. Abd-Allah, A. Abdelalim, M. Abdollahi, I. Abdollahpour, et al. 2020. Global burden of 87 risk factors in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet* 396:223–249. doi:[10.1016/S0140-6736\(20\)30752-2](https://doi.org/10.1016/S0140-6736(20)30752-2)

O’Connor, L.E., J.E. Kim, and W.W. Campbell. 2017. 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. *Am. J. Clin. Nutr.* 105:57–69. doi:[10.3945/ajcn.116.142521](https://doi.org/10.3945/ajcn.116.142521)
- O'Connor, L.E., J.E. Kim, C.M. Clark, W. Zhu, and W.W. Campbell. 2021. Effects of total red meat intake on glycemic control and inflammatory biomarkers: a meta-analysis of randomized controlled trials. *Adv. Nutr.* 12:115–127. doi:[10.1093/advances/nmaa096](https://doi.org/10.1093/advances/nmaa096)
- Pierre, F.H.F., O.C.B. Martin, R.L. Santarelli, S. Tache, N. Naud, F. Gueraud, M. Audebert, J. Dupuy, N. Meunier, D. Attaix, et al. 2013. Calcium and alpha-tocopherol suppress cured-meat promotion of chemically induced colon carcinogenesis in rats and reduce associated biomarkers in human volunteers. *Am. J. Clin. Nutr.* 98:1255–1262. doi:[10.3945/ajcn.113.061069](https://doi.org/10.3945/ajcn.113.061069)
- Qian, F., M.C. Riddle, J. Wylie-Rosett, and F.B. Hu. 2020. Red and processed meats and health risks: how strong is the evidence? *Diabetes Care* 43:265–271. doi:[10.2337/dci19-0063](https://doi.org/10.2337/dci19-0063)
- Rubin, R. 2020. Backlash over meat dietary recommendations raises questions about corporate ties to nutrition scientists. *JAMA* 323:401–404. doi:[10.1001/jama.2019.21441](https://doi.org/10.1001/jama.2019.21441)
- Schünemann, H., S. Hill, G. Guyatt, E.A. Akl, and F. Ahmed. 2011. The GRADE approach and Bradford Hill's criteria for causation. *J. Epidemiol. Community Health* 65:392–395. doi:[10.1136/jech.2010.119933](https://doi.org/10.1136/jech.2010.119933)
- Stanton, A.V., F. Leroy, C. Elliott, N. Mann, P. Wall, and S. De Smet. 2022. 36-fold higher estimate of deaths attributable to red meat intake in GBD 2019: is this reliable? *Lancet* 399:e23–e26. doi:[10.1016/S0140-6736\(22\)00311-7](https://doi.org/10.1016/S0140-6736(22)00311-7)
- Stylianou, K.S., V.L. Fulgoni, and O. Jolliet. 2021. Small targeted dietary changes can yield substantial gains for human health and the environment. *Nat. Food* 2:616–627. doi:[10.1038/s43016-021-00343-4](https://doi.org/10.1038/s43016-021-00343-4)
- Turner, N.D., and S.K. Lloyd. 2017. Association between red meat consumption and colon cancer: a systematic review of experimental results. *Exp. Biol. Med.* 242:813–839. doi:[10.1177/1535370217693117](https://doi.org/10.1177/1535370217693117)
- Van Hecke, T., J. Van Camp, and S. De Smet. 2017. Oxidation during digestion of meat: interactions with the diet and *Helicobacter pylori* gastritis, and implications on human health. *Comprehensive Rev. Food Sci. Food Safety* 16:214–233. doi:[10.1111/1541-4337.12248](https://doi.org/10.1111/1541-4337.12248)
- Vernooij, R.W.M., G.H. Guyatt, D. Zeraatkar, M.A. Han, C. Valli, R. El Dib, P. Alonso-Coello, M.M. Bala, and B.C. Johnston. 2021. Reconciling contrasting guideline recommendations on red and processed meat for health outcomes. *J. Clin. Epidemiol.* 138:215–218. doi:[10.1016/j.jclinepi.2021.07.008](https://doi.org/10.1016/j.jclinepi.2021.07.008)
- Watts, N., M. Amann, N. Arnell, S. Ayeb-Karlsson, J. Beagley, K. Belesova, M. Boykoff, P. Byass, W. Cai, D. Campbell-Lendrum, et al. 2021. The 2020 report of the Lancet countdown on health and climate change: responding to converging crises. *Lancet* 397:129–170. doi:[10.1016/S0140-6736\(20\)32290-X](https://doi.org/10.1016/S0140-6736(20)32290-X)
- Willett, W., J. Rockström, B. Loken, M. Springmann, T. Lang, S. Vermeulen, T. Garnett, D. Tilman, F. DeClerck, A. Wood, et al. 2019. Food in the Anthropocene: the EAT–Lancet Commission on healthy diets from sustainable food systems. *Lancet* 393:447–492. doi:[10.1016/S0140-6736\(18\)31788-4](https://doi.org/10.1016/S0140-6736(18)31788-4)
- Zeraatkar, D., and B.C. Johnston. 2019. A novel approach to evaluating the plausibility of causal relationships from non-randomized studies. *Int. Soc. Evidence-Based Health Care*, 26th Newsletter Edition. Retrieved on 1 September 2022, from https://ebm.mcmaster.ca/docs/librariesprovider31/newsletters/international-society-for-evidence-based-health-care-newsletter-december-2019.pdf?sfvrsn=1bef3db2_4.
- Zeraatkar, D., B.C. Johnston, J. Bartoszko, K. Cheung, M.M. Bala, C. Valli, M. Rabassa, D. Sit, K. Milio, B. Sadeghirad, et al. 2019. Effect of lower versus higher red meat intake on cardiometabolic and cancer outcomes: a systematic review of randomized trials. *Ann. Intern. Med.* 171:721–731. doi:[10.7326/M19-0622](https://doi.org/10.7326/M19-0622)
- Zheng, C., M. Pettinger, G.A. Nagana Gowda, J.W. Lampe, D. Raftery, L.F. Tinker, et al. 2022. Biomarker-calibrated red and combined red and processed meat intakes with chronic disease risk in a cohort of postmenopausal women. *J. Nutr.* 152:1711–1720. doi:[10.1093/jn/nxac067](https://doi.org/10.1093/jn/nxac067)