BMJ 2019;365:l1579 doi: 10.1136/bmj.l1579 (Published 16 April 2019)

ANALYSIS

FOOD FOR THOUGHT

Making nutrition guidelines fit for purpose

Guidelines must ask the right questions and incorporate complexity to improve their relevance and quality, argue **Lisa Bero and colleagues**

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Dietary risk factors are the leading contributors to the global burden of disease.[1] But what we choose to eat also affects the health of the planet.[2] Nutrition guidance therefore serves multiple purposes, including promoting health and wellbeing, maintaining adequate nutrition, combating dietary excesses and imbalances associated with non-communicable diseases, and protecting sustainable food systems. However, existing nutritional guidelines often do not consider the right questions or fail to take full account of available evidence because they rely on methods borrowed from other fields. We need different types of evidence informed nutrition guidelines to tackle these unprecedented challenges to population health.[3]

Unsuitability of current approaches

The current approach to developing nutrition guidelines has been adapted from established methods for clinical practice guidelines and was not created with nutrition questions and evidence in mind.[4] Although these methods are applicable to some types of nutrition guidelines, such as setting dietary or nutrient reference intake values, they are unsuitable for food and diet based guidelines for several reasons.[5-7]

Important questions related to nutrient interactions, dietary patterns, or food systems are studied mostly using observational designs rather than the randomised controlled trial that predominates in clinical studies. Randomised trials present several problems when studying nutrition exposures or interventions,[8 9] although advances in trial design, such as pragmatic trials, can help improve problems related to generalisability of results.[9]

Rigorous guidelines are usually underpinned by a systematic review of available trials, and although review methods have also been evolving, they are optimised for randomised trials of single component interventions. Most of the nutrition guidelines and policy statements in the World Health Organization's e-Library of Evidence for Nutrition Actions (eLENA) database of systematic reviews and the Cochrane Library relate to single nutrient interventions, which can be evaluated by randomised trials.[10] And the majority of nutrition systematic reviews in the Cochrane Library relate to evidence derived from studies of specific nutrients rather than of foods, dietary pattern, or food systems.[11] As well as availability of evidence, selection of topics for systematic reviews may be affected by reviewers' interest in narrower, clinical topics.

A critical step to including observational studies in the systematic review process is assessing risks of bias. Tools for assessing human observational studies of exposure effects need further development.[12 13] A recent review of 62 tools for assessing observational studies of exposures could not recommend a specific tool but provided guidance for selecting one.[14] Stakeholders from the nutrition field, including nutrition researchers and policy makers, should be involved in evaluating and achieving consensus on the most suitable tools for nutrition research.

The last crucial steps in guideline development are rating the certainty of the evidence and formulating recommendations based on the evidence and other considerations. Methods such as GRADE (Grading of Recommendations, Assessment, Development and Evaluation) are used infrequently, although guideline developers are starting to adopt this approach.[4] But these methods typically rate randomised trials as higher quality than a body of evidence consisting of other study designs, which means the recommendations for broad nutritional interventions are likely to be less strong than those focused on narrow questions studied with randomised trials.

Skewed evidence

Because recommendations are based on a body of evidence, they are heavily influenced by the availability of research on particular topics, which, in turn, is influenced by funding

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sources. A recent scoping review examined original research and systematic reviews that assessed corporate influence on research agendas across different fields.[15] The review found that industry tends to prioritise lines of inquiry that focus on products, processes, or activities that can be commercialised and marketed. For example, randomised trials sponsored by the food industry were more likely to test an intervention that manipulated a particular nutrient than trials with other sponsors.[16] This could allow food companies to market manufactured products containing certain nutrients as beneficial to health. Additional studies in the scoping review analysed internal industry documents from the tobacco, alcohol, sugar, and mining industries. These highlighted the strategies used to reshape entire fields of research,[15] including establishing research agendas that support industry policy positions, distract from research on harms of products, and protect industry from litigation.

Lack of transparency on funding sources makes it difficult to study differences between research with and without food industry sponsorship.[17] But Coca-Cola makes sufficient information available on its funded projects to track its publications. Along with a focus on single nutrient research, over 40% of Coca-Cola funded projects focused on physical activity, suggesting that the company attempted to shift attention from the role of sugary drinks in obesity to the role of sedentary behaviour.[18 19]

Nutrition researchers[10 20-23] and organisations such as Cochrane[11] are calling for reform of conventional evidence synthesis and translation approaches so they are better able to overcome limitations in available evidence and include evidence relevant to modern nutrition problems. Below we give two examples of reforms in public health.

Incorporating complexity into systematic reviews

Recent work on incorporating complexity into systematic reviews and guidelines will help to inform work in nutrition, particularly food and diet based guidelines.[24] Taking a "complexity perspective" involves considering theory of change, causal pathways, complex systems properties, and context when conceptualising a review and when interpreting the evidence and formulating recommendations.[25] Nutrition recommendations should be framed in a broader context than clinical recommendations, emphasising equity, human rights, and sociocultural acceptability as well as the benefits and harms of an intervention.[26] Qualitative evidence can be synthesised to inform critical considerations such as acceptability and feasibility of complex interventions.[27]

Context is especially important when developing nutrition guidelines because of the diversity of purposes, exposure types, and intervention targets. The purpose of nutrition guidance extends across promoting health and wellbeing; nutritional adequacy for growth, maintenance, and repair; tackling dietary excesses and imbalances associated with non-communicable diseases and obesity; and protecting sustainable food systems.[28] Nutrition exposure spans nutrients, foods, diets, and food systems. The intervention may target downstream, midstream, or upstream causes of nutrition problems. Thus, observational study designs that produce findings with high external validity are needed to account for the contextual characteristics of links between health and food and dietary patterns.[29-31]

Advances in environmental health guidelines

Environmental health science, which synthesises evidence to assess harms of environmental exposures, faces similar challenges to nutrition.[32] Randomised trials of exposure to environmental risks are not available, and evidence syntheses must use data from observational human, animal, and in vitro mechanistic studies. In addition, environmental exposures are inherently complex and inter-related, making a randomised trial of a single chemical uninformative as well as unethical.

Environmental health researchers are innovating systematic review methods to evaluate and synthesise evidence from multiple data streams.[32-35] Such integrative approaches may be useful for complex nutrition questions such as how evolutionary changes in animal diets affect health outcomes.[36] GRADE is being modified for application to environmental health topics.[37] For example, some frameworks for assessing research on environmental hazards start with an initial higher rating for observational studies than GRADE would apply.[38] Importantly, the process for formulating the research questions is based on criteria such as priority and uncertainty rather than the availability of certain types of evidence or the methods needed to synthesise it.[34]

Putting the horse before the cart

The selection and evaluation of evidence for nutrition guidance are currently being driven by the methods for evidence synthesis rather than the questions that need to be answered. This is analogous to putting the cart before the horse; narrow questions studied with randomised trials are driving the development of guidelines rather than the complex nutrition problems that need to be solved to improve nutrition.

We believe this problem can be tackled by using theory and logic models to drive the development of nutrition guidelines. They can be used to strategically guide formulation of the research question(s), to hypothesise causal mechanisms, to identify the methods that best measure the hypothesised causal mechanism, and for evidence synthesis and translation.[39]

Formulate the research question

The first step in the development of nutrition guidance is to formulate research questions in relation to the type of nutrition exposure (nutrient, food, dietary pattern, food system, or interactions of these) or intervention target and health outcome. Research questions about risks or associations need to be differentiated from those about causation because they require different study designs. Questions related to nutrition exposure typically assess associations (eg, is energy intake associated with obesity?) whereas questions about interventions typically assess causality (eg, does menu labelling reduce food consumption?). These questions will then dictate the types of evidence that must be considered to answer the questions.

Use theory to hypothesise causal mechanisms

Building a logic model based on nutrition and health promotion science theory can help identify the causal mechanisms that need to be studied to answer a particular set of nutrition questions. For example, building a logic model to examine the question, "How can we improve the nutritional quality of the food supply and change consumer demand patterns to benefit population health, particularly obesity?" led to a series of

systematic reviews of different strategies.[39] Comparative studies of other species can also contribute theory for structuring research into the complex relationships between humans and food environments.[36]

Nutrition and health promotion science can provide theoretical insights to hypothesise the causal mechanism linking a nutrition exposure or intervention to a health outcome. Nutrition science theory helps explain the nature and scope of the associations between nutrients, foods, diets, food systems, and health outcomes[40-44] and to model them.[36] Health promotion science can help suggest causal mechanisms that link intervention types with health outcomes. Nutrition interventions can target downstream (treatment), midstream (prevention), or upstream (promotion) factors for a particular nutrition problem. For instance, interventions to reduce obesity could focus on gastroplasty (downstream), dietary behaviour (midstream), or social circumstances (upstream). Health promotion science theory can help explain the nature and scope of the relations between these nutrition interventions and health outcomes. Describing the potential causal relations can guide the development of questions to examine different parts of the model.

Identify the type of evidence that should be included

The questions developed from the logic model will then drive the selection of evidence for the systematic reviews. What constitutes the best evidence varies with the question being asked, and multiple types of evidence may be needed.[45 46] The method selected to assess the hypothesised causal mechanism will be the one best able to account for the particular exposure type or intervention, as well as the contextual characteristics associated with the exposure or intervention. Narrow, nutrient specific questions can be examined with randomised trials whereas broader dietary pattern questions will usually require observational study designs. In addition, animal studies can provide mechanistic information or provide data on diet interactions with the environment. For example, nutritional ecology studies aim to understand how nutrition mediates the relations between animals and their environments, from short term homeostatic responses to longer term developmental and evolutionary adaptation.[47]

Synthesise the evidence

The challenge for guideline developers is to synthesise evidence from these different evidence streams, as sometimes done in environmental health. For example, to examine the effect of perfluorooctanoic acid on fetal growth systematic reviewers used predefined structured methods for integrating human and non-human evidence from different systematic reviews and linked these to describing the strength of the evidence.[48]

For public health guidelines examining broad questions for which the evidence comes from observational data, new ways of rating the evidence need to be considered that acknowledge factors such as generalisability and relevance for translation into practice.[49 50] This means that observational studies might start out with a higher rating if they are the best fit for answering a question within the logic model. For example, a process such as GRADE could be modified to initially assign a "moderate" rather than "low" quality rating to human observational evidence, upgrading or downgrading based on predefined criteria relevant to the specific type of study.[32]

Other structured processes such as the Hill criteria, navigation guide, and US National Toxicology Program methods have also been proposed for rating the quality of diverse types of evidence.[51] The main value of these approaches is that the judgments used to make recommendations are systematic and transparent.

Influencing policy

Systematic reviews are increasingly used to inform policy related to health, criminal justice, social welfare, and environmental risks.[35 52] However, opposition to using systematic reviews is persistent and often led by commercial organisations. For example, drug companies have paid authors to criticise systematic review methods or challenge specific reviews and erroneously suggested that using evidence limits decisions and personal choice.[52 53] These criticisms can discourage policy makers from using systematic reviews of drug efficacy and safety to inform decisions. Mislabelling poorly conducted and methodologically unsound reviews as "systematic" also increases policy makers' distrust.[54]

Some countries now require systematic reviews to support claims about the health benefits of foods[55] and for environmental risk assessments.[51] Commercial interests then produce systematic reviews that meet regulatory requirements but not high methodological standards.[54] The resistance to using systematic reviews as an evidence base for nutrition guidelines may be particularly hard to overcome because of the well documented industry influence on nutrition evidence. Systematic review methods may be unfamiliar to nutrition policy makers and the questions addressed by existing systematic reviews may not be relevant to them.

Our proposed approach to developing nutrition guidelines offers solutions to enhance the use of systematic reviews. Including policy makers in the production and prioritisation of systematic reviews can increase their uptake.[52] Using theory and logic models to drive the development of nutrition guidelines is a way to incorporate policy makers' input early in the process of formulating questions and systematic reviews. Training policy makers, researchers, and nutrition scientists in systematic review methods can enable them to identify reviews that have high methodological standards. Lastly, transparency about industry influence in the production or evaluation of systematic reviews can enable policy makers to detect trustworthy reviews.

Although innovation is needed to fill some of the gaps in evidence synthesis methods, our approach offers opportunities for funders, researchers, and systematic reviewers to produce studies and synthesise evidence that can be used to inform optimal nutrition policy. Involving these stakeholders and policy makers in improving the methods for systematic reviews in nutrition will make the reviews underpinning nutrition guidelines more rigorous, transparent, usable, and relevant.

Key messages

- Methods for developing clinical practice guidelines are not suitable for nutrition
- The nutrition questions that need to be answered, rather than the availability of evidence, should drive nutrition guidance
- Logic models and theory should be used to develop questions for review, identify and evaluate the most suitable types of study, and formulate recommendations
- Innovation in evidence synthesis methods will be needed to assess properly the relevant evidence

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Contributors and sources: LB has a research track record related to studying bias, systematic review methods, commercial influences on health, and policy making.

SN is an expert in guideline development and systematic review methods and has extensive experience at health systems, national, and global levels. ML is a public health nutritionist with extensive research experience in food policy, sustainable diets, and dietary guideline development. LB was invited by *The BMJ* to submit the paper and wrote the first draft. SN and ML made significant contributions to revisions of the paper. LB serves as guarantor.

Competing interests: We have read and understood BMJ policy on declaration of interest and declare that we have no competing interests. The authors alone are responsible for the views expressed in this article and they do not necessarily represent the views, decisions, or policies of the institutions with which they are affiliated.

Provenance and peer review: Commissioned; externally peer reviewed.

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