



Strengthening Knowledge and Understanding of Dietary Supplements

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Dietary Supplement Fact Sheet:

# Multivitamin/mineral Supplements

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## Introduction

Americans have been taking multivitamin/mineral (MVM) supplements since the early 1940s, when the first such products became available [1]. MVMs are still popular dietary supplements and, according to estimates, more than one-third of all Americans take these supplements [1,2]. MVMs account for almost one-fifth of all purchases of dietary supplements and more than 40% of all sales of vitamin and mineral supplements. (Sales of all dietary supplements in the United States totaled an estimated \$30.0 billion in 2011. This amount included \$12.4 billion for all vitamin- and mineral-containing supplements, of which \$5.2 billion was for MVMs [3].)

No standard or regulatory definition is available for an MVM supplement such as what nutrients it must contain and at what levels. Therefore, the term can refer to products of widely varied compositions and characteristics [4]. These products go by various names, including multis, multiples, and MVMs. Manufacturers determine the types and levels of vitamins, minerals, and other ingredients in their MVMs. As a result, many types of MVMs are available in the marketplace.



See QuickFacts for easy-to-read facts about MVM supplements.

One way to group them is as follows:

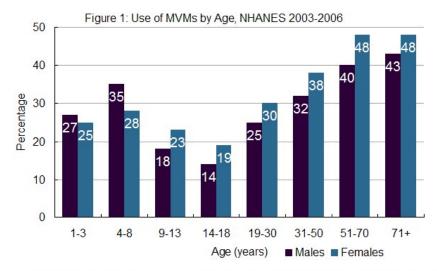
- · Many are once-daily MVMs that contain all or most of the recognized vitamins and minerals, generally at levels close to the Daily Values (DVs) or Recommended Dietary Allowances (RDAs) or Adequate Intakes (AIs) for these nutrients.1 This fact sheet focuses primarily on these basic "broad-spectrum" MVMs. Formulations for children, adults, men, women, pregnant women, and seniors typically provide different amounts of the same vitamins and minerals based on the specific needs of these populations.
- Some MVMs contain levels of certain vitamins and minerals that are substantially higher than the DV, RDA, AI, and even, in some cases, the established tolerable upper intake level (UL).2 These MVMs might also include other nutritional and herbal ingredients. Manufacturers sometimes offer these MVMs in packages or packs of two or more pills that users are supposed to take each day.
- · Specialized MVMs—such as those for enhanced performance or energy, weight control, improved immune function, or management of menopause symptoms-often include vitamins and minerals in combination with herbal and specialty ingredients, such as sterols, coenzyme Q10, probiotics, and glucosamine. A few nutrients might be present at levels substantially above the DV, RDA, AI and, in some cases, the UL.

To complicate further this product category, many dietary supplements are not labeled as MVMs even though they contain similar types and amounts of vitamins and minerals to some products labeled as MVMs [4]. For example, a manufacturer might label a product containing vitamins C and E, selenium, and beta-carotene as an antioxidant formula rather than an MVM even though it contains several vitamins and a mineral.

Given the diversity of available MVMs, investigators define these products differently (or sometimes not at all) in studies to evaluate their potential health benefits. For example, the Agency for Healthcare Research and Quality, in an evidence-based review in 2006 of the role of MVM supplements in chronic disease prevention, defined MVMs as "any supplement containing three or more vitamins and minerals but no herbs, hormones, or drugs, with each component at a dose less than the tolerable upper level determined by the Food and Nutrition Board..." [5]. Another study defined MVMs more ambiguously as "stress-tab-type," "therapeutic or theragran type," and "one-a-day" type [6]. Varying definitions of MVMs, and the fact that manufacturers can change the composition of their MVMs at will, complicate the study of the potential impacts of MVMs on health because equivalent products are not used across studies.

# Extent of MVM Use

According to an analysis of data that the National Health and Nutrition Examination Survey (NHANES) collected in 2003-2006, 33% of the U.S. population aged 1 year and older took an MVM in a given month (see Figure 1) [2]. The authors of this analysis defined MVMs as products containing at least three vitamins and at least one mineral. Overall, females (36%) were more likely to take an MVM than males (31%). Use rates of MVMs were 25%-27% at age 1-3 years and 14%-19% at 14-18 years. After age 18, use rates increased by age so that by age 71 years or older, 48% of women and 43% of men were taking MVMs.



Estimating the prevalence of MVM use is challenging because of differences in definitions of these products, varying frequency of use, and the increasing complexity of MVM formulations (e.g., more and more products contain non-vitamin, non-mineral ingredients and specialized formulations) [1]. Overall, however, studies show that MVM use is more frequent among women and the children of women who use supplements; the elderly; those with more education, higher incomes, healthier lifestyles and diets, and lower body-mass indexes; and residents of the western United States. MVM use is lower among smokers and members of certain ethnic and racial groups, such as African Americans, Hispanics, and Native Americans [1].

## MVMs and Health

People take MVMs for numerous reasons. Here we evaluate the impact of MVMs on two of these factors: to increase nutrient intakes and to improve health, prevent chronic disease, or both.

## Increase Nutrient Intakes

Taking an MVM increases nutrient intakes and helps people obtain recommended intakes of vitamins and minerals when they cannot meet these needs from food alone. The Food and Nutrition Board (FNB) notes that RDAs and AIs for nutrients are levels of intake one should ingest, on average, each day from the diet [7]; the FNB does not address whether or to what extent nutrient supplements can compensate for dietary inadequacies. Nevertheless, some consider use of an MVM as a form of dietary or nutritional "insurance," a concept first introduced by Miles Laboratories in marketing its One-A-Day® line of nutrient supplements [8].

Although MVMs can improve the intake adequacy of various nutrients, they can also increase the likelihood that users will have intakes of other nutrients at levels that are higher than ULs. Results from several studies exemplify both the issues of nutritional insurance for some individuals and the concern of excessive intakes for others.

In one study, for example, investigators assessed the diets and use of multivitamins in a large multiethnic cohort from Los Angeles and Hawaii [9]. The investigators calculated nutrient intakes from diet using a food frequency questionnaire and from multivitamins using a default profile based on the two most commonly reported MVMs. Approximately three-quarters of participants had adequate intakes from food alone, but use of multivitamins increased the prevalence of adequacy by an average of eight percentage points for both men and women. The greatest improvements in intake were for vitamin E, vitamin A, and zinc. However, the prevalence of potentially excessive intakes among the MVM users was 10%–15% for vitamin A, iron, and zinc and 48%–61% for niacin. The investigators concluded that MVMs "could be better formulated to target public health concerns." They added that an ideal MVM would help fill gaps in nutrient adequacy (e.g., for vitamin E, potassium, and calcium) and provide low levels of nutrients whose amounts in MVMs could be excessive (e.g., vitamin A, iron, and niacin).

A second study, a national survey of infants and children younger than 4 years, found that usual nutrient intakes from food alone were adequate for most of the infants and children [10]. However, the results showed inadequate intakes of iron and zinc in a small subset of older infants and for vitamin E and potassium in a sizeable proportion of young children. Although supplements would help reduce the prevalence of these inadequacies, use of supplements tended to push intakes of some nutrients— particularly vitamin A, folic acid, and (for the older preschool children) zinc—over the UL. The investigators advised parents not to give young children dietary supplements or fortified foods containing high levels of vitamin A and zinc [11].

A study of folic acid, the synthetic form of folate added to fortified foods and available in supplement form, provides another example of research on the impact of MVMs on nutritional adequacy. According to an analysis of data from the 2003–2006 NHANES, 34.5% of participants reported using supplements (MVMs and others) containing folic acid [12]. Although these supplements lowered the prevalence of inadequate intakes of this nutrient, 4% of users exceeded the UL (1,000 mcg/day) for folic acid from the supplements alone. Approximately 5% of persons aged 50 years or older had total folic acid intakes above the UL. Among children aged 1–13 years, 28% of whom took folic acid-containing dietary supplements, more than half exceeded the UL for folic acid compared with 5% of nonusers [13]. Not surprisingly, excessive nutrient intakes are more likely among MVM users who also take single vitamin and mineral supplements [14].

Several studies have found that MVM users tend to have higher micronutrient intakes from their diet than nonusers [14]. Ironically, the populations at highest risk of nutritional inadequacy who might benefit the most from MVMs are the least likely to take them [1].

#### Health Promotion and Chronic Disease Prevention

In 2006, researchers published a comprehensive evidence-based review of the relationship between studies on nutrients that most strongly suggested potential impacts on health and on conditions (cancer; age-related sensory loss; and cardiovascular, endocrine, neurologic, musculoskeletal, gastroenterologic, renal, and pulmonary diseases) on which experts believe that nutrient supplements have the most potential influence [5]. Considering only published randomized, controlled clinical trials, the investigators found that use of MVMs did not reduce the risk of any chronic disease. (The authors defined MVMs as products containing three or more vitamins and minerals at levels below the UL and no herbs).

An expert panel that reviewed this report and participated in a state-of-the-science conference on MVMs in chronic disease prevention at the National Institutes of Health in 2006 concluded that "the present evidence is insufficient to recommend either for or against the use of MVMs by the American public to prevent chronic disease" [1]. An earlier assessment of the evidence by the U.S. Preventive Services Task Force [15] came to a similar conclusion: the evidence for or against the use of MVMs to prevent cancer or cardiovascular disease was insufficient. A comprehensive evaluation of research by the World Cancer Research Fund and the American Institute for Cancer Research [16] recommended against the use of dietary supplements for cancer prevention by the public because of the unpredictability of potential benefits and risks, as well as the possibility of unexpected adverse events.

Most of the studies of the potential value of MVMs to enhance health and prevent disease have been observational, which can only suggest an association but do not prove a cause-effect relationship. Some have suggested potential benefits or adverse effects, while others have found none. Participants in these studies used different MVMs or the studies included different mixes and doses of nutrients. One of the largest of these prospective observational studies included 161,808 postmenopausal women aged 50–79 years who were participating in the Women's Health Initiative to study health and risks for cancer, heart disease, and osteoporosis. Approximately 41.5% of the women took an MVM, but over the median of 8 years of observation, the investigators found no association between use of these products and the risk of any common cancer or total cancers, cardiovascular disease, or total mortality [17]. Similar results were reported by investigators who followed 182,099 men and women aged 45–75 years living in Hawaii and California over an average 11 years of followup. Among this cohort of mostly African Americans, Native Hawaiians, Japanese Americans, Latinos, and non-Hispanic whites, approximately 48% of the men and 52% of the women reported taking a multivitamin with or without minerals [18].

A prospective study of Swedish women found an association between MVM use and an increased breast cancer risk [19]. Another study of U.S. health professionals found no such association but did find indications that MVM use might reduce the risk of estrogen- and progesterone-receptor-negative breast cancer and breast cancer overall in women who consume alcohol [20]. A large prospective study found a higher risk of advanced and fatal prostate cancers among men who took an MVM more than seven times a week than in nonusers [6]. A prospective study of male physicians found that MVM use had no association with cardiovascular disease [21]. However, among Swedish adult women, use of MVMs was associated with a reduced risk of myocardial infarction, especially when taken for at least 5 years [22]. A study in which postmenopausal women in Iowa were followed for 18 years found that those taking MVMs (or specific nutrients like iron) had a slight but significant increased total mortality risk as compared to nonusers [23].

Randomized controlled trials are a superior study design to investigate whether MVMs might affect disease risk, but few have been conducted. The Physicians Health Study II was the longest clinical trial to investigate whether MVMs might help prevent chronic disease. The study randomly assigned 14,641 male physicians in the United States aged 50 and older to take a daily MVM (Centrum Silver®) or placebo and followed participants for a median of 11.2 years. Participants taking the MVM did not have fewer major cardiovascular events, myocardial infarctions, strokes, or cardiovascular-related deaths [24]. However, MVM supplementation modestly but significantly reduced their risk of developing cancer by 8%, although it did not reduce the risk of prostate cancer or overall cancer mortality [25].

Two other well-known trials of the impact of MVMs on disease risk and progression used combinations of antioxidant nutrients. In the first of these studies, the French Supplémentation en Vitamines et Minéraux Antioxydants (SU.VI.MAX) study, investigators randomly assigned 13,017 adults to receive a placebo or a daily supplement containing moderate amounts of vitamin C (120 mg), vitamin E (30 mg), beta-carotene (6 mg), selenium (100 mcg), and zinc (20 mg) [26]. After 7.5 years of use, the supplements lowered total cancer incidence and all-cause mortality in men but not women. The supplements provided no protection against cardiovascular disease.

In the Age-Related Eye Disease Study, investigators randomly assigned individuals with varying degrees of age-related macular degeneration to receive a placebo or a daily supplement containing high doses of vitamin C (500 mg), vitamin E (400 international units [IU]), beta-carotene (15 mg), zinc (80 mg), and copper (2 mg) [27]. (These nutrients are present in most basic MVMs but usually in substantially smaller amounts.) Over an average followup period of 6.3 years, the supplements significantly reduced the risk of developing advancedage-related macular degeneration and reduced loss of visual acuity.

A small randomized controlled trial in Sri Lankan adults with diabetes found that using a specially prepared MVM with zinc for 4 months led to a significant reduction in fasting blood sugar and glycosylated hemoglobin compared to individuals who received either a placebo or the MVM without zinc [28]. The MVM contained

moderate amounts of various vitamins and minerals, including 22 mg zinc. However, a large prospective study, observational in nature, found no association between MVM use among adults aged 50–71 years and risk of developing diabetes [29].

Because people with healthier diets and lifestyles are more likely to use dietary supplements, attributing potential health benefits that are distinct from the proven and predictable benefits of health-promoting behaviors to the use of supplements is difficult [8]. Furthermore, whether studies find any benefits (or risks) depends on the combinations and amounts of nutrients in the MVMs used as well as the populations studied and duration of follow-up, and these results are not generalizable to the enormous variety of MVMs available in the marketplace.

Special Considerations for Certain Population Groups

Although MVMs do not appear to reduce overall chronic disease risk, several nutrients in MVMs might benefit certain population groups. For example:

- Supplementation with calcium and vitamin D might increase bone mineral density and decrease fracture rates in postmenopausal women [1,30].
- Women of childbearing age who might become pregnant should obtain 400 mcg/day of synthetic folic acid from fortified foods or dietary supplements. Taking sufficient amounts of folic acid in the first month of pregnancy (a time when many women do not yet know that they are pregnant) reduces the risk of neural tube defects in newborns [7.31.32].
- People over age 50 should obtain recommended intakes of vitamin B12 mainly from fortified foods or dietary supplements, because they could be less able than younger people to absorb the proteinbound, naturally occurring vitamin B12 in food [7,32]. In addition, vegans should ensure that their intakes of vitamin B12 from fortified foods or supplements are adequate [32].
- Pregnant women should take an iron supplement as recommended by an obstetrician or other health care provider [32].
- The American Academy of Pediatrics recommends that exclusively and partially breastfed infants receive supplements of 400 IU/day of vitamin D shortly after birth and continue to receive these supplements until they are weaned and consume at least 1,000 mL/day of vitamin D-fortified formula or whole milk [33]. Similarly, all non-breastfed infants ingesting less than 1,000 mL/day of vitamin D-fortified formula or milk should receive a vitamin D supplement of 400 IU/day [33]. According to the Academy, children at nutritional risk who might benefit from supplementation include those who have anorexia or an inadequate appetite, follow fad diets, have chronic disease, come from deprived families or suffer parental neglect or abuse, participate in dietary programs for managing obesity, consume a vegetarian diet without adequate dairy products, and have failure to thrive [34].

No U.S. government health agency, private health group, or health professional organization promotes regular use of an MVM or individual nutrients without considering first the quality of a person's diet. However, individuals with poor nutrient intakes from diet alone, who consume low-calorie diets, or who avoid certain foods (such as strict vegetarians and vegans) might benefit from taking MVMs [35]. Health care providers sometimes prescribe MVMs for people with medical conditions and diseases that impair digestion, absorption, or use of nutrients. In general, some supplements might help people who do not eat a nutritious variety of foods to obtain adequate amounts of essential nutrients. However, supplements cannot take the place of the variety of foods that are important to a healthy diet.

## Safety Issues

Taking a basic MVM that provides nutrients approximating recommended intakes should pose no safety risks to healthy people. However, individuals who take MVMs and other supplements and who eat fortified foods and beverages might consume some nutrients at levels exceeding the UL, increasing the possibility of adverse effects [36]. This can also be a concern for people taking MVMs that contain some vitamins or minerals at doses approaching or exceeding the UL.

Smokers and, possibly, former smokers should avoid MVM products providing large amounts of beta-carotene or vitamin A because two studies have linked these nutrients to an increased risk of lung cancer in smokers [37]. In one randomized, controlled clinical trial, male Finnish smokers who took supplemental beta-carotene (20 mg/day) had an 18% higher lung cancer rate than smokers who took a placebo over 5–8 years of followup [38]. In another study, smokers, former smokers, and asbestos-exposed persons who took a combination of 30 mg/day of beta-carotene plus 25,000 IU/day of vitamin A (as retinol) had a 28% increase in lung cancer risk after an average 4-year followup compared to participants taking a placebo [39].

Taking excess vitamin A (as preformed retinol but not beta-carotene) during pregnancy can increase the risk of birth defects in infants. The vitamin A UL during pregnancy is 9,240 IU/day for adolescents and 10,000 IU/day for adult women [40].

Unless a physician diagnoses iron deficiency or inadequacy, adult males should avoid taking MVMs containing the DV for iron. At 18 mg, this amount is more than twice their RDA of 8 mg/day. Postmenopausal women, for whom the RDA for iron is also 8 mg/day, should also avoid MVMs containing the DV for iron unless a physician recommends otherwise. Iron supplements are a leading cause of poisoning in children until age 6 years, so parents and guardians should keep iron-containing supplements out of children's reach [41].

# Interactions with Medications

MVMs providing nutrients at recommended intake levels do not ordinarily interact with medications, with one important exception. People who take medicines to reduce blood clotting, such as warfarin (Coumadin®), should talk with their health care providers before taking any MVM or dietary supplement containing vitamin K

[42,43]. Vitamin K is involved in blood clotting and decreases the effectiveness of warfarin and similar drugs. The dose of medication is determined in part by the amount of vitamin K routinely consumed.

## Choosing an MVM

Basic MVMs contain both vitamins and minerals, mostly at levels that do not exceed the DVs for these nutrients. MVMs usually have low levels of nutrients whose required intake is relatively large, such as calcium and magnesium, so people might need to take supplements containing these nutrients separately from their MVMs. In contrast, as noted above, some people should pay special attention to the vitamin A and iron content of any MVM they take so as to avoid overconsuming these nutrients.

When choosing an MVM product, people should try to find one tailored to their age, gender, and other characteristics (e.g., pregnancy). MVMs for men often contain little or no iron, for example, whereas those for seniors typically provide more calcium and vitamins D and B12 than MVMs for younger adults. Prenatal supplements generally provide no vitamin A as retinol, and most children's MVMs provide age-appropriate amounts of nutrients. The U.S. Food and Drug Administration (FDA) has developed good manufacturing practices for dietary supplements to help ensure their identity, purity, strength, and composition [44]. The FDA also periodically inspects facilities that manufacture dietary supplements.

## MVMs and Healthful Diets

According to the federal government's 2010 Dietary Guidelines for Americans, "nutrients should come primarily from foods. Foods in nutrient-dense, mostly intact forms contain not only the essential vitamins and minerals that are often contained in nutrient supplements, but also dietary fiber and other naturally occurring substances that may have positive health effects. ... Dietary supplements...may be advantageous in specific situations to increase intake of a specific vitamin or mineral" [32]. With respect to MVMs, the report's authors note that "[s]ufficient evidence is not available to support a recommendation for or against the use of multivitamin/mineral supplements in the primary prevention of chronic disease for the healthy American population." However, the authors acknowledge that Americans consume insufficient nutrient-dense foods and beverages. Nutrients of special public health concern in American diets are potassium, dietary fiber, calcium, and vitamin D in both adults and children.

For more information about building a healthful diet, refer to the <u>Dietary Guidelines for Americans</u> and the U.S. Department of Agriculture's food guidance system, <u>MyPlate</u>.

<sup>1</sup> The Food and Nutrition Board (FNB) at the Institute of Medicine of The National Academies (formerly National Academy of Sciences) establishes RDAs and AIs. RDAs are the average daily intake level of essential nutrients sufficient to meet the nutrient requirements of nearly all (97%–98%) healthy people. These values vary by age, gender, and nutrient. The FNB establishes AIs for nutrients for which evidence is insufficient to develop an RDA; the FNB sets AIs at levels that the board's experts assume will ensure nutritional adequacy and that are high enough to meet or exceed the needs of most "apparently healthy" people [7]. The U.S. Food and Drug Administration (FDA) develops DVs to help consumers compare the nutrient content of products within the context of a total diet. The FDA establishes a single DV for each nutrient for adults and children from age 4 years, and the DV is usually similar to the RDA or AI for that nutrient. [back]

<sup>2</sup> ULs, which the FNB establishes for many nutrients, are the maximum daily intakes unlikely to cause adverse health effects. As intake increases above the UL, the potential risk for adverse effects increases. [back]

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## Disclaimer

This fact sheet by the Office of Dietary Supplements provides information that should not take the place of medical advice. We encourage you to talk to your health care providers (doctor, registered dietitian, pharmacist, etc.) about your interest in, questions about, or use of dietary supplements and what may be best for your overall health. Any mention in this publication of a specific brand name is not an endorsement of the product.

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