NIH National Institutes of Health
Office of Dietary Supplements

Zinc

Fact Sheet for Health Professionals

Introduction

Zinc, an essential mineral, is naturally present in some foods, added to others, and available as a dietary supplement. Zinc is also found in some cold lozenges, over-the-counter drugs sold as cold remedies, and some denture adhesive creams.

Zinc is involved in many aspects of cellular metabolism. It is required for the catalytic activity of hundreds of enzymes, and it plays a role in enhancing immune function, protein and DNA synthesis, wound healing, and cell signaling and division [1-4]. Zinc also supports healthy growth and development during pregnancy, infancy, childhood, and adolescence and is involved in the sense of taste [2,3,5].

The total amount of zinc in the body is approximately 1.5 g in women and 2.5 g in men [2]. Most of this zinc is stored in skeletal muscle and bone [1-3].

The processes that maintain zinc homeostasis are absorption of zinc from the diet, excretion into the gastrointestinal tract, and reabsorption in the gastrointestinal lumen [2,3]. In general, as zinc intakes rise, the amount of zinc absorbed also increases, but its fractional absorption drops [2,3].

Serum or plasma zinc levels are typically used in clinical practice to assess zinc status. In healthy people, the amount of zinc in serum or plasma is 80 to 120 mcg/dL (12 to 18 mcmol/L) [2]. Serum zinc levels below 70 mcg/dL in women and 74 mcg/dL in men indicate inadequate zinc status. However, both serum and plasma measures have important limitations. Zinc concentrations in serum are associated with the patient's sex and age as well as the time of the blood draw (morning vs. evening) and do not always correlate with dietary or supplemental zinc intakes [6]. Zinc levels also fluctuate in response to other factors, including infections, changes in steroid hormones, and muscle catabolism during weight loss or illness [1,3]. Clinicians consider risk factors (such as inadequate caloric intake, chronic alcohol use, and malabsorptive digestive diseases) and signs of zinc deficiency (such as impaired growth in infants and children) when they assess a patient's zinc status [1].

Recommended Intakes

Intake recommendations for zinc 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 [1]. 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: Recommended Dietary Allowances (RDAs) for Zinc [1]

Age	Male	Female	Pregnancy	Lactation
Birth to 6 months*	2 mg	2 mg		
7–12 months	3 mg	3 mg		
1–3 years	3 mg	3 mg		
4–8 years	5 mg	5 mg		
9–13 years	8 mg	8 mg		
14–18 years	11 mg	9 mg	12 mg	13 mg
19+ years	11 mg	8 mg	11 mg	12 mg

*Adequate Intake (AI), equivalent to the mean intake of zinc in healthy, breastfed infants.

Sources of Zinc

Food

The richest food sources of zinc include meat, fish, and seafood [3]. Oysters contain more zinc per serving than any other food, but beef contributes 20% of zinc intakes from food in the United States because it is commonly consumed [7]. Eggs and dairy products also contain zinc [3]. Beans, nuts, and whole grains contain zinc, but the bioavailability of zinc from these foods is lower than that from animal foods because these foods contain phytates. Phytates, the storage form of phosphorus in plants, bind some minerals such as zinc in the intestine and form an insoluble complex that inhibits zinc absorption [1-3,8]. Fruits and vegetables contain very little zinc.

Breakfast cereals, which are often fortified with zinc, are a major source of zinc in the U.S. diet [3]. In U.S. children and adolescents, 12.1% to 18.4% of daily zinc intakes come from enriched and fortified foods [9].

The amount of zinc absorbed from food ranges from 5% to more than 50%, depending on the amount of plant-based foods (and thus of phytate) in the diet [3]. The absorption of zinc from mixed meals or diets containing a combination of animal-based and plant-based foods is lower than from diets or meals containing animal-based foods only [10].

Table 2 lists a variety of foods and their zinc content per serving [11].

Table 2: Zinc Content of Selected Foods [11]

Food	Milligrams (mg) per serving	Percent DV*
Oysters, Eastern, farmed, raw, 3 ounces	32	291
Oysters, Pacific, cooked, 3 ounces	28.2	256
Beef, bottom sirloin, roasted, 3 ounces	3.8	35
Blue crab, cooked, 3 ounces	3.2	29
Breakfast cereals, fortified with 25% of the DV for zinc, 1 serving	2.8	25
Cereals, oats, regular and quick, unenriched, cooked with water, 1 cup	2.3	21
Pumpkin seeds, roasted, 1 ounce	2.2	20
Pork, center loin (chops), bone in, broiled, 3 ounces	1.9	17
Turkey breast, meat only, roasted, 3 ounces	1.5	14
Cheese, cheddar, 1.5 ounces	1.5	14
Shrimp, cooked, 3 ounces	1.4	13
Lentils, boiled, ½ cup	1.3	12
Sardines, canned in oil, drained solids with bone, 3 ounces	1.1	10
Greek yogurt, plain, 6 ounces	1.0	9
Milk, 1% milkfat, 1 cup	1.0	9
Peanuts, dry roasted, 1 ounce	0.8	7
Rice, brown, long grain, cooked, ½ cup	0.7	6
Egg, large, 1	0.6	5
Kidney beans, canned, ½ cup	0.6	5
Bread, whole wheat, 1 slice	0.6	5
Fish, salmon, cooked, 3 ounces	0.5	5
Broccoli, chopped, cooked, ½ cup	0.4	4
Rice, white, long grain, cooked, ½ cup	0.3	3
Bread, white, 1 slice	0.2	2
Cherry tomatoes, raw, ½ cup	0.1	1
Blueberries, raw, ½ cup	0.1	1

*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 zinc is 11 mg for adults and children age 4 years and older [12]. FDA does not require food labels to list zinc content unless zinc 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.

The U.S. Department of Agriculture's (USDA's) FoodData Central (https://fdc.nal.usda.gov/) lists the nutrient content of many foods and provides a comprehensive list of foods containing zinc arranged by nutrient content (https://ods.od.nih.gov/pubs/usdandb/Zinc-Content.pdf) and by food name (https://ods.od.nih.gov/pubs/usdandb/Zinc-Food.pdf).

Dietary supplements

Zinc is available in supplements containing only zinc; supplements containing zinc in combination with other ingredients; and in many multivitamin/mineral products [13]. Supplements can contain any of a variety of forms of zinc, including zinc sulfate, zinc acetate, and zinc gluconate [14]. The Supplement Facts panel on a dietary supplement label declares the amount of elemental zinc in the product, not the weight of the entire zinc-containing compound.

Absorption of zinc from supplements containing zinc citrate or zinc gluconate is similar, at approximately 61% in young adults; the absorption from supplements containing zinc oxide is 50% [15]. Taking supplements containing 25 mg elemental iron or more at the same time as zinc supplements can reduce zinc absorption and plasma zinc concentrations [16-19]. However, the iron added to enriched or fortified foods does not interfere with zinc absorption.

Other sources

Products containing zinc include some labeled as homeopathic medications as well as nasal sprays that are sold over the counter to treat or prevent the common cold, manage flu symptoms, and support immune system health.

Some denture adhesive creams contain 17–34 mg/g zinc to enhance their adhesive properties [20]. Use as directed, resulting in intakes of 0.5–1.5 g zinc from these products per day, is not a concern. However, chronic, excessive use can lead to zinc toxicity, which can cause copper deficiency and neurologic diseases. Such toxicity has been reported in individuals who use at least one tube containing a total of 2.4 g or more denture cream each week for several years [21-23]. Many denture creams have been reformulated to omit zinc.

Zinc Intakes and Status

Most people in the United States consume adequate amounts of zinc, but people in certain age groups, especially older adults, might have marginal intakes. The average daily zinc intake from foods is 7.6–9.7 mg/day in children age 2–11 years, 10.1 mg/day in children and teens age 12–19 years, 13 mg/day in men older than 19, and 9.2 mg/day in women [24]. The average daily zinc intake from foods and supplements is 8.4–10.4 mg/day in children age 2–11 years, 10.7 mg/day in children and teens age 12–19 years, 16.4 mg/day in men, and 12.6 mg/day in women. In pregnant people age 20–40 years, the mean zinc intake is 12.4 mg/day from foods alone and 22.7 mg/day from foods and supplements [25].

Less than 1% of U.S. children age 2 to 8 years have zinc intakes from foods and supplements that are lower than the EAR. Among boys age 14 to 18 years, 1% have intakes below the EAR [9]. However, the proportion is much higher, 20.9%, in girls in this age group. National Health and Nutrition Examination

Survey (NHANES) data from 2005 to 2016 show that among U.S. adults age 19 years and older, 15% have zinc intakes below the EAR [26].

In the United States, 3.8% of children younger than 10, 8.6% of males age 10 and older, and 8.2% of females have serum zinc concentrations below the serum zinc cutoff for sufficiency for their age and sex according to an analysis of 2011–2014 NHANES data [6,8]. The investigators used cutoffs developed by the Biomarkers of Nutrition for Development Zinc Expert Panel on the basis of a statistical definition: 57–65 mcg/dL for children younger than 10, 69–70 mcg/dL for females age 10 and older, and 61–74 mcg/dL for males age 10 and older [8].

Zinc deficiency based on serum or plasma concentrations is much more common in low-income and middle-income countries [27]. According to an estimate based on analyses of zinc and phytate available in national food supplies and the prevalence of stunting, approximately 17% of the world's population is likely to have zinc deficiency [28].

Zinc Deficiency

Because zinc has many functions throughout the body, zinc deficiency affects many different tissues and organs [29]. Zinc deficiency can affect, for example, skin; bones; and the digestive, reproductive, central nervous, and immune systems [29].

The manifestations of zinc deficiency vary by age [29]. In infants and children, diarrhea is a common sign. In older children, alopecia, delayed growth, and frequent infections become more prevalent. In both infants and children, zinc deficiency can impair growth and lead to a loss of appetite and reproductive problems when they reach adulthood [2,3,27,30]. In populations with low intakes of absorbable zinc (e.g., from meat and fish), including many low-income and middle-income countries, zinc deficiency affects the health of pregnant people and their infants by increasing the risk of child morbidity (including premature birth and low birthweight) and mortality, maternal morbidity, and adverse birth outcomes [27]. In addition, zinc deficiency can interfere with the senses of taste and smell [5]. Zinc deficiency in older adults can cause delays in wound healing and changes in cognitive and psychological function [29].

Groups at Risk of Zinc Inadequacy

The following groups are among those most likely to have inadequate zinc status.

People with gastrointestinal disorders or who have had bariatric surgery

Zinc inadequacy is common in people with inflammatory bowel disease (IBD, which includes ulcerative colitis and Crohn's disease) or bariatric surgery involving resection of the gastrointestinal tract because of poor dietary intakes, decreased absorption, or increased urinary excretion as a result of inflammation [31,32]. Approximately 15% to 40% of people with IBD have zinc deficiency during active disease states and while in remission [31,32]. In patients with zinc deficiency, the risk of IBD-related symptoms (including anemia, hemorrhage, and abdominal or perianal fistula) increases, and these patients are more likely to need hospitalization or surgery. Zinc supplementation might reduce these risks [31].

Approximately 50% of people with newly diagnosed celiac disease have a high risk of zinc inadequacy or deficiency; potential contributors to this risk might include zinc malabsorption and mucosal inflammation [33,34]. These deficiencies sometimes persist even when people with celiac disease avoid foods containing gluten [34].

Vegetarians (especially vegans)

The bioavailability of zinc from vegetarian diets is lower than from nonvegetarian diets because vegetarians typically eat large amounts of legumes and whole grains, which contain phytates that bind zinc and inhibit its absorption [2]. In addition, meat is high in bioavailable zinc [35]. As a result, vegetarians and vegans usually have lower dietary intakes of zinc and lower serum zinc levels than nonvegetarians [36].

Vegetarians and vegans might benefit from using certain food preparation techniques that reduce the binding of zinc by phytates and increase its bioavailability, such as soaking beans, grains, and seeds in water for several hours before cooking them [37]. In addition, organic acids in fermented foods might increase zinc absorption [37]. Vegetarians and vegans might also benefit from zinc supplements [38].

People who are pregnant or lactating

During pregnancy, the amount of zinc needed increases to accommodate fetal growth, and the FNB therefore recommends that pregnant people consume 3 mg/day more zinc than nonpregnant people in the same age group [1,3]. Similarly, the zinc requirement increases by 4 mg/day during lactation.

NHANES data from 2001 to 2014 show that 11% of pregnant people in the United States have total zinc intakes from foods and supplements that are below the EAR [25]. Low serum zinc concentrations during pregnancy might increase the risk of preeclampsia and low-birthweight infants [39,40]. Routine zinc supplementation during pregnancy does not appear to reduce the risk of low birthweight, stillbirth, or neonatal death, but it might lower the risk of preterm birth [41].

During lactation, some [42,43] but not all [44] studies show that adequate intakes of foods rich in zinc increase concentrations of the mineral in breast milk. Evidence is also conflicting on whether zinc supplementation during lactation increases the zinc content of breast milk [45,46].

Older infants who are exclusively breastfed

Zinc concentrations in breast milk peak during the first month after birth and then decline by approximately 75% by the ninth month [3]. Because of this sharp drop, human breast milk alone is not sufficient to meet the infant’s zinc requirement after age 6 months [3,47]. The FNB recommends that in addition to breast milk, infants age 7–12 months consume age-appropriate foods or formula containing zinc [1].

Children with sickle cell disease

Children with sickle cell disease (SCD) have a high risk of zinc insufficiency or deficiency, possibly as a result of the chelation therapy used to treat iron overload [3,48]. Children with SCD and low zinc status often are shorter and weigh less than age-matched peers, and they also have a higher risk of maturation delays, vaso-occlusive pain crises (blockages of blood flow to an area of the body), and associated hospitalizations [48]. Supplemental zinc might enhance growth in children with SCD and decrease the risk of bacterial infections, hospitalizations, and vaso-occlusive pain crises [3,48,49].

People with alcohol use disorder

Low zinc status has been observed in 30% to 50% of people with alcohol use disorder [1,50]. Ethanol consumption decreases intestinal absorption of zinc and increases urinary zinc excretion [1,50,51,52]. In addition, the variety and amount of food consumed by many people with alcohol use disorder is limited, leading to inadequate zinc intake [53,54].

Zinc and Health

This section focuses on the following diseases and disorders in which zinc might play a role: the common cold, pneumonia in children, HIV in children and adults, acute childhood diarrhea (which often results from infections), age-related macular degeneration (AMD), and type 2 diabetes (T2D). For information on zinc and COVID-19, see Dietary Supplements in the Time of COVID-19.

The common cold

Researchers have hypothesized that zinc could reduce the severity and duration of cold signs and symptoms by directly inhibiting rhinovirus binding and replication in the nasal mucosa and suppressing inflammation [55,56]. In studies examining the effects of zinc supplements on the common cold, zinc is usually administered in a lozenge or syrup that temporarily sticks to the mouth and throat, placing the zinc in contact with the rhinovirus in those areas.

The results from clinical trials that have examined the effects of zinc supplements on the common cold have been inconsistent. Overall, however, supplemental zinc in lozenge or syrup form appears to reduce the duration, but not the severity, of signs and symptoms of the common cold when taken shortly after a person develops a cold [57-60].

In one clinical trial, 50 adults took a zinc acetate lozenge (13.3 mg zinc) or placebo every 2–3 wakeful hours within 24 hours of developing the common cold for as long as they had cold symptoms. In comparison with placebo, the zinc lozenges reduced the duration of colds by 3 days and the severity of cold symptoms (cough, nasal discharge, and muscle aches) [61]. In another clinical trial, 273 adults with experimentally induced colds were randomly assigned to take zinc gluconate (13.3 mg zinc) or zinc acetate (5.0 mg or 11.5 mg) lozenges every 2 to 3 hours while awake, for a total of six lozenges per day, or placebo, for up to 14 days [62]. Duration of illness was 1 day less with the zinc gluconate supplements than with the placebo, but the lozenges had no effect on symptom severity. Furthermore, the 5.0 and 11.5 mg zinc acetate lozenges had no effect on either cold duration or severity. In a second trial described in the same report, neither zinc gluconate nor zinc acetate lozenges affected the duration or severity of cold symptoms in comparison with placebo in 281 adults with colds [62].

A 2021 systematic review and meta-analysis included 28 randomized controlled trials (including the three described above) with a total of 5,446 participants (mostly adults younger than 65 years) who had a community-acquired viral respiratory tract infection or were inoculated with a rhinovirus [57]. Most trials provided zinc in the form of zinc acetate or gluconate lozenges at total daily doses of 45 mg to 300 mg for up to 2 weeks, but some trials used nasal sprays or gels. In participants who used products containing zinc, symptoms resolved an average of 2 days earlier than in those who received a placebo. However, average daily symptom severity did not differ between those who were and were not treated with zinc. The author of an earlier systematic review concluded that the use of zinc lozenges at doses of over 75 mg/day reduced the duration of the common cold, whereas lower doses did not [59].

Additional research is needed to determine the optimal dosage, formulation, and administration schedule before a general recommendation can be made regarding the use of lozenges, gels, and sprays containing zinc to reduce the severity and duration of symptoms of the common cold [58-60].

Pneumonia in children

In low-income countries, pneumonia is responsible for 15% of all deaths in children younger than 5 years and for 19% of all childhood deaths [63]. Poor zinc status is associated with greater susceptibility to pneumonia, more severe disease, and higher mortality risk in children [64-67].

Several clinical trials have examined the effects of zinc supplementation on the incidence of pneumonia and as an adjunctive treatment for pneumonia. A 2016 Cochrane Review of six trials in low-income countries found that supplementation with 10–20 mg zinc for up to 20 months in a total of 5,193 children age 2 to 59 months resulted in lower incidence and prevalence of pneumonia than placebo [63].

However, most research suggests that the adjunctive use of zinc supplements to treat pneumonia in children does not affect mortality or time to recovery. A 2020 systematic review and meta-analysis included 11 clinical trials in children age 2 to 60 months with mostly severe pneumonia in low- and middle-income countries [68]. Mortality rates from pneumonia and time to recovery from severe pneumonia did not differ between children treated with 10–20 mg/day supplemental zinc and those treated with placebo for 7–14 days or until discharge. Another meta-analysis of six placebo-controlled trials that included 2,216 children age 2 to 60 months found that zinc supplementation reduced mortality rates from severe pneumonia but not rates of treatment failure or of changes in antibiotic therapy [69].

HIV in children and adults

HIV infection reduces the absorption and metabolism of zinc from foods [3]. In addition, people with HIV often have diarrhea, which can result in excessive losses of zinc. For these reasons, people with HIV often have low plasma or serum zinc levels.

Several clinical trials have found some beneficial effects of zinc supplementation to manage the morbidity and mortality associated with HIV infection. One trial, for example, randomly assigned 231 adults who had HIV and plasma zinc levels lower than 75 mcg/dL to supplemental zinc (12 mg/day for women or 15 mg/day for men) or placebo for 18 months [70]. The supplements reduced rates of immunological failure events (CD4+ T-cell counts less than 200 cells/mL) by 76% and rates of diarrhea by 60% but had no effect on mortality. In another trial in Iran that randomized 146 adults with HIV to 50 mg/day zinc, 200 mcg/day selenium, or placebo for 6 months and then followed participants for another 3 months, the zinc supplements decreased rates of opportunistic infections but did not improve CD4+ T-cell counts [71].

However, findings were less positive in two Cochrane Reviews and another trial (not included in either Cochrane Review) that assessed the potential benefits of supplementation with micronutrients, including zinc, or placebo in various populations with HIV. The first Cochrane Review, which focused on micronutrient supplementation for children with HIV, included two trials that administered 10 mg/day zinc with or without vitamin A for up to 15 months in a total of 128 children with HIV in South Africa [72]. One of these trials found that zinc supplementation had no beneficial effects in comparison with vitamin A, whereas the other found that the risk of watery diarrhea was 49% lower with zinc supplements than with placebo.

A subsequent Cochrane Review that evaluated micronutrient supplements for adults with HIV included six placebo-controlled trials of zinc supplements (12–50 mg/day for 14 days to 18 months or 1 weekly 90 mg dose for 6 months) in a total of 826 participants [73]. The authors concluded that although zinc supplements might improve zinc status, the supplements appeared to have little if any effect on CD4+ T-cell counts or viral load and inconclusive effects on mortality and diarrhea frequency. In a trial in 400 pregnant people with HIV in Tanzania, 25 mg/day zinc until 6 weeks after delivery did not result in any differences in birth weight, duration of gestation, or rates of fetal mortality or early mother-to-child transmission of HIV in comparison with placebo [74,75]. In addition, zinc supplementation did not affect maternal viral load or CD4+, CD8+, or CD3+ T-cell counts. However, the supplements blunted the rise in hemoglobin concentrations between baseline and 6 weeks postpartum.

More evidence is required to determine whether zinc supplements might be helpful for people with HIV.

Childhood acute diarrhea

Acute diarrhea is associated with high mortality rates among children in low-income countries, where it causes about 525,000 deaths annually [76,77]. Zinc is used to treat acute diarrhea in children, especially in low-income countries where zinc deficiency is common. Scientists believe that zinc's beneficial effects stem from its role in supporting adaptive immunity and maintaining the mucosal integrity of the gastrointestinal system [76].

Clinical trials show that zinc supplementation helps shorten the duration of diarrhea in children in low-income countries. A 2016 Cochrane Review included 33 trials that compared the effects of zinc supplementation with placebo in 10,841 children age 1 month to 5 years with acute or persistent diarrhea [78]. Most studies were conducted in Asian countries with high rates of zinc deficiency. The investigators administered zinc in the form of zinc acetate, zinc gluconate, or zinc sulfate. The most common dose was 20 mg/day, and about half the studies administered zinc for 2 weeks. The authors concluded, on the basis of evidence of low to moderate certainty, that zinc supplementation shortens the duration of diarrhea by about half a day in children older than 6 months and reduces the likelihood that diarrhea will persist for at least 7 days by 27%. In children younger than 6 months, however, zinc supplementation did not affect mean duration of diarrhea or persistence of diarrhea for 7 days. In addition, evidence that the authors deemed to have high certainty showed that zinc supplementation reduces the duration of diarrhea in children with signs of malnutrition by about a day.

A 2018 systematic review and meta-analysis had similar findings. It examined the use of zinc alone or in combination with other treatments for acute diarrhea and gastroenteritis in 174 studies in 32,430 children, mostly from low- and middle-income countries [79]. The authors concluded that zinc was one of the most effective interventions of those examined, especially when it was combined with *Saccharomyces boulardii* (a probiotic) or smectite (a natural clay that contains minerals), for reducing the duration of acute diarrhea and gastroenteritis in children. Analyses showed that zinc alone or in combination reduced the duration of diarrhea by about ¾ to 1½ days.

The World Health Organization and UNICEF recommend short-term zinc supplementation—20 mg zinc per day, or 10 mg for infants under 6 months, for 10 to 14 days—to treat acute childhood diarrhea [80]. Most trials of zinc supplementation for diarrhea have been conducted in low-income countries [76]. Zinc supplements might have only a marginal effect on diarrhea duration in well-nourished children.

Age-related macular degeneration

AMD is the leading cause of significant vision loss in older people [81]. The human retina has a high zinc concentration, and research has shown that supplements containing both zinc and antioxidants might delay the progression of AMD and vision loss, possibly by preventing cellular damage in the retina [3,82,83].

Observational evidence suggests a link between higher zinc intakes and a lower risk of AMD. In a population-based cohort study in the Netherlands that included 4,170 adults age 55 or older, dietary zinc intake was inversely associated with the risk of AMD over a mean follow-up period of 8 years [84]. Similarly, a study of 2,464 adults age 49 or older in Australia found that at 5-year and 10-year follow-up, participants with intakes of zinc from food and supplements in the top decile (at least 15.8 mg/day) had a 44% lower risk of any AMD and a 46% lower risk of early AMD than participants in all other deciles [85].

Clinical trial evidence has confirmed the benefits of zinc supplementation, in combination with certain antioxidants, for slowing the progression of AMD. The Age-Related Eye Disease Study (AREDS) was a clinical trial in 4,757 participants age 50 to 80 years with a high risk of advanced AMD (i.e., they had intermediate AMD or advanced AMD in one eye and good vision in the other eye) [83]. AREDS found that participants who took a supplement each day containing 80 mg zinc in the form of zinc oxide, 15 mg (7,500 mcg retinol activity equivalent [RAE]) beta-carotene, 180 mg (400 International Units [IU]) vitamin E in the form of dl-alpha-tocopheryl acetate, 500 mg vitamin C, and 2 mg copper for 5 years had a 25% lower risk of advanced AMD than those taking a placebo.

The follow-up AREDS2 study confirmed the value of the AREDS supplement in reducing the progression of AMD in 4,203 participants over a median follow-up period of 5 years [86]. AREDS2 also showed that a formulation providing 25 mg zinc (about one-third the amount in the original formulation) provided the same protective effect against advanced AMD. However, because AREDS2 had fewer participants than the original AREDS study, and fewer than half took the formula containing less zinc, the researchers viewed this finding as preliminary. The National Eye Institute recommends use of an AREDS formulation providing 80 mg zinc [87,88].

Individuals who have or are developing AMD should talk to their health care provider about their zinc intakes and the supplement formulations used in the AREDS studies.

Type 2 diabetes

Zinc concentrations are often low in people with T2D [2,3]. Researchers therefore hypothesize that zinc depletion might play a role in diabetes progression.

Several observational studies have found an association between zinc intakes and risk of T2D. In a systematic review and meta-analysis that included 16 observational studies conducted in the United States, Australia, Sweden, India, and Japan with a total of 146,027 men and women age 18 to 84 years, the risk of T2D was 13% lower in participants with the highest zinc intakes than in those with the lowest intakes [89]. When the researchers analyzed the influence of area of residence on the results, the associations between zinc intakes and T2D risk were significant only for studies conducted in rural areas and not those conducted in urban areas.

Clinical trials have assessed the utility of zinc supplements to reduce the risk of T2D or to manage its complications. In a 2015 Cochrane Review of the clinical trial evidence on zinc supplementation for T2D prevention, only three trials with a total of 128 participants met the inclusion criteria [90]. These studies administered 30 mg to 100 mg zinc (in the form of zinc sulfate or zinc amino chelate) per day for 4 to 12 weeks, but the quality of these studies could not be assessed because of the lack of relevant information in the study reports. The Cochrane Review authors concluded that evidence is lacking on which to base conclusions about the use of zinc supplementation to prevent T2D.

However, studies published since the Cochrane Review have had more positive findings. A systematic review and meta-analysis included nine placebo-controlled trials assessing the effects of zinc supplementation (7 mg/day to 150 mg/day) for 6 to 52 weeks on lipid profiles in a total of 424 people with T2D [91]. The supplements had beneficial effects on serum levels of triglycerides and total cholesterol but not on serum low-density lipoprotein (LDL) cholesterol or high-density lipoprotein (HDL) cholesterol levels.

A second systematic review and meta-analysis compared the effects of low-dose zinc supplements (less than 25 mg/day) with those of high-dose supplements (25 to 75 mg/day) on risk factors for T2D and cardiovascular disease in 27 clinical trials (including two from the 2015 Cochrane Review) [92]. Zinc supplements were administered for 4 weeks to 12 months (mean 11 weeks) to a total of 1,042 participants age 6 to 106 years (but most studies included adults age 20 to 70 years) and placebo to 974 participants. Although low-dose and high-dose zinc supplements had beneficial effects on several outcomes assessed, low doses of zinc and longer administration improved a larger number of risk factors. For example, studies that administered zinc supplements for less than 12 weeks had beneficial effects on fasting blood glucose, insulin resistance, and triglyceride levels, whereas studies that administered the supplements for longer had positive effects on fasting blood glucose, hemoglobin A1c, triglyceride, total cholesterol, and LDL cholesterol levels. Sensitivity analyses showed no significant effect of zinc dosage on these outcomes.

A third systematic review and meta-analysis evaluated the effects of zinc supplements on T2D prevention and management in 32 trials that administered zinc supplements (4 to 240 mg/day zinc, mean 35 mg/day) or placebo for 1 to 12 months to a total of 1,700 adults age 18 and older with T2D (except that one included study was in children age 6 to 10 years) [93]. The supplements reduced fasting glucose, 2-hour postprandial glucose, fasting insulin, insulin resistance, glycated hemoglobin, and C-reactive protein levels. Glycemic indicators did not vary by zinc dosage (less than 30 mg/day or at least 30 mg/day) or duration of supplementation (1 month or more than 1 month).

Research has also explored the potential benefits of zinc supplementation in people with gestational diabetes. A systematic review and meta-analysis of five placebo-controlled trials that included 263 people with gestational diabetes evaluated the effects of zinc supplementation (4 to 30 mg/day zinc with or without vitamin E, magnesium, calcium, vitamin D, or a combination) on metabolic status [94]. The supplements had beneficial effects on fasting plasma glucose, insulin, and insulin resistance, but did not affect LDL or total cholesterol levels. However, because this analysis included studies that administered zinc in combination with other nutrients, the potential contribution of zinc by itself cannot be assessed.

Up to one quarter of people with T2D develop diabetic foot ulcers, which can result in amputation [95]. A Cochrane Review of nutritional interventions to treat diabetic foot ulcers included one trial in 60 participants of 50 mg zinc (in the form of zinc sulfate) or placebo for 12 weeks [96]. The authors concluded that whether zinc supplements affect diabetic foot ulcers over time is uncertain.

Overall, the evidence to date is insufficient to support any conclusions about the impact of zinc supplementation on the prevalence or severity of T2D, gestational diabetes, or diabetic foot ulcers.

Health Risks from Excessive Zinc

High zinc intakes can cause nausea, dizziness, headaches, gastric distress, vomiting, and loss of appetite [2,3]. If used for weeks, doses of 50 mg zinc or more—typically from supplements or excessive use of denture adhesive creams that contain zinc—can interfere with copper absorption (which can cause low copper status), reduce immune function, and lower HDL cholesterol levels [1-3,97]. The amount of zinc obtained from food is rarely as high as 50 mg, so the zinc in foods is unlikely to cause zinc toxicity. Very high doses of zinc from supplements (142 mg/day) might also interfere with magnesium absorption and disrupt magnesium balance [98].

According to a few reports, overuse of denture adhesive creams containing up to 34 mg zinc per gram of product can lead to neurological symptoms (including sensory ataxia and myelopathy) and anemia. Zinc-free formulations are available to prevent these effects [2,20,21].

The FNB has established ULs for zinc from food and supplements for healthy individuals on the basis of levels that have an adverse effect on copper status (Table 3) [1]. The ULs do not apply to individuals receiving zinc for medical treatment, but such individuals should be under the care of a physician.

Table 3: Tolerable Upper Intake Levels (ULs) for Zinc [1]

Age	Male	Female	Pregnancy	Lactation
Birth to 6 months	4 mg	4 mg		
7–12 months	5 mg	5 mg		
1–3 years	7 mg	7 mg		
4–8 years	12 mg	12 mg		
9–13 years	23 mg	23 mg		
14–18 years	34 mg	34 mg	34 mg	34 mg
19+ years	40 mg	40 mg	40 mg	40 mg

Interactions with Medications

Zinc has the potential to interact with certain medications. In addition, several types of medications might adversely affect zinc levels. A few examples are provided below. Individuals taking these and other medications on a regular basis should discuss their zinc status with their health care providers.

Antibiotics

Both quinolone antibiotics (such as Cipro) and tetracycline antibiotics (such as Achromycin and Sumycin) might interact with zinc in the gastrointestinal tract, which could inhibit the absorption of both zinc and the antibiotic if they are taken at the same time [99,100]. Taking the antibiotic at least 2 hours before or 4–6 hours after the zinc supplement minimizes this interaction [99].

Penicillamine

Zinc can reduce the absorption and action of penicillamine, a drug used to treat rheumatoid arthritis and Wilson disease [101]. To minimize this interaction, people should take zinc supplements and penicillamine at least 1 hour apart.

Diuretics

Thiazide diuretics, such as chlorthalidone (Hygroton and Thalitone) and hydrochlorothiazide (e.g., Esidrix and HydroDIURIL), increase zinc excretion in the urine. This increased excretion, in turn, decreases serum zinc concentrations [102].

Zinc 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)."

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.myplate.gov/).

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

- Includes a variety of vegetables, fruits, whole grains, fat-free or low-fat milk and milk products, and oils.
    - Some dairy products are good sources of zinc. Some ready-to-eat breakfast cereals are fortified with zinc.
- Includes a variety of protein foods, including seafood, lean meats and poultry, eggs, legumes (beans and peas), nuts, seeds, and soy products.
    - Some meats contain high amounts of zinc. Fish and seafood are good sources of zinc.
- 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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