

## Vitamin and Mineral Supplements: Do We Really Need Them?

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### ABSTRACT

In the United States, 40 – 50% of the men and women 50 years of age or older regularly use multivitamin/mineral (MVM) supplements, making the annual sales of these supplements over \$11 billion. However, the question remains whether using MVM supplements is beneficial to health. This article reviews the results of randomized studies of MVM supplements and individual vitamins/mineral supplements in relation to overall mortality and incidence of chronic diseases, particularly cancer and ischemic heart disease. The results of large-scale randomized trials show that, for the majority of the population, there is no overall benefit from taking MVM supplements. Indeed, some studies have shown increased risk of cancers in relation to using certain vitamins.

**Keywords:** vitamins, minerals, cancer, coronary heart disease, mortality.

### INTRODUCTION

Multivitamin / mineral (MVM) supplements certainly sell well in the United States. According to the National Health and Nutrition Examination Survey (NHANES) data, collected between 2003 and 2006, 40 – 50% of the men and women 50 years of age or older regularly consume MVM supplements.<sup>[1]</sup> In 2009, the total sale of nutritional supplements in the United States was approximately \$27 billion,<sup>[2]</sup> and in 2010, despite the economic downturn, this number grew by 4.4% to over \$28 billion.<sup>[3]</sup> Of this, over \$11 billion was the sales of MVM or MVM-containing supplements.<sup>[2,3]</sup> However, do *healthy individuals* really need MVM supplements? Are they beneficial in reducing the risk of chronic diseases such as ischemic heart disease, cancer, and stroke? The answer is most likely *NO*. The results of large-scale randomized trials in the past two decades have shown that *for the majority of the population*, MVM supplements are not only ineffective, but they may be deleterious to health.

When the Alpha-Tocopherol Beta-Carotene Cancer Prevention (ATBC) study presented the first strong evidence for a harmful effect of vitamins in 1994,<sup>[4]</sup> health scientists were caught by surprise. The results of this large-scale 2 × 2 factorial design trial, which randomized over 29,000 middle-aged Finnish smoker men to receive  $\alpha$ -tocopherol (a form of vitamin E),

beta-carotene (a precursor of vitamin A), both, or neither, showed that  $\beta$ -carotene statistically significantly increased lung cancer incidence by 18% and total mortality by 8%, mainly due to increased deaths from lung cancer and ischemic cardiac disease.<sup>[4]</sup>  $\alpha$ -tocopherol did not materially change the risk of lung cancer or total deaths. Despite the strong design of this trial and its large sample size, the results were met with skepticism. The results were deemed to be inconsistent with several of the previously published observational studies, based on which the trial had been designed to reduce the risk of lung cancer.<sup>[5,6]</sup> Several of the accompanying letters of correspondence, published in *the New England Journal of Medicine*, pointed to the potential shortcomings of this study, such as short duration of the study (i.e., a median follow-up of six years). Nevertheless, results of most of the subsequent trials, using other forms of vitamins and supplements, conducted in different populations and with different durations of use, have confirmed no benefit or even harm from the use of such vitamin supplements [Table 1].<sup>[4,7-17]</sup> The most recent notable one was the Selenium and Vitamin E Cancer Prevention Trial (SELECT Trial), the extended results of which showed that vitamin E supplements could increase the risk of prostate cancer among healthy men.<sup>[17]</sup> One exception to these null or deleterious effects was the result of the General Population Nutrition Intervention Trial conducted in Linxian, China,<sup>[7,18]</sup> which tested four combinations of vitamins and supplements (namely, factors A, B, C, and D). Factor D (a combination of selenium,  $\alpha$ -tocopherol, and  $\beta$ -carotene) reduced overall mortality by approximately 10%. However, this trial was conducted in an area where micronutrient intake was quite poor, and thus supplements might have had a beneficial role. Even in this nutrition-deficient population, results of the trial showed no benefit for two of the other MVM supplements (factors B and C; see Table 1), and extended follow-up showed adverse results for one of the supplements (factor A containing zinc and vitamin A).<sup>[18]</sup>

Thus far, several meta-analyses, authoritative reviews, and expert panel reports have been published on the use of MVMs in preventing chronic diseases in healthy individuals. Almost all have found no overall benefit. For example, a

systematic review and meta-analysis, published in the *Journal of the American Medical Association* (JAMA), in 2007, concluded that, “*Treatment with  $\beta$ -carotene, vitamin A, and vitamin E may increase mortality. The potential roles of vitamin C and selenium on mortality need further study*”.<sup>[19]</sup> Another more recent meta-analysis concluded that, “*Dietary supplementation with folic acid to lower homocysteine levels had no significant effects within five years on cardiovascular events or on overall cancer or mortality in the populations studied*”.<sup>[20]</sup> A recent re-analysis of the Women’s Health Initiative, which was published along with the meta-analysis of the available literature, concluded that calcium supplements with or without vitamin D increased the risk of the cardiovascular events, particularly myocardial infarction.<sup>[21]</sup> An expert panel meeting at the National Institutes of Health, in 2006, concluded that there was ‘*insufficient evidence*’ to recommend for or against the use of MVMs by the American public to prevent chronic diseases.<sup>[22]</sup> The World Cancer Research Fund and the American Institute for Cancer Research has recommended against the use of dietary supplements by the public, for cancer prevention.<sup>[23]</sup> These expert panel reports appeared prior to the publication of the recent results from the SELECT Trial or those from the Women’s Health Initiative, which bolstered the ‘*no benefit or even harm*’ conclusion.

We would like to emphasize that these conclusions are for *the general population*, and for prevention of chronic diseases such as cancer and cardiovascular disease. In special cases, individuals may need vitamins or supplements. For example, periconceptional folate supplements substantially reduce the risk of neural tube defects.<sup>[24]</sup> Likewise, iron supplements during pregnancy can substantially reduce the risk of anemia and perinatal complications in mothers.<sup>[25]</sup> Physician-recommended treatment of disorders such as osteoporosis,<sup>[26]</sup> as well as other diseases, may require use of MVMs or individual vitamins or minerals, but these are not the subject of this article. In addition, these conclusions do not negate the potential health benefits of eating fresh fruits and vegetables.

One might ask then, given substantial evidence for lack of any health benefit from MVM use for the majority of the adult population, why are these products so widely marketed in the United States

**Table 1:** Randomized, double-blind, placebo-controlled, primary prevention trials designed to reduce risk of major chronic diseases

Study	Population	N	Agents, dose, and mean duration	Main outcomes	Results
Alpha-Tocopherol, Beta-Carotene Cancer Prevention (ATBC) Study <sup>[4]</sup>	Male Smokers aged 50 – 69 years (Finland)	29,133	$\alpha$ -tocopherol (50 mg daily) and / or $\beta$ -carotene (20 mg daily) for six years	Lung cancer incidence	$\alpha$ -tocopherol did not affect the risk of lung cancer or total mortality, but it increased the risk of hemorrhagic stroke by 50%. $\beta$ -carotene increased the incidence of lung cancer by 18% and total mortality by 8% (mainly due to lung cancer and ischemic heart disease).
Beta-Carotene and Retinol Efficacy Trial (CARET) <sup>[7]</sup>	Smokers, former smokers, and workers exposed to asbestos > 45 years of age (United States)	18,314	$\beta$ -carotene (30 mg) plus retinol (25,000 IU) daily for 4 years	Lung cancer incidence	Supplements increased the incidence of lung cancer by 28% and total mortality by 17%.
Physicians' Health Study (PHS) <sup>[8]</sup>	Male physicians 40 – 84 years old (United States)	22,071	$\beta$ -carotene (50 mg on alternate days) and / or aspirin for 12 years	Overall, cardiovascular, and cancer mortality	There was virtually no difference in any of the main outcomes when comparing those who received and did not receive $\beta$ -carotene.
Physicians' Health Study II (PHS II) <sup>[9,10]</sup>	Male physicians > 50 years (United States)	14,641	Vitamin E (400 IU every other day) and / or vitamin C (500 mg daily) for eight years	Major cardiovascular events, prostate and overall cancer incidence	Compared with the placebo, vitamin E or vitamin C had no effect on the incidence of major cardiovascular events, cancer, or total mortality. Vitamin E was associated with an increased risk of hemorrhagic stroke.
Nutrition Intervention Trials (NIT) General Population Trial <sup>[11]</sup>	Linxian general population, 40 – 69 years old (China)	29,584	Half 2 <sup>4</sup> factorial design of four different combinations of vitamins and minerals, namely factor A (retinol + zinc), factor B (riboflavin + niacin), factor C (ascorbic acid + molybdenum), factor D ( $\beta$ -carotene + selenium + $\alpha$ -tocopherol) for six years	Overall mortality, esophageal / gastric cardia cancer incidence and mortality	Factor D reduced total mortality by 9%, total cancer mortality by 13%, and stomach cancer mortality by 21%. In the extended follow-up (10 years after termination of the trial), the group receiving factor C still had a reduced risk of mortality, but factor A, containing vitamin A and zinc, increased the overall mortality.
Women's Health Initiative <sup>[12]</sup>	Postmenopausal women (United States)	36,282	Calcium (500 mg) and vitamin D (200 IU vitamin D3) twice daily for seven years	Risk of hip fracture, colorectal cancer risk	Calcium and vitamin D had no effect on colorectal cancer incidence. Further analysis suggested that calcium increased the risk of cardiovascular events.

Table 1 Contd...

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Study	Population	N	Agents, dose, and mean duration	Main outcomes	Results
Women's Health Study <sup>[13,14]</sup>	Healthy women, 45 years or older (United States)	39,876	Vitamin E (600 mg every other day) for 10 years and / or $\beta$ -carotene (50 mg every other day) for two years	Incidence of cardiovascular disease and cancer	Neither vitamin E nor $\beta$ -carotene significantly changed the risk of any of the main outcomes of the study or total mortality.
Supplémentation en Vitamines et Minéraux Antioxydants (SU.VI. MAX) <sup>[15]</sup>	Men and women 35 – 60 years (France)	13,017 (5141 men and 7876 women)	Vitamin C (120 mg), $\alpha$ -tocopherol (30 mg), $\beta$ -carotene (6 mg), selenium (100 $\mu$ g), zinc (20 mg) daily for eight years	Risk of cancer and heart disease	A moderate (12%), but not statistically significant, reduction in prostate cancer incidence.
Selenium and Vitamin E Cancer Prevention Trial (SELECT) <sup>[16,17]</sup>	Healthy men, 50 years or older (North America)	35,534	Selenium (200 $\mu$ g / day) and / or vitamin E (400 IU / day) for 5.5 years	Prostate cancer incidence	Vitamin E increased the risk of prostate cancer by 17%. Selenium did not significantly affect the risk of prostate cancer. There was no overall effect on mortality from either of these agents or their combination.

and elsewhere? Or why would over 40% of the older population of the United States regularly use them? The answer is perhaps multifactorial. First, the belief in the use of vitamins has deep roots. The immense beneficial effects of vitamins in preventing pellagra, rickets, and scurvy at a period when overt nutritional deficiencies were common, gave the halo of a magical effect to these drugs. Before the 1990s, some eminent scientists strongly advocated the use of vitamins and supplements. Most notably, Linus Pauling, a two-time Nobel Laureate and a towering figure in chemistry, believed that vitamin C could prevent cancer and increase the life expectancy of cancer patients.<sup>[27]</sup> Pauling and Cameron supplemented 100 terminal cancer patients with vitamin C and compared them with 1000 similar patients who did not receive such supplementation and concluded that the lives of those receiving vitamin C were prolonged by one year.<sup>[28]</sup> However, this study was not randomized, and two subsequent double-blind randomized trials sponsored by the National Cancer Institute and conducted in the Mayo Clinic, did not find any benefit from oral supplementation with vitamin C.<sup>[29,30]</sup> Despite such negative results, the effect of Pauling's and other scientists' highly publicized comments still linger in the media and in people's minds.

Second, in the United States, unlike the case for drugs, human research is not required to prove that supplements are safe or effective.<sup>[31]</sup> Only if the Food and Drug Administration (FDA) finds that supplements are unsafe, can they stop the distribution of the products.<sup>[31]</sup> Third, there exists substantial inaccurate or misleading advertising in the media, which might be expected, given the annual \$27 billion business. For example, a TV commercial has advertised the use of a certain brand of MVMs based on the results of a 'Harvard Study,' which had shown that lycopene use may reduce risk of prostate cancer. Although a Harvard Study' has indeed shown an inverse association between dietary lycopene intake and prostate cancer risk,<sup>[32]</sup> the inference that one must use MVMs is incorrect for various reasons: (a) MVMs contain many vitamins and elements other than lycopene; (b) the results had come from an observational study and not a randomized trial, hence the results are subject to confounding factors; (c) prostate cancer is not the only meaningful health outcome, and the overall effect of MVMs on health needs to be considered. Fourth, many believe that MVMs, if not useful, will not harm. As the results of ATBC have shown, such a belief may be false. Fifth, many people want to take an active



role in improving their health and increasing their longevity. Avoiding tasty, but unhealthy food, may be difficult, but taking a pill once a day is relatively easy. As others have discussed, prescription is more convenient than proscriptioin.<sup>[5,33]</sup>

In summary, although in the long run MVMs may slightly increase the risk of cancer and cardiovascular diseases, in the short run they produce little harm or no harm, and thus negative consequences will not be discernible by individuals taking them. MVM sales benefit from misleading commercials, and people are pleased by the well-known placebo effects. Therefore, Americans who have been using MVMs since the early 1940s,<sup>[22]</sup> will most likely continue to use them in the foreseeable future, and the rest of the world will follow.

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