

Title: Meat, vegetables and health – interpreting the evidence

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One sentence summary: Although questions remain about several diet and disease associations, current evidence supports dietary guidelines to limit red meat and increase vegetable intake.

Previous research, including several meta-analyses, have reported on associations of red meat and vegetable consumption with health, but questions remain regarding the strength of the evidence. In this issue of *Nature Medicine*, Lescinsky *et al.*¹ and Stanaway *et al.*² applied a new meta-analysis approach to evaluate the evidence on red meat and vegetable consumption, respectively, and risks for several major health outcomes. For unprocessed red meat, they concluded that there is weak evidence for higher risks of ischaemic heart disease (IHD), type 2 diabetes, colorectal and breast cancer with higher consumption.¹ For vegetable intake, moderate evidence for protection was reported for ischaemic stroke, and weak evidence of a protective effect was reported for IHD, haemorrhagic stroke and oesophageal cancer.² The findings are broadly in support of national dietary guidelines, such as the Eatwell guide³ in the UK, to limit red meat and increase vegetable intake.

These new meta-analyses used a star rating system based on the relative risk differences, to rank the strength of evidence from no evidence (1 star) to very strong evidence (5 stars). The strength of evidence and associated star ratings need to be appraised in context; dietary factors (excluding severe deficiencies) typically only have small to moderate quantitative impacts on health, with common dietary exposures showing at most 15-20% risk difference for most health outcomes — which would equate to no more than two stars (weak evidence) or three stars (moderate evidence) under the proposed rating system. However, as the authors acknowledged¹, the combination of a universal exposure (e.g. diet) and common health outcome (e.g. IHD) may translate to a major overall disease burden, warranting a policy focus. The star rating should therefore be just one component among other metrics to consider when making policy recommendations.

Ideally, a known causal relationship should underpin any policy change. In turn, for any disease risk factor to be causal, there should be a plausible biological mechanism with supportive evidence from different study designs, including from randomised clinical trials where feasible. The potential mechanisms linking unprocessed red meat and vegetable intake with selected health outcomes are summarised in Figure 1. In general, the biological plausibility of diet-disease associations would be expected to be disease specific, and thus associations would vary depending on the risk-outcome pair of interest. For example, on the one hand, the saturated fat content in red meat could lead to an increase in low-density-lipoprotein cholesterol⁴ and thus increase the risk of IHD⁵, while on the other hand, the iron and vitamin B₁₂ content in meat can reduce the risk of nutritional anaemia. Any dietary component that appears to be associated with numerous health outcomes in the same direction should be critically scrutinised, because it might be an indicator of overall health

and healthy lifestyle but not have a true causal role. Outcome-wide analyses⁶, and the use of negative controls, could be considered to assess the specificity of associations.

While the meta-analyses carried out by Lescinsky *et al.*¹ and Stanaway *et al.*² pool together all available evidence, thus reducing the likelihood of spurious findings arising by chance, they do not fully address other issues which may need to be considered at the individual study level. In general, people who eat more vegetables may have healthier diets overall, and might exhibit other health behaviours such as smoking less or being more physically active, and having a higher educational and socio-economic status; these other factors are thus potential “confounders” of the associations of interest. Confounding of apparent diet-disease associations by other dietary and non-dietary risks factors is almost always present in observational research, and can remain – so-called residual confounding - despite rigorous attempts to correct for known confounders. For example, smoking is a major cause of many diseases including IHD and, in many populations, smokers eat less fruit and vegetables and more meat than non-smokers. Studies can adjust for self-reported smoking history, but this cannot be a fully accurate measure of actual lifetime exposure — so that even after adjusting as carefully as possible, there could still be apparent adverse and protective associations, respectively, for meat and vegetables in relation to risk for IHD which are in fact driven by smoking. Studies included in meta-analyses can also vary in the degree of adjustment for confounders, which may have an impact on the overall risk estimates.

In the current meta-analyses, the majority of studies included were conducted in North American and Western European countries, with a few studies in Asia and Australia; but there is a notable lack of data from other regions. People in different parts of the world have different diets, including different ranges of intakes and opting for different foods within the same food group. For example, unprocessed red meat consumption is predominantly from pork in China, but from beef in many Western countries.⁷ People in many low-income countries also have substantially lower intakes of any meat types compared with people living in high-income countries.⁸ These distinctions, combined with differences in the prevalence of other risk factors (e.g. rates of smoking or range of BMI) as well as varying disease rates across various regions, could result in true heterogeneity in diet-disease associations by geographical location — in which case it might not be appropriate to combine the data. More data are therefore needed from diverse populations to determine the health risk differences at different levels of intake, and attention should be given to identify any true heterogeneity by populations and the reasons for this heterogeneity.

The overall dietary composition and ‘substitution’ of some foods by others is another important consideration.⁹ For example, a decrease in red meat consumption could either result in lower total energy intake, or could more likely be replaced by energy from eating more of other foods. The health impact of decreasing meat consumption would therefore be dependent on the health effects of the foods that replace the meat. Further work, including future meta-analyses, should aim to assess the substitution effects of different foods, and dietary guidelines should include realistic alternative options to replace foods such as meat, for which lower consumption is recommended.

The work by Lescinsky *et al.*¹ and Stanaway *et al.*² provides a contemporary and extensive summary of the current evidence on unprocessed red meat and vegetable consumption for a number of major health outcomes. Although some questions remain, and careful interpretation is needed, this update supports common national and international dietary guidelines. Dietary choices also have important environmental impacts. The potential

environmental benefits of reducing meat and increasing plant food consumption are substantial¹⁰, and future evaluations of dietary guidelines should consider environmental and societal impacts, as well as health.

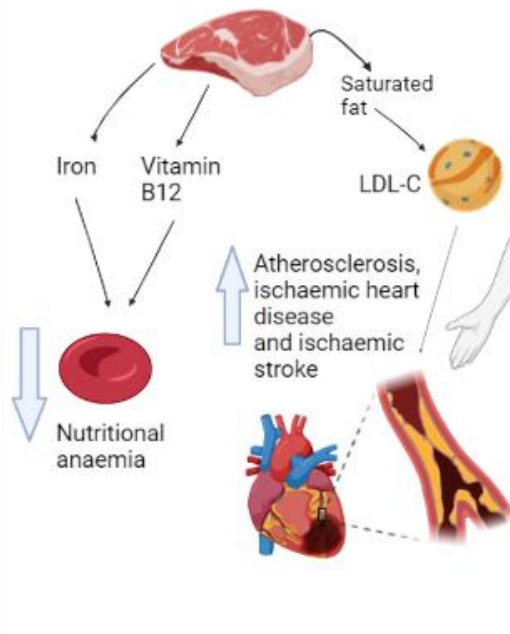
1. Lescinsky, H. *et al.* Evidence on health effects of unprocessed red meat consumption: an updated systematic review and doseresponse meta-analysis. *Nat. Med.* (2022).
2. Stanaway, J. D. *et al.* Evidence on health effects of vegetable consumption: a systematic review and dose-response meta-analysis. *Nat. Med.* (2022).
3. Public Health England. Guidance: The Eatwell guide. <https://www.gov.uk/government/publications/the-eatwell-guide> (2018).
4. Clarke, R., Frost, C., Collins, R., Appleby, P. & Peto, R. Dietary lipids and blood cholesterol: quantitative meta-analysis of metabolic ward studies. *BMJ* **314**, 112–7 (1997).
5. Ference, B. A. *et al.* Effect of long-term exposure to lower low-density lipoprotein cholesterol beginning early in life on the risk of coronary heart disease: a mendelian randomization analysis. *J. Am. Coll. Cardiol.* **60**, 2631–2639 (2012).
6. Vanderweele, T. J. Outcome-wide epidemiology. *Epidemiology* **28**, 399–402 (2017).
7. Takata, Y. *et al.* Red meat and poultry intakes and risk of total and cause-specific mortality: results from cohort studies of Chinese adults in Shanghai. *PLoS One* **8**, e56963 (2013).
8. Data published by United Nations Food and Agricultural Organization (FAO). Our World in Data: Meat consumption vs. GDP per capita, 2017. <https://ourworldindata.org/grapher/meat-consumption-vs-gdp-per-capita> (2020).
9. Ibsen, D. B. *et al.* Food substitution models for nutritional epidemiology. *Am. J. Clin. Nutr.* **113**, 294–303 (2021).
10. Clark, M. A., Springmann, M., Hill, J. & Tilman, D. Multiple health and environmental impacts of foods. *Proc. Natl. Acad. Sci.* **116**, 23357–23362 (2019).

Conflicts of interest: None

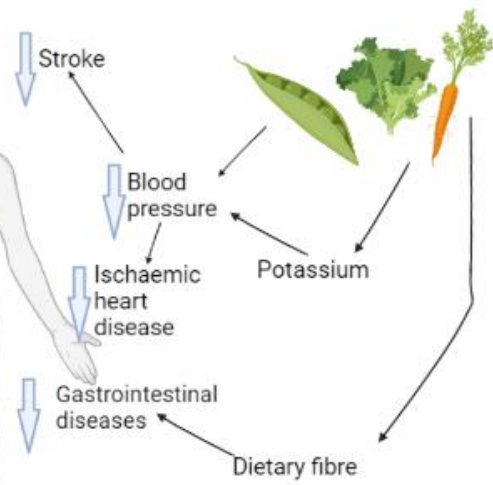
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Figure 1: Selected established or suggested mechanisms for meat, vegetables and health

Established beneficial and adverse mechanisms for meat



Suggested beneficial mechanisms for vegetables



Established beneficial mechanisms for vegetables