

May 16, 2022

VIA ELECTRONIC SUBMISSION

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Office of Disease Prevention and Health Promotion (ODPHP)
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Re: Request for Comments on Scientific Questions To Be Examined To Support the Development of the Dietary Guidelines for Americans, 2025–2030. Docket ID: HHS-OASH-2022-0005. 87 FR 22540.

The Council for Responsible Nutrition (CRN)¹ appreciates the opportunity to provide comments to the U.S. Department of Health and Human Services (HHS) and Department of Agriculture (USDA) and looks forward to engaging throughout the Departments' transparent process for developing the *2025-2030 Dietary Guidelines for Americans*.

CRN notes that the list of proposed questions does not include questions related to dietary supplements and fortified foods. In the 2020-2025 Dietary Guidelines process, dietary supplements were included as a topic for two specific life stages – infancy and toddlerhood and pregnancy and lactation. In addition, across life stages, a question was posed to examine whether there is evidence to support supplementation and/or fortified food consumption to meet nutrient adequacy if USDA Dietary Patterns do not provide recommended nutrient targets. CRN believes questions about supplementation should be examined by the 2025 Dietary Guidelines Advisory Committee (DGAC), including questions relating to pregnancy and lactation as there are increased nutrient needs during this life stage that are difficult to meet from foods and beverages alone.

¹The Council for Responsible Nutrition (CRN), founded in 1973, is a Washington, D.C.-based trade association representing more than 200 dietary supplement and functional food manufacturers, ingredient suppliers, and companies providing services to those manufacturers and suppliers. In addition to complying with a host of federal and state regulations governing dietary supplements and food in the areas of manufacturing, marketing, quality control and safety, our manufacturer and supplier members also agree to adhere to additional voluntary guidelines as well as to CRN's Code of Ethics. For more information, visit www.crnusa.org.

Dietary supplement use is prevalent in the U.S.² and the current Dietary Guidelines recognize that in some cases dietary supplements may be useful in providing nutrients that are consumed in less than recommended amounts.³ The 2020 DGAC scientific report indicates that the U.S. population (1 year and older) does not meet recommended intakes of vitamins A, C, D, E, and K, calcium, dietary fiber, potassium, magnesium, and choline and identified vitamin D, calcium, dietary fiber, and potassium as underconsumed food components of public health concern. Moreover, many pregnant women do not meet recommendations for key nutrients, including vitamins A, C, D, E, K, B6, folate, choline, iron, potassium, calcium, magnesium, and zinc. Fortunately, about 70 percent of pregnant women consumed nutrient supplements, which reduced the prevalence of inadequate nutrient intakes.⁴

Due to their prevalence in American diets, nutrient intakes from dietary supplements have been analyzed in conjunction with foods and beverages to estimate overall nutrient intakes in the population, an important part of the DGAC scientific review. Beyond nutrient adequacy, the 2020 DGAC examined relationships between intakes of specific nutrients and dietary components and maternal and child outcomes. Due to time constraints, the 2020 DGAC did not examine some scientific questions and recommended the next DGAC to do so; however, these were not included in the proposed list of questions. CRN recommends adding questions left unstudied by the 2020 DGAC as well as questions about specific nutritional needs of older adults, possible new USDA Dietary Patterns, and dietary pattern components with scientific evidence suggesting benefits for health. Thus, this comment proposes new scientific questions.

CRN notes HHS and USDA proposed a question examining the relationship between consumption of dietary patterns with varying amounts of ultra-processed foods and growth, size, body composition, risk of overweight and obesity, and weight loss and maintenance. We suggest modification to this question to consider the varying nutritional quality of ultra-processed foods. Thus, this comment also proposes modification to a proposed question.

New Scientific Questions

1. Iodine status in pregnancy and lactation

Suggested question wording:

²Mishra S, Stierman B, Gahche JJ, Potischman N. Dietary Supplement Use Among Adults: United States, 2017-2018. NCHS Data Brief. 2021;(399):1-8.

³U.S. Department of Agriculture and U.S. Department of Health and Human Services. Dietary Guidelines for Americans, 2020-2025. 9th Edition. December 2020. Available at [DietaryGuidelines.gov](https://www.dietaryguidelines.gov).

⁴Dietary Guidelines Advisory Committee. 2020. Scientific Report of the 2020 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Agriculture and the Secretary of Health and Human Services. U.S. Department of Agriculture, Agricultural Research Service, Washington, DC. Available at: <https://doi.org/10.52570/DGAC2020>.

- What are the dietary determinants of maternal iodine status in both pregnancy and lactation?

Rationale for inclusion:

The need for iodine increases during pregnancy to support neurological development and fetal growth. Iodine inadequacy during pregnancy is associated with impaired neurological development. Based on biomarker data, the 2020 DGAC concluded low iodine intake is of public health concern among women who are pregnant, especially those not using iodine-containing prenatal supplements. Dietary data were not available for iodine; therefore, the 2020 DGAC recommended that food values for iodine be included in the USDA database so that intakes can be estimated. The iodine content of common foods and dietary supplements is now available.⁵

2. Relationship between maternal dietary supplement and/or fortified food intakes of vitamin B12, vitamin D, iron, iodine, and choline and maternal and child outcomes

Suggested questions and wording:

- What is the relationship between specific nutrients from supplements and/or fortified foods consumed before and during pregnancy and lactation and micronutrient status? (vitamin B12, vitamin D, iron, iodine, and choline)
- What is the relationship between specific nutrients from supplements and/or fortified foods consumed before and during pregnancy and lactation and risk of gestational diabetes? (vitamin B12, vitamin D, iron, iodine, and choline)
- What is the relationship between specific nutrients from supplements and/or fortified foods consumed before and during pregnancy and lactation and risk of hypertensive disorders during pregnancy? (vitamin B12, vitamin D, iron, iodine, and choline)
- What is the relationship between specific nutrients from supplements and/or fortified foods consumed before and during pregnancy and lactation and developmental milestones, including neurocognitive development? (vitamin B12, vitamin D, iron, iodine, and choline)

Rationale for inclusion:

These questions were previously included in the list of questions for the 2020 DGAC but were not examined due to lack of time. The 2020 DGAC recognized that these nutrients play an important role in achieving optimal pregnancy outcomes and emphasized that

⁵USDA, FDA and ODS-NIH Database for the Iodine Content of Common Foods. Agricultural Research Service – U.S. Department of Agriculture. Updated March 24, 2022. Accessed May 12, 2022. <https://www.ars.usda.gov/northeast-area/beltsville-md-bhnrc/beltsville-human-nutrition-research-center/methods-and-application-of-food-composition-laboratory/mafcl-site-pages/iodine>.

further examination by the next DGAC is needed given that all are nutrients of public health concern among women of reproductive age.

3. Omega 3 fatty acids and maternal and child outcomes

Suggested question wording:

- What is the relationship between omega-3 fatty acid supplements consumed before and during pregnancy and pregnancy outcomes and developmental milestones?

Rationale for inclusion:

The 2020 DGAC recognized the importance of adequate intake of omega-3 fatty acids for fetal brain development. Further, a recent systematic review suggests that increasing intake of omega-3 long-chain polyunsaturated fatty acids from food or supplements in pregnant women lowers the risk of early preterm and preterm birth.⁶ The 2020 DGAC recommended that the next DGAC assess both seafood and omega-3 fatty acid supplementation on pregnancy outcomes and child development.

4. Nutritional needs of older adults

Suggested questions and wording:

- What age-related factors impact the ability of older adults to meet nutritional needs?
- What nutritional strategies help mitigate age-related challenges affecting the ability of older adults to meet nutritional needs?

Rationale for inclusion:

Older Americans are one of the fastest-growing demographics. The number of people age 65 and older increased from 39.6 million in 2009 to 54.1 million in 2019 and is projected to top 80 million by 2040.⁷ In less than two decades, older adults are expected to outnumber children for the first time in the U.S.⁸ As the population ages, the

⁶Middleton P, Gomersall JC, Gould JF, Shepherd E, Olsen SF, Makrides M. Omega-3 fatty acid addition during pregnancy. *Cochrane Database Syst Rev.* 2018;11(11):CD003402. Published 2018 Nov 15. doi:10.1002/14651858.CD003402.pub3.

⁷Administration for Community Living. Projected Future Growth of Older Population. Accessed 6 May 2022. Available at: <https://acl.gov/aging-and-disability-in-america/data-and-research/projected-future-growth-older-population>.

⁸United States Census Bureau. The U.S. Joins Other Countries With Large Aging Populations. Accessed 6 May 2022. Available at: <https://www.census.gov/library/stories/2018/03/graying-america.html>.

prevalence of chronic disease increases; 85% of older adults have at least one chronic health condition and 60% have at least two.⁹ While the *2020-2025 Dietary Guidelines for Americans* advise consistent consumption of healthy dietary pattern components for adults of all age groups and health status, and experimenting with food preparation that “can help identify textures that are acceptable, appealing, and enjoyable,” there should be more guidance on how to maintain proper nutrition in the face of age-related challenges. Many older adults experience decreased food consumption due to reduced energy needs; changes in appetite, sense of taste, and sense of smell; physical impairment such as inability to chew or swallow food; decreased ability to consume and/or absorb nutrients related to use of medication and their side effects.¹⁰ The 2020-2025 Dietary Guidelines recognized such “heightened risk of malnutrition that occurs with age.” Importantly, the Centers for Medicare & Medicaid Services recently commented in their proposed 2023 Inpatient Prospective Payment System rule that “One factor contributing to the burden of malnutrition is health disparity across racial and ethnic groups.”¹¹

As the HHS and USDA continue to take a life stage approach towards updating the Dietary Guidelines with more information on life-stage specific nutritional concerns, the Departments should expand scientific questions related to the nutritional needs specific to older adults, a rapidly growing population with unique age-related challenges impacting the ability to consume nutrient dense foods. Further, additional guidance would better inform federal nutrition programs that rely on the Dietary Guideline’s recommendations to assist older adults in meeting nutritional needs, including HHS’s Home-Delivered Nutrition Program and USDA’s Supplemental Nutrition Assistance Program (SNAP).

5. Additional Dietary Patterns

Suggested question wording:

⁹National Institute on Aging. Talking to Your Older Patient: Supporting Older Patients with Chronic Conditions: Accessed 6 May 2022. Available at: <https://www.nia.nih.gov/health/supporting-older-patients-chronic-conditions#:~:text=Approximately%2085%25%20of%20older%20adults,for%20Disease%20Control%20and%20Prevention.>

¹⁰U.S. Government Accountability Office. Report to Congressional Requesters. Nutrition Assistance Programs: Agencies Could Do More to Help Address the Nutritional Needs of Older Adults. Accessed 6 May 2022. Available at: <https://www.gao.gov/assets/gao-20-18.pdf>.

¹¹Medicare Program: Hospital Inpatient Prospective Payment Systems for Acute Care Hospitals and the Long-Term Care Hospital Prospective Payment System and Proposed Policy Changes and Fiscal Year 2023 Rates, etc. 87 Fed. Reg. 28108 (May 10, 2022).

- If nutrient needs are not met by additional Dietary Patterns, is there evidence to support supplementation and/or consumption of fortified foods to meet nutrient adequacy?

Rationale for inclusion:

The 2020 DGAC examined a similar question regarding the three USDA Dietary Patterns. The list of proposed questions includes the following under “Food Pattern Modeling”:

Considering each life stage, should changes be made to the USDA Dietary Patterns (Healthy U.S.-Style, Healthy Mediterranean-Style, and/or Healthy Vegetarian), and should additional Dietary Patterns be developed/proposed based on:

- *Findings from systematic reviews, data analysis, and/or food pattern modeling analyses*
- *Population norms (e.g., starchy vegetables are often consumed interchangeably with grains), preferences (e.g., emphasis on one staple grain versus another), or needs (e.g., lactose intolerance) of the diverse individuals and cultural foodways within the U.S. population?*

The DGAC may find that additional Dietary Patterns should be developed; in that case, a question should examine whether additional Dietary Patterns meet nutrient needs across life stages, and if not, whether there is evidence to support supplementation and/or consumption of fortified foods to meet nutrient adequacy in each life stage.

6. Relationship between specific dietary pattern components (micronutrients; flavonoids; omega-3 fatty acids; and lutein/zeaxanthin; fermented foods or probiotics, NAD) and health

Suggested questions and wording:

- What is the relationship between micronutrients, including B vitamins, from foods, beverages, and dietary supplements and cognitive health in older adults?
- What is the relationship between flavonoids and omega-3 fatty acids from foods, beverages, and dietary supplements and cardiovascular health?
- What is the relationship between lutein and zeaxanthin from foods, beverages, and dietary supplements and ocular health?
- What is the relationship between fermented foods or probiotics from foods, beverages, and dietary supplements and gut health?
- What is the relationship between nicotinamide adenine dinucleotide (NAD) status and age-related cognitive decline?

Rationale for inclusion:

A wide range of dietary pattern components have been studied for their potential role in supporting health and preventing diet-related health conditions. Beyond food groups to include and food components to limit, dietary advice would be more robust with recommendations about dietary pattern components to increase that are beneficial for health and healthy aging. As the U.S. population ages it becomes imperative to optimize cognitive health. The 2020 DGAC noted in its scientific report that optimal nutrient intake for prevention of cognitive decline should be examined given that various food components, such as vitamin B12, have been associated with cognitive function. The prevalence of cardiovascular disease (CVD) (including hypertension) among U.S. adults is 49.2% (126.9 million in 2018) and increases with age. The annual economic burden of CVD was estimated to be \$363.4 billion.¹² The prevalence of age-related macular degeneration (AMD) is 2.09% (2.07 million in 2010) and the estimated number of people with AMD is expected to more than double by 2050 to 5.44 million as the population ages.¹³ Recent systematic reviews and meta-analyses have shown that micronutrients support cognitive health^{14,15,16,17}; omega-3 fatty acids^{18,19,20} and flavonoids support

¹²Virani SS, Alonso A, Aparicio HJ, Benjamin EJ, Bittencourt MS, Callaway CW, et al. Heart disease and stroke statistics—2021 update: a report from the American Heart Association. *Circulation*. 2021;143:e254–e743.

¹³National Eye Institute. Age-Related Macular Degeneration (AMD) Data and Statistics. Accessed 2 May 2022. Available at: <https://www.nei.nih.gov/learn-about-eye-health/outreach-campaigns-and-resources/eye-health-data-and-statistics/age-related-macular-degeneration-amd-data-and-statistics>.

¹⁴Olaso-Gonzalez G, Inzitari M, Bellelli G, Morandi A, Barcons N, Viña J. Impact of supplementation with vitamins B6, B12, and/or folic acid on the reduction of homocysteine levels in patients with mild cognitive impairment: A systematic review. *IUBMB Life*. 2022 Jan;74(1):74-84. doi: 10.1002/iub.2507.

¹⁵Wang Z, Zhu W, Xing Y, Jia J, Tang Y. B vitamins and prevention of cognitive decline and incident dementia: a systematic review and meta-analysis. *Nutr Rev*. 2022 Mar 10;80(4):931-949. doi: 10.1093/nutrit/nuab057.

¹⁶Suh SW, Kim HS, Han JH, Bae JB, Oh DJ, Han JW, Kim KW. Efficacy of Vitamins on Cognitive Function of Non-Demented People: A Systematic Review and Meta-Analysis. *Nutrients*. 2020 Apr 22;12(4):1168. doi:10.3390/nu12041168.

¹⁷Baker L, Manson J, Rapp S, et al. OC-11 Multivitamins on cognitive function: findings of the cocoa supplement and multivitamin outcomes study of cognition (COSMOS-MIND)[Oral Communication]. In: Abstract: Symposia, Conferences, Oral communications: 14th Clinical Trials on Alzheimer's Disease (CTAD) November 9-12, 2021. *J Prev Alzheimers Dis*. 2021;8(S1):S2-S72. doi: 10.14283/jpad.2021.57.

¹⁸Shen S, Gong C, Jin K, Zhou L, Xiao Y, Ma L. Omega-3 Fatty Acid Supplementation and Coronary Heart Disease Risks: A Meta-Analysis of Randomized Controlled Clinical Trials. *Front Nutr*. 2022;9:809311. Published 2022 Feb 3. doi:10.3389/fnut.2022.809311.

¹⁹Khan SU, Lone AN, Khan MS, et al. Effect of omega-3 fatty acids on cardiovascular outcomes: A systematic review and meta-analysis. *EClinicalMedicine*. 2021;38:100997. Published 2021 Jul 8. doi:10.1016/j.eclinm.2021.100997.

²⁰Hu Y, Hu FB, Manson JE. Marine Omega-3 Supplementation and Cardiovascular Disease: An Updated Meta-Analysis of 13 Randomized Controlled Trials Involving 127 477 Participants. *J Am Heart Assoc*. 2019;8(19):e013543. doi:10.1161/JAHA.119.013543.

cardiovascular health^{21,22}, lutein and zeaxanthin support ocular health,^{23,24} and probiotics support gut health.^{25,26,27} Aging may be associated with decline in NAD.^{28,29} A growing body of evidence suggests boosting cellular NAD may provide neuroprotective effects in healthy aging and neurodegeneration.³⁰

The benefits of these dietary pattern components should be examined to help inform guidance on health-promoting dietary patterns across the lifespan. Further, findings related to these questions could help inform development of additional dietary patterns for diverse groups within the U.S. population.

Modification of a Proposed Question:

1. Relationship between ultra-processed foods and health

Suggested question modification (in red):

- What is the relationship between consumption of dietary patterns with varying amounts of ultra-processed foods **of varying nutritional quality** and growth, size, body composition, risk of overweight and obesity, and weight loss and maintenance?

²¹Raman G, Avendano EE, Chen S, et al. Dietary intakes of flavan-3-ols and cardiometabolic health: systematic review and meta-analysis of randomized trials and prospective cohort studies. *Am J Clin Nutr.* 2019;110(5):1067-1078. doi:10.1093/ajcn/nqz178.

²²Wang X, Ouyang YY, Liu J, Zhao G. Flavonoid intake and risk of CVD: a systematic review and meta-analysis of prospective cohort studies. *Br J Nutr.* 2014;111(1):1-11. doi:10.1017/S000711451300278X.

²³Wilson LM, Tharmarajah S, Jia Y, Semba RD, Schaumberg DA, Robinson KA. The Effect of Lutein/Zeaxanthin Intake on Human Macular Pigment Optical Density: A Systematic Review and Meta-Analysis. *Adv Nutr.* 2021;12(6):2244-2254. doi:10.1093/advances/nmab071.

²⁴Johnson EJ, Avendano EE, Mohn ES, Raman G. The association between macular pigment optical density and visual function outcomes: a systematic review and meta-analysis. *Eye (Lond).* 2021;35(6):1620-1628. doi:10.1038/s41433-020-01124-2.

²⁵Singh RK, Chang HW, Yan D, Lee KM, Ucmak D, Wong K, Abrouk M, Farahnik B, Nakamura M, Zhu TH, Bhutani T, Liao W. Influence of diet on the gut microbiome and implications for human health. *J Transl Med.* 2017 Apr 8;15(1):73. doi: 10.1186/s12967-017-1175-y.

²⁶Rajkumar H, Mahmood N, Kumar M, Varikuti SR, Challa HR, Myakala SP. Effect of probiotic (VSL#3) and omega-3 on lipid profile, insulin sensitivity, inflammatory markers, and gut colonization in overweight adults: a randomized, controlled trial. *Mediators Inflamm.* 2014;2014:348959. doi: 10.1155/2014/348959.

²⁷Sergeev IN, Aljutaily T, Walton G, Huarte E. Effects of Synbiotic Supplement on Human Gut Microbiota, Body Composition and Weight Loss in Obesity. *Nutrients.* 2020 Jan 15;12(1):222. doi: 10.3390/nu12010222.

²⁸Braidy N, Liu Y. Can nicotinamide riboside protect against cognitive impairment?. *Curr Opin Clin Nutr Metab Care.* 2020;23(6):413-420. doi:10.1097/MCO.0000000000000691.

²⁹Braidy N, Berg J, Clement J, et al. Role of Nicotinamide Adenine Dinucleotide and Related Precursors as Therapeutic Targets for Age-Related Degenerative Diseases: Rationale, Biochemistry, Pharmacokinetics, and Outcomes. *Antioxid Redox Signal.* 2019;30(2):251-294. doi:10.1089/ars.2017.7269.

³⁰Brakedal B, Dölle C, Riemer F, et al. The NADPARK study: A randomized phase I trial of nicotinamide riboside supplementation in Parkinson's disease. *Cell Metab.* 2022;34(3):396-407.e6. doi:10.1016/j.cmet.2022.02.001.

Rationale for modification:

Currently there is no definition for “ultra-processed food” in U.S. regulation. The term “ultra-processed food” was developed in the newly proposed NOVA classification from researchers in Brazil, which is solely based on the extent and degree of processing of foods but not on nutrient content.³¹ Group 4 within the NOVA classification is “ultra-processed foods” (UPF), which are “formulations of ingredients, mostly of exclusive industrial use, typically created by series of industrial techniques and processes.”³² One of its assumptions is that all commercially manufactured foods which fall into Group 4 in the NOVA system have low nutritional value and increase the risks of chronic diseases and mortality. However, this assumption is not necessarily in line with science that has demonstrated health benefits of diets comprising foods at all levels of processing.³³ The NOVA classification has significant limitations when trying to apply the simplistic concept on nutrition policy as it completely overlooks nutrient density or nutritional attributes of food.^{34, 35} Within Group 4 of NOVA classifications, one may find a wide range and varying degree of nutrient density and nutritional quality of products. Group 4 contains not only foods high in added sugar, salt, and saturated fat, but it also contains plant-based beverages, plant-based foods, as well as meal replacements that have high nutrient density. Therefore, when evaluating the relationships between ultra-processed foods and health outcomes, it is critical to consider not only the amount but also the nutritional quality of the products consumed as part of dietary patterns.

The original question, which focuses only on the amount of ultra-processed foods, may lead to conclusions that can be potentially misleading. Furthermore, the 2020-2025 Dietary Guidelines encourage Americans to consume foods which include many products made from processed soybeans (fortified soy beverages, soy yogurt, and tofu) that fall under “ultra-processed food” within the NOVA classification. In addition, many fortified foods, despite being classified as “ultra-processed,” play an important role in public health by contributing to the dietary intakes of desired nutrients including those that are under-consumed by the U.S. population (calcium, potassium, dietary fiber, and

³¹Gibney MJ. Ultra-Processed Foods: Definitions and Policy Issues. *Curr Dev Nutr*. 2018 Sep 14;3(2):nzy077. doi: 10.1093/cdn/nzy077.

³²Monteiro, C.A., Cannon, G., Lawrence, M., Costa Louzada, M.L. and Pereira Machado, P. 2019. Ultra-processed foods, diet quality, and health using the NOVA classification system. Rome, FAO.

³³Petrusa RR, Sobralac PJA, Tadinibc CC, Gonçalves CB. The NOVA classification system: A critical perspective in food science. *Trends in Food Science & Technology*. 2021 Oct;116:603-608.

³⁴Hallinan S, Rose C, Buszkiewicz J, Drewnowski A. Some Ultra-Processed Foods Are Needed for Nutrient Adequate Diets: Linear Programming Analyses of the Seattle Obesity Study. *Nutrients*. 2021 Oct 28;13(11):3838. doi: 10.3390/nu13113838.

³⁵ Messina M, Sievenpiper JL, Williamson P, Kiel J, Erdman JW. Perspective: Soy-Based Meat and Dairy Alternatives, Despite Classification as Ultra-Processed Foods, Deliver High-Quality Nutrition on Par With Unprocessed or Minimally Processed Animal-Based Counterparts [published online ahead of print, 2022 Mar 23]. *Adv Nutr*. 2022;nmac026. doi:10.1093/advances/nmac026.

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May 16, 2022

10

vitamin D) and are of public health concern.³⁶ It is strongly recommended that HHS and USDA take a science-based, balanced approach when addressing the relationship between ultra-processed foods and health outcomes in the development of the *2025-2030 Dietary Guidelines for Americans*.

Thank you for considering our comments.



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³⁶Weaver CM, Dwyer J, Fulgoni VL 3rd, et al. Processed foods: contributions to nutrition. *Am J Clin Nutr.* 2014;99(6):1525-1542. doi:10.3945/ajcn.114.089284.