# Multivitamins and Supplements—Benign Prevention or Potentially Harmful Distraction?

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**More than half of adults** take dietary supplements, and use of supplements in the US is projected to increase.<sup>1,2</sup> In 2021, people in the US spent an estimated almost \$50 billion on dietary supplements and the dietary supplement industry spent

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Related article at iamainternalmedicine.com about \$900 million on marketing.<sup>2</sup>

The appeal of supplements is obvious. In theory, vitamins and minerals have antioxidative and anti-inflammatory effects that should decrease the development of cardiovascular disease and cancer. Eating fruits and veg-

etables is associated with decreased cardiovascular disease and cancer risk.<sup>3,4</sup> It is reasonable to think that key vitamins and minerals could be extracted from fruits and vegetables, packaged into a pill, and people could avoid the difficulty and expense of maintaining a balanced diet. The most common reason people report taking supplements is to improve or maintain overall health.<sup>5</sup> However, whole fruits and vegetables contain a mixture of vitamins, phytochemicals, fiber, and other nutrients that probably act synergistically to deliver health benefits. Micronutrients in isolation may act differently in the body than when naturally packaged with a host of other dietary components.<sup>6</sup>

In the right circumstances, supplements have health benefits. Vitamin and mineral deficiencies cause myriad illnesses. For individuals who are or may soon become pregnant, folic acid is recommended to prevent neural tube defects and iron is recommended to prevent preterm birth and low birth weight, as well as improve fetal brain development.<sup>7,8</sup>

For otherwise healthy, nonpregnant adults, the US Preventive Services Task Force (USPSTF) has updated its recommendation about the use of supplements to prevent cardiovascular disease or cancer.9 This updated recommendation is based on a new evidence report and systematic review, both in this issue of JAMA, of 84 studies, including 52 new studies since the last USPSTF recommendation on this topic in 2014.10 The USPSTF concluded that the current evidence is insufficient to assess the balance of benefits and harms of the use of multivitamin supplements, single supplements, or most paired supplements for the prevention of cardiovascular disease or cancer (I statement). The USPSTF specifically recommends against the use of beta carotene supplements for prevention of cardiovascular disease or cancer (D recommendation) because of a possible increased risk of mortality, cardiovascular mortality, and lung cancer. The USPSTF also specifically recommends against the use of vitamin E supplements for prevention of cardiovascular disease or cancer (D recommendation) because it probably has no net benefit in reducing mortality, cardiovascular disease, or cancer.

For multivitamins, proving the absence of a benefit is challenging and an I statement (ie, "insufficient" evidence) is not a recommendation for or against use. However, at best, current evidence suggests that any potential benefits of a multivitamin on reducing mortality are likely to be small. For example, for a healthy 65-year-old woman, who has a 9-year estimated mortality risk of about 8.0%, taking a multivitamin for 5 to 10 years might reduce estimated mortality risk to 7.5% (based on an odds ratio of 0.94). In addition to showing small potential benefit, this estimate is based on imperfect evidence, is imprecise, and is highly sensitive to how the data are interpreted and analyzed. The available evidence is limited by heterogeneity in the multivitamins studied, short follow-up times, and nondiverse study samples.

Lifestyle counseling to prevent chronic diseases in patients should continue to focus on evidence-based approaches, including balanced diets that are high in fruits and vegetables and physical activity. However, healthy eating can be a challenge when the US industrialized food system does not prioritize health, and healthy foods tend to be more expensive, leading to access problems and food insecurity. At the patient level, screening for food insecurity and linkage of affected households to public and community resources are essential for equitable chronic disease prevention. At the local level, community organizations must have the support to integrate health promotion into their services as they address the needs of underserved populations. At the government level, public policies must ensure that healthy foods and environments for physical activity are accessible to all US residents.

Importantly, the current USPSTF recommendations do not apply to preconception or pregnancy-related care. While the task force has separately recommended that all individuals capable of or planning pregnancy take 0.4 to 0.8 mg of folic acid daily, robust data regarding the potential benefits of additional multivitamin supplementation in preventing cardiovascular complications of pregnancy (eg, hypertensive disorders of pregnancy) associated with long-term risk of cardiovascular disease are lacking.<sup>7,11</sup> Determining if and how supplementation with other single or combined nutrients before and during pregnancy may modify risk of these adverse pregnancy outcomes could have important implications for cardiovascular disease prevention efforts. Regardless of multivitamin use, promoting primordial and primary prevention efforts that optimize cardiovascular health early in the life course should be a cornerstone of cardiovascular disease prevention.

The substantial marketing budget of the supplement industry generates interest, attention, and billions of dollars in revenue. Most people view supplements as, at worst, benign preventive products. However, in the US, dietary supplements are relatively unregulated and required to disclaim that health claims have "not been evaluated by the Food and Drug Administration" and they are "not intended to diagnose, treat, cure, or prevent any disease." The very real harms of supplements are not studied as extensively as those of pharmaceuticals.<sup>12</sup> Many patients do not report their use of dietary supplements, leading to a missed opportunity to discuss safety concerns with patients.<sup>13</sup> Beyond wasted money, the focus on supplements might be viewed as a potentially harmful distraction. Rather than focusing money, time, and attention on supplements, it would be better to emphasize lower-risk, higher-benefit activities. Individual, public health, public policy, and civic efforts should focus on supporting people in regular preventive care,<sup>14,15</sup> following a healthful diet, getting exercise, maintaining a healthy weight, and avoiding smoking. Health systems and health care professionals should focus on evidence-based preventive services recommended by the USPSTF, including controlling high blood pressure and behavioral counseling to encourage physical activity and a healthy diet.<sup>14,15</sup>

#### ARTICLE INFORMATION

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#### REFERENCES

1. Mishra S, Stierman B, Gahche JJ, Potischman N. Dietary Supplement Use Among Adults: United States, 2017-2018. NCHS Data Brief. National Center for Health Statistics; 2021. doi:10.15620/cdc: 101131

2. North America dietary supplements market report, 2021-2028. Accessed May 26, 2022. https://www.grandviewresearch.com/industryanalysis/north-america-dietary-supplementsmarket

**3**. Arnett DK, Blumenthal RS, Albert MA, et al 2019 ACC/AHA guideline on the primary prevention of

cardiovascular disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation*. 2019;140(11). doi:10.1161/CIR. 000000000000678

4. Aune D, Giovannucci E, Boffetta P, et al. Fruit and vegetable intake and the risk of cardiovascular disease, total cancer and all-cause mortality-a systematic review and dose-response meta-analysis of prospective studies. *Int J Epidemiol.* 2017;46(3):1029-1056. doi:10.1093/ije/dyw319

5. Bailey RL, Gahche JJ, Miller PE, Thomas PR, Dwyer JT. Why US adults use dietary supplements. *JAMA Intern Med*. 2013;173(5):355-361. doi:10.1001/ jamainternmed.2013.2299

6. Alissa EM, Ferns GA. Dietary fruits and vegetables and cardiovascular diseases risk. *Crit Rev Food Sci Nutr.* 2017;57(9):1950-1962. doi:10.1080/10408398.2015.1040487

7. Bibbins-Domingo K, Grossman DC, Curry SJ, et al; US Preventive Services Task Force. Folic acid supplementation for the prevention of neural tube defects: US Preventive Services Task Force recommendation statement. *JAMA*. 2017;317(2): 183-189. doi:10.1001/jama.2016.19438

8. American College of Obstetricians and Gynecologists' Committee on Practice Bulletins—Obstetrics. Anemia in pregnancy: ACOG Practice Bulletin, Number 233. *Obstet Gynecol.* 2021;138(2):e55-e64. doi:10.1097/AOG. 00000000004477

**9**. US Preventive Services Task Force. Vitamin, mineral, and multivitamin supplementation to prevent cardiovascular disease and cancer: US Preventive Services Task Force recommendation statement. JAMA. Published June 21, 2022. doi:10. 1001/jama.2022.8970

**10.** O'Connor EA, Evans CV, Ivlev I, et al. Vitamin and mineral supplements for the primary prevention of cardiovascular disease and cancer: updated evidence report and systematic review for the US Preventive Services Task Force. *JAMA*. Published June 21, 2022. doi:10.1001/jama.2021. 15650

 Gestational hypertension and preeclampsia.
Accessed May 26, 2022. https://www.acog.org/ clinical/clinical-guidance/practice-bulletin/articles/ 2020/06/gestational-hypertension-andpreeclampsia

12. White CM. Dietary supplements pose real dangers to patients. *Ann Pharmacother*. 2020;54 (8):815-819. doi:10.1177/1060028019900504

13. Tarn DM, Karlamangla A, Coulter ID, et al. A cross-sectional study of provider and patient characteristics associated with outpatient disclosures of dietary supplement use. *Patient Educ Couns*. 2015;98(7):830-836. doi:10.1016/j.pec. 2015.03.020

14. Liss DT, Uchida T, Wilkes CL, Radakrishnan A, Linder JA. General health checks in adult primary care: a review. *JAMA*. 2021;325(22):2294-2306. doi:10.1001/jama.2021.6524

**15.** US Preventive Services Task Force. Accessed May 26, 2022. https://www. uspreventiveservicestaskforce.org/uspstf/