Red and Processed Meats and Health Risks: How Strong Is the Evidence?

Frank Qian,[1,2] Matthew C. Riddle,[3] Judith Wylie-Rosett,[4] and Frank B. Hu[1,5,6]

Diabetes Care 2020;43:265–271 | https://doi.org/10.2337/dci19-0063

Prevailing dietary guidelines have widely recommended diets relatively low in red and processed meats and high in minimally processed plant foods for the prevention of chronic diseases. However, an ad hoc research group called the Nutritional Recommendations (NutriRECS) consortium recently issued "new dietary guidelines" encouraging individuals to continue their current meat consumption habits due to "low certainty" of the evidence, difficulty of altering meat eaters' habits and preferences, and the lack of need to consider environmental impacts of red meat consumption. These recommendations are not justified, in large part because of the flawed methodologies used to review and grade nutritional evidence. The evidence evaluation was largely based on the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) criteria, which are primarily designed to grade the strength of evidence for clinical interventions especially pharmacotherapy. However, the infeasibility for conducting large, long-term randomized clinical trials on most dietary, lifestyle, and environmental exposures makes the criteria inappropriate in these areas. A separate research group proposed a modified and validated system for rating the meta-evidence on nutritional studies (NutriGRADE) to address several limitations of the GRADE criteria. Applying NutriGRADE, the evidence on the positive association between red and processed meats and type 2 diabetes was rated to be of "high quality," while the evidence on the association between red and processed meats and mortality was rated to be of "moderate quality." Another important limitation is that inadequate attention was paid to what might be replacing red meat, be it plant-based proteins, refined carbohydrates, or other foods. In summary, the red/processed meat recommendations by NutriRECS suffer from important methodological limitations and involve misinterpretations of nutritional evidence. To improve human and planetary health, dietary guidelines should continue to emphasize dietary patterns low in red and processed meats and high in minimally processed plant foods such as fruits and vegetables, whole grains, nuts, and legumes.

Consumption of red meats (meats of mammalian origin including beef, pork, and lamb) and processed meats (meats transformed through salting, curing, fermentation, smoking, or other processes to enhance flavor or improve preservation) has been increasing rapidly worldwide (1–3). These trends can have major health and environmental consequences. Considerable evidence from long-term prospective cohort studies has demonstrated that diets high in red and processed meats are associated with increased risk of type 2 diabetes (T2D), cardiovascular disease (CVD), cancer (particularly colorectal cancer), and all-cause mortality (4–6). Similarly, such evidence along with the evidence from short-term intervention trials strongly suggests that replacing red and processed meats with plant-based protein sources (including

[1]*Department of Nutrition, Harvard T.H. Chan School of Public Health, Boston, MA*
[2]*Department of Medicine, University of Chicago, Chicago, IL*
[3]*Division of Endocrinology, Diabetes & Clinical Nutrition, Oregon Health & Science University, Portland, OR*
[4]*Department of Epidemiology & Population Health, Albert Einstein College of Medicine, The Bronx, NY*
[5]*Department of Epidemiology, Harvard T.H. Chan School of Public Health, Boston, MA*
[6]*Channing Division of Network Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, MA*

Corresponding author: Frank B. Hu, frank.hu@channing.harvard.edu

legumes and nuts), poultry, and seafood has the potential to reduce risk of chronic diseases and premature death (7–10,11). For example, in two meta-analyses of randomized feeding trials (10,12), replacement of red meat with nuts or legumes significantly reduced total and LDL cholesterol. On the environmental side, livestock production (particularly ruminant animals) contributes the vast majority of the greenhouse gas emissions attributable to the agricultural sector, which comprises 22% of global total emissions, and also leads to environmental degradation by means of fertilizer run-off, deforestation, and desertification (13).

Based on the cumulative evidence, the majority of existing dietary guidelines, including the *Dietary Guidelines for Americans 2015–2020* (14), recommend dietary patterns relatively low in red and processed meats and high in minimally processed plant foods. Similarly, a consensus report of the American Diabetes Association recommends multiple dietary patterns for preventing and managing T2D, most of which emphasize modest or no consumption of red or processed meats (15). These include the Dietary Approaches to Stop Hypertension (DASH) (16), the traditional Mediterranean-style diet (17), and vegetarian/plant-based regimens (2,9,18). The American College of Cardiology/American Heart Association Guideline on the Primary Prevention of Cardiovascular Disease also recommends consuming diets low in red and processed meats (19). In 2015, the International Agency for Research on Cancer (IARC) classified processed meats as a Group 1 carcinogen for human colorectal cancer, and red meat was classified as probably carcinogenic to humans (Group 2A) based on a comprehensive review of epidemiologic evidence, combined with "strong mechanistic evidence supporting a carcinogenic effect" (20). Based on the review, the IARC has recommended reducing consumption of red and processed meats for cancer prevention.

However, a recent collection of systematic reviews and meta-analyses and accompanying dietary guidelines by the "Nutritional Recommendations (NutriRECS) consortium," published in the *Annals of Internal Medicine* (21–25), has challenged these recommendations. This group also systematically reviewed health-related values and preferences regarding red/processed meat consumption (25) and concluded that most people are generally unwilling to alter their current meat consumption habits. Contradicting both the current dietary recommendations and some of the findings of their own analyses, the authors issued "new dietary guidelines" that individuals should be advised to continue their current meat consumption habits due to the "low certainty" of the evidence, the weak associations, and the difficulty of altering meat eaters' habits and preferences.

Limitations of the GRADE System in Evaluating Nutritional Evidence

A careful examination of these systematic reviews and meta-analyses and accompanying recommendations reveals several serious weaknesses. First, the analyses and recommendations were largely based on the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) criteria (26). Although the meta-analyses conducted by the NutriRECS group found a significantly lower risk of total, CVD, and cancer mortality, as well as lower incidence of T2D for low versus high red meat intakes and dietary patterns, this evidence was rated low or very low quality and thus dismissed by the authors. While the GRADE approach is well established for evaluating the efficacy of clinical interventions, in particular pharmacotherapy, it has serious limitations when used to evaluate the efficacy of most dietary, lifestyle, and environmental exposures. The GRADE system rates all observational studies (without clear distinction between their different types) as offering a low degree of evidence because of their potential for confounding, and instead considers randomized controlled trials (RCTs) of hard end points to be the pinnacle of evidence. Hence, even if results from multiple lines of evidence converge to support benefit, the lack of RCTs of clinical outcomes will lead to the majority of nutrition evidence being graded as of "low quality." However, while RCTs are highly reliable in assessing clinical interventions, especially pharmacotherapy, they have key limitations when used to assess long-term dietary or lifestyle factors. These include their relatively short follow-up time, impracticality in the masking of treatment groups, and low adherence to the assigned dietary interventions, particularly in the long-term period that should be required in primary prevention trials to observe effects on hard end points like heart disease or cancer (27,28). Clearly, long-term RCTs are not suitable for assessing the effects of many important lifestyle and environmental exposures (e.g., *trans* fat intake, secondhand smoking, physical activity, and air pollution) on disease outcomes. Therefore, the GRADE system, heavily relying on the drug trial paradigm, is not adequate for evaluating most nutritional evidence.

In addition to these general limitations of the GRADE system, the methods applied by the NutriRECS group in their recent analyses involved several seemingly arbitrary decisions. For example, their assessment of risks of developing T2D associated with reducing processed meat consumption, based on 14 large prospective cohort studies including 669,530 participants, demonstrated a robustly significant association (relative risk and 95% CI 0.78 (0.72–0.84) (29). The authors downgraded their evidence rating for this outcome due to the presence of significant heterogeneity as calculated by the Cochran Q test ($P < 0.001$) and I^2 statistic (54.5%). However, both of these statistics are known to yield uninformative statistically significant findings with a very large sample size and may detect heterogeneity that is not meaningful for causal interpretation.

In addition, statistical heterogeneity with respect to the observed associations may suggest true etiological differences that should be examined in future research rather than dismissed outright. For example, heterogeneities could have arisen due to differences in study populations (e.g., Asian vs. Western), baseline diet, and replacement food source (refined carbohydrates vs. other animal-based or plant-based protein sources) (7–9,30).

The strength of observational evidence should have been upgraded when there is supporting evidence from RCTs on relevant risk factors or biological mechanisms or if observational studies satisfy multiple Bradford Hill criteria (e.g., dose-response, consistency across studies) (4,10,28). This approach was alluded to but not applied by the authors, despite findings of dose-response relationships between red and processed meat intake and well-accepted risk factors such as LDL cholesterol.

Modifying GRADE for Nutritional Studies: The NutriGRADE System

Previous studies have shown low reliability of the GRADE system in assessing

complex as opposed to simple interventions or evidence from a combination of observational studies and intervention trials (31,32). Alternative approaches such as that of the World Cancer Research Fund (20), the Hierarchies of Evidence Applied to Lifestyle Medicine (HEALM) (27), and NutriGRADE (33) have been developed to specifically evaluate evidence from studies of nutritional and lifestyle factors.

The NutriGRADE system is a modification of GRADE developed and validated specifically to address some limitations of the existing GRADE criteria (Table 1) (33). The NutriGRADE scoring criteria were found to have good agreement between raters and reasonably high reliability when evaluating the quality of evidence from nutritional intervention trials and cohort studies (intraclass correlation coefficient 0.81 (95% CI 0.69–0.90). NutriGRADE evaluates several unique attributes of nutritional studies, including dietary assessment methods, the potential for funding bias, the comparative value of using cohort studies versus RCTs, and dose-response relationships between dietary factors and health outcomes. Applying the NutriGRADE criteria to recent systematic reviews, the evidence for the association between red and processed meats and development of T2D was rated to be of "high quality" (5), while that for the association between red and processed meats and mortality was rated to be of "moderate quality" (34). The NutriGRADE system, which still requires further fine-tuning, or similar systems as mentioned above, should be more widely used in assessing the strength of nutritional evidence.

Misinterpretation of the Women's Health Initiative as a Meat Reduction Trial

In their assessment of existing RCTs testing the effects of reducing consumption of red or processed meats on hard clinical end points, the NutriRECS group correctly stated that no such studies have ever been conducted. Nevertheless, they used data from the Women's Health Initiative (WHI) to support their conclusion that meat reduction had no significant effect on CVD or cancer (35). This is a misinterpretation of the WHI data, because the randomized dietary intervention in WHI was a low-fat dietary pattern rather than an intervention aimed to reduce consumption of red or processed meat. The overall achieved difference in meat consumption was quite small, only 1.4 fewer servings per week at 3 years of follow-up, and adherence to the low-fat dietary intervention decayed substantially over time. This decline in adherence was further corroborated by a lack of difference in cardiometabolic risk markers between the two arms (36). Furthermore, the potential benefits of this small reduction in meat consumption could have been counterbalanced by reductions in healthful fat intake from plant oils, nuts, or fish. Despite inclusion of the WHI findings in this review, other interventional studies that included red meat reduction as a component of a more general dietary approach were excluded from the systematic review. Notably, the Lyon Diet Heart Trial (37), the Prevención con Dieta Mediterránea (PREDIMED) study (17), and a meta-analysis of eight RCTs assessing replacement of saturated fat (predominantly found in meat and high-fat dairy products) with polyunsaturated fat (38) demonstrated clear reduction of CVD risk, yet they were not included.

Food Preferences as a Justification for Continued Meat Consumption

The NutriRECS group's mixed-methods systematic review of health-related values and preferences regarding meat consumption synthesized data from 13 qualitative studies and 41 quantitative studies (25). Evaluation by the GRADE criteria indicated that the majority of the studies had a high risk of bias and methodological limitations. The qualitative studies primarily used focus groups and interviews with varying levels of question structure, and the majority were conducted in individuals who self-identified as vegetarians. The quantitative studies used multiple choice and rating scale questions and food-frequency questionnaires to characterize the attitudes and behaviors of population subgroups ranging from self-identified meat lovers to vegans. The reliability and validity of the questionnaires were not addressed, and no quantitative analyses were included in the systematic review. The conclusion that most people are attached to eating meat and are unwilling to change this behavior to avoid undesirable effects is not justified. Systematically reviewing studies considered to have high risk of bias and methodological limitations will not increase understanding of people's health-related values and preferences on meat consumption, which is the stated intent for the review. Although individual food preferences are useful for personalized nutritional advice, they should not be considered as a major factor in developing dietary guidelines for health promotion purposes.

Environmental Impact of Red Meat Declared out of the Scope of the Meat Guidelines

In making their recommendations, the NutriRECS authors declared that the scope of their report would not include an assessment of the environmental impacts of red and processed meat. This represents a major missed opportunity to improve population health given the large environmental impact of red meat production and the interrelationships between human health and planetary health. Climate change in the form of rising ambient temperatures (39), air pollution (40), and extreme weather events (41) poses serious threats to future human health, particularly among the most vulnerable populations (42). Multiple lines of evidence support an enormous potential benefit to the environment by greater reliance on plant-based protein sources (2). Environmental benefits are closely intertwined with the consumption of red and processed meats and should be considered when making dietary recommendations regarding optimal levels of meat consumption.

The Role of Prospective Observational Studies in Nutritional Research and Developing Dietary Guidelines

As noted earlier, the ideal randomized, double-blind, placebo-controlled trial is rarely feasible or ethical when evaluating the effects of dietary and lifestyle factors on long-term health outcomes (28). The effects of nutritional factors on disease and mortality risk often manifest over a span of years to decades, compared with the typically shorter span for drugs or devices. Such long-term follow-up is extremely costly and long-term trials are prone to increasing dropout rates and steep declines in adherence to the

Table 1—Comparison of the rating criteria between GRADE and NutriGRADE for assessing evidence from systematic reviews and meta-analyses[1]

	GRADE		NutriGRADE	
	RCTs	Observational studies	RCTs	Observational studies
Assessment criteria				
Risk of bias	*1*) Random sequence generation; *2*) Allocation concealment; *3*) Blinding of participants and researchers; *4*) Blinding of outcome assessment; *5*) Incomplete outcome data; *6*) Selective reporting; *7*) Other biases	*1*) Exposed and nonexposed cohorts from same population; *2*) Confidence in exposure assessment; *3*) Outcome of interest not present at start of study; *4*) Match or adjusted for confounding variables; *5*) Confidence in assessment of confounding factors; *6*) Confidence in assessment of outcome; *7*) Follow-up adequate	Same as GRADE, except blinding of participants and researchers cannot readily be achieved	*1*) Ascertainment of exposure (criteria specific to type of dietary assessment, i.e., validated food-frequency questionnaire, diet-associated biomarkers); *2*) Basic and outcome-relevant statistical adjustments; *3*) Assessment of outcome; *4*) Adequacy of follow-up
Precision	Number of cases (events), sample size, and inspection of the 95% CIs around the best estimate of the absolute effect	Same as for RCTs	Similar to GRADE, additional point awarded for *1*) 400–2,000 participants, but 95% CI excludes the null value; *2*) >2000 participants	Similar to GRADE, additional point awarded for *1*) ≥500 events and the 95% CI excludes the null value; *2*) ≥500 events, but 95% CI overlaps the null value (i.e., CI includes RR of 1.0), and 95% CI excludes important benefit (RR of <0.8) or harm (RR of >1.2)
Consistency	Similarity of point estimates and the overlap of their confidence intervals, as well as statistical criteria for heterogeneity (e.g., I^2 and Cochrane *Q* test)	Same as for RCTs	Same as GRADE	Same as GRADE
Directness	No important differences in the population or intervention; hard clinical outcome (vs. surrogate marker)	Same as for RCTs	Same as GRADE	Same as GRADE
Publication bias	*1*) Number of studies; *2*) Evidence for publication bias detected using funnel plots or statistical tests (e.g., Egger, Begg-Mazumdar)	Same as for RCTs	Same as GRADE	Same as GRADE
Funding bias	N/A	N/A	Higher points awarded for academic or research institutions, without industry funding or significant conflicts of interest	Same as for RCTs
Criteria for upgrading	N/A	*1*) Large magnitude of effect (+1 for RR >2 or <0.5 or +2 for RR >5 or <0.2, in situations with an effect); *2*) Dose-response gradient; *3*) Adjustment for any potential residual confounders would only strengthen the observed association	These criteria are imbedded in the NutriGRADE scoring system, including for moderate (+1 for RR or HR <0.80–0.50 and >1.20–2 comparing extreme quantiles) or large effect size (+2 for RR or HR <0.5 or >2 comparing extreme quantiles) and dose-response analysis	Same as for RCTs

Continued on p. 269

Table 1—Continued

	GRADE		NutriGRADE	
	RCTs	Observational studies	RCTs	Observational studies
Criteria for downgrading	*1*) Risk of bias; *2*) Imprecision; *3*) Inconsistency; *4*) Indirectness; *5*) Publication bias	Same as for RCTs	These criteria are imbedded in the NutriGRADE scoring system, including for moderate (+1 for RR or HR <0.80–0.50 and >1.20–2 comparing extreme quantiles) or large effect size (+2 for RR or HR <0.5 or >2 comparing extreme quantiles) and dose-response analysis	Same as for RCTs
Overall assessment	Initially rated as high, downgrade per above criteria	Initially rated as low, upgrade or downgrade per above criteria	Initial rating does not depend explicitly on study design, only on the overall score: *1*) ≥8 points: high; *2*) 6–7.99 points: moderate; *3*) 4–5.99 points: low; *4*) 0–3.99 points: very low	Same as for RCTs

HR, hazard ratio; N/A, not applicable; RR, relative risk. [1]Original reference article for GRADE: (26); and for NutriGRADE: (33).

originally assigned intervention, as seen in the WHI dietary modification trial (35). Therefore, most existing RCTs testing nutritional interventions have examined intermediate outcomes such as CVD risk factors that can be more quickly observed. Furthermore, while it is relatively easy to achieve masking of the intervention for both the participants and investigators in RCTs of drugs or devices, this is seldom possible in dietary studies, potentially resulting in further biases related to poor adherence and cross-over. Identifying an appropriate control group when assessing dietary factors or patterns is particularly difficult, given that the changes of consumption of foods and nutrients and their medical consequences do not occur in isolation and also depend heavily on the replacement food or nutrient. This is readily seen in studies on the health effects of saturated fat, where replacement with polyunsaturated fat confers a significant benefit on developing coronary heart disease and replacement with carbohydrates does not (38,43). Moreover, relatively limited funding is available to conduct large-scale RCTs in nutrition, compared to those for pharmaceuticals or devices (44). Given all of these constraints, while RCTs in nutritional science are desirable when feasible, such RCTs are extremely rare and the field of nutritional research cannot depend on them. Well-conducted prospective cohort studies, which are considered the strongest observational study design, are indispensable for this purpose. Although confounding is a threat to the validity of any observational research, bias from confounding and other sources can be limited through judicious study design and careful statistical adjustment, while interpretation can be assisted by corroborating evidence from small-scale intervention trials. In the future, maturation of electronic medical records and other systems for collecting and handling objective data should assist in the design and conduct of improved prospective observational studies.

Consistent evidence from prospective cohort studies with hard clinical end points and intervention trials with intermediate outcomes is particularly informative in inferring causality and developing public health recommendations. For example, epidemiologic studies were instrumental in the identification of associations between *trans* fat intake and increased risk of cardiovascular disease, and sugar-sweetened beverages and increased risk of T2D, consistent with the evidence from short-term intervention studies showing adverse effects of these dietary factors on blood lipids and other cardiometabolic risk factors (28,45,46). These findings contributed substantially to the evidence base for developing public health recommendations and nutrition policies for reducing intakes of *trans* fatty acids and added sugars. In addition, observational studies can and should continue to play an important role in identifying potentially harmful exposures in the diet and the environment, particularly when the exposures affect a large segment of the population. For red and processed meat, where substantial and consistent evidence shows adverse health outcomes and environmental impacts, action is warranted to limit the potential harms, despite the scarcity of definitive evidence.

Conclusions

The "dietary guideline recommendations" by the NutriRECS consortium suffer from multiple methodological limitations and involve misinterpretations of nutritional evidence. These recommendations are not justified by current evidence and have led to considerable confusion among health professionals and the general public. While more evidence regarding the health effects of red and processed meats is needed, the body of epidemiologic data showing their associations with T2D, CVD, and cancer is large and consistent. Meanwhile, short-term randomized intervention trials have demonstrated the benefits of replacing red meat with plant protein sources in reducing LDL cholesterol and other cardiometabolic risk factors (10). For the prevention and management of diabetes and other chronic diseases, it is important to follow current nutritional recommendations by the American Diabetes Association (15) and other professional and governmental organizations that allow for personalized choices but also emphasize dietary patterns high in minimally processed fruits and vegetables, whole grains, nuts, and legumes, while limiting red and

processed meats, refined carbohydrates, saturated fats, and sugar-sweetened beverages. Although there is still some uncertainty regarding current evidence, we should not fall into the trap of demanding absolute proof before taking public health actions. As Sir Austin Bradford Hill succinctly articulated nearly half a century ago (47):

> *All scientific work is incomplete—whether it be observational or experimental. All scientific work is liable to be upset or modified by advancing knowledge. That does not confer upon us a freedom to ignore the knowledge we already have, or to postpone the action it appears to demand at a given time.*

Funding. J.W.-R. is supported in part by a National Institute of Diabetes and Digestive and Kidney Diseases grant for the New York Regional Center for Diabetes Translational Research (DK111022). F.B.H. is supported by National Institutes of Health grants DK112940, DK102896, and HL60712.

Duality of Interest. M.C.R. reports research support through Oregon Health & Science University from AstraZeneca, Eli Lilly, and Novo Nordisk and honoraria for consulting from Adocia, AstraZeneca, Dance, Eli Lilly, GlaxoSmithKline, Novo Nordisk, Sanofi, and Theracos. These dualities have been reviewed and managed by Oregon Health & Science University. F.B.H. reports receiving research support from the California Walnut Commission, honoraria for lectures from Metagenics and Standard Process, and honoraria from Diet Quality Photo Navigation, outside the submitted work. No other potential conflicts of interest relevant to this article were reported.

References

1. GBD 2017 Diet Collaborators. Health effects of dietary risks in 195 countries, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet 2019;393:1958–1972
2. Willett W, Rockström J, Loken B, et al. Food in the Anthropocene: the EAT-Lancet Commission on healthy diets from sustainable food systems. Lancet 2019;393:447–492
3. Godfray HCJ, Aveyard P, Garnett T, et al. Meat consumption, health, and the environment. Science 2018;361:eaam5324
4. Mozaffarian D. Dietary and policy priorities for cardiovascular disease, diabetes, and obesity: a comprehensive review. Circulation 2016;133:187–225
5. Neuenschwander M, Ballon A, Weber KS, et al. Role of diet in type 2 diabetes incidence: umbrella review of meta-analyses of prospective observational studies. BMJ 2019;366:l2368
6. Abete I, Romaguera D, Vieira AR, Lopez de Munain A, Norat T. Association between total, processed, red and white meat consumption and all-cause, CVD and IHD mortality: a meta-analysis of cohort studies. Br J Nutr 2014;112:762–775
7. Song M, Fung TT, Hu FB, et al. Association of animal and plant protein intake with all-cause and cause-specific mortality. JAMA Intern Med 2016;176:1453–1463
8. Budhathoki S, Sawada N, Iwasaki M, et al.; Japan Public Health Center-based Prospective Study Group. Association of animal and plant protein intake with all-cause and cause-specific mortality. JAMA Intern Med 2019;179:1509–1518
9. Qian F, Liu G, Hu FB, Bhupathiraju SN, Sun Q. Association between plant-based dietary patterns and risk of type 2 diabetes: a systematic review and meta-analysis. JAMA Intern Med 2019;179:1335–1344
10. Guasch-Ferré M, Satija A, Blondin SA, et al. Meta-analysis of randomized controlled trials of red meat consumption in comparison with various comparison diets on cardiovascular risk factors. Circulation 2019;139:1828–1845
11. Imamura F, Micha R, Wu JH, et al. Effects of saturated fat, polyunsaturated fat, monounsaturated fat, and carbohydrate on glucose-insulin homeostasis: a systematic review and meta-analysis of randomised controlled feeding trials. PLoS Med 2016;13:e1002087
12. Schwingshackl L, Hoffmann G, Iqbal K, Schwedhelm C, Boeing H. Food groups and intermediate disease markers: a systematic review and network meta-analysis of randomized trials. Am J Clin Nutr 2018;108:576–586
13. McMichael AJ, Powles JW, Butler CD, Uauy R.: Food, livestock production, energy, climate change, and health. Lancet 2007;370:1253–1263
14. U.S. Department of Health and Human Services and U.S. Department of Agriculture. 2015–2020 Dietary Guidelines for Americans, 8th Edition. December 2015. Available from https://health.gov/dietaryguidelines/2015/guidelines/. Accessed 14 November 2019
15. Evert AB, Dennison M, Gardner CD, et al. Nutrition therapy for adults with diabetes or prediabetes: a consensus report. Diabetes Care 2019;42:731–754
16. Sacks FM, Svetkey LP, Vollmer WM, et al.; DASH-Sodium Collaborative Research Group. Effects on blood pressure of reduced dietary sodium and the Dietary Approaches to Stop Hypertension (DASH) diet. N Engl J Med 2001;344:3–10
17. Estruch R, Ros E, Salas-Salvadó J, et al.; PREDIMED Study Investigators. Primary prevention of cardiovascular disease with a Mediterranean diet supplemented with extra-virgin olive oil or nuts. N Engl J Med 2018;378:e34
18. Kahleova H, Levin S, Barnard N. Cardiometabolic benefits of plant-based diets. Nutrients 2017;9:E848
19. Arnett DK, Blumenthal RS, Albert MA, et al. 2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation 2019;140:e596–e646
20. Bouvard V, Loomis D, Guyton KZ, et al.; International Agency for Research on Cancer Monograph Working Group. Carcinogenicity of consumption of red and processed meat. Lancet Oncol 2015;16:1599–1600
21. Johnston BC, Zeraatkar D, Han MA, et al. Unprocessed red meat and processed meat consumption: dietary guideline recommendations from the Nutritional Recommendations (NutriRECS) consortium. Ann Intern Med 2019;171:756–764
22. Han MA, Zeraatkar D, Guyatt GH, et al. Reduction of red and processed meat intake and cancer mortality and incidence: a systematic review and meta-analysis of cohort studies. Ann Intern Med 2019;171:711–720
23. Vernooij RWM, Zeraatkar D, Han MA, et al. Patterns of red and processed meat consumption and risk for cardiometabolic and cancer outcomes: a systematic review and meta-analysis of cohort studies. Ann Intern Med 2019;171:732–741
24. Zeraatkar D, Johnston BC, Bartoszko J, et al. Effect of lower versus higher red meat intake on cardiometabolic and cancer outcomes: a systematic review of randomized trials. Ann Intern Med 2019;171:721–731
25. Valli C, Rabassa M, Johnston BC, et al.; NutriRECS Working Group. Health-related values and preferences regarding meat consumption: a mixed-methods systematic review. Ann Intern Med 2019;171:742–755
26. Guyatt GH, Oxman AD, Vist GE, et al.; GRADE Working Group. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. BMJ 2008;336:924–926
27. Katz DL, Karlsen MC, Chung M, et al. Hierarchies of evidence applied to lifestyle medicine (HEALM): introduction of a strength-of-evidence approach based on a methodological systematic review. BMC Med Res Methodol 2019;19:178
28. Satija A, Yu E, Willett WC, Hu FB. Understanding nutritional epidemiology and its role in policy. Adv Nutr 2015;6:5–18
29. Zeraatkar D, Han MA, Guyatt GH, et al. Red and processed meat consumption and risk for all-cause mortality and cardiometabolic outcomes: a systematic review and meta-analysis of cohort studies. Ann Intern Med 2019;171:703–710
30. Hutcheon JA, Chiolero A, Hanley JA. Random measurement error and regression dilution bias. BMJ 2010;340:c2289
31. Movsisyan A, Melendez-Torres GJ, Montgomery P. Outcomes in systematic reviews of complex interventions never reached "high" GRADE ratings when compared with those of simple interventions. J Clin Epidemiol 2016;78:22–33
32. Movsisyan A, Melendez-Torres GJ, Montgomery P. Users identified challenges in applying GRADE to complex interventions and suggested an extension to GRADE. J Clin Epidemiol 2016;70:191–199
33. Schwingshackl L, Knüppel S, Schwedhelm C, et al. Perspective: NutriGrade: a scoring system to assess and judge the meta-evidence of randomized controlled trials and cohort studies in nutrition research. Adv Nutr 2016;7:994–1004
34. Schwingshackl L, Schwedhelm C, Hoffmann G, et al. Food groups and risk of all-cause mortality: a systematic review and meta-analysis of prospective studies. Am J Clin Nutr 2017;105:1462–1473
35. Howard BV, Manson JE, Stefanick ML, et al. Low-fat dietary pattern and weight change over 7 years: the Women's Health Initiative Dietary Modification Trial. JAMA 2006;295:39–49

36. Howard BV, Curb JD, Eaton CB, et al. Low-fat dietary pattern and lipoprotein risk factors: the Women's Health Initiative Dietary Modification Trial. Am J Clin Nutr 2010;91:860–874
37. de Lorgeril M, Renaud S, Mamelle N, et al. Mediterranean alpha-linolenic acid-rich diet in secondary prevention of coronary heart disease. Lancet 1994;343:1454–1459
38. Mozaffarian D, Micha R, Wallace S. Effects on coronary heart disease of increasing polyunsaturated fat in place of saturated fat: a systematic review and meta-analysis of randomized controlled trials. PLoS Med 2010;7:e1000252
39. Hajat S, Haines A, Sarran C, Sharma A, Bates C, Fleming LE. The effect of ambient temperature on type-2-diabetes: case-crossover analysis of 4+ million GP consultations across England. Environ Health 2017;16:73
40. Doherty RM, Heal MR, O'Connor FM. Climate change impacts on human health over Europe through its effect on air quality. Environ Health 2017;16(Suppl. 1):118
41. Ghazali DA, Guericolas M, Thys F, Sarasin F, Arcos González P, Casalino E. Climate change impacts on disaster and emergency medicine focusing on mitigation disruptive effects: an international perspective. Int J Environ Res Public Health 2018;15:E1379
42. Climate change preparations must focus on health disparities. Lancet 2006;368:1624
43. Jakobsen MU, O'Reilly EJ, Heitmann BL, et al. Major types of dietary fat and risk of coronary heart disease: a pooled analysis of 11 cohort studies. Am J Clin Nutr 2009;89:1425–1432
44. Weaver CM, Miller JW. Challenges in conducting clinical nutrition research. Nutr Rev 2017;75:491–499
45. Mozaffarian D, Aro A, Willett WC. Health effects of trans-fatty acids: experimental and observational evidence. Eur J Clin Nutr 2009;63(Suppl. 2):S5–S21
46. Malik VS, Pan A, Willett WC, Hu FB. Sugar-sweetened beverages and weight gain in children and adults: a systematic review and meta-analysis. Am J Clin Nutr 2013;98:1084–1102
47. Rosner D. Criteria for action in population health: the Hill criteria a half century later. Milbank Q 2015;93:259–262