

Fact Sheet for Health Professionals

Introduction

Fluoride, a mineral, is naturally present in many foods and available as a dietary supplement.

Fluoride is the ionic form of the element fluorine, and it inhibits or reverses the initiation

Consumer

Datos en español

Health Professional

Other Resources

and progression of dental caries (tooth decay) and stimulates new bone formation [1].

Soil, water, plants, and foods contain trace amounts of fluoride. Most of the fluoride that people consume comes from fluoridated water, foods and beverages prepared with fluoridated water, and toothpaste and other dental products containing fluoride [2,3].

Approximately 80% or more of orally ingested fluoride is absorbed in the gastrointestinal tract [1]. In adults, about 50% of absorbed fluoride is retained, and bones and teeth store about 99% of fluoride in the body [1,3]. The other 50% is excreted in urine [1]. In young children, up to 80% of absorbed fluoride is retained because more is taken up by bones and teeth than in adults [1].

Individual fluoride status is not typically assessed, although fluoride concentrations can be measured in plasma, saliva, urine, bones, nails, hair, and teeth [4,5]. Criteria for adequate, high, or low levels of fluoride in the body have not been established.

Recommended Intakes

Intake recommendations for fluoride 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]. DRIs 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:

- 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.

The FNB found the data insufficient to derive EARs for fluoride. Therefore, the board established AIs for all ages using estimated intakes shown to maximize reductions in the incidence of dental caries without unwanted side effects, such as dental fluorosis, a chronic condition resulting from the consumption of too much fluoride when teeth are developing [1]. Table 1 lists the current AIs for fluoride for healthy individuals.

Table 1: Daily Adequate Intakes (Als) for Fluoride [1]

Age	Male	Female	Pregnancy	Lactation
Birth to 6 months	0.01 mg	0.01 mg		
7-12 months	0.5 mg	0.5 mg		
1-3 years	0.7 mg	0.7 mg		
4-8 years	1 mg	1 mg		
9-13 years	2 mg	2 mg		
14-18 years	3 mg	3 mg	3 mg	3 mg
19+ years	4 mg	3 mg	3 mg	3 mg

Sources of Fluoride

Food

Food

Brewed tea typically contains higher levels of fluoride than most foods, depending on the type of tea and its source, because tea plants take up fluoride from soil [1,3]. Fluoride levels can range from 0.3 to 6.5 mg/L (0.07 to 1.5 mg/cup) in brewed tea made with distilled water [3].

Fluoride concentrations in breast milk are so low that they cannot always be detected; when these levels can be measured, they range from less than 0.002 to 0.01 mg/L, even when mothers live in communities with fluoridated water [3]. Fluoride concentrations in cow's milk are also very low, ranging from 0.007 to 0.086 mg/L [3]. Fluoride levels in infant formulas in the United States vary, depending on the type of formula and the fluoride content of the water used to prepare the formula [3]. The typical fluoride concentration is less than 0.2 mg/L in milk-based infant formula and 0.2 to 0.3 mg/L in soybased infant formula (not including contributions from tap water used to prepare the formula).

Only trace amounts of fluoride are naturally present in most foods, and most foods not prepared with fluoridated water provide less than $0.05 \text{ mg}/100 \text{ g} [\underline{1,6}]$.

A variety of types of foods and their fluoride levels per serving are listed in Table 2.

Table 2: Fluoride Content of Selected Foods [3,6]

Milligrams per
Serving

Food	Milligrams per Serving
Tea, black, brewed, 1 cup	0.07 to 1.5*
Coffee, brewed, 1 cup	0.22*
Bottled water with added fluoride, 1 cup	0.19 to 0.24*
Shrimp, canned, 3 ounces	0.17
Raisins, ¼ cup	0.08
Oatmeal, cooked, ½ cup	0.08*
Grapefruit juice, ¾ cup	0.08
Potatoes, russet, baked, 1 medium	0.08
Rice, cooked, ½ cup	0.04*
Cottage cheese, ½ cup	0.04
Pork chop, baked, 3 ounces	0.03
Yogurt, plain, low-fat, 1 cup	0.03
Lamb chop, cooked, 3 ounces	0.03
Tortilla, flour, 1 tortilla, approx. 10" diameter	0.02
Corn, canned, ½ cup	0.02
Beef, cooked, 3 ounces	0.02
Tuna, light, canned in water, 3 ounces	0.02
Cheese, cheddar, 1½ ounces	0.01
Bread, white or whole wheat, 1 slice	0.01
Asparagus, cooked, 4 spears	0.01
Chicken, cooked, 3 ounces	0.01
Milk, fat-free or 1%, 1 cup	0.01
Apple, raw, with skin, 1 medium	0.01
Avocado, raw, ½ cup sliced	0.01
Macaroni, plain, cooked, ½ cup	0.00*
Tomato, raw, 1 medium	0.00
Bananas, 1 medium	0.00
Egg, cooked, 1 large	0.00
Carrots, raw, 1 medium	0.00
Peanut butter, 1 tbsp	0.00

^{*}Amounts of fluoride might vary by levels in the water used to prepare these foods and beverages.

Fluoridated drinking water

Since 1962, the U.S. Public Health Service has recommended the addition of fluoride to drinking (tap) water to reduce the risk and severity of dental caries, one of the most common chronic diseases in

children [7]. Many countries around the world now adjust the fluoride concentration of community drinking water supplies to the level recommended for the prevention of dental caries [8].

Although the U.S. Public Health Service recommended fluoride concentrations of 0.7 in warmer climates (where children were expected to drink more water) to 1.2 mg/L in cooler climates to prevent dental caries in 1962, it amended its recommended level in 2015 to 0.7 mg/L to maintain the ability to prevent caries while minimizing the risk of dental fluorosis [7,9]. In 1986, guidelines from the U.S. Environmental Protection Agency (EPA) established a maximum allowable concentration of 4.0 mg/L fluoride in public drinking water systems to prevent adverse effects from fluoride exposure (such as bone disease) and a recommended maximum concentration of 2.0 mg/L to prevent dental fluorosis [3,10]. A review of this regulation is a currently a low priority for the EPA [11].

Fluoridated municipal drinking water—including water that people drink as well as foods and beverages prepared using municipal drinking water—accounts for about 60% of fluoride intakes in the United States [3,7]. In 2016, 62.4% of the U.S. population had access to a fluoridated community water system [12]. The fluoride additives used to fluoridate drinking water in the United States are fluosilicic acid, sodium fluosilicate, and sodium fluoride [13]. The Centers for Disease Control and Prevention publishes fluoride levels in tapwater by county [14]. Because of differences in amounts of fluoride in groundwater, private water sources (including well water) have variable fluoride concentrations [10].

Fluoride is not typically added to bottled drinking waters. However, when fluoride is added, the bottle's label is not required to list the amount unless the label makes a claim about the product's fluoride content [15]. By law, the amount of fluoride added to bottled water cannot exceed 1.7 mg/L [3]. In 2019, FDA proposed revising the quality standard for bottled water and thereby limiting the amount of fluoride to no more than 0.7 mg/L, but this rule has not yet been finalized [16].

Dietary supplements

Only a few dietary supplements contain fluoride, usually in the form of sodium fluoride [17]. Most of these products are multivitamin/multimineral supplements, multivitamins plus fluoride, or supplements containing trace minerals only. Some fluoride supplements, usually intended for children, are in the form of drops. The most common amount of fluoride in supplements is 0.25 mg, although a few products contain 0.5 or 1 mg [17].

Dental products

Most toothpaste sold in the United States contains fluoride in the form of sodium fluoride or monofluorophosphate, most commonly at a level of 1,000 to 1,100 mg/L (about 1.3 mg in a quarter teaspoon, a typical amount of toothpaste used for one brushing) [3]. The amount of fluoride ingested from toothpaste depends on the amount used, the person's swallowing control, and how often the person uses toothpaste. Estimated typical amounts of fluoride ingested daily from toothpaste are 0.1 mg to 0.25 mg for infants and children aged 0 to 5 years, 0.2 to 0.3 mg for children aged 6–12 years, and 0.1 mg for adults [3]. Fluoride in toothpaste, regardless of its form, is well absorbed [1].

Other dental products that provide fluoride include mouth rinses for home use, topical fluoride preparations applied in dentists' offices or through school-based programs, and dental devices (e.g.,

orthodontic bracket adhesives, glass-ionomer and some composite resin dental restorative materials, and some dental sealants and cavity liners) [3,18]. Gels used by dentists are typically applied one to four times a year and can lead to ingestions of 1.3 to 31.2 mg fluoride each time; varnishes are least likely to produce a high bolus of fluoride [3].

Medications

Medications can contain fluoride. For example, voriconazole (VFEND or Vfend) is an oral antifungal medication used to treat several infectious conditions, including invasive aspergillosis, candidemia, and candidiasis [19]. Typical doses of voriconazole provide 65 mg/day fluoride. Long-term use (e.g., for 4 months or more) of this medication can lead to high fluoride concentrations in serum [20,21]. The prescribing information for voriconazole advises discontinuation of voriconazole if skeletal fluorosis and periostitis (inflammation of the membrane surrounding and protecting the bones) develop [19].

Fluoride Intakes and Status

Most people in the United States consume adequate amounts of fluoride through foods containing naturally occurring fluoride, fluoridated tap water, and food products made with fluoridated tap water. According to the EPA, typical daily fluoride intakes in the United States from foods and beverages (including fluoridated drinking water) are 1.2 to 1.6 mg for infants and toddlers younger than 4 years, 2.0 to 2.2 mg for children aged 4–11 years, 2.4 mg for those aged 11–14 years, and 2.9 mg for adults [10].

Fluoride and Health

This section focuses on two conditions in which fluoride might play a role: dental caries and bone fractures.

Dental caries

Dental caries occurs when cariogenic bacteria in the mouth ferment foods and produce acids that dissolve tooth mineral [22]. Over time, this tooth decay can cause pain and tooth loss. Without treatment, dental caries can cause infections, impair growth, lead to weight gain, affect school performance, impair quality of life, and possibly result in death [23-26]. Adequate fluoride intakes reduce the risk of dental caries in its initial stages by inhibiting demineralization and the activity of bacteria in dental plaque and by enhancing tooth remineralization [24].

<u>Impact of water fluoridation on dental caries</u>: Water fluoridation protects teeth in two main ways—by preventing the development of caries through ingestion of drinking water during the tooth-forming years and through direct contact of fluoride with teeth throughout life [27,28].

A 2015 Cochrane review included 20 prospective observational studies (most conducted before 1975) [8]. The results showed that water fluoridation reduces the risk of decay and fillings, as well as of premature loss of primary (baby) teeth, by 35% and loss of permanent (adult) teeth by 26% in children receiving fluoridated water in comparison with children receiving unfluoridated water. Fluoridation also increases the number of children with no decay in their baby teeth by 15% and the number of children with no decay in their permanent teeth by 14%. The authors concluded that water fluoridation is

effective for reducing dental caries rates in both primary and permanent teeth in children. However, the reviewers were unable to assess the effectiveness of water fluoridation for preventing caries in adults because no evidence met the review's inclusion criteria (which required studies to include at least two groups, one receiving fluoridated water and one receiving unfluoridated water).

The Cochrane review's findings were confirmed by a 2018 cross-sectional study on the associations between fluoridated community water and dental caries in the United States [29]. The authors analyzed data on 7,000 children aged 2 to 8 years and 12,604 children and adolescents aged 6 to 17 years who participated in the National Health and Nutrition Examination Study (NHANES) from 1999 to 2004 and 2011 to 2014, respectively. The results showed that living in a county in which 75% or more of the drinking water contained at least 0.7 mg/L fluoride was associated with a 30% reduction in the rate of caries in primary teeth and a 12% reduction in the rate of caries in permanent teeth.

Some evidence shows that the addition of fluoride to drinking water can also prevent dental caries in adults. An observational study included 3,779 individuals in Australia aged 15 and older who participated in the Australian 2004–2006 National Survey of Adult Oral Health [30]. In adults exposed to fluoridated community water supplies for at least 14 years, rates of decayed, missing, or filled teeth were 11–12% lower than in adults whose drinking water during this period had negligible amounts of fluoride. An earlier study in 876 Australian Defence Force members aged 17–56 years found that the average rate of decayed, missing, and filled teeth was 24% lower in those with access to water containing 0.5 to 1 mg/L fluoride for at least half of their lifetime than in those exposed for less than 10% of their lifetime [31].

These findings show that fluoridated drinking water can prevent dental caries in children and adults.

Impact of fluoride dietary supplements on dental caries in children: Some studies have assessed the impact of fluoride supplements on caries development in children. For example, a 2011 Cochrane review of 11 randomized or quasi-randomized studies in a total of 7,196 children (most living in communities lacking access to fluoridated drinking water) found that 0.25–1 mg/day supplemental fluoride for 24–55 months reduced rates of decayed, missing, and filled tooth surfaces by 24% [32]. The authors concluded that fluoride supplements were associated with a lower caries incidence rate in permanent teeth. A 2013 systematic review found an even greater preventive effect of fluoride supplements on the basis of one randomized and four nonrandomized clinical trials in children [25]. The results showed that 0.25–1 mg/day fluoride supplementation reduced caries incidence rates in primary teeth by 48–72% in areas where water fluoridation levels were lower than 0.6 mg/L. In two of these trials that monitored the children for 6–10 years, supplements were associated with a 33–80% reduction in the incidence of caries at ages 7–10 years.

The U.S. Preventive Services Task Force (USPSTF) and the American Dental Association have issued fluoride supplement recommendations for children whose water supply contains little or no fluoride [23]. These recommendations are summarized in Table 3.

Table 3: Expert Panel Recommendations for Fluoride Supplementation in Children

Source	Age Range	Recommendation
USPSTF [<u>23</u>]	6 months and older	 Fluoride supplement (dose not specified) for children whose water supply contains little or no fluoride*
American Dental Association [33]**	6 months to 3 years	• Fluoride supplement (0.25 mg/day) for children whose water supply contains less than 0.3 ppm (0.3 mg/L) fluoride
	3-6 years	 Fluoride supplement (0.5 mg/day) for children whose water supply contains less than 0.3 ppm (0.3 mg/L) fluoride Fluoride supplement (0.25 mg/day) for children whose water supply contains 0.3 to 0.6 ppm (0.3 to 0.6 mg/L) fluoride
	6-16 years	 Fluoride supplement (1 mg/day) for children whose water supply contains less than 0.3 ppm (0.3 mg/L) fluoride Fluoride supplement (0.5 mg/day) for children whose water supply contains 0.3 to 0.6 ppm (0.3 to 0.6 mg/L) fluoride

^{*}No studies have addressed the dosage or duration of oral fluoride supplementation in this population.

Overall, the available evidence suggests that dietary supplements containing fluoride can reduce rates of dental caries in children who lack access to fluoridated drinking water. No studies have assessed the impact of fluoride supplements on caries development in adults.

Fluoride dietary supplements in pregnant women: Like other nutrients, fluoride is transferred from a pregnant woman to her fetus, so a few studies have evaluated the use of fluoride supplements by pregnant women to prevent dental caries in their children. However, the authors of a 2017 Cochrane review found only one randomized controlled trial published in 1997 that met the review's inclusion criteria [34]. This study assessed caries rates in 798 3-year-old children whose mothers had received 1 mg/day fluoride during the last 6 months of pregnancy [35]. The results showed no significant difference in the proportions of children who had decayed or filled primary tooth surfaces or who had caries. The authors of the Cochrane review concluded that the 1997 study was of very low quality and that no evidence shows that fluoride supplementation in pregnant women prevents dental caries in their offspring.

Bone fractures

Because fluoride helps stimulate the formation of new bone, researchers have hypothesized that fluoride supplements might reduce bone fracture risk. However, research to date has provided only limited evidence supporting this hypothesis [36-38].

The findings of observational studies on the impact of fluoride levels in water on bone mineral density (BMD) and fracture risk have been mixed. A study of 7,129 white women found no significant differences in bone mineral density or risk of hip, vertebral, wrist, or humerus fracture between those exposed and those not exposed to fluoridated water between 1950 and 1994 [37]. In contrast, in a study in 8,266 Chinese residents aged 50 years or older, people with access to water fluoride levels of

^{**}Recommended doses are based on poor-quality evidence.

approximately 1 mg/L had a lower overall risk of fractures, but not of hip fractures, than those with access to water containing negligible fluoride levels [38].

Clinical trials have also had conflicting findings about the efficacy of fluoride dietary supplements to prevent bone fractures. For example, a meta-analysis of 25 randomized controlled trials in a total of 954 participants (four of the studies included people with osteoporosis) showed a significant reduction in vertebral and nonvertebral fracture risk with daily doses of up to 20 mg fluoride (in the form of monofluorophosphate or sodium fluoride), but not with higher doses [39]. A more recent randomized controlled trial found that 2.5, 5, or 10 mg/day fluoride for 1 year in 180 postmenopausal women did not change BMD at any site assessed [40].

Health Risks from Excessive Fluoride

Long-term ingestion of excess fluoride in infancy and childhood, when the teeth are being formed, can lead to dental fluorosis [41]. The characteristics of this chronic condition usually vary from almost imperceptible white lines or flecks to white or brown stains on teeth [2]. Severe dental fluorosis can lead to pitting in tooth enamel. The risk of dental fluorosis increases with fluoride intakes above recommended amounts [42]. Severe enamel fluorosis is very rare, and no evidence indicates that recommended levels of community water fluoridation lead to severe dental fluorosis [3,28].

Analysis of 1999–2004 NHANES data showed that 22.8% of persons aged 6–49 had dental fluorosis, although less than 1% had severe fluorosis and less than 2% had moderate fluorosis [41]. The prevalence rate of dental fluorosis was highest, 41%, in adolescents and lowest, 8.7%, in those aged 40–49. A more recent analysis of NHANES data in 2001–2002 and 2011–2012 found that rates of dental fluorosis (from very mild to severe) increased during this 10-year period, from 29.7% to 61.3% [43].

High doses of fluoride (typically from rare accidents resulting in excessively high levels of fluoridation of water, unintentional ingestion of fluoride products intended for topical use in dentists' offices, or fluoride supplements inappropriately given to children) can result in nausea, vomiting, abdominal pain, diarrhea, periostitis, and even death in rare cases [3,19,44]. According to one estimate, the acute dose that could cause serious systemic toxicity for fluoride is 5 mg/kg (e.g., 375 mg for someone who weighs 75 kg [165 pounds]) [44]. This dose would be virtually impossible to achieve from water or toothpaste containing standard levels of added fluoride.

Chronic, excess intakes of fluoride are also associated with skeletal fluorosis, although this condition is extremely rare in the United States. Its effects can range from occasional joint pain or stiffness to osteoporosis, muscle wasting, and neurological defects [1,45].

In addition to the potential to damage teeth and bones, some evidence suggests that higher fluoride intakes during early development, including during gestation, might be associated with a lower IQ and other cognitive impairments (e.g., delays in cognitive development) in children [46-49]. However, many experts consider this evidence to be weak and methodologically flawed [50-58].

The FNB has established ULs for fluoride from all sources for healthy individuals (Table 4) based on levels associated with dental and skeletal fluorosis [1].

Table 4: Daily Tolerable Upper Intake Levels for Fluoride [1]

Age	Male	Female	Pregnancy	Lactation
Birth to 6 months	0.7 mg	0.7 mg		
7-12 months	0.9 mg	0.9 mg		
1−3 years	1.3 mg	1.3 mg		
4-8 years	2.2 mg	2.2 mg		
9-13 years	10 mg	10 mg		
14-18 years	10 mg	10 mg	10 mg	10 mg
19-51 years	10 mg	10 mg	10 mg	10 mg
51+ years	10 mg	10 mg		

Interactions with Fluoride

Fluoride has no known, clinically relevant interactions with medications [59].

Fluoride 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 <u>Dietary Guidelines for Americans (https://www.dietaryguidelines.gov)</u> and the U.S. Department of Agriculture's <u>MyPlate.</u> (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.
- Includes a variety of protein foods such as lean meats; poultry; eggs; seafood; beans, peas, and lentils; nuts and seeds; and soy products.
- Limits foods and beverages higher in added sugars, saturated fat, and sodium.
- Limits alcoholic beverages.
- Stays within your daily calorie needs.

References

- 1. Institute of Medicine, Food and Nutrition Board. Dietary Reference Intakes for Calcium, Phosphorus, Magnesium, Vitamin D, and Fluoride. Washington, DC: National Academies Press; 1997.
- 2. Touger-Decker R, Radler DR, Depaola DP. Nutrition and dental medicine. In: Ross AC, Caballero B, Cousins RJ, Tucker KL, Ziegler TR, eds. Modern Nutrition in Health and Disease. 11th ed. Baltimore, MD: Lippincott Williams & Wilkins; 2014:1016-40.
- 3. National Research Council. <u>Fluoride in Drinking Water: A Scientific Review of EPA's Standards.</u> (https://www.nap.edu/catalog/11571/fluoride-in-drinking-water-a-scientific-review-of-epas-standards) The National Academies Press, 2006.
- 4. Pessan JP, Buzalaf MR. Historical and recent biological markers of exposure to fluoride. Monogr Oral Sci 2011;22:52-65. [PubMed abstract (https://www.ncbi.nlm.nih.gov/pubmed/21701191? dopt=Abstract)]
- 5. Rango T, Vengosh A, Jeuland M, Whitford GM, Tekle-Haimanot R. Biomarkers of chronic fluoride exposure in groundwater in a highly exposed population. Sci Total Environ 2017;596-597:1-11. [PubMed abstract (https://www.ncbi.nlm.nih.gov/pubmed/28411405?dopt=Abstract)]
- 6. U.S. Department of Agriculture. <u>USDA National Fluoride Database of Selected Beverages and Foods, Release 2. (https://www.ars.usda.gov/ARSUserFiles/80400525/Data/Fluoride/F02.pdf)</u> U.S. Department of Agriculture, 2005.
- 7. U. S. Department of Health and Human Services Federal Panel on Community Water Fluoridation. U.S. Public Health Service Recommendation for Fluoride Concentration in Drinking Water for the Prevention of Dental Caries. Public Health Reports 2015;130:318-31. [PubMed abstract (https://www.ncbi.nlm.nih.gov/pubmed/26346489?dopt=Abstract)]
- 8. Iheozor-Ejiofor Z, Worthington HV, Walsh T, O'Malley L, Clarkson JE, Macey R, et al. Water fluoridation for the prevention of dental caries. Cochrane Database Syst Rev 2015:Cd010856. [PubMed abstract (https://www.ncbi.nlm.nih.gov/pubmed/26092033?dopt=Abstract)]
- 9. U.S. Department of Health, Education, and Welfare. Public Health Service drinking water standards, revised 1962. Washington, DC: PHS Publication No. 956; 1962.
- 10. U.S. Environmental Protection Agency. <u>Fluoride: Exposure and Relative Source Contribution Analysis.</u> (https://www.epa.gov/sites/production/files/2019-03/documents/fluoride-exposure-relative-report.pdf) 2010.
- 11. U.S. Environmental Protection Agency. <u>Review of the Fluoride Drinking Water Regulation</u>. (https://www.epa.gov/dwsixyearreview/review-fluoride-drinking-water-regulation) 2019.
- 12. Centers for Disease Control and Prevention. <u>Water Fluoridation Data & Statistics</u>. (https://www.cdc.gov/fluoridation/statistics/FSGrowth.htm) 2016.

- 13. Centers for Disease Control and Prevention. <u>Water Fluoridation Additives</u>. (https://www.cdc.gov/fluoridation/engineering/wfadditives.htm) 2014.
- 14. Centers for Disease Control and Prevention. <u>My Water's Fluoride</u> (https://nccd.cdc.gov/doh_mwf/Default/Default.aspx). 2020.
- 15. U.S. Food and Drug Administration. <u>Small Entity Compliance Guide: Revision of the Nutrition and Supplement Facts Labels (https://www.fda.gov/regulatory-information/search-fda-guidance-documents/small-entity-compliance-guide-revision-nutrition-and-supplement-facts-labels)</u>. 2020.
- 16. U.S. Food and Drug Administration. <u>FDA Announces Proposed Ruling on Fluoride in Bottled Water</u> (https://www.fda.gov/food/cfsan-constituent-updates/fda-announces-proposed-ruling-fluoride-bottled-water). 2019.
- 17. National Institutes of Health. <u>Dietary Supplement Label Database. (http://http://www.dsld.nlm.nih.gov/dsld) 2020.</u>
- 18. Cressey P, Gaw S, Love J. Estimated dietary fluoride intake for New Zealanders. J Public Health Dent 2010;70:327-36. [PubMed abstract (https://www.ncbi.nlm.nih.gov/pubmed/20735718? dopt=Abstract)]
- 19. U.S. Food and Drug Administration. <u>VFEND Prescribing Information</u> (https://www.accessdata.fda.gov/drugsatfda_docs/label/2015/021266s038,021267s047,021630s028lbl.pd <u>f.)</u> 2015.
- 20. Barajas MR, McCullough KB, Merten JA, Dierkhising RA, Bartoo GT, Hashmi SK, et al. Correlation of Pain and Fluoride Concentration in Allogeneic Hematopoietic Stem Cell Transplant Recipients on Voriconazole. Biology of Blood and Marrow Transplantation 2016;22:579-83. [PubMed abstract (https://www.ncbi.nlm.nih.gov/pubmed/26524731?dopt=Abstract)]
- 21. Tan I, Lomasney L, Stacy GS, Lazarus M, Mar WA. Spectrum of Voriconazole-Induced Periostitis With Review of the Differential Diagnosis. American Journal of Roentgenology 2018;212:157-65. [PubMed abstract (https://www.ncbi.nlm.nih.gov/pubmed/30403528?dopt=Abstract)]
- 22. Featherstone JD. Dental caries: a dynamic disease process. Australian Dental Journal 2008;53:286-91. [PubMed abstract (https://www.ncbi.nlm.nih.gov/pubmed/18782377?dopt=Abstract)]
- 23. Moyer VA, Force USPST. Prevention of dental caries in children from birth through age 5 years: US Preventive Services Task Force recommendation statement. Pediatrics 2014;133:1102-11. [PubMed abstract (https://www.ncbi.nlm.nih.gov/pubmed/24799546?dopt=Abstract)]
- 24. Institute of Medicine. <u>Advancing Oral Health in America.</u>
 (https://www.hrsa.gov/sites/default/files/publichealth/clinical/oralhealth/advancingoralhealth.pdf)
 National Academy of Science, 2011.
- 25. Chou R, Cantor A, Zakher B, Mitchell JP, Pappas M. Preventing dental caries in children <5 years: systematic review updating USPSTF recommendation. Pediatrics 2013;132:332-50. [PubMed abstract (https://www.ncbi.nlm.nih.gov/pubmed/23858419?dopt=Abstract)]

- 26. Kim JK, Baker LA, Davarian S, Crimmins E. Oral health problems and mortality. J Dent Sci 2013;8. [PubMed abstract (https://www.ncbi.nlm.nih.gov/pubmed/24416472?dopt=Abstract)]
- 27. National institute of Dental and Craniofacial Research. <u>Fluoride & Dental Health.</u> (https://www.nidcr.nih.gov/health-info/fluoride) 2020.
- 28. Community Preventive Services Task Force. <u>Dental Caries (Cavities): Community Water Fluoridation.</u> (https://www.thecommunityguide.org/sites/default/files/assets/Oral-Health-Caries-Community-Water-Fluoridation_3.pdf) 2013.
- 29. Slade GD, Grider WB, Maas WR, Sanders AE. Water Fluoridation and Dental Caries in U.S. Children and Adolescents. Journal of dental research 2018;97:1122-8. [PubMed abstract (https://www.ncbi.nlm.nih.gov/pubmed/29900806?dopt=Abstract)]
- 30. Slade GD, Sanders AE, Do L, Roberts-Thomson K, Spencer AJ. Effects of fluoridated drinking water on dental caries in Australian adults. J Dent Res 2013;92:376-82. [PubMed abstract (https://www.ncbi.nlm.nih.gov/pubmed/23456704?dopt=Abstract)]
- 31. Mahoney G, Slade GD, Kitchener S, Barnett A. Lifetime fluoridation exposure and dental caries experience in a military population. Community Dent Oral Epidemiol 2008;36:485-92. [PubMed abstract (https://www.ncbi.nlm.nih.gov/pubmed/18422709?dopt=Abstract)]
- 32. Tubert-Jeannin S, Auclair C, Amsallem E, Tramini P, Gerbaud L, Ruffieux C, et al. Fluoride supplements (tablets, drops, lozenges or chewing gums) for preventing dental caries in children. Cochrane Database Syst Rev 2011:Cd007592. [PubMed abstract (https://www.ncbi.nlm.nih.gov/pubmed/22161414?dopt=Abstract)]
- 33. Rozier RG, Adair S, Graham F, Iafolla T, Kingman A, Kohn W, et al. Evidence-based clinical recommendations on the prescription of dietary fluoride supplements for caries prevention: a report of the American Dental Association Council on Scientific Affairs. J Am Dent Assoc 2010;141:1480-9. [PubMed abstract (https://www.ncbi.nlm.nih.gov/pubmed/21158195?dopt=Abstract)]
- 34. Takahashi R, Ota E, Hoshi K, Naito T, Toyoshima Y, Yuasa H, et al. Fluoride supplementation (with tablets, drops, lozenges or chewing gum) in pregnant women for preventing dental caries in the primary teeth of their children. Cochrane Database Syst Rev 2017;10:Cd011850. [PubMed abstract (https://www.ncbi.nlm.nih.gov/pubmed/29059464?dopt=Abstract)]
- 35. Leverett DH, Adair SM, Vaughan BW, Proskin HM, Moss ME. Randomized clinical trial of the effect of prenatal fluoride supplements in preventing dental caries. Caries research 1997;31:174-9. [PubMed abstract (https://www.ncbi.nlm.nih.gov/pubmed/9165186?dopt=Abstract)]
- 36. Nasman P, Ekstrand J, Granath F, Ekbom A, Fored CM. Estimated drinking water fluoride exposure and risk of hip fracture: a cohort study. J Dent Res 2013;92:1029-34. [PubMed abstract (https://www.ncbi.nlm.nih.gov/pubmed/24084670?dopt=Abstract)]
- 37. Phipps KR, Orwoll ES, Mason JD, Cauley JA. Community water fluoridation, bone mineral density, and fractures: prospective study of effects in older women. Bmj 2000;321:860-4. [PubMed

- abstract (https://www.ncbi.nlm.nih.gov/pubmed/11021862?dopt=Abstract)]
- 38. Li Y, Liang C, Slemenda CW, Ji R, Sun S, Cao J, et al. Effect of long-term exposure to fluoride in drinking water on risks of bone fractures. J Bone Miner Res 2001;16:932-9. [PubMed abstract (https://www.ncbi.nlm.nih.gov/pubmed/11341339?dopt=Abstract)
- 39. Vestergaard P, Jorgensen NR, Schwarz P, Mosekilde L. Effects of treatment with fluoride on bone mineral density and fracture risk—a meta-analysis. Osteoporos Int 2008;19:257-68. [PubMed abstract (https://www.ncbi.nlm.nih.gov/pubmed/17701094?dopt=Abstract)]
- 40. Grey A, Garg S, Dray M, Purvis L, Horne A, Callon K, et al. Low-dose fluoride in postmenopausal women: a randomized controlled trial. J Clin Endocrinol Metab 2013;98:2301-7. [PubMed abstract (https://www.ncbi.nlm.nih.gov/pubmed/23553866?dopt=Abstract)]
- 41. Beltran-Aguilar ED, Barker L, Dye BA. Prevalence and severity of dental fluorosis in the United States, 1999-2004. NCHS Data Brief 2010:1-8. [PubMed abstract (https://www.ncbi.nlm.nih.gov/pubmed/21211168?dopt=Abstract)]
- 42. Bhagavatula P, Curtis A, Broffitt B, Weber-Gasparoni K, Warren J, Levy SM. The relationships between fluoride intake levels and fluorosis of late-erupting permanent teeth. J Public Health Dent 2018;78:165-74. [PubMed abstract (https://www.ncbi.nlm.nih.gov/pubmed/29286185? dopt=Abstract)]
- 43. Wiener RC, Shen C, Findley P, Tan X, Sambamoorthi U. Dental Fluorosis over Time: A comparison of National Health and Nutrition Examination Survey data from 2001-2002 and 2011-2012. J Dent Hyg 2018;92:23-9. [PubMed abstract (https://www.ncbi.nlm.nih.gov/pubmed/29500282?dopt=Abstract)]
- 44. Whitford GM. Acute toxicity of ingested fluoride. Monogr Oral Sci 2011;22:66-80. [PubMed abstract (https://www.ncbi.nlm.nih.gov/pubmed/21701192?dopt=Abstract)]
- 45. Gutteridge DH, Stewart GO, Prince RL, Price RI, Retallack RW, Dhaliwal SS, et al. A randomized trial of sodium fluoride (60 mg) +/- estrogen in postmenopausal osteoporotic vertebral fractures: increased vertebral fractures and peripheral bone loss with sodium fluoride; concurrent estrogen prevents peripheral loss, but not vertebral fractures. Osteoporos Int 2002;13:158-70. [PubMed abstract (https://www.ncbi.nlm.nih.gov/pubmed/11908491?dopt=Abstract)]
- 46. Green R, Lanphear B, Hornung R, Flora D, Martinez-Mier EA, Neufeld R, et al. Association Between Maternal Fluoride Exposure During Pregnancy and IQ Scores in Offspring in Canada. JAMA Pediatr 2019;173:940-8. [PubMed abstract (https://www.ncbi.nlm.nih.gov/pubmed/31424532? dopt=Abstract)]
- 47. Grandjean P. Developmental fluoride neurotoxicity: an updated review. Environ Health 2019;18:110. [PubMed abstract (https://www.ncbi.nlm.nih.gov/pubmed/31856837?dopt=Abstract)]
- 48. Office of Health Assessment and Translation, Division of the National Toxicology Program, National Institute of Environmental Health Sciences, National Institutes of Health. <u>Systematic Review of Fluoride Exposure and Neurodevelopmental and Cognitive Health Effects.</u>

- (https://www.asdwa.org/wp-content/uploads/2019/10/draft_fluoride_monograph_20190906_5081.pdf) 2019.
- 49. Valdez Jimenez L, Lopez Guzman OD, Cervantes Flores M, Costilla-Salazar R, Calderon Hernandez J, Alcaraz Contreras Y, et al. In utero exposure to fluoride and cognitive development delay in infants. Neurotoxicology 2017;59:65-70. [PubMed abstract (https://www.ncbi.nlm.nih.gov/pubmed/28077305?dopt=Abstract)]
- 50. Canadian Agency for Drugs and Technologies in Health. <u>Community Water Fluoridation: A Review of Neurological and Cognitive Effects.</u>
 (https://www.cadth.ca/sites/default/files/pdf/htis/2019/RC1198%20Community%20Water%20Fluoridation%20Exposure%20Final.pdf) 2019.
- 51. Aghaji QN, Nwabuo CC. Association Between Maternal Fluoride Exposure and Child IQ. JAMA Pediatrics 2020;174:210-1. [PubMed abstract (https://www.ncbi.nlm.nih.gov/pubmed/31886833? dopt=Abstract)]
- 52. Berezow AB. Association Between Maternal Fluoride Exposure and Child IQ. JAMA Pediatr 2019;174:210-7. [PubMed abstract (https://www.ncbi.nlm.nih.gov/pubmed/31886848?dopt=Abstract)]
- 53. Bledsoe J, Breiger D, McKeever J. Association Between Maternal Fluoride Exposure and Child IQ. JAMA Pediatrics 2020;174:213. [PubMed abstract (https://www.ncbi.nlm.nih.gov/pubmed/31886845? dopt=Abstract)]
- 54. Farrow S, Joffe AR. Association Between Maternal Fluoride Exposure and Child IQ. JAMA Pediatrics 2020;174:214. [PubMed abstract (https://www.ncbi.nlm.nih.gov/pubmed/31886840? dopt=Abstract)]
- 55. Gehani CP, Pollick H, Stevenson RA. Association Between Maternal Fluoride Exposure and Child IQ. JAMA Pediatrics 2020;174:215-6. [PubMed abstract (https://www.ncbi.nlm.nih.gov/pubmed/31886843?dopt=Abstract)]
- 56. Gong CX, James NE. Association Between Maternal Fluoride Exposure and Child IQ. JAMA Pediatrics 2020;174:212-3. [PubMed abstract (https://www.ncbi.nlm.nih.gov/pubmed/31886860? dopt=Abstract)]
- 57. Ritchie SJ, Morris AJ, McConway K. Association Between Maternal Fluoride Exposure and Child IQ. JAMA Pediatrics 2020;174:213-4. [PubMed abstract (https://www.ncbi.nlm.nih.gov/pubmed/31886842?dopt=Abstract)]
- 58. Waugh D. Association Between Maternal Fluoride Exposure and Child IQ. JAMA Pediatrics 2020;174:211-2. [PubMed abstract (https://www.ncbi.nlm.nih.gov/pubmed/31886836?dopt=Abstract)]
- 59. Natural Medicines. Fluoride. (https://naturalmedicines.therapeuticresearch.com) 2019.

Disclaimer

This fact sheet by the National Institutes of Health (NIH) Office of Dietary Supplements (ODS) provides information that should not take the place of medical advice. We encourage you to talk to your healthcare 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 product or service, or recommendation from an organization or professional society, does not represent an endorsement by ODS of that product, service, or expert advice.

Updated: March 29, 2021 <u>History of changes to this fact sheet</u>