"Modified" GRADE Approach Not GRADE, Not Rigorous

To USDA-HHS,

For the 2020-2025 U.S. Dietary Guidelines for Americans, the USDA office leading this effort (Center for Nutrition Policy and Promotion, or CNPP) made an announcement in March of this year, at the first meeting of the Dietary Guidelines Advisory Committee, in Washington, D.C., regarding its intention to use a "modified GRADE" for the systematic reviews of the scientific literature in order to ensure the trustworthiness of nutrition guidelines.

CNPP stated that the announcement regarding GRADE was in response to a recommendation made by the National Academies of Sciences, Engineering, and Medicine, in its 2017 review of the Dietary Guidelines, which found that the Guidelines' process fell short of meeting the "best practices for conducting systematic reviews" and that the "methodological approaches and scientific rigor for evaluating the scientific evidence need[ed] to "be strengthened."[1] The report recommended GRADE as an option.

As a co-founder of GRADE, and current GRADE working group co-chair, with extensive, senior-level experience in the development of international treatment guidelines, I feel I can comment with authority regarding the intent to use "modified GRADE".

The GRADE working group strongly discourages any modification of GRADE – indeed, our request is that any group diverging in important ways from key GRADE principles and practice not refer to GRADE. We of course have no authority to stop anyone from doing so.

GRADE has been adopted by over 110 organizations worldwide, many with the highest prestige and standards. We make the request to refrain from referring to a "modified GRADE" because we feel that the core principles are crucial, and the aura of scientific credibility given by reference to GRADE is, when there are important modifications, illusory.

My concern is that CNPP's stated methodological approach, presented on its website [2] diverges from GRADE standards in critical ways:

- Most importantly, CNPP says nothing about the basic prioritization of types of evidence. Fundamental to the GRADE methodology is an approach where, when assessing the quality of evidence, systematic reviews of randomized controlled clinical trials begin as "high-quality" evidence, while systematic reviews of observational studies (for example, cohort and case-control studies) begin as "low quality" evidence. The reason for this guidance is that observational studies inevitably suffer from a risk of substantial residual confounding, and only in the presence of large effects (RR > 2 or < 0.5) or clear dose-response gradients can provide higher quality evidence.

This distinction between high- and low-quality evidence lies at the core of any rigorous evaluation of science and is at the heart of the GRADE methodology.[3] Thus, CNPP's omission on this point is a fundamental problem in its approach.

- Further, the CNPP approach does not include the full range of factors for modification of ratings of quality of evidence from the starting point based on study design.
    - CNPP provides only reasons for rating down the quality of evidence and omits the reasons for rating up;
    - CNPP includes only four of the five GRADE reasons for rating down evidence. Absent is an evaluation of "publication bias," which may be an important problem in nutrition science;
    - CNPP presents two factors, called "directness" and "generalizability" - an unnecessarily duplication. The issue that GRADE labels "directness" includes generalizability.

CNPP justifies its modifications to GRADE by suggesting that nutrition guidelines inform population-based nutrition guidance, rather than medical guidance, for which GRADE was originally developed. GRADE initially asserted, and maintains, that standards of judgment of quality of evidence for causation remain the same irrespective of the field of inquiry. This includes nutrition, where GRADE has previously been applied.[4] Although I am personally sympathetic with nutrition guideline members who may find it painful and vexing to acknowledge that only low quality evidence underlies their recommendations, revising the standards of what constitutes moderate or high quality evidence is not a satisfactory remedy. If they choose to do so, I would appeal to them not to refer to GRADE in any way.

There is an additional limitation in the CNPP's reference to GRADE. The statement does not refer to GRADE guidance for moving from evidence to recommendations, and in particular to the crucial role of peoples' values and preferences. Systematic reviews of the available evidence regarding values and preferences should be part of the guideline effort – in our experience, they have been crucial in guiding the panel to recommendations that consider public attitudes. Consideration of public values and preferences has been widely neglected, including in previous USDA guidelines. Appropriate use of GRADE must include explicit value and preference judgments based on systematic reviews of the relevant evidence, as well as considerations of feasibility, acceptability, and equity.

CNPP's significant deviations from the GRADE methodology will result in nutritional guidelines recommendations that, without proper evaluation of the evidence, are unlikely to be trustworthy. The best solution would be adherence to GRADE guidance. The alternative solution is less satisfactory, but is required if USDA is to act with scientific integrity, which is to remove any claim that its approach adheres to GRADE guidance, however "modified."

Sincerely,
Gordon Guyatt MD MSc O.C.

[1] The National Academies of Sciences, Engineering and Medicine, "Redesigning the Process for Establishing the Dietary Guidelines for Americans," September, 2017, http://nationalacademies.org/hmd/Reports/2017/redesigning-the-process-for-establishing-the-dietary-guidelines-for-americans.aspx, pp. S-4 and 2-15.
[2] https://nesr.usda.gov/2020-dietary-guidelines-advisory-committee-systematic-reviews
https://nesr.usda.gov/sites/default/files/2019-03/Nutrition%20Evidence%20Systematic%20Review%20Grading%20Rubric.pdf
Note: CNPP has confirmed that, as of this writing, these website pages and those linked to them represent the totality of its methodology.
[3] Guyatt G. et al., *BMJ* 2008;336:924.
[4] E.g., Johnston BC, et al. Comparison of weight loss among named diet programs in overweight and obese adults: a meta-analysis. *JAMA*. 2014 Sep 3;312(9):923-33.

Note: "NESR" refers to Nutrition Evidence Systematic Review, which is the office within CNPP in charge of these scientific reviews.