

# Selenium

## Fact Sheet for Health Professionals

### Introduction

Selenium is an essential mineral that is naturally present in many foods and added to others. It is also available as a dietary supplement. Selenium is a constituent of 25 selenoproteins, including thioredoxin reductases, glutathione peroxidases, and selenoprotein P [1]. Selenoproteins play critical roles in thyroid hormone metabolism, DNA synthesis, reproduction, and protection from oxidative damage and infection [2-4].

Soil and ground water contain inorganic forms of selenium (e.g., selenites and selenates) that plants accumulate and convert to organic forms, mostly selenomethionine and selenocysteine and their methylated derivatives. In foods, selenium is present primarily as selenomethionine along with selenocysteine. Dietary selenium is readily absorbed by the body and absorption is largely not affected by selenium status [4-6].

Absorbed selenomethionine and inorganic selenium is rapidly metabolized to a common intermediate that is used for synthesizing selenocysteine, the form of selenium found in the 25 human selenoproteins. Approximately 28% to 46% of the total body's selenium content is found in skeletal muscle [7]. Selenium homeostasis is maintained primarily by urinary excretion and, in cases of higher selenium intake, through the lungs and feces [3,4,6].

The most commonly used measures of selenium status are plasma and serum selenium concentrations [2,4]. Plasma or serum selenium concentrations of 8 micrograms (mcg)/dL or higher in healthy people are considered sufficient for selenoprotein synthesis [8]. Concentrations in plasma, serum, and urine reflect recent selenium intake whereas selenium concentrations in whole blood (including erythrocytes) indicate long term status. Analyses of hair and nail selenium content are also used to monitor long term intakes, over months or years [3,4].

The two predominant selenoproteins in plasma are glutathione peroxidase 3 and selenoprotein P, and both can be used as functional biomarkers of selenium status [1,3,9]. However, some experts question the reliability of these two biomarkers to indicate selenium deficiency because plasma selenoprotein concentrations can be affected by inflammation and oxidative stress [4,10]. In addition, research suggests that selenium supplementation does not increase selenoprotein P concentration and glutathione peroxidase activity unless individuals are selenium deficient [3,4,6,9,11,12]. Urinary methylated selenometabolites are not reliable selenium status biomarkers because many people lack the methylation enzymes due to genetic polymorphisms [4].

# Recommended Intakes

Intake recommendations for selenium and other nutrients are provided in the Dietary Reference Intakes (DRIs) developed by the Food and Nutrition Board (FNB) at the National Academies of Sciences, Engineering, and Medicine [13]. DRI is the general term for a set of reference values used for planning and assessing nutrient intakes of healthy people. These values, which vary by age and sex, include the following:

- Recommended Dietary Allowance (RDA): Average daily level of intake sufficient to meet the nutrient requirements of nearly all (97%–98%) healthy individuals; often used to plan nutritionally adequate diets for individuals
- Adequate Intake (AI): Intake at this level is assumed to ensure nutritional adequacy; established when evidence is insufficient to develop an RDA
- Estimated Average Requirement (EAR): Average daily level of intake estimated to meet the requirements of 50% of healthy individuals; usually used to assess the nutrient intakes of groups of people and to plan nutritionally adequate diets for them; can also be used to assess the nutrient intakes of individuals
- Tolerable Upper Intake Level (UL): Maximum daily intake unlikely to cause adverse health effects

Table 1 lists the current RDAs for selenium in mcg. For infants from birth to 12 months, the FNB established an AI for selenium that is equivalent to the mean intake of selenium in healthy, breastfed infants.

**Table 1: Recommended Dietary Allowances (RDAs) for Selenium [13]**

Age	Male	Female	Pregnancy	Lactation
Birth to 6 months	15 mcg*	15 mcg*		
7–12 months	20 mcg*	20 mcg*		
1–3 years	20 mcg	20 mcg		
4–8 years	30 mcg	30 mcg		
9–13 years	40 mcg	40 mcg		
14–18 years	55 mcg	55 mcg	60 mcg	70 mcg
19–50 years	55 mcg	55 mcg	60 mcg	70 mcg
51+ years	55 mcg	55 mcg		

\*Adequate Intake (AI)

## Sources of Selenium

Because selenium in foods is protein bound, foods that are high in protein tend to be the best sources of selenium. Brazil nuts, seafood, meat, poultry, and organ meats are the richest food sources of selenium. Other sources include cereals and other grains, and dairy products [6]. The amount of selenium in drinking water is not nutritionally significant in most geographic regions [3,13]. The major

food sources of selenium in the diets of people in the United States are breads, grains, meat, poultry, seafood, and eggs [14].

The amount of selenium in a given type of plant-based food depends on the amount and form of selenium in the soil and several other factors, such as soil pH and amount of organic matter in the soil [3,13,15]. As a result, selenium concentrations in plant-based foods vary widely by geographic location [2,15]. For example, according to FoodData Central from the U.S. Department of Agriculture (USDA), Brazil nuts have an average of 544 mcg selenium/ounce, but values from other analyses vary widely [16-18].

The selenium content of soil affects the amount of selenium in the plants that animals eat. However, this does not substantially affect the amount of selenium in animal products because animals maintain predictable tissue concentrations of selenium through homeostatic mechanisms [3,6]. Furthermore, formulated livestock feeds generally contain selenium at consistent levels [19].

Several food sources of selenium are listed in Table 2.

**Table 2: Selenium Content of Selected Foods [18]**

Food	Micrograms (mcg) per serving	Percent DV*
Brazil nuts, 1 ounce (6–8 nuts)	544	989
Tuna, yellowfin, cooked, 3 ounces	92	167
Sardines, canned in oil, drained solids with bone, 3 ounces	45	82
Shrimp, cooked, 3 ounces	42	76
Pork chop, bone-in, broiled, 3 ounces	37	67
Beef steak, bottom round, roasted, 3 ounces	37	67
Spaghetti, cooked, 1 cup	33	60
Beef liver, pan fried, 3 ounces	28	51
Turkey, boneless, roasted, 3 ounces	26	47
Ham, roasted, 3 ounces	24	44
Cod, Pacific, cooked, 3 ounces	24	44
Chicken, light meat, roasted, 3 ounces	22	40
Cottage cheese, 1% milkfat, 1 cup	20	36
Beef, ground, 25% fat, broiled, 3 ounces	18	33
Egg, hard-boiled, 1 large	15	27
Baked beans, canned, plain or vegetarian, 1 cup	13	24
Oatmeal, regular and quick, unenriched, cooked with water, 1 cup	13	24
Mushrooms, portabella, grilled, ½ cup	13	24
Rice, brown, long-grain, cooked, 1 cup	12	22
Bread, whole-wheat, 1 slice	8	15

Food	Micrograms (mcg) per serving	Percent DV*
Yogurt, plain, low fat, 1 cup	8	15
Milk, 1% fat, 1 cup	6	11
Lentils, boiled, 1 cup	6	11
Bread, white, 1 slice	6	11
Spinach, frozen, boiled, ½ cup	5	9
Spaghetti sauce, marinara, 1 cup	4	7
Pistachio nuts, dry roasted, 1 ounce	3	5
Corn flakes, 1 cup	1	2
Green peas, frozen, boiled, ½ cup	1	2
Bananas, sliced, ½ cup	1	2
Potato, baked, flesh and skin, 1 potato	1	2
Peanut butter, smooth, 2 tablespoons	1	2
Peach, yellow, raw, 1 medium	0	0
Carrots, raw, ½ cup	0	0
Lettuce, iceberg, raw, 1 cup	0	0

\*DV = Daily Value. The U.S. Food and Drug Administration (FDA) developed DVs to help consumers compare the nutrient contents of foods and dietary supplements within the context of a total diet. The DV for selenium is 55 mcg for adults and children age 4 years and older [20]. FDA does not require food labels to list selenium content unless selenium has been added to the food. Foods providing 20% or more of the DV are considered to be high sources of a nutrient, but foods providing lower percentages of the DV also contribute to a healthful diet. USDA's [FoodData Central](https://fdc.nal.usda.gov/) [18] lists the nutrient content of many foods and provides a comprehensive list of foods containing selenium arranged by [nutrient content](https://ods.od.nih.gov/pubs/usdandb/Selenium-Content.pdf) and by [food name](https://ods.od.nih.gov/pubs/usdandb/Selenium-Food.pdf).

## Dietary Supplements

Selenium is available in multivitamin/mineral supplements, in supplements containing vitamin E and other ingredients, and as stand-alone supplements. Common forms include selenomethionine, selenium-enriched yeast (grown in a high-selenium medium, predominantly as selenomethionine), sodium selenite, and sodium selenate [21-23]. Doses of selenium in multivitamin/mineral supplements vary, but many contain 55 mcg. The amount of selenium is often higher in supplements with fewer ingredients. For example, supplements that combine selenium with vitamin E or other ingredients generally contain 50 to 200 mcg of selenium. Selenium-only supplements typically contain 100 to 400 mcg [21].

The human body absorbs up to about 90% of selenium from selenomethionine, selenium-enriched yeast, selenite, and selenate [4-6,9,12,24].

## Selenium Intakes and Status

Most people in the United States consume adequate amounts of selenium. In addition, 17% to 19% of adults use a dietary supplement containing selenium [25].

According to an analysis of data from the 2017–March 2020 National Health and Nutrition Examination Survey (NHANES), the average daily selenium intake in people age 2 years and older from foods and beverages is 108 mcg and from foods, beverages, and supplements is 116 mcg [25]. Adult men have higher daily intakes (132 mcg from foods and beverages and 145 mcg from foods, beverages, and supplements) than adult women (94 mcg from foods and beverages and 102 mcg from foods, beverages, and supplements).

Dietary selenium intakes are similar among people who are Black and those who are White. People who follow a vegetarian or vegan dietary pattern may have lower selenium intakes than others [26-28].

According to an analysis of NHANES data from 2011 to 2016, the mean serum selenium concentration in males and females age 8 to 80 years is 12.7 mcg/dL [29]. Research indicates that men have slightly higher serum selenium concentrations than women, and people who are White have higher concentrations than those who are Black [30-33]. Selenium status is lower in people who smoke, possibly because smoking increases oxidative stress [34].

Selenium intakes and serum concentrations in the United States and Canada vary somewhat by region because of differences in the amounts of selenium in soil and in local foods consumed [3,13]. For example, residents of the Midwestern and Western United States have higher concentrations than those living in the South and Northeast [32,35]. However, the extensive transport of food in the United States typically allows people living in low-selenium areas to obtain sufficient amounts of selenium [13].

## Selenium Deficiency

Selenium deficiency alone rarely causes overt illness, but it produces biochemical changes that might predispose people who experience additional stresses to develop certain illnesses [13,36]. For example, Keshan disease is an endemic cardiomyopathy that was first identified in 1935 in parts of China where the soil is low in selenium. Adults in these areas had average selenium intakes of no more than 10 mcg/day whereas intakes of at least 20 mcg/day protect adults from the disease [3,13].

Keshan disease mainly affects women of childbearing age and preschool children. Although prevalence is low today, the disease still exists [3,36,37]. The etiology of Keshan disease remains unknown, but disease incidence dramatically reduced following several large intervention trials in the 1970s to 1990s that provided selenium selenite supplements. A 2018 systematic review and meta-analysis of 41 studies found that selenium supplements (doses not indicated) reduce the risk of Keshan Disease by 86% [38].

Selenium deficiency is also associated with Kashin-Beck disease, a type of osteoarthritis that commonly presents in childhood and puberty and occurs in certain low-selenium and low-iodine areas

of China, Tibet, Siberia, and North Korea [3,13,39,40].

Selenium deficiency could exacerbate iodine deficiency, potentially increasing the risk of congenital hypothyroidism in infants [3,8]. Endemic myxedematous hypothyroidism is a disease that occurs in regions with very low selenium levels, such as Central Africa, and is thought to develop during gestation or early childhood. Individuals with this condition produce insufficient thyroid hormone and present with very low plasma triiodothyronine (T3) and thyroxine (T4) levels and extremely high thyroid stimulating hormone (TSH) levels [3].

## Groups at Risk of Selenium Inadequacy

Selenium deficiency is very rare in the United States and Canada [13]. However, some people, including those living in certain other countries, may obtain insufficient amounts of selenium. The following groups are among those most likely to have inadequate intakes of selenium.

### People living in selenium-deficient regions

Selenium intakes in North America, even in low-selenium regions, are well above the RDA [41], likely because most people consume foods originating from a wide geographic area. However, people in some countries whose diet consists primarily of vegetables grown in low-selenium areas are at risk of deficiency [13]. The lowest selenium intakes in the world are in certain parts of China, where large proportions of the population have a primarily vegetarian diet and soil selenium levels are very low [3]. Average selenium intakes are also low in some European countries, especially among populations consuming vegan diets [4,42]. Although intakes in New Zealand were low in the past, they rose after the country increased its importation of high-selenium wheat [15].

### People undergoing kidney dialysis

Selenium concentrations are often significantly lower in patients undergoing long-term hemodialysis than in healthy individuals partly because hemodialysis removes some selenium from the blood [43-46]. In addition, hemodialysis patients are at risk of low dietary selenium intakes due to anorexia resulting from uremia and dietary restrictions [44,46,47]. However, whether selenium concentrations are sufficient in hemodialysis patients also depends on individual selenium status. For example, median selenium concentrations were above the 95th percentile of normal (normal reference: median 9.2 mcg/dL) at baseline and remained elevated in a 2-year prospective cohort study of 198 hemodialysis patients in Western Canada [47]. Although selenium supplementation increases blood concentrations in hemodialysis patients, more evidence is needed to determine whether supplements have beneficial clinical effects in these individuals.

### People living with HIV

People living with HIV often have low selenium concentrations, possibly due to malabsorption or inadequate selenium intakes [48]. The prevalence of selenium deficiency in people living with HIV varies by country, reflecting variable selenium content of the soil [49]. Observational studies have found an association between lower selenium concentrations in people with HIV and an increased risk of cardiomyopathy; worsening of disease progression; death; and, in pregnant women, HIV transmission

to offspring and early death of offspring [50-54]. However, randomized trials suggest selenium supplementation has little effect on HIV disease progression or treatment.

## Selenium and Health

This section focuses on six diseases and conditions in which selenium might play a role: cancer, cardiovascular disease, cognitive decline and Alzheimer's disease, HIV infection, male fertility, and thyroid disease.

### Cancer

Because of its effects on DNA repair, apoptosis, and the endocrine and immune systems as well as other mechanisms, including its antioxidant properties, selenium has been hypothesized to play a role in the prevention of cancer [15,55-57]. Results from animal studies also suggest that selenium may have chemopreventive properties [3,6]. Researchers have examined the effects of selenium primarily for prostate, breast, lung, and colorectal cancers, with prostate cancer being the most extensively studied.

Epidemiological studies have suggested an inverse association between selenium status and the risk of colorectal, prostate, lung, bladder, skin, esophageal, and gastric cancers. In addition, a few early clinical trials found that selenium supplements reduced the risk of some forms of cancer, but more recent trials have not supported these findings [58,59].

The Nutritional Prevention of Cancer Trial, which began recruitment in 1983, was a randomized controlled trial that investigated 200 mcg/day selenium as selenium yeast or placebo for a mean of 4.5 years in 1,312 men and women in the United States with histories of nonmelanoma skin cancer [60,61]. Although selenium supplementation did not reduce the recurrence of nonmelanoma skin cancer, a secondary analysis of the trial found that men who took selenium had a 49% lower risk of prostate cancer than those who took placebo over a mean follow-up of about 7.5 years. The effect was strongest among men with the lowest baseline plasma selenium concentrations (below 10.6 mcg/dL), with no effect among men with plasma selenium concentrations greater than 12.3 mcg/dL.

The subsequent Selenium and Vitamin E Cancer Prevention Trial (SELECT), however, did not find that selenium supplementation reduced the risk of prostate cancer. This randomized, controlled trial in 35,533 men age 50 years or older from the United States, Canada, and Puerto Rico was discontinued after 5.5 years when analyses showed no association between prostate cancer risk and supplementation with 200 mcg/day selenium as selenomethionine with or without 400 international units (IU)/day vitamin E [62]. An additional 1.5 years of follow-up data on participants after they stopped taking the study supplements confirmed the lack of a significant association between selenium supplementation and prostate cancer risk [63]. Further investigation in a case-cohort of 1,739 men diagnosed with prostate cancer and 3,117 matched controls from the SELECT trial found that selenium supplementation did not affect prostate cancer risk in men with low baseline selenium status (based on toenail selenium levels) [64]. However, the researchers did find an increased risk of high-grade prostate cancer in men with higher baseline selenium status ( $\geq 60^{\text{th}}$  percentile of toenail



selenium) and recommended that men over age 55 avoid selenium supplementation at doses that exceed recommended dietary intakes.

A 2018 Cochrane Review on selenium for the prevention of cancer included 83 studies (including the studies described above) [59]. Among the 70 observational cohort studies reviewed, participants with the highest baseline selenium status had a 28% lower cancer risk and a 24% lower cancer mortality than those with the lowest status. In addition, these participants had a 33% lower risk of bladder cancer; an 18% lower risk of lung cancer; an 18% lower risk of colorectal cancer; and, in men, a 16% lower risk of prostate cancer. The authors found no association between selenium status in women and risk of breast cancer. However, due to major weaknesses in study design, confounders, and limitations in the assessment of selenium exposure, the certainty of evidence for these findings was very low. In addition, no evidence of a dose-response relationship between selenium status and cancer risk was observed.

The 10 randomized, placebo-controlled trials examined in the 2018 Cochrane Review included a total of 27,232 participants, 94% of which were men [59]. Results from these studies showed that supplementing with 200 to 500 mcg/day selenium, primarily as selenomethionine, for 2 to 10.3 years had little to no effect on cancer incidence or mortality. The certainty of evidence was high for prostate, colorectal, lung, and bladder cancers and moderate for breast and nonmelanoma skin cancers. Because most of the studies used 200 mcg/day selenium, the authors concluded that 200 mcg/day selenium does not reduce the overall risk of cancer or the risk of individual cancer types. They also concluded that more research is needed to determine if selenium supplementation might modify cancer risk in individuals with specific genetic backgrounds or nutritional status or if different forms of selenium have different effects [10,59].

Starting in 2003, FDA allowed two qualified health claims that some scientific evidence suggests consumption of selenium “may reduce the risk of certain forms of cancer” and “may produce anticarcinogenic effects.” However, FDA determined that this evidence is limited and not conclusive [65]. In 2009, FDA evaluated additional qualified health claims for selenium and denied claims for many forms of cancer but allowed qualified health claims for three forms of cancer, noting that FDA concludes it is “highly uncertain” that selenium supplements reduce the risk of bladder cancer in women or the risk of thyroid cancer, and “highly unlikely” that selenium supplements reduce the risk of prostate cancer [66].

More research is needed to fully understand the relationship between selenium status and cancer risk and to determine whether selenium supplements can help prevent any form of cancer.

## **Cardiovascular disease**

Selenoproteins help reduce inflammation and prevent lipid oxidation and platelet aggregation [67,68]. For these reasons, experts have hypothesized that selenium supplements could reduce the risk of cardiovascular disease or deaths associated with cardiovascular disease.

Results from early observational studies suggested that low selenium status might increase the risk of cardiovascular disease. A 2006 meta-analysis of 25 observational studies primarily in men over age 40



reported an inverse association between selenium concentrations and risk of coronary heart disease [69]. Mean serum selenium concentrations ranged from 5.18 to 13.07 mcg/dL; men with the highest selenium concentrations had a 15% lower risk of coronary heart disease than those with the lowest.

Since then, epidemiological studies on the role of selenium in cardiovascular disease have yielded conflicting findings. A study in 1,042 middle-age White men and women (mean age 40.8 years) reported that higher plasma selenium concentrations (mean 12.4 mcg/dL) were associated with higher total and non-high-density lipoprotein (HDL) cholesterol levels [70]. On the other hand, a study in 13,887 adults in the United States showed no association between baseline serum selenium concentrations (mean 12.56 mcg/dL) and cardiovascular mortality over 12 years of follow-up [71]. Similarly, an 18-year prospective study in 3,112 young adult men and women (age 20–32 years at baseline) reported no association between baseline toenail selenium levels and changes in carotid intima-media thickness or coronary artery calcium score at the end of the study [72].

Several clinical trials have examined whether selenium supplementation alone or as part of a multivitamin/mineral supplement reduces the risk of cardiovascular disease. In one trial, 474 healthy adults age 60 to 74 years with a mean baseline plasma selenium concentration of 9.12 mcg/dL took 100, 200, or 300 mcg/day selenium as selenium yeast or placebo for 6 months [73]. Selenium supplements providing 100 and 200 mcg/day lowered total plasma cholesterol an average of 8.5 and 9.7 mg/dL and non-HDL cholesterol by 7.7 and 10.4 mg/dL, respectively, while 300 mcg/day selenium increased HDL levels by 2.3 mg/dL. However, the study authors noted that the clinical significance of these findings is unclear. Other trials have found that supplementation with selenium alone (100, 200, or 300 mcg/day) or supplementation with a multivitamin/mineral product containing selenium (100 mcg/day) does not reduce the risk of cardiovascular disease or cardiac death [67,74-76].

The SELECT trial (detailed in the Cancer section, above) assessed cardiovascular risk as a secondary outcome in 17,488 well-nourished men and found no effect of 200 mcg/day selenium on risk of cardiovascular events over 7 to 12 years, compared with placebo [63]. A Cochrane Review of SELECT and 11 other smaller randomized trials providing 100 to 800 mcg/day selenium supplementation for 2 weeks to 12 years in a total of 19,715 predominantly male adults also found that selenium supplements did not reduce the risk of fatal and nonfatal cardiovascular events [68]. All studies were assessed as having a low risk of bias.

Although studies suggest that supplementing with selenium does not reduce the risk of cardiovascular disease, including selenium in antioxidant mixtures may reduce the risk of cardiovascular mortality. A meta-analysis and systematic review included 43 randomized trials in adults who took either selenium supplements alone or as part of antioxidant formulas for at least 24 weeks (antioxidant formulas were defined by the researchers as containing two or more of the following: selenium, retinol, beta-carotene, vitamin C, vitamin E, zinc, or copper) [77]. Selenium alone, providing 100 to 400 mcg/day, or antioxidant formulas with or without 50 to 200 mcg selenium were not associated with cardiovascular disease or cardiovascular mortality, compared with placebo. However, when the antioxidant formula trials were separated into selenium-containing or not, cardiovascular mortality was reduced by 23% in participants

taking the antioxidant formulas containing selenium, compared with those who took antioxidant formulas that did not contain selenium.

Overall, clinical trial evidence does not support the use of selenium supplementation for reducing the risk of heart disease, particularly in healthy people who obtain sufficient selenium from food. Additional clinical trials are needed to better understand any contributions of selenium from food and dietary supplements to cardiovascular health.

## **Cognitive decline and Alzheimer's disease**

Selenoproteins have antioxidant and anti-inflammatory activities, and serum selenium concentrations decline with age [78,79]. In addition, chronic selenium deficiencies are correlated with cognitive decline [80,81]. For these reasons, researchers have hypothesized that higher selenium intakes might reduce the risk of cognitive decline.

An analysis of 2011–2014 NHANES data showed that higher whole blood selenium concentrations and higher selenium intakes were associated with higher cognitive scores in older adults [33,82]. However, results from other observational studies have been mixed [83–86]. A study in 1,012 men and women in Italy (mean age 75 years) reported that lower plasma selenium concentrations were associated with subtle neurological impairments [79]. Participants in the lowest quartile of plasma selenium (less than 6.67 mcg/dL) had worse neuro-motor performance than those in the highest quartile (more than 8.23 mcg/dL). In contrast, a study in 154 healthy people in Australia (96% women, average age 71 years), 85% of whom had replete selenium concentrations (average plasma selenium 16.9 mcg/dL), found no association between plasma selenium concentrations and cognitive outcomes [81].

Researchers have evaluated whether taking an antioxidant supplement containing selenium reduces the risk of cognitive impairment in older adults. A post hoc analysis of the Supplémentation en Vitamines et Minéraux Antioxydants (SU.VI.MAX) study in 4,447 participants age 45 to 60 years in France found that, compared with placebo, people who took a daily supplement containing 100 mcg selenium with 120 mg ascorbic acid, 30 mg vitamin E, 6 mg beta-carotene, and 20 mg zinc for 8 years had higher episodic memory and semantic fluency test scores 6 years after supplementation ended [87]. However, selenium's independent contribution to the observed effects in this study cannot be determined.

Observational studies have found that individuals with Alzheimer's disease (AD) have lower blood selenium concentrations compared with cognitively healthy older adults [88,89]. The Prevention of Alzheimer's Disease with Vitamin E and Selenium (PREADVISE) trial was the first large-scale primary prevention trial to study the effects of selenium (200 mcg/day as selenomethionine) and vitamin E (400 IU/day) in 7,540 cognitively healthy men age 60 years and older [90]. However, during the 5.4 years of supplement use, the trial found no difference in the incidence of new AD or dementia among participants taking selenium only, vitamin E only, or selenium plus vitamin E, compared with placebo.

A 2022 systematic review and meta-analysis of 11 clinical trials evaluated the effects of supplements containing selenium only or selenium plus other nutrients in adults age 69 to 89 years with mild cognitive impairment or AD [91]. Supplements containing both organic and inorganic forms of

selenium were used. Results from these studies showed that selenium-only supplements at various doses and selenium plus other nutrient supplements for 12 to 24 weeks did not improve cognitive test scores.

Selenium may play a role in maintaining healthy brain function, but clinical evidence does not support the use of selenium supplementation in replete individuals for reducing the risk of cognitive decline and dementia in older adults.

## **HIV infection**

In children and adults with HIV, selenium deficiency is associated with a higher risk of morbidity and mortality [54]. However, studies examining whether micronutrient supplementation, including selenium, affects risk of HIV transmission or disease outcomes in children and adults have had mixed results. An observational study in Thailand did not identify associations between selenium status in children with HIV and treatment outcomes [92]. This study included 141 boys and girls with HIV (median age 7.3 years), 97 of whom started antiretroviral therapy (ART) over a period of 48 weeks. Baseline selenium concentrations (all of which were adequate) showed no associations with ART treatment outcomes.

Clinical trials have found limited benefits of selenium supplementation on immune function in people with HIV. A clinical trial in Rwanda examined the effects of selenium supplementation on CD4+ T-cell counts in 300 men and women age 21 years and older with HIV [93]. Participants had CD4+ T-cell counts between 400 and 650 cells/mcL, so they were not yet eligible for ART and they took 200 mcg/day selenium or placebo for 24 months. During the trial, average CD4+ T-cell counts declined in both the treatment and placebo groups, but the rate of depletion was 43.8% lower in those who took selenium. However, selenium supplementation had no effect on the composite endpoint of a CD4+ count less than 350 cells/mcL or initiation of ART.

Selenium supplementation provided no benefits in a randomized controlled trial in Iran in which 146 men and women receiving ART for HIV (mean age 38.6 years) took 50 mg/day zinc, 200 mcg/day selenium, or placebo for 6 months. The investigators then followed participants for another 3 months but found that selenium supplementation did not raise CD4+ T-cell counts [94].

Two Cochrane Reviews also concluded that selenium supplements offer little, if any, benefit for people with HIV. The first review examined whether micronutrient supplementation reduces the burden of HIV infection in children [95]. It included 3 clinical trials that administered 30 or 60 mcg/day selenium as part of a multiple-micronutrient formulation in children with HIV who were living in South Africa or Uganda. The authors found that evidence was insufficient to determine whether supplementation with selenium alone is beneficial. Similarly, the authors of a second Cochrane Review of 4 clinical trials in a total of 1,187 adults with HIV concluded that 200 mcg/day selenium for 9 to 24 months may have little to no effect on CD4+ T-cell count and viral load [96]. They also concluded the evidence was insufficient to determine whether selenium supplementation affects the risk of hospital admission in adults with HIV.

Researchers have also examined whether blood selenium concentration or selenium supplementation affects pregnancy outcomes in people with HIV. These studies have found associations between low

blood selenium concentrations and higher risk of preterm birth, and they suggest that selenium supplementation might reduce the risk of preterm birth. For example, a cross-sectional study in Nigeria of 113 pregnant individuals age 15 to 49 years with HIV found that those with a selenium deficiency (defined as blood selenium less than 7 mcg/dL) at 14 to 26 weeks of gestation were almost eight times as likely to have a preterm birth as those with normal selenium concentrations [97]. Individuals with a low CD4+ T-cell count also had an eight-fold higher risk of preterm birth. In a clinical trial in Nigeria, researchers examined whether selenium supplementation affected pregnancy outcomes and disease progression in 90 pregnant individuals with HIV (mean age 29.7 years) at 14 to 27 weeks of gestation [98]. In this trial, participants took 200 mcg/day selenium or placebo between enrollment and delivery. Those who took selenium had a 68% lower risk of preterm birth than those who took placebo, but the risk of low birthweight did not differ between the two groups. In addition, selenium supplementation did not affect the levels of HIV infection markers (CD4+ T-cell counts and viral load).

Overall, clinical evidence on whether selenium supplementation affects risk of HIV transmission or disease outcomes is inconclusive, although limited evidence suggests that it might reduce the risk of preterm birth in people with HIV. More research is needed to determine whether selenium supplementation benefits children and adults with HIV.

## **Male fertility**

Infertility is considered a global public health issue, affecting about 15% of the world's population. Observational studies suggest that consuming a healthy diet may improve sperm quality [99]. Certain nutrients, such as selenium, may also play a role, possibly because they reduce oxidative stress that has been linked to male infertility. In addition, the selenoprotein phospholipid hydroperoxide glutathione peroxidase is a major constituent and structural component of mature sperm [100]. A 5-year prospective study in idiopathic infertile men found that both low and high selenium semen concentrations were associated with male infertility and reproductive failures [101,102].

Clinical trials evaluating selenium supplementation on sperm quality have had conflicting findings. A trial in 54 healthy men (nonsmokers) age 18 to 45 years administered 300 mcg/day selenium (as selenium yeast) or placebo for 48 weeks [103]. No differences in sperm concentration or motility were found between groups, and semen volume declined in both groups.

In contrast, a 3-month trial in Scotland in 69 men (mean age 33 years) with reduced sperm motility and low selenium plasma concentrations (mean 8.1 mcg/dL) found that 100 mcg/day selenium as selenomethionine improved plasma selenium concentrations, sperm motility, and chance of conception compared with placebo. No additional benefits were found when vitamins A, C, and E were included with the selenium supplement [102]. Another 3-month trial that provided 200 mcg/day selenium as selenium yeast or 200 mg/day coenzyme Q10 to 70 men (average age 25 years) with idiopathic infertility reported increases in total and progressive sperm motility in those taking selenium [104]. However, this trial did not have a placebo group or measure baseline selenium status.

More research is needed to determine whether selenium supplements affect male fertility.

## **Thyroid disease**

Selenium concentration is higher in the thyroid gland than in any other organ in the body and, like iodine, selenium has important functions in thyroid hormone synthesis and metabolism [105]. For example, selenoproteins play critical roles in the conversion of the prohormone T4 to the active T3. In addition, the selenoproteins glutathione peroxidase and thioredoxin reductase help protect the thyroid gland from the hydrogen peroxide produced during thyroid hormone synthesis [15,105].

Epidemiological studies have found associations between low selenium status and increased risk of thyroid disease. However, this effect has been observed only in women [23,106,107]. For example, data from 1,900 middle-age men and women with mean serum selenium concentrations of 12.4 mcg/dL showed an inverse association between serum selenium concentrations and thyroid volume and a protective effect of selenium against risk of goiter in the women participants, but not the men [108]. A cross-sectional study in 805 women age 18 to 65 and men age 60 to 65 years in Denmark with mean serum selenium concentrations of 9.7 mcg/dL and mild iodine deficiency also found an inverse association between serum selenium concentration and thyroid volume in the women only [107].

A randomized trial administered 100, 200, or 300 mcg/day selenium as selenium yeast for 6 months in 368 healthy men and women age 60 to 74 years with mean baseline plasma selenium concentrations of 9.13 mcg/dL. It reported no effect on thyroid function, even though plasma selenium concentrations increased in all three groups [109].

Chronic autoimmune thyroiditis (AIT), also called Hashimoto's thyroiditis, affects 1 to 2 percent of the population, particularly middle-age females [110]. Several clinical trials have investigated the effect of selenium supplementation on thyroid antibodies in people with AIT. A systematic review and meta-analysis of 16 trials assessed the effects of selenium supplementation on serum thyroid peroxidase antibody (TPOAb) and thyroglobulin antibody (TgAb) levels in those with AIT who were treated with levothyroxine compared with those newly diagnosed and not treated with levothyroxine [111]. The trials included a total 1,494 adults (mainly women) who were administered 80 to 200 mcg/day selenium (as selenomethionine or sodium selenite) for 3 to 12 months and all but two trials were placebo controlled. Five trials reported baseline serum selenium concentrations ranging from 3.7 to 8.5 mcg/dL, indicating deficient to marginal selenium status in many participants; the other trials did not report baseline selenium status. In the levothyroxine-treated groups, selenium supplementation lowered TPOAb levels. In addition, selenomethionine was more effective than sodium selenite at lowering TPOAb, possibly because of higher absorption. In the levothyroxine-untreated groups of newly diagnosed participants, selenium supplementation lowered TPOAb and TgAb levels in the 3-month studies but not in the 6- or 12-month studies.

Other trials have evaluated the effects of selenium supplementation on thyroid function and quality of life in adults with AIT. A systematic review included 9 controlled trials (all of which were included in the 16-study review described above) in 679 predominantly female participants (mean age approximately 39–48 years) [110]. Some of the trials also administered levothyroxine, but analyses were limited to trials using selenium alone. Results showed that selenium supplementation ranging from 80 to 200 mcg/day as selenomethionine or sodium selenite for 3 to 12 months did not affect TSH levels, thyroid echogenicity (ultrasound, a measure of hypothyroidism), or health-related quality of life. As in the

above-mentioned review, participants had deficient to marginal selenium status in seven of the nine trials that reported on status. The authors concluded that the evidence does not support the use of selenium supplementation for AIT.

Up to 50% of pregnant people who are TPOAb or TgAb positive in the first trimester will develop postpartum thyroiditis, and 20% to 40% of these people will develop permanent primary hypothyroidism [23]. However, results have been mixed from clinical trials examining the effects of selenium supplementation in this population. In one trial, 151 pregnant White women age 18 to 36 years who were TPOAb positive with normal thyroid function and marginal selenium status (mean 8.09 mcg/dL) took 200 mcg/day selenium as selenomethionine or placebo from 12.5 weeks of gestation through 12 months postpartum [112]. Of the participants in the selenium group, 28.6% developed postpartum thyroid disorders compared with 48.6% of those in the placebo group. In addition, 11.7% of participants in the selenium group developed permanent hypothyroidism compared with 20.3% in the placebo group. Another trial provided 83 mcg/day selenium as selenomethionine to 45 pregnant women who were TPOAb and/or TgAb positive. It also reported reductions in these antibodies at 6 months postpartum compared with placebo [113]. However, a trial that provided 60 mcg/day selenium as selenium yeast to TPOAb positive pregnant women who were mild to moderately iodine deficient showed no reduction in TPOAb levels at delivery [114].

In 2017, the American Thyroid Association issued a weak recommendation against the use of selenium supplementation for pregnant people who are TPOAb positive based on moderate quality evidence [115].

Although selenium is involved with normal thyroid function, more research is needed to understand the role of selenium supplements in thyroid disease, particularly by gender and selenium status.

## Health Risks from Excessive Selenium

Chronically high intakes of the organic and inorganic forms of selenium have similar effects [13]. Early indicators of excess intake are a garlic odor in the breath and a metallic taste in the mouth. The most common clinical signs of chronically high selenium intakes, or selenosis, are hair loss and nail brittleness or loss. Other signs and symptoms include skin rash, nausea, diarrhea, fatigue, irritability, and nervous system abnormalities [3,13,62].

As discussed earlier, Brazil nuts contain very high amounts of selenium (68–91 mcg per nut) and could cause selenium toxicity if consumed regularly. Acute selenium toxicity has resulted from the ingestion of misformulated over-the-counter products containing very large amounts of selenium [8,55]. In 2008, for example, 201 people experienced severe adverse reactions from taking a liquid dietary supplement containing 200 times the labeled amount of selenium [116]. Acute selenium toxicity can cause severe gastrointestinal and neurological symptoms; acute respiratory distress syndrome; myocardial infarction; hair loss; muscle tenderness; tremors; lightheadedness; facial flushing; kidney failure; cardiac failure; and, in rare cases, death [13,55].

The FNB has established ULs for selenium from food and supplements based on the amounts of selenium that are associated with hair and nail brittleness and loss (see Table 3) [13]. These ULs, however, do not apply to people taking selenium under the care of a physician.

**Table 3: Tolerable Upper Intake Levels (ULs) for Selenium [13]**

Age	Male	Female	Pregnancy	Lactation
Birth to 6 months	45 mcg	45 mcg		
7–12 months	60 mcg	60 mcg		
1–3 years	90 mcg	90 mcg		
4–8 years	150 mcg	150 mcg		
9–13 years	280 mcg	280 mcg		
14–18 years	400 mcg	400 mcg	400 mcg	400 mcg
19+ years	400 mcg	400 mcg	400 mcg	400 mcg

In 2023, the Panel on Nutrition, Novel Foods and Food Allergens of the European Food Safety Authority released a scientific opinion on the ULs for selenium [117]. Based on systematic reviews that examined associations between excess selenium intake and clinical effects, specifically alopecia, the panel set an upper limit for selenium of 255 mcg/day for all adults, including those who are pregnant or lactating, with lower amounts ranging from 70 to 230 mcg/day for children and teens, depending on age.

## Interactions with Medications

Selenium can interact with certain medications, and some medications can have an adverse effect on selenium levels. One example is provided below. Individuals taking this and other medications on a regular basis should discuss their selenium status with their health care providers.

### Cisplatin

Cisplatin, an inorganic platinum chemotherapy agent, is used to treat ovarian, bladder, lung, and other cancers. Cisplatin can reduce selenium levels in hair and serum but whether these reductions have a clinically significant impact is not known [118,119]. Some small studies have shown that selenium supplementation can reduce cisplatin’s toxicity [120], but the authors of a Cochrane Review concluded that the evidence that selenium supplementation alleviates the side effects of chemotherapy is insufficient [121].

## Selenium and Healthful Diets

The federal government’s 2020–2025 Dietary Guidelines for Americans notes that “Because foods provide an array of nutrients and other components that have benefits for health, nutritional needs should be met primarily through foods. ... In some cases, fortified foods and dietary supplements are useful when it is not possible otherwise to meet needs for one or more nutrients (e.g., during specific life stages such as pregnancy).” [122]

For more information about building a healthy dietary pattern, refer to the *Dietary Guidelines for Americans* (<https://www.dietaryguidelines.gov/>) and the USDA’s *MyPlate* (<https://www.choosemyplate.gov/>).



The *Dietary Guidelines for Americans* describes a healthy dietary pattern as one that

- Includes a variety of vegetables; fruits; grains (at least half whole grains); fat-free and low-fat milk, yogurt, and cheese; and oils.
  - Many whole grains and dairy products, including milk and yogurt, are good sources of selenium. Some ready-to-eat breakfast cereals are fortified with selenium, and some fruits and vegetables contain selenium.
- Includes a variety of protein foods such as lean meats; poultry; eggs; seafood; beans, peas, and lentils; nuts and seeds; and soy products.
  - Pork, beef, turkey, chicken, fish, shellfish, and eggs contain high amounts of selenium. Brazil nuts contain particularly high levels of selenium.
- Limits foods and beverages higher in added sugars, saturated fat, and sodium.
- Limits alcoholic beverages.
- Stays within your daily calorie needs.

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