36-fold higher estimate of deaths attributable to red meat intake in GBD 2019: is this reliable?

We wish to compliment the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) Collaborators for their important contributions to global health metrics over the past 30 years. Their standardised and comprehensive estimates of the global burden of diseases, injuries, and risk factors have been used by researchers, government officials, and non-governmental organisations to make comparisons among populations, to track changes over time, and to monitor progress towards key policy targets, such as the Sustainable Development Goals.

However, we have some serious concerns about the most recent GBD systematic analysis of risk factors.[1] In particular, we wish to highlight the substantial changes in the GBD 2019 estimates of the disease burdens attributable to many of the dietary risk factors compared with the GBD 2017 estimates.[2] Disease burdens (as measured by deaths and disability-adjusted life-years [DALYs]) attributed to diets low in fruit, nuts and seeds, vegetables, seafood omega-3 fatty acids, and polyunsaturated fatty acids have declined by more than 50%. However, the most substantial change in the estimates is the disease burden attributed to diets high in unprocessed red meat. In 2019, a diet high in red meat was reported to be responsible for 896 000 deaths (95% uncertainty interval [UI] 536 000–1 250 000) and 23·9 million DALYs (15·6–32·0), and was considered to be the fifth leading dietary risk factor for attributable DALYs.[1] By contrast, the GBD 2017 analysis only attributed 25 000 deaths (95% UI 11 000–40 000) and 1·3 million DALYs (0·5–2·3) to diets high in red meat, and red meat intake was the least important of 15 dietary risk factors.[2] Hence, by comparison with previous estimates, the 2019 estimates of deaths attributable to unprocessed red meat intake have increased 36-fold, and estimates of DALYs attributable to unprocessed red meat intake have increased 18-fold.

The GBD 2019 Risk Factors Collaborators acknowledge the substantial differences in the estimates for many of the dietary risk factors and suggest three major sources for these differences: changes in the crosswalks between alternative and reference methods for estimating diet intake, new systematic reviews and meta-regressions, and more empirical standardised methods for selecting the theoretical minimum risk exposure level (TMREL) for protective factors. For red meat, all three sources influence the estimates; however, the new systematic reviews and meta-regressions and the setting of the red meat TMREL to 0 g per day appear to be two sources of particular importance.

All previous GBD Risk Factor analyses used data from published peer-reviewed systematic reviews and meta-analyses,[2] as well as the World Cancer Research Fund criteria for convincing or probable evidence of risk–outcome pairs,[3] to construct the relative risk curves and to determine the TMREL for each risk factor. The GBD 2019 analysis differs from this approach in that the GBD 2019 Risk Factors Collaborators performed or updated their own systematic reviews for each dietary risk and its related outcomes. On the basis of these reviews, the GBD 2019 Risk Factors Collaborators reported "sufficient evidence supporting the causal relationship of red meat intake with ischaemic heart disease, breast cancer, haemorrhagic stroke, and ischaemic stroke"[1] and added these outcomes to previously identified relationships with diabetes and colon cancer.

These findings of additional causal relationships for red meat are not in agreement with other recently conducted systematic reviews and meta-analyses. The Nutritional Recommendations (also known as NutriRECS) international consortium performed four parallel systematic reviews of randomised trials and observational studies.[4–7] The consortium reported finding low to very low certainty evidence that diets lower in unprocessed red meat might result in very small reductions in risk of cardiovascular disease, stroke, myocardial infarction, type 2 diabetes, and overall lifetime cancer mortality.[8] The 2018 World Cancer Research Fund's Continuous Update Project Expert Report judged the evidence for a link between red meat intake and breast cancer to be limited and that no conclusion could be reached regarding a causal or protective relationship.[9]

Furthermore, there appears to be a considerable disparity between the updated relative risk curves of GBD 2019 (appendix 1 of GBD 2019 [p 349]) and the dose–response curves of peer-reviewed cohort studies that examine the relationship between red meat intake and adverse outcomes. This disparity is particularly evident for moderate intakes of red meat, up to 50 g per day or three portions of red meat per week. According to the GBD 2019 analysis,[1] the relative risk of suffering an ischaemic stroke, an intracerebral haemorrhage, or a subarachnoid haemorrhage for people aged 55–59 years who are consuming 50 g per day of red meat versus those consuming no red meat is 1·20 [95% CI 1·11–1·26], 1·20 [1·1–1·28], and 1·20 [1·1–1·28], respectively. By contrast, only one[10] of nine studies examining the relationship between red meat intake and ischaemic stroke[10–16] reports a relative risk of 1·20 or greater for an intake of 50 g per day. None of eleven studies of haemorrhagic stroke,[10–17] or the single study of subarachnoid haemorrhage,[12] report a relative risk as high as 1·20 for a red meat intake of 50 g per day. Indeed, only one[17] of the 11 cohort studies of haemorrhagic stroke reports an estimated relative risk of more than 1 for red meat intakes up to 50 g per day.

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In attempting to understand these highly divergent conclusions, it is problematic that the GBD 2019 analysis provides little information concerning their updated systematic reviews.

The Lancet, along with all top ranked medical journals, rightly requires that global health estimates be reported according to the Guidelines for Accurate and Transparent Health Estimates Reporting (GATHER) statement.[18] GATHER recognises that accurate interpretation and responsible use of health estimates, by both decision makers and researchers, requires understanding of the input data on which estimates were based, including their quality, and of the methods used to derive the estimates from the input data. GATHER comprises a checklist of 18 items, which are organised into four sections: objectives and funding, data inputs, data analysis, and results and discussion. With regard to data inputs, GBD 2019 does indicate that 92 sources are used in the estimations of relative risk of diets high in red meat.[1] However, those 92 publications are not specifically identified, and we cannot find any reporting of GATHER items 3–6, which pertain to how the data from each source were identified and accessed, the inclusion and exclusion criteria, the characteristics of the populations, the data collection methods, and any potentially important biases. This non-adherence to agreed best practice is deeply concerning.

Furthermore, since the GBD 2019 analysis had new or updated systematic reviews and meta-analyses, *The Lancet* requires that each of these reviews be reported according to the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) 2009 guidelines.[19] We note that advances in systematic review methodology and terminology over the past decade have very recently mandated the updated PRISMA 2020 statement.[20] Key changes include a requirement to specify the methods used to assess the risk of bias in the included studies, a shift from assessing quality to assessing certainty in the body of evidence, and a recommendation that systematic review protocols are prospectively registered with a publicly accessible repository. We can find no record in the main GBD 2019 Article, nor in the appendices, of the GBD 2019 systematic review protocols, nor of the required peer-reviewed publications that comprehensively address the 27-item PRISMA (2009 or 2020) checklists.

Additionally, we are puzzled by the reference to more empirical standardised methods for selecting the TMREL for risk factors in GBD 2019. For protective factors, it appears that considerable care was taken to select the level of exposure with the lowest level of risk that was supported by the available data. The GBD 2019 Risk Factors Collaborators recognised that projecting beyond the level of exposure supported by the available studies could exaggerate the attributable burden for a risk factor. Hence, for protective dietary components, the TMREL was set using the 85th percentile of levels of exposure included in the published cohort studies or randomised controlled trials. By contrast, the TMREL for risk factors viewed as harmful was, by default, set to zero. Therefore, the red meat TMREL changed from 22·5 g per day to 0 g per day. The assumption of a red meat TMREL of zero is counterintuitive given the role of meat in evolutionary diets and in contemporary hunter-gatherer populations, in which cardiometabolic diseases were and still are uncommon.[21,22] Furthermore, recently published results from one of the largest multinational studies, which was conducted in five continents and examined the association between different types of meat and health outcomes, the Prospective Urban Rural Epidemiology study,[23] contradicts this premise. It is of considerable importance that the GBD 2019 Risk Factors Collaborators provide the empirical evidence for this change in TMREL and confirm that there was no projection beyond the available evidence.

We further question if the totality of nutritional effects of red meat have been considered in the meta-regressions. If the TMREL is assumed to be zero, red meat would then de facto be presented as an inherently harmful food. This assumption would ignore the well documented nutritional benefits with respect to the supply of essential nutrients and bioactive components.[24,25] If the current public health message advising moderate consumption of red meat as part of a healthy balanced diet is replaced by the message that any intake of red meat is harmful, this change will probably adversely affect iron deficiency anaemia, sarcopenia, and child and maternal malnutrition—these conditions and their associated risk factors are already responsible for considerably greater global disease burdens than a diet high in red meat, particularly in low-income and middle-income countries.

Since publication, GBD 2019 has been cited by 635 documents, including 351 scientific papers and nine policy documents. Using data from GBD 2019, Chung and colleagues[26] concluded that global increases in the red and processed meat trade contributed to an abrupt increase of diet-related non-communicable diseases. The GBD 2019 Stroke Collaborators[27] recently reported that greater numbers of stroke and subarachnoid haemorrhage DALYs were attributable to diets high in red meat, than were attributable to diets high in salt, in 11 of 21 world regions. Of great concern is the extensive quoting of GBD 2019 risk factor data in the evidence document of the UK's National Food Strategy.[28] Figures in this policy document indicate that diets high in red meat

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are responsible for greater numbers of DALYs than diets high in salt, trans-fatty acids, or sugar-sweetened beverages.

Given the substantial influence of GBD reports on worldwide nutritional policy decision making, it is of considerable importance that the GBD estimates are subject to critical scrutiny and that they continue to be rigorously and transparently evidence-based. Hence, we call on the GBD 2019 Risk Factors Collaborators to address two key concerns. First, the GBD 2019 Risk Factors Collaborators should clarify where the peer-reviewed publications of their updated or new systematic reviews are that comprehensively address the 27-item PRISMA statement and the 20-item GATHER statement checklists; that justify the updated dose–response curves of the relative risks of red meat for breast cancer, colorectal cancer, type 2 diabetes, ischaemic heart disease, ischaemic stroke, haemorrhagic stroke, and subarachnoid haemorrhage; and that provide the empirical evidence for the changing of the red meat TMREL from 22·5 g per day to 0 g per day. Finally, the GBD 2019 Risk Factors Collaborators should clarify if the additional deaths and DALYs from iron deficiency anaemia, sarcopenia, and child and maternal malnutrition that would result from the imposition of a red meat TMREL of zero have been included in the GBD 2019 estimates.

Unless, and until, all new or updated reviews and meta-analyses pertaining to all dietary risk factors are published, having undergone comprehensive independent peer review, we think it would be highly inappropriate and imprudent for the GBD 2019 dietary risk estimates to be used in any national or international policy documents, nor in any regulatory nor legislative decisions.

All authors declare no competing interests related to this Correspondence. Unrelated to this Correspondence, AVS serves as a non-remunerated member of the Irish 2030 Agri-Food Strategy Committee, Horizon Europe's Cancer Mission Assembly, the Irish Climate and Health Coalition, the Council on High Blood Pressure of the Irish Heart Foundation, and the World Action against Salt, Sugar, and Health; is a part-time employee of Devenish Nutrition; and owns stock in Devenish Nutrition. FL serves as a non-remunerated officer with the following scientific not-for-profit organisations: the Belgian Association for Meat Science and Technology, the Belgian Society for Food Microbiology, and the Belgian Nutrition Society; and is a member of the following scientific committees: the World Farmers Organization, the Institute Danone Belgium, and the Advisory Commission for the Protection of Geographical Denominations and Guaranteed Traditional Specialties for Agricultural Products and Foods of the Ministry of the Brussels Capital Region. CE reports grants to his institute from Devenish Nutrition; serves as an independent scientific expert to the World Food Programme; and serves as chair of the Scientific Advisory Committee of Foundation Earth. SDS serves as vice-president (non-remunerated) to the Belgian Association for Meat Science and Technology; is a member (non-remunerated) of the Scientific Advisory Board of Bleu-Blanc-Coeur; and is a member of the Flemish Strategic Advisory Council for Agriculture and Fisheries.

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