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ANALYSIS

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Dietary guidelines and health—is nutrition science up to the task?

Despite criticism and controversy, nutrition science can be relied on to improve our understanding of food and health, argue **Dariush Mozaffarian** and **Nita Forouhi**

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Nutrition science has been much criticised. Two concerns stand out. The first is that it relies too much on observational studies susceptible to confounding and errors in self reported dietary assessments and on small short term interventions with questionable relevance to the real world. The second is that the conclusions are ever changing: a given nutrient or food is said to be harmful one moment, then healthy, then harmful again.

Is nutrition science methodologically inferior to other fields? Is nutrition knowledge insufficiently stable to be useful? Is it even causing harm? To examine these questions, we consider the evolution of modern nutrition science and the reliability of nutrition evidence compared with other disciplines.

History of modern nutrition science

A reasonable birthdate for modern nutrition science is 1932, when vitamin C was first isolated and proved to cure scurvy. Other single nutrient deficiencies were identified in the following decades, including vitamin A and night blindness, vitamin D and rickets, thiamine and beriberi, niacin and pellagra. At the same time, the Great Depression and second world war heightened concern over food shortages. This coincidence of scientific discovery and geopolitics produced a strong focus on single nutrient deficits.

By 1980, less than 50 years later, these diseases had been largely eradicated in wealthier nations through successes in nutrition science and improvements in farming and food production. As chronic diseases such as cancer and heart disease began to take centre stage, the previously successful, reductionist approach to nutrition science was carried forward[1]: identify the relevant nutrient for a disease, establish its target intake, and translate this as a simple message. Thus, saturated fat and dietary cholesterol became "the" causes of heart disease and total fat (and, more recently, total calories) "the" cause of obesity. This nutrient focus was evident in the 1980 US dietary guidelines: "avoid too much fat, saturated fat, and cholesterol; eat foods with adequate starch and fibre; avoid too much sugar; avoid too much sodium."[2] However, such reductionist thinking, instrumental in conquering deficiency diseases, was inadequate to tackle chronic disease.

Fortunately, new research models emerged,[3,4] driven by scientific inquiry and growing public interest in food and nutrition. These included advanced study designs such as prospective cohorts, carefully designed metabolic studies, and long term clinical trials; methods to assess validity and reproducibility of dietary assessment tools and approaches to reduce bias; complementary assessment methods such as 24 hour recall, weighed food records, food frequency questionnaires, and biochemical indicators; energy adjustment to help account for age, sex, body size, physical activity, and systematic over-reporting or under-reporting; use of repeated measures to reduce error and account for within person variability; new technologies to scale up use of assessment tools and nutritional biomarkers; and the study of foods and dietary patterns rather than single nutrients.

The number of relevant studies also increased (fig 1). Ironically, this growth in quality and quantity provides the foundation for nutrition science's most ardent critics, allowing them to show which past guidelines and priorities were unsound and which questions remain.

Alongside these improvements in the quality and quantity of evidence has come a better understanding of how to integrate results from different study designs when making causal inferences. Core to this has been elucidation of the relative strengths and limitations of interventional and observational studies. Just as observational studies can vary greatly in design and quality of execution, dietary trials can vary substantially in whether they evaluate in vitro, animal, or human populations; short or long term treatment; healthy or diseased individuals; free living or tightly controlled populations; and single or multiple surrogates or clinical outcomes.

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Fortunately, these different study designs have complementary strengths and limitations. Although randomised trials can eliminate confounding at baseline, interpretation can be challenged by problems in blinding, compliance, crossover, ethical constraints, unequal dropout, and practical restraints on doses, durations, disease stages, and populations that can be evaluated. Trials must further balance optimal methods, expense, and statistical power against real world, holistic populations and interventions, especially when evaluating lifestyle or environmental factors. Conversely, long term prospective cohort studies are limited by residual confounding, yet possess numerous strengths that complement trials' shortcomings. Thus, scientists such as Austin Bradford Hill have developed appropriate criteria to infer causality from prospective cohorts.[7]

Arguments that science can be advanced only by "pivotal mega-trials of comprehensive interventions" appear attractive.[5 6] But such trials are often unfeasible outside the world of drugs because of problems with blinding, randomisation, contamination, attrition, dose, adherence, and energy intake, let alone cost. Furthermore, to reliably detect effects on chronic disease, trials must evaluate changes in eating behaviour in large, compliant, and generalisable populations over long periods. Thus, the tested interventions are often superseded by new science by the time the trial is completed.

Several problematic mega-trials of lifestyle factors have been described.[7 8] The Women's Health Initiative is a sobering example: a mega-trial of both hormone replacement and a low fat diet, it cost around $700m (£500m; €570m) and ultimately confirmed the findings of prospective observational cohorts (box 1). Such concordance in results between randomised trials and observational studies often goes unremarked but is not unusual. Indeed, in most cases, when properly evaluated, prospective cohort studies and randomised trials of a range of foods, nutrients, and dietary patterns produce generally concordant findings (table 2).[18-22]

Box 1: Women's Health Initiative trial—concordance with observational results

One of the most commonly cited examples of why observational studies should not be trusted comes outside nutrition. Observational studies found lower rates of heart disease in women taking hormone replacement therapy, but the Women's Health Initiative trial found the opposite.

This was widely thought to show insurmountable limitations of observational research. Yet, additional follow-up in the trial showed benefit in younger women (who were most representative of the observational cohorts) and not in older women who had been enrolled to increase statistical power because of their higher risk of heart disease.[9-15]

This concordance between observational and interventional findings, which was also striking for other clinical endpoints (table 1), has been largely overlooked. Systematic comparisons, including up to 1583 meta-analyses of 228 conditions, find similar close concordance between randomised trials and observational studies.[16 17]

Evidence based nutrition is therefore best served by incorporating all the evidence and evaluating consistency across multiple types of studies. Diverse types of evidence, considered together, best support causal inference (box 2).[4]

Box 2: How different types of study contribute to continuum of nutritional evidence: example of polyunsaturated fatty acids[23-29]

Randomised trials

- Confirm changes in blood concentrations of specific omega 3 and omega 6 fatty acids after controlled feeding of foods rich in these fats
- Document effects of such supplementation on physiological risk factors
- Evaluate effects on hard clinical endpoints

Observational cohort studies

- Document relations of estimated omega 3 and omega 6 fatty acid consumption from the diet and omega 3 and omega 6 fatty acid biomarkers in the blood with observed dietary habits, clinical risk factors, and hard clinical endpoints in different, more varied populations

Experimental and preclinical studies

- Elucidate mechanisms and pathways of effects
- Each of these lines of evidence contributes complementary data, and no single study is by itself necessary or sufficient for achieving overall actionable evidence

Advances in nutrition science

With each scientific shift—from a focus on single nutrient deficiencies to overall diets and chronic disease, from simple approaches to more rigorous methods, and from a few individual studies to diverse research designs with complementary findings—has come greater understanding. This includes better recognition of the diverse, complex biological pathways by which dietary habits influence health, limiting the value of any single surrogate outcome,[21] and the complex health effects of different foods and dietary patterns beyond individual nutrients.[30] The calorie independent effects of diverse foods on modulators of long term weight regulation are also emerging—for example, hunger, satiety, brain reward, metabolic responses, hepatic fat synthesis, adipocyte function, metabolic expenditure, and the microbiome—highlighting the importance of food quality rather than energy balance and calorie counting to prevent obesity.[21] The comparative effects of dietary factors are also now being characterised: we should not ask simply whether a given food is healthy or harmful, but compared with what?

These advances have brought new questions and uncertainties. Current controversies include the relevance of saturated fat and its diverse food sources, including dairy foods; the value of very low carbohydrate diets; the optimal lowest intake of sodium; the effects of fish oil or vitamin D supplements; the role of non-calorific sweeteners; the health effects of starchy foods such as potatoes and fat sources such as plant oils; and the relevance of calorie counting versus diet quality for long term weight control.[21] The time lag between the generation of new knowledge and its implementation creates the appearance of additional controversy and exacerbates public confusion. This can be seen, for example, in the continued public and industry focus on low fat foods, despite new evidence that total fat is less important than the relative types of fat (saturated, unsaturated, trans) as well as quality of carbohydrate (eg, starch and sugar, fibre, glycaemic response, whole grain content).[31]

Uncertainty exists in all scientific fields

Nutrition science is evolving, but does this mean we should be sceptical of current conclusions? No: comparison with other scientific fields suggests that the scope and pace of these discoveries, evolving priorities, and remaining uncertainties are not only natural and appropriate, but expected and reassuring.

Take cardiology. Major uncertainties and controversies still exist in cardiovascular medicine: such as the choices and durations of anti-thrombotic therapy after coronary intervention; the timing and patient selection for transcatheter versus surgical aortic valve replacement; the treatment of asymptomatic carotid atherosclerosis; the usefulness of anti-diabetic drugs and glucose control for reducing heart attacks and death; and the role of and potential treatments to raise high density lipoprotein cholesterol levels or lower systemic inflammation. Even for seemingly straightforward and heavily studied markers of coronary risk such as lipids, knowledge and recommendations have evolved substantially over time: uncertainty has actually grown about optimal screening, risk versus benefit, and patient selection for statins, one of the most widely studied drugs in the world.

But these uncertainties in cardiovascular medicine do not leave us sceptical and distrustful of all modern cardiovascular treatments and recommendations. Instead we are reassured that cardiovascular science and its application through clinical practice, public guidance, and policy continue to evolve with new findings. Similarly, advances in the science and application of nutrition represent expected, reassuring progress. For both the patient in our clinic and the population around us, it is appropriate to act on reasonable conclusions based on the totality of existing evidence and expected risks versus benefits. As in all fields, application cannot await flawless evidence or perfect understanding.

Vested interests

The optimal role for industry in nutrition research remains unclear.[32 33] Given the scale of diet related diseases, funding for research on foods and nutrients is limited. Total annual federal spending on nutrition research across all US agencies was about $1.5bn in 2009,[34] whereas industry spends more than $60bn a year on research into drugs, biotechnology, and medical devices.

Since government and non-profit organisational support for nutrition research is limited, the food industry has a key role in funding studies. Concerns have been raised about bias in such work, with skewing of findings towards industry benefit. For example, evidence for substantial bias has been identified in industry sponsored research on health effects of sugar sweetened beverages[35 36] and artificial sweeteners.[37] Evidence for bias in industry sponsored research on other nutritional topics is less strong, with a non-significant trend towards about 30% higher likelihood of favourable conclusions.[38] This figure is similar to that found in analyses of industry sponsored studies of drugs or medical devices.[39] Despite the potential for bias, the food industry's expertise, reach, and innovation can help address challenges in food production, formulation, and distribution; facilitate greater innovation for the public good; and build capacity.[40]

The difficulties of food industry involvement in research are profound and not easily dismissed. Given the scale of nutritional challenges globally, all parts of the food system, including the food industry, will need to be part of the solution, whether through voluntary action or legislation. Any partnership between research and the food industry must be governed by clear principles, as have been proposed elsewhere,[33 40] and continue to be developed, such as by the UK Medical Research Council and the UK Prevention Research Partnership.[41 42]

Coherent public messaging

Dietary guidelines from government and advocacy organisations compete with messages from other sources. Almost everyone seems to have an opinion on food and nutrition. We speculate this may relate to the deeply personal, palpable, and cultural aspects of food. We all eat, interacting with our food multiple times each day over a lifetime, making food and nutrition seem tangible and accessible. Yet opinion is not always based on science, and often the loudest, most extreme voices drown out the well informed.

There is also money to be made. Nutrition books and resources and the related dieting, supplement, and functional food industries generate billions of dollars in revenue. In a digital era, stories need clicks and instant comment, and sensational headlines promising miracle breakthroughs or "new" findings that overturn established dogma generate traffic, advertising revenue, and sales. This confusion is further harnessed by some sections of the food industry, whose documented tactics may include promotion of unhealthy products, misleading marketing campaigns, targeting of children and other susceptible groups, corporate lobbying, co-opting of organisations and social media through financial support, and attacks against science and scientists.[43] And, least understood by a bewildered public, the science itself changes. Together these factors cause great misinformation.

The optimal solutions for this confusion remain unclear. Enhancing the quality of dietary guidelines is one important strategy. The US National Academies recently reviewed the process for developing US dietary guidelines and recommended several new approaches to increase transparency and reduce potential for bias, including in selection of the advisory committee and appraisal of the evidence.[44 45] Recommendations include establishing separate groups for identifying new research questions or conducting new systematic reviews, evaluating and integrating the evidence and developing recommendations, and translating these into draft policy recommendations. Standardisation of methods and criteria is also recommended, although critics argue this may not go far enough to tackle underlying biases in the research agenda, sources of funding, and conflicts of interest.[46] Nonetheless, these are steps in the right direction. Academic institutions, which are the main repositories of the science, must also take a more active role as a "trusted voice" in direct communication to the public.[47] To keep pace with the rapid advances in nutritional science, future research should consider and test new approaches to increase coherent public messaging.

Nutrition science: up to the task

Nutrition science is moving away from focusing on isolated nutrients, deficiency diseases, calorie counting, and simple surrogate outcomes and towards foods, chronic diseases, diet quality, and complex biological mechanisms and pathways. These advances are founded on methodological progress, gains in the numbers and types of studies, and better incorporation of diverse evidence from multiple study designs.

Accurate translation is crucial. Although not unique to nutritional science, vested interests can influence research priorities and interpretation of findings. Emerging frameworks for partnerships between researchers and industry are a positive step. The competing sources of nutritional messaging represent a more insidious layer of vested interests. There is an urgent need for more coherent public messaging, including more robust processes for transparency and timeliness in the development of evidence based dietary guidelines.

An upcoming series in *The BMJ*, launching in June, aims to provide some much needed clarity. Examining the science and politics of nutrition and its role in health, the series brings together experts with diverse perspectives to advance objective evidence and rational debate on what we know, and what we need to learn, in this crucial area of health and healthcare.

Advances in nutritional science enable reasonable conclusions about dietary priorities for general health: eat minimally processed, bioactive rich foods (fruits, nuts, seeds, beans, vegetables, whole grains, plant oils, yogurt, fish) and avoid ultraprocessed foods rich in refined starch, sugars, and industrial additives such as trans fat and sodium.[21] And, there is much we still don't know, setting the stage for further advances in our understanding of areas such as food preparation and processing, fatty acid metabolites, flavonoids, gut-brain-metabolic communication, brown and beige fat, the microbiome, early life influences, and yet to be discovered pathways and mechanisms. Modern nutrition science is up to the task.

Key messages

- Nutrition science has often been criticised as unreliable but has made vital contributions to human health
- Understanding has advanced from isolated nutrient deficiencies to the importance of foods and overall dietary patterns in chronic disease
- Improvements in complementary research methods have generated sufficient scientific evidence to formulate key public health guidelines
- Management of vested interests is needed to avoid potential bias in research findings and public messaging of dietary advice
- All stakeholders, including the food industry, must be part of a collective effort to solve the tremendous global challenge of nutrition and health

The BMJ will shortly be publishing a major international series of articles on the science and politics of nutrition. The series will launch at a two day interactive conference in Zurich in June, cohosted by *The BMJ* and the global insurance group Swiss-Re. See http://institute.swissre.com/events/food_for_thought_bmj.html .

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1 Messina M, Lampe JW, Birt DF, etal . Reductionism and the narrowing nutrition perspective: time for reevaluation and emphasis on food synergy . *J Am Diet Assoc* 2001;101:1416-9. 10.1016/S0002-8223(01)00342-X 11762736
2 Davis C, Saltos E. *Dietary recommendations and how they have changed over time. America's Eating habits: changes and consequences: Agriculture Information Bulletin No 750.* ERA, 1999.
3 Willett WC. *Nutritional epidemiology.* 3rd ed. Oxford University Press, 201210.1093/acprof:oso/9780199754038.001.0001.
4 Frieden TR. Evidence for health decision making—beyond randomized, controlled trials[Review]. *N Engl J Med* 2017;377:465-75. 10.1056/NEJMra1614394 28767357
5 Ioannidis JP. Implausible results in human nutrition research. *BMJ* 2013;347:f6698. 10.1136/bmj.f6698 24231028
6 Nissen SEUS. US dietary guidelines: an evidence-free zone. *Ann Intern Med* 2016;164:558-9. 10.7326/M16-0035 26783992
7 Kones R, Rumana U, Merino J. Exclusion of 'nonRCT evidence' in guidelines for chronic diseases - is it always appropriate? The Look AHEAD study. *Curr Med Res Opin* 2014;30:2009-19. 10.1185/03007995.2014.925438 24841173
8 Multiple Risk Factor Intervention Trial Research Group. Multiple risk factor intervention trial. Risk factor changes and mortality results. *JAMA* 1982;248:1465-77. 10.1001/jama.1982.03330120023025 7050440
9 Boardman HM, Hartley L, Eisinga A, etal . Hormone therapy for preventing cardiovascular disease in post-menopausal women. *Cochrane Database Syst Rev* 2015;(3):CD002229.25754617
10 Grodstein F, Stampfer MJ, Colditz GA, etal . Postmenopausal hormone therapy and mortality. *N Engl J Med* 1997;336:1769-75. 10.1056/NEJM199706193362501 9187066
11 Nelson HD, Humphrey LL, Nygren P, Teutsch SM, Allan JD. Postmenopausal hormone replacement therapy: scientific review. *JAMA* 2002;288:872-81. 10.1001/jama.288.7.872 12186605
12 Mohammed K, Abu Dabrh AM, Benkhadra K, etal . Oral vs transdermal estrogen therapy and vascular events: a systematic review and meta-analysis. *J Clin Endocrinol Metab* 2015;100:4012-20. 10.1210/jc.2015-2237 26544651
13 Rossouw JE, Anderson GL, Prentice RL, etal. Writing Group for the Women's Health Initiative Investigators. Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results from the Women's Health Initiative randomized controlled trial. *JAMA* 2002;288:321-33. 10.1001/jama.288.3.321 12117397
14 Colditz GA, Egan KM, Stampfer MJ. Hormone replacement therapy and risk of breast cancer: results from epidemiologic studies. *Am J Obstet Gynecol* 1993;168:1473-80. 10.1016/S0002-9378(11)90784-4 8498430
15 Zhu L, Jiang X, Sun Y, Shu W. Effect of hormone therapy on the risk of bone fractures: a systematic review and meta-analysis of randomized controlled trials. *Menopause* 2016;23:461-70.26529613
16 Concato J, Shah N, Horwitz RI. Randomized, controlled trials, observational studies, and the hierarchy of research designs. *N Engl J Med* 2000;342:1887-92. 10.1056/NEJM200006223422507 10861325
17 Anglemyer A, Horvath HT, Bero L. Healthcare outcomes assessed with observational study designs compared with those assessed in randomized trials. *Cochrane Database Syst Rev* 2014;(4):MR000034.24782322
18 Mozaffarian D, Appel LJ, Van Horn L. Components of a cardioprotective diet: new insights. *Circulation* 2011;123:2870-91. 10.1161/CIRCULATIONAHA.110.968735 21690503
19 Mozaffarian D. Mediterranean diet for primary prevention of cardiovascular disease. *N Engl J Med* 2013;369:673-4.23944310
20 Mozaffarian D. Nutrition and cardiovascular and metabolic diseases. In: Mann DLZD, Libby P, Bonow RO, Braunwald E, eds. *Braunwald's heart disease: a textbook of cardiovascular medicine.* 10th ed. Elsevier, 2015:1001-14.
21 Mozaffarian D. Dietary and policy priorities for cardiovascular disease, diabetes, and obesity: a comprehensive review. *Circulation* 2016;133:187-225. 10.1161/CIRCULATIONAHA.115.018585 26746178
22 Micha R, Peñalvo JL, Cudhea F, Imamura F, Rehm CD, Mozaffarian D. Association between dietary factors and mortality from heart disease, stroke, and diabetes in the United States. *JAMA* 2017;317:912-24. 10.1001/jama.2017.0947 28267855
23 Hodson L, Skeaff CM, Fielding BA. Fatty acid composition of adipose tissue and blood in humans and its use as a biomarker of dietary intake. *Prog Lipid Res* 2008;47:348-80. 10.1016/j.plipres.2008.03.003 18435934
24 Mensink RP, Zock PL, Kester AD, Katan MB. Effects of dietary fatty acids and carbohydrates on the ratio of serum total to HDL cholesterol and on serum lipids and apolipoproteins: a meta-analysis of 60 controlled trials. *Am J Clin Nutr* 2003;77:1146-55. 10.1093/ajcn/77.5.1146 12716665
25 Mozaffarian D, Wu JH. Omega-3 fatty acids and cardiovascular disease: effects on risk factors, molecular pathways, and clinical events. *J Am Coll Cardiol* 2011;58:2047-67. 10.1016/j.jacc.2011.06.063 22051327
26 Imamura F, Micha R, Wu JH, etal . 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. 10.1371/journal.pmed.1002087 27434027
27 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. 10.1371/journal.pmed.1000252 20351774
28 Del Gobbo LC, Imamura F, Aslibekyan S, etal. Cohorts for Heart and Aging Research in Genomic Epidemiology (CHARGE) Fatty Acids and Outcomes Research Consortium (FORCe). ω-3 Polyunsaturated Fatty Acid Biomarkers and Coronary Heart Disease: Pooling Project of 19 Cohort Studies. *JAMA Intern Med* 2016;176:1155-66. 10.1001/jamainternmed.2016.2925 27357102
29 Forouhi NG, Imamura F, Sharp SJ, etal . Association of plasma phospholipid n-3 and n-6 polyunsaturated fatty acids with type 2 diabetes: The EPIC-InterAct Case-Cohort Study. *PLoS Med* 2016;13:e1002094. 10.1371/journal.pmed.1002094 27434045
30 Dietary Guidelines Advisory Committee. Scientific Report of the 2015 Dietary Guidelines Advisory Committee. US Department of Agriculture, Agriculutural Research Service; 2015: http://www.health.gov/dietaryguidelines/2015-scientific-report/.
31 Mozaffarian D, Ludwig DS. The 2015 US Dietary Guidelines: Lifting the ban on total dietary fat. *JAMA* 2015;313:2421-2. 10.1001/jama.2015.5941 26103023
32 Aveyard P, Yach D, Gilmore AB, Capewell S. Should we welcome food industry funding of public health research?*BMJ* 2016;353:i2161. 10.1136/bmj.i2161 27098491
33 Mozaffarian D. Conflict of interest and the role of the food industry in nutrition research. *JAMA* 2017;317:1755-6. 10.1001/jama.2017.3456 28464165
34 Kuchler F, Toole A. Federal Support for nutrition research trends upward as USDA share declines. United States Department of Agriculture, Economic Research Service. 2015 https://www.ers.usda.gov/amber-waves/2015/june/federal-support-for-nutrition-research-trends-upward-as-usda-share-declines.
35 Bes-Rastrollo M, Schulze MB, Ruiz-Canela M, Martinez-Gonzalez MA. Financial conflicts of interest and reporting bias regarding the association between sugar-sweetened beverages and weight gain: a systematic review of systematic reviews. *PLoS Med* 2013;10:e1001578, e1001578. 10.1371/journal.pmed.1001578 24391479
36 Schillinger D, Tran J, Mangurian C, Kearns C. Do sugar-sweetened beverages cause obesity and diabetes? industry and the manufacture of scientific controversy. *Ann Intern Med* 2016;165:895-7. 10.7326/L16-0534 27802504
37 Mandrioli D, Kearns CE, Bero LA. Relationship between research outcomes and risk of bias, study sponsorship, and author financial conflicts of interest in reviews of the effects

of artificially sweetened beverages on weight outcomes: a systematic review of reviews. *PLoS One* 2016;11:e0162198. 10.1371/journal.pone.0162198 27606602

38 Chartres N, Fabbri A, Bero LA. Association of industry sponsorship with outcomes of nutrition studies: a systematic review and meta-analysis. *JAMA Intern Med* 2016;176:1769-77. 10.1001/jamainternmed.2016.6721 27802480

39 Lundh A, Lexchin J, Mintzes B, Schroll JB, Bero L. Industry sponsorship and research outcome. *Cochrane Database Syst Rev* 2017;2:MR000033.28207928

40 Centers for Disease Control and Prevention. CDC's guiding principles for public-private partnerships. 2014. https://www.cdc.gov/about/pdf/business/partnershipguidance-4-16-14.pdf.

41 UK Prevention Research Partnership. UKPRP principles for working with industry. 2017. https://www.mrc.ac.uk/documents/pdf/ukprp-principles-for-working-with-industry/.

42 Medical Research Council. MRC priorities for nutrition research. 2017. https://www.mrc.ac.uk/funding/science-areas/population-systems-medicine/mrc-priorities-for-nutrition-research/

43 Nestle M. *Soda politics: taking on big soda (and winning)*. Oxford University Press, 2015.

44 National Academies of Sciences, Engineering, and Medicine. Redesigning the process for establishing the Dietary Guidelines for Americans. 2017. https://www.nap.edu/catalog/24883/redesigning-the-process-for-establishing-the-dietary-guidelines-for-americans.

45 National Academies of Sciences, Engineering, and Medicine. Optimizing the process for establishing the Dietary Guidelines for Americans: the selection process. 2017. https://www.nap.edu/catalog/24637/optimizing-the-process-for-establishing-the-dietary-guidelines-for-americans.

46 Bero L. Developing reliable dietary guidelines. *BMJ* 2017;359:j4845. 10.1136/bmj.j4845 29101096

47 Friedman School of Nutrition Science & Policy. Public impact initiative. 2016 https://nutrition.tufts.edu/strategic-plan-aims/public-impact-initiative

Tables

Table 1| Comparison of results from randomised controlled trials and prospective observational studies in hormone replacement therapy

Outcome	Relative risk (95% CI) of outcome	
	Randomised trials	Observational cohorts
Total mortality	<10 years since menopause 0.70 (0.52 to 0.95); ≥10 years 1.06 (0.95 to 1.18)[9]	0.63 (0.56 to 0.70) [10]
Heart disease	<10 years since menopause 0.52 (0.29 to 0.96); ≥10 years 1.07 (0.96 to 1.20)[9]	0.62 (0.40 to 0.90)*[11]
Stroke	1.24 (1.10 to 1.41) [9]	1.12 (1.01 to 1.23) [11]
Venous thromboembolism	1.92 (1.36 to 2.69) [9]	1.63 (1.40 to 1.90) [12]
Breast cancer	1.26 (1.02 to 1.59) [13]	1.40 (1.20 to 1.63) [14]
Colorectal cancer	0.63 (0.43 to 0.92) [13]	0.66 (0.59 to 0.74) [11]
Hip fracture	0.72 (0.53 to 0.98) [15]	0.64 (0.32 to 1.04) [11]

* Coronary heart disease mortality (the reported meta-analysis of total heart disease included randomised trials).

Table 2| Comparison of quality of evidence from different study designs for cardiometabolic health effects of increased consumption of selected foods, nutrients, and dietary patterns*

	Ecological studies of clinical endpoints	Randomised trials of risk factors†	Prospective cohort studies of clinical endpoints	Randomised trials of clinical endpoints
Foods and beverages				
Fruits	++++ Benefit	++ Benefit	++++ Benefit	–
Vegetables	++++ Benefit	++ Benefit	++++ Benefit	–
Whole grains	–	++ Benefit	++++ Benefit	–
Beans/legumes	–	++ Benefit	+++ Benefit	–
Fish	++++ Benefit	++ Benefit	++++ Benefit	+ Benefit
Nuts	–	+++ Benefit	++++ Benefit	++ Benefit
Processed meats	+++Harm	–	++++Harm	–
Unprocessed red meats	+++Harm	–	++No effect ‡	–
Eggs	–	++No effect	++No effect	–
Dairy	–	++ Benefit	+++ Benefit	–
Sugar sweetened beverages	++Harm	+++Harm	++Harm	–
Alcohol	+++ Benefit	+++ Benefit	++++ Benefit	–
Nutrients				
Sodium	++++Harm	++++Harm	++Harm	+Harm
Potassium	–	+++ Benefit	+++ Benefit	+ Benefit
Antioxidant vitamins	–	+ Benefit	+++ Benefit	++++No effect
Calcium	–	+ Benefit	+++No effect	++No effect
Dietary fibre	++++ Benefit	++++ Benefit	++++ Benefit	+No effect
Refined carbohydrates/starches	++Harm	++Harm	++++Harm	–
Total fat	+++Harm	++No effect	+++No effect	+++No effect
Trans fat	+++Harm	++++Harm	++++Harm	–
Polyunsaturated fat in place of:				
saturated fat	+++ Benefit	++++ Benefit	++++ Benefit	++ Benefit
carbohydrate	++ Benefit	++++ Benefit	++ Benefit	–
Monounsaturated fat in place of				
Saturated fat	++ Benefit	++++ Benefit	+No effect / benefit	–
Carbohydrate	++ Benefit	++++ Benefit	++ Benefit	++ Benefit
Saturated fat in place of: §				
Carbohydrate	+++Harm	++++Harm/ No effect /§	++++No effect	+No effect
Seafood omega 3 fatty acids	+++ Benefit	++++ Benefit	++++ Benefit †	++ Benefit
Plant omega 3 fatty acids	++ Benefit	++ Benefit	++ Benefit †	+No effect
Dietary cholesterol	+++Harm	+++Harm	+Harm	–
Dietary patterns				
DASH	–	++++ Benefit	++++ Benefit	+ Benefit
Mediterranean	++++ Benefit	++++ Benefit	++++ Benefit	+++ Benefit
Vegetarian	+ Benefit	+ Benefit	++ Benefit	–
Japanese	++++ Benefit	–	++ Benefit	–

–Too few studies performed to provide meaningful evidence; + Conflicting or limited supporting evidence; ++ Some evidence from a relatively limited number of studies, although with relevant shortcomings (eg, insufficient numbers of studies, limited types of populations, inadequate sample sizes, or insufficient follow-up) or relevant evidence to the contrary which raises important questions; +++ Fairly consistent evidence from several well conducted studies, but with some perceived shortcomings in the available evidence or some evidence to the contrary which precludes a more definite judgment; ++++Consistent evidence from multiple well conducted studies, with little or no evidence to the contrary.

* Each of these types of study designs provide complementary evidence for assessing strength, plausibility, and causality of diet-disease relations——see text for details. The entries in this table are based on the strongest evidence for effects on any single major cardiometabolic endpoint, including coronary heart disease, stroke, or diabetes. Table adapted, with new updates, from Mozaffarian et al.[18]

† Based on the strongest evidence for effects on any single major risk factor, including blood pressure, blood lipids, plasma glucose or insulin resistance, heart rate, or systemic inflammation.

Table 2 (continued)

	Ecological studies of clinical endpoints	Randomised trials of risk factors†	Prospective cohort studies of clinical endpoints	Randomised trials of clinical endpoints

‡ Relatively little effect for heart disease and stroke; modestly higher risk for diabetes.

§ Lowering of LDL cholesterol, but also lowering of HD cholesterol and no change in the total cholesterol:HDL cholesterol ratio.

Figure

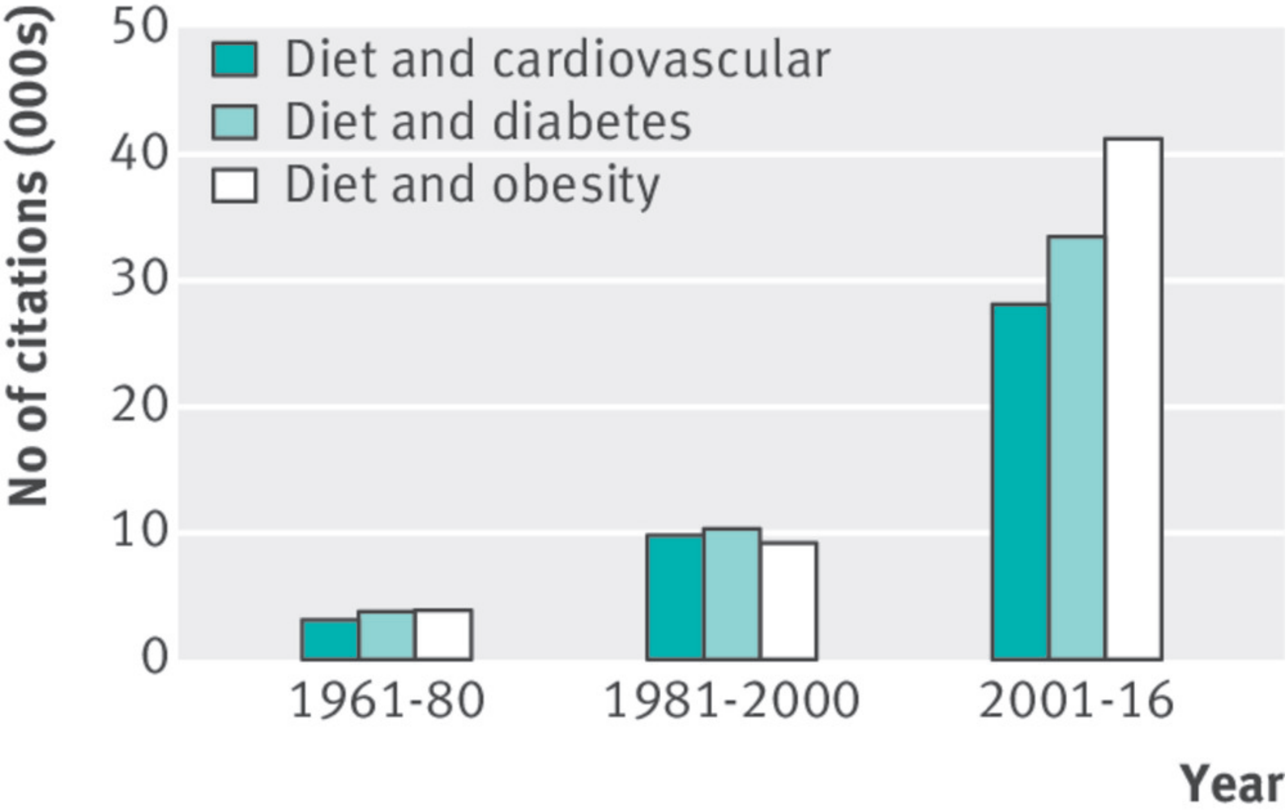

Fig 1 Numbers of publications retrieved by PubMed searches using the terms diet and cardiovascular, diabetes, or obesity by year