Calcium and Vitamin D

modified August 2024

Questions arise about adequate calcium intake; the safety of calcium supplements; and about adequate, optimal, and excessive vitamin D intake. The chart below addresses frequently asked questions about calcium (including dosing, benefits, and risks) and vitamin D (including signs and symptoms of vitamin D deficiency, measurement and interpretation of levels, and recommendations for vitamin D intake and supplementation).

Clinical Question	Answer/Pertinent Information
Calcium	
What is the physiologic role of calcium?	• Calcium is an important structural component of bones and teeth.[1] ○ Bones serve as a repository for calcium. Parathyroid hormone and calcitriol act on bones, the intestines, and kidney through a feedback mechanism to help keep serum calcium levels within a tightly regulated range.[1] • Calcium plays a role in muscle contraction, blood vessel contraction/relaxation, nerve conduction, intracellular signaling, and hormone secretion.[1]
What are the consequences of calcium deficiency?	• Hypocalcemia is usually secondary to illness (e.g., kidney failure), medications (e.g., bisphosphonates, cisplatin), impaired parathyroid hormone production, etc.[2] • Hypocalcemia can be asymptomatic. The most common symptoms are muscle spasms and tingling in the hands and feet. Kidney or brain calcification, cataracts, congestive heart failure, and seizures can also result.[2] • Long term, inadequate calcium intake can lead to osteomalacia, rickets (children), osteoporosis, and fractures.[2]

How much calcium should **adults** get?	• The recommended daily intake from food and/or supplements for adults is:[1,3-5]
	  ○ 1,000 mg.
	  ○ 1,200 mg for females 51 years and older and males 71 years and older.

How much calcium should **children** get?	• The recommended calcium dietary reference intakes for children are:[1,5]
	  ○ Adequate intake:
	  ▪ birth to six months: 200 mg per day.
	  ▪ >six months to 12 months: 260 mg per day.
	  ○ Recommended dietary allowance:
	  ▪ one to three years: 700 mg.
	  ▪ four to eight years: 1,000 mg.
	  ▪ nine to 18 years: 1,300 mg.

Calcium, continued	

Clinical Question	Answer/Pertinent Information
How can patients get adequate calcium from food?	• Teach patients to read food labels. If the label provides calcium in a percentage of the DV, it is based on 1,000 mg of calcium per day. For example, 30% DV of calcium = 300 mg.[3] • High-calcium foods include servings of milk (~300 mg) and yogurt (340 mg to 450 mg). Non-dairy choices include cooked collard greens (~325 mg) and calcium-fortified foods soy milk [80 mg to 300 mg], cereal [up to 1,000 mg]).[4] • A guide to calcium-rich foods is available at https://www.nof.org/patients/treatment/calciumvitamin-d/. • A **calcium calculator** is available at https://www.iofbonehealth.org/calcium-calculator.
Which adults need to take a calcium supplement?	• Calculate the amount of calcium patients are getting from food, then supplement only to make up any deficit.[3,6] • Patients typically get 250 to 300 mg per day of calcium from their diet, not including dairy products.[7,8] Adding two to three servings of high-calcium foods can provide adequate intake or reduce supplement needs. • A chart to help patients estimate their calcium intake is available at https://www.nof.org/patients/treatment/calciumvitamin-d/steps-to-estimate-your-calcium-intake/.

What calcium supplements are available, and how should they be taken?	• Choose calcium carbonate or calcium citrate as they provide the most elemental calcium (see below).
	  ○ Calcium gluconate and calcium lactate are impractical due to low amounts of calcium provided.[9]
	  ○ Calcium D-glucarate [US]) lacks sufficient safety and efficacy information.[10]
	  ○ Calcium acetate is used as a phosphate binder in patients with kidney disease.
	• Calcium carbonate is 40% elemental calcium.[4]
	  ○ Dissolves best in an acidic environment; however, effects of older age (who have reduced acid) or acid-reducing meds (e.g., PPIs) is unclear.[11]
	• Calcium citrate is 21% elemental calcium; however, it is better absorbed compared to calcium carbonate.[4,11]
	• Additional ingredients (e.g., magnesium, vitamin K) have no proof of better efficacy compared to calcium alone.
	• It is generally recommended that calcium carbonate should be taken with food to improve absorption.[2]
	• Calcium absorption is highest with elemental calcium doses of 500 mg or less.[2]
	• Recommend USP verified products (US) or, in Canada, products with a Natural Product Number (NPN), to ensure the product meets purity and quality standards.[3]
	  ○ Excess lead (and sometimes other heavy minerals) is a concern with some coral or dolomite calcium products (both sources of calcium carbonate) contain excess lead.[10] The lead content of oyster shell and refined calcium products is considered to be clinically insignificant.[10]

Calcium, continued	

Clinical Question	Answer/Pertinent Information
How is hypocalcemia managed in inpatients?	• Most commonly, symptomatic hypocalcemia (i.e., severe, possibly with hyperreflexia, tetany, generalized seizures) occurs in a hospital setting, with serum ionized calcium less than 4.3 mg/dL (1.1 mmol/L) or serum total calcium less than 7 mg/dL (1.8 mmol/L).[12] • Management includes correction of causes (e.g., hypoparathyroidism, vitamin D deficiency, kidney failure).[12] • Replacement is often a bolus dose of calcium **gluconate** 1 g (or may be standardized to 2 g or 4 g), administered over an hour. Dose can be repeated every six hours as needed.[64] • Patients with severe symptoms (e.g., seizures, tetany) can be given a calcium gluconate intravenous bolus (1 g) over ten minutes. The bolus can be repeated, or a continuous infusion may be needed (2 to 3 g calcium gluconate in 1 L of D5W). Note that hypomagnesemia (if present) must also be corrected to maintain normal calcium levels.[12] • Calcium gluconate is the preferred salt for IV replacement due to the risk of tissue necrosis with extravasation with calcium chloride. However, calcium chloride is sometimes used during shortages of calcium gluconate. Note that it is not a one-to-one switch between calcium salts. Calcium chloride contains three times the amount of elemental calcium compared to calcium gluconate. Therefore, calcium doses should always be ordered as milliequivalents, mg, or g (never as mLs or amps).[64]
Can adults get too much calcium from supplements plus diet?	• The upper daily limit for calcium is 2,500 mg for adults 19 to 50 years and 2,000 mg for people 51 years and older.[2] • Getting too much calcium from foods alone in healthy people is rare.[2]
Does calcium supplementation prevent fractures?	• Hip and nonvertebral fracture reduction has been demonstrated with daily supplementation with vitamin D 800 IU and calcium 1,200 mg **in nursing home residents with vitamin D deficiency and low dietary calcium intake**.[13] • There is insufficient evidence to recommend use of calcium and vitamin D supplements for **primary** fracture prevention in premenopausal females, males, or in community-dwelling postmenopausal females.[14,15] (Note that USPSTF recommends against supplementing with 400 IU or less/day of vitamin D or 1,000 mg or less/day of calcium for primary prevention of fractures in community-dwelling postmenopausal females.[14])
Can calcium supplements reduce colorectal adenomas?	• Calcium supplementation might moderately help prevent colorectal adenomas, but there is not enough evidence to recommend calcium supplements for this purpose.[16]
Does calcium pose a cardiovascular risk?	• Calcium intake (dietary + supplement) that does not exceed 2,000 to 2,500 mg/day poses neither CV harm (MI, stroke, or death) nor benefit for generally healthy adults [Evidence Level A-2].[17,18] • Signals that calcium might be associated with an increase in CV risk are reported in several large cohort studies.[19-22] No prospective RCTs studies have been done to examine the effect of calcium on CV risk. • There are several theories on how calcium could increase CV risk by causing vascular calcification.[20] Supplements (as opposed to dietary calcium) might cause a spike in serum calcium concentrations that acutely adversely affects blood coagulability or flow.[20,23] Levels of fibroblast growth factor 23 and inflammatory cytokines are also increased by high levels of calcium.[23]
Calcium, continued	

Clinical Question	Answer/Pertinent Information
Does calcium cause dementia?	• A small observational study found an association between an increased risk of dementia and females (with a history of cerebrovascular disease) taking a calcium supplement.[24] • In theory, calcium could increase dementia risk by causing vascular calcification.[24] Supplements (as opposed to dietary calcium) might cause a spike in serum calcium concentrations that acutely adversely affect blood coagulability or flow or hasten programmed cell death.[24]
Does calcium cause prostate cancer?	• Observational studies have found an association between prostate cancer and calcium/dairy intake.[25] Results of studies differ based on types of dairy products and the source of calcium, which suggests the contribution of some other dairy component.[26] • A meta-analysis of observational studies showed an increased risk of prostate cancer with high intakes of dairy products, dietary calcium, and total calcium. Higher total and dietary calcium intake (approximately 1,500 mg/day or more) had the most pronounced association. Dietary calcium appears to have an increase in risk. Supplemental calcium was not associated with an increase in total risk; however, limited evidence suggests it may be associated with an increased risk of fatal prostate cancer.[26]
Does calcium cause kidney stones?	• Large cohort studies show a positive association between higher intakes of supplemental calcium (1,000 mg/day for seven years) and risk of kidney stones. However, subsequent systematic reviews and RCTs (e.g., 1,000 to 1,600 mg/day for two to seven years) did not find an association between calcium and kidney stones.[2]
Vitamin D	
In which patients should you check a vitamin D level?	• There is insufficient evidence to recommend routine screening for vitamin D deficiency in community-dwelling,, asymptomatic adults.[27,30] • Suggest checking 25-hydroxyvitamin D serum levels in patients with established indications (e.g., hypocalcemia, malabsorption syndromes (e.g., inflammatory bowel disease, bariatric surgery, chronic kidney or liver disease, metabolic bone disease).[30]
Vitamin D, continued	

Clinical Question	Answer/Pertinent Information
How do you measure vitamin D levels?	• The best indication of vitamin D status is the 25-hydroxyvitamin D level.[31] • Be sure to measure **25-hydroxyvitamin D**, NOT 1,25-dihydroxyvitamin D, in most patients.[32] 1,25-dihydroxyvitamin D levels do not correlate with vitamin D stores; they are regulated by parathyroid hormone.[32] In vitamin D deficiency, 1,25-hydroxyvitamin D levels actually go **up**. It is appropriate to check 1,25-dihydroxyvitamin D levels in patients with hypercalcemia (as part of the diagnostic workup), and perhaps end-stage kidney disease (because vitamin D activation is impaired).[32] • There is no standard test for measuring 25-hydroxyvitamin D levels.[33] There are two general categories of 25-hydroxyvitamin D level assays: immunoassays (e.g., radioimmunoassay, chemiluminescent assay) and high-performance liquid chromatography (HPLC) assays (e.g., HPLC with UV detection, HPLC with liquid chromatography-mass spectrometry [LC-MS]).[33] • LC-MS/MS (liquid chromatography/tandem mass spectrometry) is the gold standard because it is the most accurate.[33] Immunoassays are less specific.[4] However, there can be variation even with LC-MS methods due to differences in methodology and/or if quality control measures are not followed.[33,34] • It may be a good idea to stick with the same lab for follow-up to minimize variability. • Be aware that labs may report their own "normal" range that has little clinical meaning. Consider the level in the context of other information (see next section) when making treatment decisions.
How do you interpret vitamin D levels in **children**?	• Per the AAP, 25-hydroxyvitamin D levels should be 50 nmol/L (20 ng/mL) or greater in infants and children.[31] • Per the Canadian Paediatric Society, optimal vitamin D serum concentrations are 75 to 225 nmol/L (30 to 90 ng/mL).[35] Vitamin D insufficiency is defined as serum concentrations between 25 and 75 nmol/L (10 to 30 ng/mL) and deficiency is serum 25-hydroxyvitamin D concentrations less than 25 nmol/L (10 ng/mL).[35]

How do you interpret vitamin D levels and define deficiency defined in **adults**?	• When interpreting a vitamin D level, you are really asking, "Is this vitamin D level adequate to meet my patient's needs?" The problem is that some patients may have a greater or lesser need for vitamin D than others.[35] We can't actually know what an individual patient's need is.[35] For comparison, the mean vitamin D level in a healthy adult population is 16 ng/mL (40 nmol/L).[35]
	• The Institute of Medicine states that:
	  ○ patients with a 25-hydroxyvitamin D level <12 ng/mL (<30 nmol/L) are at risk of vitamin D deficiency (i.e., rickets or osteomalacia).[36]
	  ○ for almost everyone, a level of 20 ng/mL (50 nmol/L) is sufficient for bone and overall health, and that levels over 30 ng/mL are NOT consistently associated with additional health benefits.[36,37]

Vitamin D, continued	

Clinical Question	Answer/Pertinent Information
What are the consequences of vitamin D deficiency in adults?	• Symptoms of vitamin D deficiency include bone pain and muscle weakness.[36] It can lead to osteomalacia.[36] • Although low vitamin D levels have been associated with fractures, falls, diabetes, CV events, cancer, and depression, not all studies have shown an association, and for some conditions, both high and low levels have been associated with illness (i.e., a U-shaped relationship may exist).[36-39] Despite these associations, supplementation has not shown benefit for most diseases/conditions (see discussion, below).

What are the consequences of vitamin D deficiency in children?	• Reports indicate that many children in North America are deficient in vitamin D. One study found only 2% of 10- to 11-year-olds in Alberta get the Recommended Dietary Allowance of vitamin D from food, and this increases to only 22% in those taking supplements.[40] Vitamin D has a role in calcium homeostasis, and bone health. It has effects on immune function, and may help prevent infection, autoimmune diseases, and cancer. Cases of rickets continue to occur in the US and Canada.[31,35]
	• Stages of vitamin D deficiency in children:[31]
	  ○ stage 1: hypocalcemia.
	  ○ stage 2: parathyroid hormone acts to maintain calcium through bone demineralization.
	  ○ stage 3 (severe): hypocalcemia, hypophosphatemia, overt signs of bone demineralization (rickets), osteomalacia, osteopenia, abnormal immune function (increased susceptibility to acute infections).
	  ▪ Rickets is characterized by the failure of mineralization of growing bone and cartilage leading to enlargement of the skull, joints of the long bones, and rib cage, curvature of the spine and femurs, and generalized muscle weakness.
	  ▪ Physical manifestations of vitamin D deficiency that may present before rickets or radiologic findings include hypocalcemia symptoms (including seizures, especially during periods of rapid growth), growth failure, lethargy, irritability, and respiratory infections.[31]

What are the recommendations for total daily vitamin D **intake** (foods and/or supplements)? *Continued…*	• Recommended intakes are based on bone health.[37] • The **Bone Health & Osteoporosis Foundation** recommends vitamin D 400 IU (10 mcg) to 800 IU (20 mcg) daily for adults <50 years of age, and 800 IU (20 mcg) to 1,000 IU (25 mcg) daily for older adults.[41] • The **North American Menopause Society** follows the Bone Health & Osteoporosis Foundation recommendation that adults 50 and older get vitamin D3 800 IU (20 mcg) to 1,000 IU (25 mcg) daily.[42] • The **Institute of Medicine** and **Health Canada** recommend 600 IU (15 mcg) daily for everyone one year of age through age 70, and 800 IU (20 mcg) daily for people over 70 years of age.[1,5,39] • The **AAP**:[31] minimum daily intake 400 IU (infants, children, adolescents). • The **Canadian Paediatric Society**:[35] during the first year of life, daily intake should be 400 IU, except: ○ 200 to 400 IU/day: premature infants.
Vitamin D, continued	

Clinical Question	Answer/Pertinent Information
Total daily vitamin D **intake,** continued	○ 800 IU/day: between October and April, north of the 55th parallel or north of the 40th parallel in patients with deficiency risk factors. • Increased vitamin D doses are typically required in patients with obesity, malabsorption syndromes (e.g., inflammatory bowel disease), or with concomitant use of certain medications (e.g., antiseizure medications, glucocorticoids, antifungals, HIV antivirals) due to effects on vitamin D metabolism.[65]
Can patients get adequate vitamin D from sunlight?	• Sunlight is the primary natural source of vitamin D.[31] The skin produces vitamin D3 in response to sun exposure.[36] • Factors affecting the contribution of sunlight exposure to vitamin D status include skin pigmentation, body mass, living at a high latitude, season, cloud cover, time spent outdoors, air pollution, sunscreen, and clothing.[31] • Due to concerns about sun exposure and skin cancer risk, it is recommended that patients avoid sunlight (without UV protection) and instead, get vitamin D from food or supplements.[31,43-45]
Can patients (including infants and children) get adequate vitamin D from diet?	• Few foods naturally contain vitamin D (exceptions: fatty fish, egg yolks).[5,36] Many foods and products are fortified with vitamin D. Examples of high-vitamin D containing foods (values are approximate; check labels):[35,36,46] ○ salmon, three ounces (85 g), canned, 447 to 530 IU (~11 to 13 mcg). ○ tuna, canned in water, drained, three ounces (85 g), 154 IU (~4 mcg). ○ fortified orange juice, one cup (240 mL), 100 to 137 IU (2.5 to 3.4 mcg). ○ fortified milk, one cup (240 mL), ~120 IU (~3 mcg) (US), (Canada, regulated to 35 to 40 IU [~1 mcg]/100 mL). ○ fortified cereal (US), one serving, 40 IU (1 mcg) or more. ○ fortified yogurt (US), six ounces (170 g), 80 IU (2 mcg) or more. ○ fortified margarine, one tablespoon (11 g), 60 IU (1.5 mcg) (US) (Canada, regulated to at least 530 IU/100 g). ○ one large egg (yolk), 41 IU (~1 mcg). ○ plant-based beverages (e.g., soy "milk" may be fortified). Check labels. • It can be difficult for kids to obtain adequate vitamin D from food because of their eating habits and the small amounts of vitamin D found in most foods.[31] • The vitamin D content in breast milk depends on the mother's vitamin D status. In a mother supplemented with 400 IU of vitamin D daily, breast milk concentrations are only <25 to 78 IU per liter.[31] It is therefore unlikely that an infant could get adequate vitamin D from breast milk.[31] • All of the formulas available in the US and Canada contain about 400 IU/L or more vitamin D.[31,35] US infant formulas must contain 258 to 666 IU/L of vitamin D (40 to 100 IU/100 kcal; Canada: 40 to 80 IU/100 kcal).[31,36]
Vitamin D, continued	

Clinical Question	Answer/Pertinent Information
Which adults routinely need to take a vitamin D **supplement**?	• Routine supplementation with 1,000 IU (25 mcg)/day of vitamin D is **NOT recommended**.[5,37] High doses (e.g., 4,000 IU [100 mcg]/day) may be harmful, and have not shown benefit.[47,48] • Routine supplementation may be necessary in patients with bone disease, malabsorption, older age, or limited sun exposure due to the potential for limited dietary intake. Recommendations vary by organization: o **Health Canada** recommends that males and females over the age of 50 years take 400 IU (10 mcg) daily.[5] o The **Canadian Cancer Society** recommends that adults consult their healthcare provider about taking a daily 1,000 IU (25 mcg) vitamin D **supplement** during fall and winter.[44] o **Osteoporosis Canada** recommends **routine supplementation** with 400 to 1,000 IU (10 to 25 mcg) daily for adults 19 to 50 years of age, and 800 to 2,000 IU (20 to 50 mcg) daily for adults over 50 years of age or adults at risk (e.g., those with osteoporosis, multiple fractures, or vitamin D malabsorption).[49] o **The Endocrine Society** recommends **routine supplementation** for older adults (75 years and older), pregnant patients, and adults with high-risk prediabetes.[30]
Which children need to take a vitamin D supplement?	• **AAP**: children who fall into any of the following categories should receive daily supplementation of 400 IU of vitamin D:[31] o Breastfed and partially breastfed infants (begin vitamin D supplementation during the first few days of life). o All nonbreastfed infants and older children who are ingesting less than one liter (four cups or one quart) of vitamin D-fortified milk or formula a day (other dietary sources of vitamin D can be included). o Adolescents who do not obtain at least 400 IU of vitamin D through vitamin D-fortified milk and foods. o Children who are at increased risk of vitamin D deficiency such as those with fat malabsorption and those taking chronic antiseizure medications. These children may require higher doses and should have vitamin D serum levels, parathyroid hormone, and bone-mineral density status checked. • **Canadian Paediatric Society**:[35] o Breastfed, term infants can be supplemented with 400 IU/day, or the mother can be supplemented with up to 4,000 IU/day with serum calcium and vitamin D monitoring. o Supplementation with vitamin D 400 to 800 IU/day is safe for infants and children in northern latitudes. Overweight children may need higher doses. • **Health Canada**:[5] Breastfed, healthy, term infants birth to one year: supplement with 400 IU/day. • **The Endocrine Society** recommends routine supplementation for children and adolescents (1 to 18 years).[30]
Vitamin D, continued	

Clinical Question	Answer/Pertinent Information

Does vitamin D supplementation prevent fractures?	• Not all studies of vitamin D and fracture prevention have shown benefit; benefit may exist within a narrow range of doses.
	• For vitamin D 800 IU (20 mcg) daily, meta-analyses have shown the following NNTs for patients 65 and older:[50,51]
	  • To prevent one hip fracture: NNT = 88 to 168 seniors for one to seven years.[50,51]
	  • To prevent one nonvertebral fracture: NNT = 93 seniors for one to seven years.[50]
	• Vitamin D 800 IU (20 mcg) daily has not been effective for fracture prevention in all studies, and some studies using 400 IU (10 mcg) daily have shown benefit. This may reflect differences in actual intake vs assigned intake, which has been reported in some studies.[51]
	• Evidence that high-dose vitamin D supplementation may have detrimental effects on bone density comes from a small (n=311) Canadian trial in healthy (no osteoporosis) adults 55 to 70 years of age [Evidence Level B-1].[48] Over three years, bone density decreased in all groups (daily doses of 400, 4,000, and 10,000 IU), but decreased the most in the high-dose groups. In theory, high-dose vitamin D may reduce bone density by increasing osteoclast activity and/or suppression of parathyroid hormone.[48]

Can vitamin D supplementation prevent falls in older adults?	• The USPSTF recommends against vitamin D for fall prevention.[52] • There are conflicting results with interventional studies that vitamin D supplementation improves strength and physical performance and reduces falls.[30,53] • The effectiveness of vitamin D for fall prevention appears to depend on the dose and dosing frequency, concomitant supplemental calcium, and vitamin D serum levels.[66] • The Endocrine Society recommends empiric vitamin D supplementation (daily, lower-dose over non-daily higher-dose) in patients 75 years and older due to the potential for lower mortality risk (which includes the potential for lower fall risk).[30] • A dose of 2,000 IU (50 mcg) per day (given as 60,000 IU once monthly) did not decrease falls compared to 800 IU per day (given as 24,000 IU once monthly), and may even increase fall risk.[54] In a previous study, a once-yearly mega-dose of vitamin D (500,000 IU [1.25 mg] cholecalciferol) increased the risk of falls and fractures in females aged 70 years and older at high risk of fractures. Among participants in whom vitamin D levels were measured, the mean baseline level was just below the lower limit of normal. It is hypothesized that relatively high serum levels of vitamin D or its metabolites, and/or the subsequent drop in level may have played a role in the negative outcome.[55]
Does vitamin D supplementation have non-musculoskeletal benefits?	• RCTs to date have not shown that vitamin D supplementation decreases the risk of cancer, CV disease, type 2 diabetes, or depression, or improves glucose control.[36,38,39,47,56-58]
Vitamin D, continued	

Clinical Question	Answer/Pertinent Information
Does it matter whether a D2 or D3 supplement is used?	• Vitamin D2 (ergocalciferol) comes from ergosterol, a plant sterol, and yeast. Vitamin D3 (cholecalciferol) is synthesized in the skin via 7-dehydrocholesterol, a cholesterol precursor.[59] • Both vitamin D2 and vitamin D3 are effective for raising serum vitamin D levels.[30,36] But, at high doses, vitamin D3 seems to be almost twice as potent and studies suggest it may be more effective at reducing fracture risk.[50,60] Accordingly, the Osteoporosis Society of Canada recommends D3 over D2.[49] • Vitamin D2 50,000 IU is available by prescription, which may be covered by payers. • Active forms of vitamin D (e.g., calcitriol) are not routinely indicated for vitamin D deficiency.[61] Reserve these forms for patients with advanced kidney disease with severe, progressive hyperparathyroidism.[61]
What kid-friendly vitamin D supplements are available?	• Ensure caregivers understand and can accurately measure the dose volume of the chosen formulation. Some doses are per drop and others are per mL. • Single ingredient vitamin D liquids include *D-Vi-Sol*, 400 IU/mL; *Bio-D-Mulsion*, 400 IU/drop; *Bio-D-Mulsion Forte* (US), 2,000 IU/drop; *Bio-D-Mulsion 1000* (Canada), 1,000 IU/drop. • Multivitamin pediatric liquids include *Poly-Vi-Sol* and *Tri-Vi-Sol*, which each contain 400 IU per mL. • For older children, most chewable multivitamins contain 400 IU of vitamin D per tablet (e.g., *Flintstones* multivitamins, others).

Can patients get too much vitamin D (supplement, sunlight, diet)?	• Excessive sun exposure does not cause toxicity due to photodegradation of D3, thermally-mediated conversion of previtamin D3 to compounds that limit formation of vitamin D3, and conversion of vitamin D3 to nonactive forms.[36]
	• Tolerable upper intake limits:[1,37]
	  ○ one to three years: 2,500 IU.
	  ○ four to eight years: 3,000 IU.
	  ○ nine years and older: 4,000 IU.
	• Vitamin D toxicity usually doesn't develop until serum levels are greater than 200 ng/mL (500 nmol/L).[29]

How is vitamin D deficiency treated in an adult?	• Vitamin D doses to treat deficiency are different than for replacement. Higher doses must be used to replenish stores.
	• A rule of thumb: 1,000 IU (25 mcg) daily can increase levels by up to 10 ng/mL (25 nmol/L) within weeks.[62]
	• For vitamin D deficient adults, 50,000 IU (1.25 mg) of vitamin D2 or D3 can be given **once weekly** for eight weeks for replenishment.[63]
	  • Make sure patients understand this is a weekly dose, not a daily dose.
	  • This regimen can be repeated if levels are not adequate.[63]
	• Consider checking a vitamin D level every 12 weeks in patients taking more than 2,000 IU (50 mcg)/day.[62]

Vitamin D, continued	

Clinical Question	Answer/Pertinent Information

How is vitamin D deficiency treated in a child?	• Initial dose:
	  • birth to one year: 1,000 to 5,000 IU/day OR 50,000 IU/week for at least six weeks.[65]
	  • one to 18 years: 2,000 to 6,000 IU/day OR 14,000 to 50,000 IU once weekly for at least six weeks.[65]
	• Maintenance: once vitamin D level is above 30 ng/mL, reduce dose to 400 to 1,000 IU/day (birth to one year) or 600 to 1,000 IU/day (one to 18 years).[65]

Abbreviations: AAP = American Academy of Pediatrics; CV = cardiovascular; D5W = dextrose 5% in water; DV = daily value; HIV = human immunodeficiency virus; HPLC = high-performance liquid chromatography ; IU = international units; LC-MS = liquid chromatography-mass spectrometry; MI = myocardial infarction; NNT = number needed to treat; PPI = proton pump inhibitor; RCT = randomized controlled trial; UL = tolerable upper intake limit; USP = United States Pharmacopeia; USPSTF = United States Preventive Services Task Force; UV = ultraviolet.

Users of this resource are cautioned to use their own professional judgment and consult any other necessary or appropriate sources prior to making clinical judgments based on the content of this document. Our editors have researched the information with input from experts, government agencies, and national organizations. Information and internet links in this article were current as of the date of publication.

Levels of Evidence

In accordance with our goal of providing Evidence-Based information, we are citing the **LEVEL OF EVIDENCE** for the clinical recommendations we publish.

Level	Definition	Study Quality
A	Good-quality patient-oriented evidence.*****	1. High-quality randomized controlled trial (RCT) 2. Systematic review (SR)/Meta-analysis of RCTs with consistent findings 3. All-or-none study
B	Inconsistent or limited-quality patient-oriented evidence.*****	1. Lower-quality RCT 2. SR/Meta-analysis with low-quality clinical trials or of studies with inconsistent findings 3. Cohort study 4. Case control study
C	Consensus; usual practice; expert opinion; disease-oriented evidence (e.g., physiologic or surrogate endpoints); case series for studies of diagnosis, treatment, prevention, or screening.	

***Outcomes that matter to patients** (e.g., morbidity, mortality, symptom improvement, quality of life).
[Adapted from Ebell MH, Siwek J, Weiss BD, et al. Strength of recommendation taxonomy (SORT): a patient-centered approach to grading evidence in the medical literature. Am Fam Physician. 2004 Feb 1;69(3):548-56.
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