



Council for Responsible Nutrition

1828 L Street, NW, Suite 810 • Washington, DC 20036-5114
(202) 204-7700 • fax (202) 204-7701 • www.crnusa.org

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The Council for Responsible Nutrition (CRN) appreciates the opportunity to provide comments on the U.S. Preventive Services Task Force (USPSTF) **Draft Recommendation Statement: Vitamin, Mineral, and Multivitamin Supplements to Prevent Cardiovascular Disease and Cancer**. CRN, based in Washington, D.C., is the leading trade association representing dietary supplement manufacturers and ingredient suppliers. CRN's member companies manufacture popular national brands as well as the store brands marketed by major supermarkets, drug store and discount chains. They include some of the largest and most well-known ingredient suppliers, product manufacturers and marketers, direct sellers and specialty retailers of dietary supplements and dietary ingredients as well as specialty products sold by healthcare professionals.

CRN has organized its comments according to the questions posed by the USPSTF in the Public Comment Form.

Based on the evidence presented in this draft Recommendation Statement, do you believe that the USPSTF came to the right conclusions?

- Yes; I believe the USPSTF came to the right conclusions.
- Somewhat; I believe the USPSTF came to the right conclusions in some ways but not in others.
- No; I do not believe the USPSTF came to the right conclusions.
- Unsure; I am not sure if the USPSTF came to the right conclusions.

Please provide additional evidence or viewpoints that you think should have been considered.

As provided in CRN's comments on the USPSTF Draft Research Plan, we maintain that evidence surrounding surrogate endpoints for disease should be included in the review. Because there are substantial challenges to studying the effects of nutrient supplementation on chronic disease endpoints, significant gaps remain in the data regarding vitamin, mineral, and multivitamin supplementation for the prevention of cardiovascular disease and cancer when only clinical endpoints and randomized controlled trial data are considered. To broaden the evidence base for the review and further inform USPSTF's recommendations, surrogate endpoints of disease, e.g., systolic and diastolic blood pressure, serum lipid levels, markers of glucose metabolism, should be considered.

Additionally, the USPSTF should be aware of the *COcoa Supplement and Multivitamin Outcomes Study (COSMOS)*, a clinical trial investigating whether taking daily supplements of cocoa flavanols or a common multivitamin over a 5-year period reduces the risk for developing heart disease, stroke, cancer, and other important health outcomes. The intervention phase of the trial was completed on Dec 31, 2020 and the main results will most likely be available in late 2021. COSMOS is a large scale randomized clinical trial, conducted in 22,000 men and women over the age of 60. Given the size and duration of the trial, and the direct relevance of the intervention and outcome measures to the USPSTF recommendations, COSMOS will provide valuable data to inform the recommendations. CRN recommends that the USPSTF include the COSMOS trial data in its systematic review when the data become available and update the draft recommendation statement accordingly. If the review and recommendation statement are finalized without the COSMOS data, the USPSTF recommendations will soon be outdated and not serve the needs of healthcare providers and consumers.

How could the USPSTF make this draft Recommendation Statement clearer?

In the section, “USPSTF Assessment of Magnitude of Net Benefit,” it is stated that “[t]he USPSTF concludes with moderate certainty that the harms of supplementation with beta-carotene outweigh the benefits for the prevention of cardiovascular disease or cancer.” This statement lacks context and is misleading without information related to the doses at which harm has been reported. Nutrients are complex and many factors influence the benefits and risks of supplementation. However, for most nutrients both inadequate intake and supplementation at very high levels may pose a risk (classic “U” shaped curve) and benefit is achieved from regular consumption at or near recommended intake levels. It is important to identify that the evidence of harm pertains only to high doses of beta-carotene (≥ 20 mg/day) in at risk individuals.^{1,2} A more accurate statement would indicate that supplementation with beta-carotene is associated with harms at high doses and in individuals who are at increased risk of lung cancer (i.e., smokers and asbestos workers). Also, while the focus of the USPSTF recommendations is on cancer and cardiovascular disease, it should be emphasized that beta-carotene is an important nutrient at the appropriate dosages (such as the amounts contained in typical multivitamins) and that there are other documented benefits of beta-carotene supplementation, such as serving as an important source of vitamin A.

Similarly, in the section, “Supporting Evidence,” under “Harms of Supplementation,” it is stated that “[t]he most serious harm identified was increased cardiovascular disease mortality and increased risk of lung cancer in persons who smoke or had workplace asbestos exposure, associated with beta-carotene supplementation.” This statement should be modified to indicate that risk is increased at high doses of beta-carotene (≥ 20 mg/day).^{1,2} CRN believes that information about the dose of beta-carotene that has been demonstrated to pose a risk in individuals at increased risk of lung cancer is important information to communicate to health care practitioners and consumers.

¹ The Effect of Vitamin E and Beta Carotene on the Incidence of Lung Cancer and Other Cancers in Male Smokers. *New Engl J Med* 1994;330:1029-1035.

² Omenn GS, et al. Effects of a combination of beta carotene and vitamin A on lung cancer and cardiovascular disease. *New Engl J Med* 1996;334:1150-1155.

What information, if any, did you expect to find in this draft Recommendation Statement that was not included?

No comment.

What resources or tools could the USPSTF provide that would make this Recommendation Statement more useful to you in its final form?

No comment.

The USPSTF is committed to understanding the needs and perspectives of the public it serves. Please share any experiences that you think could further inform the USPSTF on this draft Recommendation Statement.

In the section, “Additional Information,” under the tab “Related Resources and Tools,” the USPSTF provided a Consumer Guide to the draft Recommendation Statement as a new resource for clinicians and patients. The Consumer Guide explains the draft recommendation in consumer-friendly language. It recognizes that people may be taking vitamin and mineral supplements with the goal of improving or maintaining overall health, but emphasizes that the recommendation is limited to the use of vitamin, mineral, and multivitamin supplementation to prevent cardiovascular disease and cancer only. The Consumer Guide also indicates that the recommendation only applies to healthy adults do not have a diagnosis or symptoms of a lack of nutrients or special nutritional needs.

CRN finds the Consumer Guide a useful new resource and suggests USPSTF promote it widely to not only clinicians and consumers, but the media as well. Currently, the Consumer Guide is not easily located on the recommendation website as the document is provided as a link under a secondary tab. CRN recommends that the Consumer Guide be prominently displayed on the recommendation website and widely publicized. Not only can it serve as a helpful resource to healthcare providers and consumers, but it can help to prevent misinterpretation of the USPSTF Recommendation Statement by these audiences, as well as the media, who report on the recommendations.

Do you have other comments on this draft Recommendation Statement?

No comment.