With as many as 1 in 3 US adults using multivitamin supplements, the question as to whether these supplements reduce mortality is an important public health issue. Drawing on 3 large cohorts including 390,124 participants and more than 20 years of follow-up data, the study by Loftfield and colleagues investigated the association between multivitamin use and mortality, while carefully controlling for potential confounders. Confirming the mostly negative results of prior studies, multivitamin supplementation was not associated with a mortality benefit. On the contrary, mortality risk was 4% higher among multivitamin users, compared with nonusers, in the initial years of follow-up (multivariable-adjusted hazard ratio, 1.04; 95% CI, 1.02-1.07).

Observations supporting the essential roles of micronutrients began centuries ago. Sailors were cured of scurvy with lime juice, which turned out to be a source of vitamin C. Beri-beri was shown to be preventable by the use of whole-grain rice, which contained a compound, now known to be thiamine, that was lost when brown rice was milled to white rice. In 1912, based on research on B vitamins, Polish biochemist Casimir Funk condensed the term *vital amines* to *vitamines*. While these essential nutrients were in foods, multivitamin supplements soon began to be offered for sale as delivery vehicles for micronutrients.

To focus research efforts, a 2007 National Institutes of Health conference defined multivitamin and multimineral supplements as products containing 3 or more vitamins and minerals, with all components below the tolerable upper levels set by the Food and Nutrition Board, and containing no herbs, hormones, or medications. In observational studies and clinical trials, they have been put to the test. For the most part, investigations have not shown reduced mortality with multivitamins. Not captured in mortality data, however, are potential benefits that do not affect longevity in cohorts of older adults. Supplementation with beta carotene, vitamins C and E, and zinc is associated with slowing the progression of age-related macular degeneration. In older individuals, multivitamin supplementation is associated with improved memory and slowed cognitive decline. Multivitamins may help offset deficiencies following bariatric surgery. Commercial products including vitamins B12 and D are a convenient source of nutrients for which many people come up short. Folate supplementation in pregnancy prevents neural tube defects in infants.

Mortality analyses also miss important risks. Although food sources of beta carotene are associated with reduced cancer risk, supplemental beta carotene was found in 2 large, randomized clinical trials in at-risk individuals (smokers and asbestos workers) to increase risk of lung cancer. Multivitamins containing vitamin K may reduce the efficacy of warfarin. The inclusion of iron in a supplement, while below the tolerable upper level, adds to that consumed in foods, increasing the risk of iron overload, which is associated with an increased risk of cardiovascular disease, diabetes, and dementia. Similar concerns may apply to copper supplementation. Calcium and zinc may reduce the absorption of certain antibiotics. Vitamin E in pills does not reflect the full range of tocopherols and tocotrienols found in foods. These findings make a case for obtaining vitamins from food sources, rather than supplements, to the extent possible.

Refocusing nutrition interventions on food, rather than supplements, may provide the mortality benefits that multivitamins cannot deliver. Vegetables, fruits, legumes, and cereal grains are staples in areas of remarkable longevity, known as Blue Zones—Okinawa, Japan; Sardinia, Italy; the Nicoya Peninsula, Costa Rica; the island of Ikaria, Greece; and Loma Linda, California. In the Nurses’ Health Study and Health Professionals Follow-up Study, increased intake of vegetables and fruits was associated with reduced mortality, with maximum benefit observed for intakes at 5 fruit or vegetable
servings per day, while substitution of plant protein in place of animal protein was also associated with reduced mortality. A healthful dietary pattern delivers micronutrients while also providing healthful macronutrients and fiber and limiting consumption of saturated fat and cholesterol.

Considerable evidence now shows that, apart from the aforementioned roles for vitamin supplementation, there is little health rationale for the use of multivitamin supplements. Micronutrients come most healthfully from food sources. When supplementation is required, it can often be limited to the micronutrients in question.

REFERENCES