Multivitamins in Prevention of Cardiovascular Disease

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C ardiovascular disease (CVD) is the major cause of death and disability globally and affects more than 50% of men and 40% of women during their lifetimes. Despite remarkable scientific advances, in 2008 CVD accounted for 1 of every 3 deaths in the United States and for health care costs estimated at close to $300 billion. The major risk factors for CVD are well known but remain ubiquitous in populations. For example, about one-third of US adults (>75 million) have hypertension; more than 20% smoke; more than one-third (>78 million) are obese; 8% (>18 million) have diagnosed diabetes, with similar rates of undiagnosed diabetes and an additional 33% with prediabetes; 15% have high cholesterol levels; and, in the 2009-2010 NHANES survey, 46.5% (102.5 million) had at least 1 major risk factor among uncontrolled blood pressure, high cholesterol levels, and current smoking. These risk factors are also major contributors to other chronic diseases such as cancer, depression, arthritis, kidney disease, and cognitive decline.

Strategies to prevent the development of these risk factors, which are largely related to lifestyle habits, and effective therapies to lower risk factor levels when these are present, can lead to substantial reductions in the burden of CVD. The sources of unfavorable lifestyle habits are largely known, and therapies that can effectively and safely lower risk factors have been identified and extensively tested. Yet the apparently simple task of implementing this knowledge grounded in decades of sound research continues to remain extremely challenging and seems at times insurmountable. Thus, even though CVD mortality rates have declined greatly in the United States and other developed countries, the disease burden remains high, and the progress that has been made is threatened by increasing rates of obesity, physical inactivity, and diabetes. Furthermore, urbanization, profound lifestyle changes, and a decline in competing risks for premature death have resulted in substantial increases in CVD in developing countries.

Numerous factors account for the current failure to achieve optimal results in CVD prevention, including (1) low adoption and adherence to healthy lifestyles and to proven, inexpensive, and safe pharmacological therapies, even when prescribed using sound evidence and to persons at highest risk; (2) the complexity of implementing meaningful lifestyle intervention programs, which require not only behavioral interventions to modify individual lifestyles but also changes in health policy, the environment, and cultural attitudes; and (3) the cost and affordability of implementing meaningful lifestyle modification programs and of using proven drugs when necessary.

Many individuals and societies as a whole resort to the use of vitamins and other dietary supplements as a simple and miraculous escape from the difficult and complex task of implementing effective prevention strategies. Most required vitamins and micronutrients can generally be derived from a healthy, well-balanced diet. In addition, many food products are already fortified with folic acid, vitamin D, calcium, fluoride, and other micronutrients, which may be needed in higher amounts by some individuals or may not be readily available to others (eg, infants, pregnant women, postmenopausal women with low exposure to sunlight, or those living in poverty).

However, despite the lack of solid evidence for benefit from the widespread use of vitamins and dietary supplements, more than half of US adults take at least 1 dietary supplement (about 10% take >5 such supplements), and these numbers continue to increase; 32% of the US population used at least 1 dietary supplement in the 1970s, 42% in 1988-1994, and 53% in 2003-2006. Moreover, such dietary supplements are used more frequently by healthier, more educated and affluent people—those at lowest risk for dietary deficiencies. Multivitamins/multiminerals are by far the most frequently used dietary supplement; 30% of the US population used them in 1988-1994 and 39% in 2003-2006. Regulations governing the approval and marketing of dietary supplements remain less strict than those for prescription or over-the-counter drugs and do not mandate conclusive proof of benefit or safety based on large randomized controlled clinical trials (RCTs). This has allowed for claims of benefit in preventing or curing an amazingly diverse and

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ever-increasing variety of illnesses ranging from CVD to cancer, arthritis, infections, macular degeneration, Alzheimer disease, wrinkles, hair loss, decreased libido, and low sexual prowess. The promise of an easy fix for multiple health problems, combined with relatively lenient regulations, fueled the growth of the dietary supplement industry from around $4 billion in 1994 to $23.7 billion in 2008.7

Given the prevalence of multivitamin use, an important question involves whether multivitamin use might be beneficial for preventing or treating CVD. Although some observational studies have reported lower CVD events in vitamin users, such studies are subject to bias, because health-minded individuals will be more likely to take vitamins6 but will also generally engage in other healthy behaviors. Moreover, data from observational studies specifically examining multivitamin use are inconsistent. Previous studies used single vitamins or combinations of few vitamins in “pharmacological” doses (ie, much higher amounts than the recommended daily intake) or in lower doses, closer to the recommended daily intake, and found no cardiovascular benefits for beta carotene, vitamin E, vitamin C, folic acid and other B vitamins, and selenium, with fewer (but also neutral) data on vitamin D.8,9

In this issue of JAMA, Sesso and colleagues8 report on the effects of multivitamins for CVD prevention in the Physicians’ Health Study (PHS) II. This was a well-conducted, large, placebo-controlled RCT. More than 14 500 middle-aged male physicians were followed up for a median of 11.2 years (>164 000 person/y of follow-up); very few were lost to follow-up and the end points, including more than 1700 confirmed major CVD events, were carefully ascertained. Compared with placebo, no significant cardiovascular benefit was seen for men randomly assigned to receive a commonly used daily multivitamin preparation. There were no significant benefits for total major CVD events, myocardial infarction, stroke, cardiovascular death, or total mortality for the entire study population or in any subgroup evaluated, including those targeted for primary or secondary prevention and those with or without various risk factors. The authors rightfully conclude that the study provides no support for the use of a multivitamin in CVD prevention.

Some limitations to generalizability of these findings include the study population (the study enrolled only a highly educated group of well-nourished male physicians) and the specific multivitamin used, which may differ in its precise composition from other multivitamin preparations. Although it appears unlikely that the results would differ in women or in other population subsets, at least in developed countries, or when using other multivitamin formulations, further data are needed.

However, not all hope is gone. An additional report from the PHS II suggests a possible reduction in incident cancers for the male physicians taking the multivitamin, although the effect was modest, derived mainly in those with a prior history of cancer and without any effect on cancer mortality.10 These data and other potential benefits of some vitamins (although not of traditional multivitamin preparations), such as effects of higher doses of vitamin D on fractures, remain of interest.

Robust data from multiple trials clearly confirm that CVD cannot be prevented or treated with vitamins. Nonetheless, many people with heart disease risk factors or previous CVD events lead sedentary lifestyles, eat processed or fast foods, continue to smoke, and stop taking lifesaving prescribed medications, but purchase and regularly use vitamins and other dietary supplements, in the hope that this approach will prevent a future myocardial infarction or stroke. This distraction from effective CVD prevention is the main hazard of using vitamins and other unproven supplements. The message needs to remain simple and focused: CVD is largely preventable, and this can be achieved by eating healthy foods, exercising regularly, avoiding tobacco products, and, for those with high risk factor levels or previous CVD events, taking proven, safe, and effective medications.

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REFERENCES


