

Enough Is Enough: Stop Wasting Money on Vitamin and Mineral Supplements

Three articles in this issue address the role of vitamin and mineral supplements for preventing the occurrence or progression of chronic diseases. First, Fortmann and colleagues (1) systematically reviewed trial evidence to update the U.S. Preventive Services Task Force recommendation on the efficacy of vitamin supplements for primary prevention in community-dwelling adults with no nutritional deficiencies. After reviewing 3 trials of multivitamin supplements and 24 trials of single or paired vitamins that randomly assigned more than 400 000 participants, the authors concluded that there was no clear evidence of a beneficial effect of supplements on all-cause mortality, cardiovascular disease, or cancer.

Second, Grodstein and coworkers (2) evaluated the efficacy of a daily multivitamin to prevent cognitive decline among 5947 men aged 65 years or older participating in the Physicians' Health Study II. After 12 years of follow-up, there were no differences between the multivitamin and placebo groups in overall cognitive performance or verbal memory. Adherence to the intervention was high, and the large sample size resulted in precise estimates showing that use of a multivitamin supplement in a well-nourished elderly population did not prevent cognitive decline. Grodstein and coworkers' findings are compatible with a recent review (3) of 12 fair- to good-quality trials that evaluated dietary supplements, including multivitamins, B vitamins, vitamins E and C, and omega-3 fatty acids, in persons with mild cognitive impairment or mild to moderate dementia. None of the supplements improved cognitive function.

Third, Lamas and associates (4) assessed the potential benefits of a high-dose, 28-component multivitamin supplement in 1708 men and women with a previous myocardial infarction participating in TACT (Trial to Assess Chelation Therapy). After a median follow-up of 4.6 years, there was no significant difference in recurrent cardiovascular events with multivitamins compared with placebo (hazard ratio, 0.89 [95% CI, 0.75 to 1.07]). The trial was limited by high rates of nonadherence and dropouts.

Other reviews and guidelines that have appraised the role of vitamin and mineral supplements in primary or secondary prevention of chronic disease have consistently found null results or possible harms (5, 6). Evidence involving tens of thousands of people randomly assigned in many clinical trials shows that β -carotene, vitamin E, and possibly high doses of vitamin A supplements increase mortality (6, 7) and that other antioxidants (6), folic acid and B vitamins (8), and multivitamin supplements (1, 5) have no clear benefit.

Despite sobering evidence of no benefit or possible harm, use of multivitamin supplements increased among

U.S. adults from 30% between 1988 to 1994 to 39% between 2003 to 2006, while overall use of dietary supplements increased from 42% to 53% (9). Longitudinal and secular trends show a steady increase in multivitamin supplement use and a decline in use of some individual supplements, such as β -carotene and vitamin E. The decline in use of β -carotene and vitamin E supplements followed reports of adverse outcomes in lung cancer and all-cause mortality, respectively. In contrast, sales of multivitamins and other supplements have not been affected by major studies with null results, and the U.S. supplement industry continues to grow, reaching \$28 billion in annual sales in 2010. Similar trends have been observed in the United Kingdom and in other European countries.

The large body of accumulated evidence has important public health and clinical implications. Evidence is sufficient to advise against routine supplementation, and we should translate null and negative findings into action. The message is simple: Most supplements do not prevent chronic disease or death, their use is not justified, and they should be avoided. This message is especially true for the general population with no clear evidence of micronutrient deficiencies, who represent most supplement users in the United States and in other countries (9).

The evidence also has implications for research. Antioxidants, folic acid, and B vitamins are harmful or ineffective for chronic disease prevention, and further large prevention trials are no longer justified. Vitamin D supplementation, however, is an open area of investigation, particularly in deficient persons. Clinical trials have been equivocal and sometimes contradictory. For example, supplemental vitamin D, which might prevent falls in older persons, reduced the risk for falls in a few trials, had no effect in most trials, and increased falls in 1 trial. Although future studies are needed to clarify the appropriate use of vitamin D supplementation, current widespread use is not based on solid evidence that benefits outweigh harms (10).

With respect to multivitamins, the studies published in this issue and previous trials indicate no substantial health benefit. This evidence, combined with biological considerations, suggests that any effect, either beneficial or harmful, is probably small. As we learned from voluminous trial data on vitamin E, however, clinical trials are not well-suited to identify very small effects, and future trials of multivitamins for chronic disease prevention in well-nourished populations are likely to be futile.

In conclusion, β -carotene, vitamin E, and possibly high doses of vitamin A supplements are harmful. Other antioxidants, folic acid and B vitamins, and multivitamin and mineral supplements are ineffective for preventing mortality or morbidity due to major chronic diseases.

Although available evidence does not rule out small benefits or harms or large benefits or harms in a small subgroup of the population, we believe that the case is closed—supplementing the diet of well-nourished adults with (most) mineral or vitamin supplements has no clear benefit and might even be harmful. These vitamins should not be used for chronic disease prevention. Enough is enough.

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References

1. Fortmann SP, Burda BU, Senger CA, Lin JS, Whitlock EP. Vitamin and mineral supplements in the primary prevention of cardiovascular disease and cancer: an updated systematic evidence review for the U.S. Preventive Services Task Force. *Ann Intern Med.* 2013;159:824-34.
2. Grodstein F, O'Brien J, Kang JH, Dushkes R, Cook NR, Okereke O, et al. Long-term multivitamin supplementation and cognitive function in men. A randomized trial. *Ann Intern Med.* 2013;159:806-14.
3. Lin JS, O'Connor E, Rossom RC, Perdue LA, Eckstrom E. Screening for cognitive impairment in older adults: a systematic review for the U.S. Preventive Services Task Force. *Ann Intern Med.* 2013;159:601-12. [PMID: 24145578]
4. Lamas GA, Boineau R, Goertz C, Mark DB, Rosenberg Y, Stylianou M, et al; TACT (Trial to Assess Chelation Therapy) Investigators. Oral high-dose multivitamins and minerals after myocardial infarction. A randomized trial. *Ann Intern Med.* 2013;159:797-804.
5. Huang HY, Caballero B, Chang S, Alberg AJ, Semba RD, Schneyer CR, et al. The efficacy and safety of multivitamin and mineral supplement use to prevent cancer and chronic disease in adults: a systematic review for a National Institutes of Health state-of-the-science conference. *Ann Intern Med.* 2006;145:372-85. [PMID: 16880453]
6. Bjelakovic G, Nikolova D, Gluud C. Antioxidant supplements to prevent mortality. *JAMA.* 2013;310:1178-9. [PMID: 24045742]
7. Miller ER 3rd, Pastor-Barriuso R, Dalal D, Riemersma RA, Appel LJ, Guallar E. Meta-analysis: high-dosage vitamin E supplementation may increase all-cause mortality. *Ann Intern Med.* 2005;142:37-46. [PMID: 15537682]
8. Miller ER 3rd, Juraschek S, Pastor-Barriuso R, Bazzano LA, Appel LJ, Guallar E. Meta-analysis of folic acid supplementation trials on risk of cardiovascular disease and risk interaction with baseline homocysteine levels. *Am J Cardiol.* 2010;106:517-27. [PMID: 20691310]
9. Gahche J, Bailey R, Burt V, Hughes J, Yetley E, Dwyer J, et al. Dietary supplement use among U.S. adults has increased since NHANES III (1988-1994). *NCHS Data Brief.* 2011:1-8. [PMID: 21592424]
10. Moyer VA; U.S. Preventive Services Task Force. Vitamin D and calcium supplementation to prevent fractures in adults: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med.* 2013;158:691-6. [PMID: 23440163]

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CORRECTION

Correction: Stop Wasting Money on Vitamin and Mineral Supplements

In a recent editorial (1), the last sentence of the first paragraph should read, “After reviewing 3 trials of multivitamin supplements and 24 trials of single or paired vitamins that randomly assigned more than 400 000 participants . . .” as opposed to 450 000.

This has been corrected in the online version.

Reference

1. Guallar E, Stranges S, Mulrow C, Appel LJ, Miller ER. Enough is enough. Stop wasting money on vitamin and mineral supplements. *Ann Intern Med.* 2013;159:850-1.