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BOLD/STRONG: Vitamin D, Diabetes, ADHD, Depression, Cognition and dementia, Schizophrenia, Pregnancy, Weight loss, United Kingdom, United States, Canada, Australia and New Zealand, European Food Safety Authority, Animal sources, Fungal sources, ^, a, b, c, d, e, f, g, h, i, j, k, l, m, n, o, p, q, r, s, t, u, v, w, x, a, b, c, d, e, f, g, h, i, j, k, l, a, b, c, d, 88, a, b, c, d, e, f, g, h, i, j, k, l, 21, ^, 102, ^, ^, 58, a, b, 68, a, b, 173, a, b, c, d, 134, a, b, c, d, 1, a, b, 383, a, b, c, d, e, f, 2, ^, a, b, 124, a, b, c, ^, ^, 88, a, b, c, d, 80, a, b, 111, ^, 93, ^, 36, a, b, c, d, e, f, g, 357, ^, 103, ^, ^, 101, ^, 3, a, b, c, d, ^, 99, a, b, 122, ^, 2010, ^, 76, ^, 99, ^, 34, ^, 100, ^, 45, a, b, 56, ^, 45, ^, 2, a, b, 80, a, b, 94, ^, ^, 20, ^, ^, ^, 69, ^, 81, ^, 141, ^, 36, ^, 9, ^, 56, a, b, 8, ^, 82, a, b, c, 96, ^, ^, 348, a, b, c, 2, ^, 37, a, b, c, d, e, f, g, h, i, j, k, a, b, 475, ^, 348, ^, 114, ^, 34, ^, 10, ^, 4, ^, 367, ^, 155, ^, 318, ^, ^, 2, ^, 4, a, b, ^, 32, ^, 11, a, b, ^, 26, ^, 8, a, b, 5, ^, 30, ^, 4, ^, 175, ^, ^, 5, ^, 50, ^, 19, ^, 183, ^, 37, ^, 341, a, b, ^, 74, ^, 13, ^, 9, ^, 185, ^, 21, ^, 26, ^, 43, ^, 34, ^, 2, ^, ^, 9, ^, 29, ^, 76, ^, 79, ^, 4, a, b, 346, a, b, 164, ^, 359, a, b, 7, a, b, 4, ^, 172, ^, 15, ^, 104, a, b, c, 8, ^, 9, ^, ^, ^, ^, a, b, c, d, a, b, c, a, b, c, a, b, c, d, 14, a, b, 10, ^, ^, ^, ^, ^, ^, ^, ^, ^, ^, 71, ^, ^, a, b, 62, ^, 4, a, b, c, d, e, f, g, 5, ^, ^, 56, ^, 39, ^, ^, ^, ^, ^, ^, ^, 38, ^, 5, ^, 98, ^, 55, ^, 148, ^, 7, ^, 8, a, b, ^, ^, a, b, 12, ^, 93, ^, 5, a, b, 96, a, b, c, a, b, c, d, 69, ^, ^, 365, ^, 57, ^, 37, ^, ^, 7, a, b, a, b, c, 317, ^, a, b, a, b, ^, 46, ^, 3, a, b, 79, ^, ^, 133, ^, ^, 1268, ^, 9, ^, 28, ^, 3, ^, ^, ^, 69, ^, 104, a, b, 135, ^, 32, a, b, c, 95, ^, 101, ^, ^, 248, ^, 261, ^, 147, ^, 8, ^, 11, ^, ^, ^, ^, ^, 51, ^, 109, ^, ^, ^, ^, 62, ^, 129, ^, 210, ^, 7, a, b, 26, ^, ^, ^, 171, ^, a, b, a, b, ^, ^, 104, a, b, 12, a, b, 211, a, b, c, d, 119, a, b, a, b, 107, ^, 114, a, b, 2021,   
Italic: : Drug class, Cladonia arbuscula, Agaricus bisporus, Cladina arbuscula, Click on genes, proteins and metabolites below to link to respective articles., Emiliania huxleyi, CYP2R1, CYP27B1, er-, ergo-, chole-, non-genomic, a, b, c, d, e, f, g, h, i, j, k, l, m, n, o, p, q, r, s, t, u, v, w, x, a, b, c, d, e, f, g, h, i, j, k, l, ods.od.nih.gov, a, b, c, d, The American Journal of Clinical Nutrition, a, b, c, d, e, f, g, h, i, j, k, l, Chemistry & Biology, The American Journal of Clinical Nutrition, Lab Tests Online (USA), Calcified Tissue International, a, b, Proceedings of the National Academy of Sciences of the United States of America, a, b, Science, a, b, c, d, The Journal of Nutrition, a, b, c, d, The Cochrane Database of Systematic Reviews, a, b, Lancet, a, b, c, d, e, f, The Lancet. 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Chem. Technol. Biotechnol, Proceedings of the Royal Society of London. Series B, Containing Papers of a Biological Character, Vitamin D, Ivory tower and industrial innovation: university-industry technology transfer before and after the Bayh-Dole Act in the United States, Elbridge a Stuart: Founder of Carnation Company, Proceedings of the National Academy of Sciences of the United States of America, Archives of Internal Medicine, Science, Frontiers in Immunology, a, b, Journal of Bone and Mineral Research, Body Metabolism and Exercise, Annals of Internal Medicine, a, b, Coronavirus Disease 2019 (COVID-19) Treatment Guidelines, This article incorporates text from this source, which is in the public domain, ., a, b, COVID-19 rapid guideline: vitamin D, International Journal of Infectious Diseases, a, b, Advances in Nutrition, a, b, The Journal of Steroid Biochemistry and Molecular Biology, a, b, c, d, Metabolism, a, b, Critical Reviews in Food Science and Nutrition, a, b, The Journal of Clinical Endocrinology and Metabolism, QJM: Monthly Journal of the Association of Physicians, a, b, The Cochrane Database of Systematic Reviews, Drug Information Portal, Drug Information Portal, Drug Information Portal, Drug Information Portal, Drug Information Portal, Agonists:, Receptor/signaling modulators,   
TEXT: Group of fat-soluble secosteroids  
  
Vitamin D is a group of fat-soluble secosteroids responsible for increasing intestinal absorption of calcium, magnesium, and phosphate, and many other biological effects.[1][2][3] In humans, the most important compounds in this group are vitamin D 3 (cholecalciferol) and vitamin D 2 (ergocalciferol).[2][3][4]  
  
The major natural source of the vitamin is synthesis of cholecalciferol in the lower layers of epidermis of the skin through a chemical reaction that is dependent on sun exposure (specifically UVB radiation).[1] Cholecalciferol and ergocalciferol can be ingested from the diet and supplements.[1][2] Only a few foods, such as the flesh of fatty fish, naturally contain significant amounts of vitamin D.[2][5] In the U.S. and other countries, cow's milk and plant-derived milk substitutes are fortified with vitamin D, as are many breakfast cereals.[1] Mushrooms exposed to ultraviolet light contribute useful amounts of vitamin D 2 .[2] Dietary recommendations typically assume that all of a person's vitamin D is taken by mouth, because sun exposure in the population is variable and recommendations about the amount of sun exposure that is safe are uncertain in view of the skin cancer risk.[2]  
  
Vitamin D from the diet, or from skin synthesis, is biologically inactive. It is activated by two protein enzyme hydroxylation steps, the first in the liver and the second in the kidneys.[1][4] Because vitamin D can be synthesized in adequate amounts by most mammals if they get enough sunlight, it is not essential and therefore is technically not a vitamin.[3] Instead it can be considered a hormone, with activation of the vitamin D pro-hormone resulting in the active form, calcitriol, which then produces effects via a nuclear receptor in multiple locations.[3]  
  
Cholecalciferol is converted in the liver to calcifediol (25-hydroxycholecalciferol); ergocalciferol is converted to 25-hydroxyergocalciferol.[1] These two vitamin D metabolites (called 25-hydroxyvitamin D or 25(OH)D) are measured in serum to determine a person's vitamin D status.[6][7] Calcifediol is further hydroxylated by the kidneys and some of the immune system cells to form calcitriol (1,25-dihydroxycholecalciferol), the biologically active form of vitamin D.[8][9] Calcitriol circulates as a hormone in the blood, having a major role regulating the concentration of calcium and phosphate, and promoting the healthy growth and remodeling of bone.[1] Calcitriol also has other effects, including some on cell growth, neuromuscular and immune functions, and reduction of inflammation.[2]  
  
Vitamin D has a significant role in calcium homeostasis and metabolism.[1] Its discovery was due to effort to find the dietary substance lacking in children with rickets (the childhood form of osteomalacia).[10] Vitamin D supplements are given to treat or to prevent osteomalacia and rickets.[1] The evidence for other health effects of vitamin D supplementation in vitamin D-replete individuals is inconsistent.[2] The effect of vitamin D supplementation on mortality is not clear, with one meta-analysis finding a small decrease in mortality in elderly people.[11] Except for the prevention of rickets and osteomalacia in high-risk groups, any benefit of vitamin D supplements to musculoskeletal or general health may be small.[12][13][14]  
  
Types [ edit ]  
  
Name Chemical composition Structure Vitamin D 1 Mixture of molecular compounds of ergocalciferol with lumisterol, 1:1 Vitamin D 2 ergocalciferol (made from ergosterol) Vitamin D 3 cholecalciferol (made from 7-dehydrocholesterol in the skin). Vitamin D 4 22-dihydroergocalciferol Vitamin D 5 sitocalciferol (made from 7-dehydrositosterol)  
  
Several forms (vitamers) of vitamin D exist.[1] The two major forms are vitamin D 2 or ergocalciferol, and vitamin D 3 or cholecalciferol. Vitamin D without a subscript refers to either D 2 or D 3 , or both, and is known collectively as calciferol.[1]  
  
Vitamin D 2 was chemically characterized in 1931. In 1935, the chemical structure of vitamin D 3 was defined and shown to result from the ultraviolet irradiation of 7-dehydrocholesterol. A chemical nomenclature for vitamin D forms was recommended in 1981,[15] but alternative names remain in common use.[4]  
  
Chemically, the various forms of vitamin D are secosteroids, that is, steroids in which one of the bonds in the steroid rings is broken.[16] The structural difference between vitamin D 2 and vitamin D 3 is in the side chain, which contains a double bond, between carbons 22 and 23, and a methyl group on carbon 24 in vitamin D 2 .[4]  
  
Many vitamin D analogues have been synthesized.[4]  
  
Biology [ edit ]  
  
[17] The role of active vitamin D (1,25-dihydroxyvitamin D, calcitriol) is shown in orange. Calcium regulation in the human body.The role of active vitamin D (1,25-dihydroxyvitamin D, calcitriol) is shown in orange.  
  
The active vitamin D metabolite calcitriol mediates its biological effects by binding to the vitamin D receptor (VDR), which is principally located in the nuclei of target cells.[1][16] The binding of calcitriol to the VDR allows the VDR to act as a transcription factor that modulates the gene expression of transport proteins (such as TRPV6 and calbindin), which are involved in calcium absorption in the intestine.[18] The vitamin D receptor belongs to the nuclear receptor superfamily of steroid/thyroid hormone receptors, and VDRs are expressed by cells in most organs, including the brain, heart, skin, gonads, prostate, and breast.  
  
VDR activation in the intestine, bone, kidney, and parathyroid gland cells leads to the maintenance of calcium and phosphorus levels in the blood (with the assistance of parathyroid hormone and calcitonin) and to the maintenance of bone content.[1][19]  
  
One of the most important roles of vitamin D is to maintain skeletal calcium balance by promoting calcium absorption in the intestines, promoting bone resorption by increasing osteoclast number, maintaining calcium and phosphate levels for bone formation, and allowing proper functioning of parathyroid hormone to maintain serum calcium levels.[1] Vitamin D deficiency can result in lower bone mineral density and an increased risk of reduced bone density (osteoporosis) or bone fracture because a lack of vitamin D alters mineral metabolism in the body.[1][20] Thus, vitamin D is also critical for bone remodeling through its role as a potent stimulator of bone resorption.[20]  
  
The VDR regulates cell proliferation and differentiation. Vitamin D also affects the immune system, and VDRs are expressed in several white blood cells, including monocytes and activated T and B cells.[21] In vitro, vitamin D increases expression of the tyrosine hydroxylase gene in adrenal medullary cells, and affects the synthesis of neurotrophic factors, nitric oxide synthase, and glutathione.[22]  
  
Vitamin D receptor expression decreases with age and findings suggest that vitamin D is directly related to muscle strength, mass and function.[1]  
  
Deficiency [ edit ]  
  
An estimated one billion people worldwide are either vitamin D insufficient or deficient.[23] Vitamin D deficiency is widespread in the European population.[24] A diet with insufficient vitamin D in conjunction with inadequate sun exposure causes vitamin D deficiency. Severe vitamin D deficiency in children causes rickets, a softening and weakening of bones, which is a rare disease in the developed world.[25]  
  
Vitamin D deficiency is found worldwide in the elderly and remains common in children and adults.[26][27][23] Deficiency results in impaired bone mineralization and bone damage which leads to bone-softening diseases,[28] including rickets in children and osteomalacia in adults. Low blood calcifediol (25-hydroxy-vitamin D) can result from avoiding the sun.[29] Being deficient in vitamin D can cause intestinal absorption of dietary calcium to fall to 15%.[19] When not deficient, an individual usually absorbs between 60 and 80%.[19]  
  
Bone health [ edit ]  
  
Rickets [ edit ]  
  
Rickets, a childhood disease, is characterized by impeded growth and soft, weak, deformed long bones that bend and bow under their weight as children start to walk. Rickets typically appears between 3 and 18 months of age.[30] Cases continue to be reported in North American and other Western Countries and is primarily seen in breastfed infants and those with darker skin complexions.[30] This condition is characterized by bow legs,[28] which can be caused by calcium or phosphorus deficiency, as well as a lack of vitamin D; in the 21st century, it is largely found in low-income countries in Africa, Asia, or the Middle East[31] and in those with genetic disorders such as pseudovitamin D deficiency rickets.[32]  
  
Maternal vitamin D deficiency may cause overt bone disease from before birth and impairment of bone quality after birth.[33][34] Nutritional rickets exists in countries with intense year-round sunlight such as Nigeria and can occur without vitamin D deficiency.[35][36]  
  
Although rickets and osteomalacia are now rare in the UK, outbreaks have happened in some immigrant communities in which osteomalacia patients included women with seemingly adequate daylight outdoor exposure wearing Western clothing.[37] Having darker skin and reduced exposure to sunshine did not produce rickets unless the diet deviated from a Western omnivore pattern characterized by high intakes of meat, fish, and eggs.[38][39][40] The dietary risk factors for rickets include abstaining from animal foods.[37][41]  
  
Vitamin D deficiency remains the main cause of rickets among young infants in most countries because breast milk is low in vitamin D and social customs and climatic conditions can prevent adequate sun exposure. In sunny countries such as Nigeria, South Africa, and Bangladesh, where rickets occurs among older toddlers and children, it has been attributed to low dietary calcium intakes, which are characteristic of cereal-based diets with limited access to dairy products.[40]  
  
Rickets was formerly a major public health problem among the US population; in Denver, where ultraviolet rays are about 20% stronger than at sea level on the same latitude,[42] almost two-thirds of 500 children had mild rickets in the late 1920s.[43] An increase in the proportion of animal protein[41][44] in the 20th century American diet coupled with increased consumption of milk[45][46] fortified with relatively small quantities of vitamin D coincided with a dramatic decline in the number of rickets cases.[19] Also, in the United States and Canada, vitamin D-fortified milk, infant vitamin supplements, and vitamin supplements have helped to eradicate the majority of cases of rickets for children with fat malabsorption conditions.[28]  
  
Osteomalacia and osteoporosis [ edit ]  
  
Osteomalacia is a disease in adults that results from vitamin D deficiency.[1] Characteristics of this disease are softening of the bones, leading to bending of the spine, bowing of the legs, proximal muscle weakness, bone fragility, and increased risk for fractures.[1] Osteomalacia reduces calcium absorption and increases calcium loss from bone, which increases the risk for bone fractures. Osteomalacia is usually present when 25-hydroxyvitamin D levels are less than about 10 ng/mL.[47] Although the effects of osteomalacia are thought to contribute to chronic musculoskeletal pain, there is no persuasive evidence of lower vitamin D levels in chronic pain sufferers[48] or that supplementation alleviates chronic nonspecific musculoskeletal pain.[49]  
  
Osteoporosis is a condition of reduced bone mineral density with increased bone fragility and risk of bone fractures. Osteoporosis can be a long-term effect of calcium and/or vitamin D insufficiency, at least in part. This may result from inadequate calcium intake, with insufficient vitamin D contributing by reducing calcium absorption.[2]  
  
Skin pigmentation [ edit ]  
  
Dark-skinned people living in temperate climates have been shown to have low vitamin D levels but the significance of this is not certain.[50][51][52] Dark-skinned people are less efficient at making vitamin D because melanin in the skin hinders vitamin D synthesis.[53] Vitamin D deficiency is common in Hispanic and African-Americans in the United States, with levels dropping significantly in the winter.[54] This is due to the levels of melanin in the skin, as it acts as a natural protectant from sun exposure.[54]  
  
Use of supplements [ edit ]  
  
Supplementation with vitamin D is a reliable method for preventing or treating rickets.[1] The effects of vitamin D supplementation on non-skeletal health are uncertain.[55][56] A 2013 review did not find any effect from supplementation on the rates of non-skeletal disease, other than a tentative decrease in mortality in the elderly.[57] Vitamin D supplements do not alter the outcomes for myocardial infarction, stroke or cerebrovascular disease, cancer, bone fractures or knee osteoarthritis.[13][58] Low vitamin D levels may result from disease rather than cause disease.[57]  
  
A United States Institute of Medicine (IOM) report states: "Outcomes related to cancer, cardiovascular disease and hypertension, and diabetes and metabolic syndrome, falls and physical performance, immune functioning and autoimmune disorders, infections, neuropsychological functioning, and preeclampsia could not be linked reliably with calcium or vitamin D intake and were often conflicting."[59]: 5 Some researchers claim the IOM was too definitive in its recommendations and made a mathematical mistake when calculating the blood level of vitamin D associated with bone health.[60] Members of the IOM panel maintain that they used a "standard procedure for dietary recommendations" and that the report is solidly based on the data. Research on vitamin D supplements, including large-scale clinical trials, is continuing.[60]  
  
Vitamin D 3 supplementation has been tentatively found to lead to a reduced risk of death in the elderly,[11][57] but the effect has not been deemed pronounced, or certain enough, to make taking supplements recommendable.[13] Other forms (vitamin D 2 , alfacalcidol, and calcitriol) do not appear to have any beneficial effects with regard to the risk of death.[11] High blood levels appear to be associated with a lower risk of death, but it is unclear if supplementation can result in this benefit.[61] Both an excess and a deficiency in vitamin D appear to cause abnormal functioning and premature aging.[62][63][64] The relationship between serum calcifediol concentrations and all-cause mortality is "U-shaped": mortality is elevated at high and low calcifediol levels, relative to moderate levels.[59] Harm from vitamin D appears to occur at a lower vitamin D level in the black population than in the white population.[59]: 435  
  
Bone health [ edit ]  
  
In general, no good evidence supports the commonly held belief that vitamin D supplements can help prevent osteoporosis.[13] Its general use for prevention of this disease in those without vitamin D deficiency is thus likely not needed.[12] For older people with osteoporosis, taking vitamin D with calcium may help prevent hip fractures, but it also slightly increases the risk of stomach and kidney problems.[65] A study found that supplementation with 800 IU or more daily, in those older than 65 years was "somewhat favorable in the prevention of hip fracture and non-vertebral fracture".[66] The effect is small or none for people living independently.[67][68] Low serum vitamin D levels have been associated with falls, and low bone mineral density.[69] Taking extra vitamin D, however, does not appear to change the risk.[70]  
  
Athletes who are vitamin D deficient are at an increased risk of stress fractures and/or major breaks, particularly those engaging in contact sports. The greatest benefit with supplementation is seen in athletes who are deficient (25(OH)D serum levels <30 ng/mL), or severely deficient (25(OH)D serum levels <25 ng/mL). Incremental decreases in risks are observed with rising serum 25(OH)D concentrations plateauing at 50 ng/mL with no additional benefits seen in levels beyond this point.[71]  
  
The US Food and Drug Administration (FDA) has required manufacturers to declare the amount of vitamin D on nutrition facts labels, as "nutrients of public health significance", since May 2016. By a proposed deadline extension, some manufacturers had until July 1, 2021, to comply.[72]  
  
Cancer [ edit ]  
  
Potential associations have been found between low vitamin D levels and the risk of developing several types of cancer.[73][74][75] Meta-analyses of observational studies have found reduced risk of cancer incidence related to vitamin D intake and 25(OH)D levels, particularly for colorectal cancer,[76] although the strength of the associations was classified as weak.[75][77][78] While randomized controlled trials have not confirmed that vitamin D supplements reduce the risk of cancer incidence, the relative risk of cancer deaths has been found to be reduced by up to 16% in several meta-analyses.[79][78]  
  
Cardiovascular disease [ edit ]  
  
Taking vitamin D supplements does not meaningfully reduce the risk of stroke, cerebrovascular disease, myocardial infarction, or ischemic heart disease.[13][80] Supplementation may have no effect on blood pressure.[81]  
  
Immune system [ edit ]  
  
Infectious diseases [ edit ]  
  
In general, vitamin D functions to activate the innate and dampen the adaptive immune systems with antibacterial, antiviral and anti-inflammatory effects.[82][83] Deficiency has been linked to increased risk or severity of viral infections, including HIV[84][85] and COVID-19.[86] Low levels of vitamin D appear to be a risk factor for tuberculosis,[87] and historically it was used as a treatment.[88]  
  
Vitamin D supplementation in low doses (400 to 1000 IU/day) may slightly decrease the overall risk of acute respiratory tract infections.[89] The benefits were found in young children and adolescents (ages 1 up to 16 years) and were not confirmed with higher doses (>1000 IU per day or more).[89] Vitamin D supplementation substantially reduces the rate of moderate or severe exacerbations of COPD in people with baseline 25(OH)D levels under 25nmol/L but not in those with less severe deficiency.[90]  
  
Asthma [ edit ]  
  
Although tentative data link low levels of vitamin D to asthma, evidence to support a beneficial effect on asthmatics from supplementation is inconclusive.[91] One review found that vitamin D supplementation could reduce the need for steroids used to inhibit episode frequency in people with mild to moderate asthma, and that supplementation had no effect on day-to-day asthma symptoms.[92] In general practice, supplementation with vitamin D is not recommended for treatment or prevention of asthma.[93]  
  
Inflammatory bowel disease [ edit ]  
  
Low levels of vitamin D are associated with two major forms of human inflammatory bowel disease (IBD): Crohn's disease and ulcerative colitis.[94] A meta-analysis of vitamin D therapy in IBD patients with vitamin D deficiency has shown that supplementation is effective at correcting vitamin D levels and is associated with improvements in scores for clinical disease activity and biochemical markers.[95]  
  
Other conditions [ edit ]  
  
Diabetes – A meta-analysis of eight studies found that vitamin D supplementation significantly reduced the risk of type 2 diabetes mellitus for non-obese prediabetic patients.[96] A meta-analysis of 37 articles found that vitamin D supplementation significantly improved glycemic control [homeostatic model assessment-insulin resistance (HOMA-IR)], hemoglobin A1C (HbA1C), and fasting blood glucose (FBG) in individuals with type 2 diabetes mellitus.[97] In prospective studies, high versus low level of vitamin D was respectively associated with significant decrease in risk of type 2 diabetes mellitus, combined type 2 diabetes mellitus and pre-diabetes, and pre-diabetes.[98] A 2011 Cochrane systematic review examined one study that showed vitamin D together with insulin maintained levels of fasting C-peptide after 12 months better than insulin alone. However, it is important to highlight that the studies available to be included in this review presented considerable flaws in quality and design.[99]  
  
ADHD - A meta-analysis of observational studies showed that children with ADHD have lower vitamin D levels, and that there was a small association between low vitamin D levels at the time of birth and later development of ADHD.[100] Several small randomized controlled trials of vitamin D supplementation indicated improved ADHD symptoms such as impulsivity and hyperactivity.[101]  
  
Depression – Clinical trials of vitamin D supplementation for depressive symptoms have generally been of low quality and show no overall effect, although subgroup analysis showed supplementation for participants with clinically significant depressive symptoms or depressive disorder had a moderate effect.[102]  
  
Cognition and dementia – A systematic review of clinical studies found an association between low vitamin D levels with cognitive impairment and a higher risk of developing Alzheimer's disease. However, lower vitamin D concentrations are also associated with poor nutrition and spending less time outdoors. Therefore, alternative explanations for the increase in cognitive impairment exist and hence a direct causal relationship between vitamin D levels and cognition could not be established.[103]  
  
Schizophrenia - Trials have demonstrated lower vitamin D levels are highly prevalent in patients with schizophrenia, particularly those with acute episodes.[104]  
  
Pregnancy – Low levels of vitamin D in pregnancy are associated with gestational diabetes, pre-eclampsia, and small (for gestational age) infants.[105] Although taking vitamin D supplements during pregnancy raises blood levels of vitamin D in the mother at term,[106] the full extent of benefits for the mother or baby is unclear.[105][106][107] Pregnant women who take an adequate amount of vitamin D during gestation may experience a lower risk of pre-eclampsia[108] and positive immune effects.[109] Vitamin D supplementation is also likely to reduce the risk of gestational diabetes, undersized babies[108] and of their poor rate of growth.[110] Pregnant women often do not take the recommended amount of vitamin D.[109]  
  
Weight loss – Though hypothesized that vitamin D supplementation may be an effective treatment for obesity apart from calorie restriction, one systematic review found no association of supplementation with body weight or fat mass.[111] A 2016 meta-analysis found that circulating vitamin D status was improved by weight loss, indicating that fat mass may be inversely associated with blood levels of vitamin D.[112]  
  
Allowable health claims [ edit ]  
  
Governmental regulatory agencies stipulate for the food and dietary supplement industries certain health claims as allowable as statements on packaging.  
  
European Food Safety Authority  
  
normal function of the immune system [113]  
  
normal inflammatory response [113]  
  
normal muscle function [113]  
  
reduced risk of falling in people over age 60[114]  
  
US Food and Drug Administration (FDA)  
  
"Adequate calcium and vitamin D, as part of a well balanced diet, along with physical activity, may reduce the risk of osteoporosis."[115]  
  
Health Canada  
  
"Adequate calcium and regular exercise may help to achieve strong bones in children and adolescents and may reduce the risk of osteoporosis in older adults. An adequate intake of vitamin D is also necessary."[116]  
  
Other possible agencies with claim guidance: Japan FOSHU[117] and Australia-New Zealand.[118]  
  
Dietary intake [ edit ]  
  
United Kingdom Age group Intake (μg/day) Maximum intake (μg/day)[119] Breast-fed infants 0–12 months 8.5 - 10 25 Formula-fed infants (<500 ml/d) 10 25 Children 1 – 10 years 10 50 Children >10 and adults 10 100 United States Age group RDA (IU/day) (μg/day)[59] Infants 0–6 months 400\* 10 Infants 6–12 months 400\* 10 1–70 years 600 15 71+ years 800 20 Pregnant/Lactating 600 15 Age group Tolerable upper intake level (IU/day) (μg/day) Infants 0–6 months 1,000 25 Infants 6–12 months 1,500 37.5 1–3 years 2,500 62.5 4–8 years 3,000 75 9+ years 4,000 100 Pregnant/lactating 4,000 100[59] Canada Age group RDA (IU) Tolerable upper intake (IU)[120] Infants 0–6 months 400\* 1,000 Infants 7–12 months 400\* 1,500 Children 1–3 years 600 2,500 Children 4–8 years 600 3,000 Children and Adults 9–70 years 600 4,000 Adults > 70 years 800 4,000 Pregnancy & Lactation 600 4,000 Australia and New Zealand Age group Adequate Intake (μg) Upper Level of Intake (μg)[121] Infants 0–12 months 5\* 25 Children 1–18 years 5\* 80 Adults 19–50 years 5\* 80 Adults 51–70 years 10\* 80 Adults > 70 years 15\* 80 European Food Safety Authority Age group Adequate Intake (μg)[122] Tolerable upper limit (μg)[123] Infants 0–12 months 10 25 Children 1–10 years 15 50 Children 11–17 years 15 100 Adults 15 100 Pregnancy & Lactation 15 100 \* Adequate intake, no RDA/RDI yet established  
  
Recommended levels [ edit ]  
  
Various institutions have proposed different recommendations for the amount of daily intake[124] of vitamin D. These vary according to precise definition, age, pregnancy or lactation, and the extent assumptions are made regarding skin synthesis of vitamin D.[119][59][120][121][122] Conversion: 1 μg (microgram) = 40 IU (international unit).[119]  
  
United Kingdom [ edit ]  
  
The UK National Health Service (NHS) recommends that people at risk of vitamin D deficiency, breast-fed babies, formula-fed babies taking less than 500ml/day, and children aged 6 months to 4 years, should take daily vitamin D supplements throughout the year to ensure sufficient intake.[119] This includes people with limited skin synthesis of vitamin D, who are not often outdoors, are frail, housebound, living in a care home, or usually wearing clothes that cover up most of the skin, or with dark skin, such as having an African, African-Caribbean or south Asian background. Other people may be able to make adequate vitamin D from sunlight exposure from April to September. The NHS and Public Health England recommend that everyone, including those who are pregnant and breastfeeding, consider taking a daily supplement containing 10 μg (400 IU) of vitamin D during autumn and winter because of inadequate sunlight for vitamin D synthesis.[125]  
  
United States [ edit ]  
  
The dietary reference intake for vitamin D issued in 2010 by the Institute of Medicine (IoM) (renamed National Academy of Medicine in 2015), superseded previous recommendations which were expressed in terms of Adequate Intake. The recommendations were formed assuming the individual has no skin synthesis of vitamin D because of inadequate sun exposure. The reference intake for vitamin D refers to total intake from food, beverages and supplements, and assumes that calcium requirements are being met.[59]: 5 The tolerable upper intake level (UL)[126] is defined as "the highest average daily intake of a nutrient that is likely to pose no risk of adverse health effects for nearly all persons in the general population."[59]: 403 Although ULs are believed to be safe, information on the long-term effects is incomplete and these levels of intake are not recommended for long-term consumption.[59]: 403 : 433  
  
For U.S food and dietary supplement labeling purposes, the amount in a serving is expressed as a percent of Daily Value (%DV). For vitamin D labeling purposes, 100% of the Daily Value was 400 IU (10 μg), but on May 27, 2016, it was revised to 800 IU (20 μg) to bring it into agreement with the RDA.[127][128] Compliance with the updated labeling regulations was required by 1 January 2020 for manufacturers with US$10 million or more in annual food sales, and by 1 January 2021 for manufacturers with lower volume food sales.[72][129] A table of the old and new adult daily values is provided at Reference Daily Intake.  
  
Canada [ edit ]  
  
Health Canada published recommended dietary allowances (RDA) and tolerable upper intake levels for vitamin D in 2012[120] based on the Institute of Medicine report.[59]  
  
Australia and New Zealand [ edit ]  
  
Australia and New Zealand published nutrient reference values including guidelines for dietary vitamin D intake in 2005.[121] About a third of Australians have vitamin D deficiency.[130]  
  
European Union [ edit ]  
  
The European Food Safety Authority (EFSA) in 2016[122] reviewed the current evidence, finding the relationship between serum 25(OH)D concentration and musculoskeletal health outcomes is widely variable. They considered that average requirements and population reference intakes values for vitamin D cannot be derived, and that a serum 25(OH)D concentration of 50 nmol/L was a suitable target value. For all people over the age of 1, including women who are pregnant or lactating, they set an adequate intake of 15 μg/day (600 IU).[122]  
  
The EFSA reviewed safe levels of intake in 2012,[123] setting the tolerable upper limit for adults at 100 μg/day (4000 IU), a similar conclusion as the IOM.  
  
The Swedish National Food Agency recommends a daily intake of 10 μg (400 IU) of vitamin D3 for children and adults up to 75 years, and 20 μg (800 IU) for adults 75 and older.[131]  
  
Non-government organisations in Europe have made their own recommendations. The German Society for Nutrition recommends 20 μg.[132] The European Menopause and Andropause Society recommends postmenopausal women consume 15 μg (600 IU) until age 70, and 20 μg (800 IU) from age 71. This dose should be increased to 100 μg (4,000 IU) in some patients with very low vitamin D status or in case of co-morbid conditions.[133]  
  
Sources [ edit ]  
  
Although vitamin D is present naturally in only a few foods,[2] it is commonly added as a fortification in manufactured foods. In some countries, staple foods are artificially fortified with vitamin D.[134]  
  
Natural sources [ edit ]  
  
In general, vitamin D 3 is found in animal source foods, particularly fish, meat, offal, egg and dairy.[137] Vitamin D 2 is found in fungi and is produced by ultraviolet irradiation of ergosterol.[138] The vitamin D 2 content in mushrooms and Cladina arbuscula, a lichen, increases with exposure to ultraviolet light,[136][139] and is stimulated by industrial ultraviolet lamps for fortification.[138] The United States Department of Agriculture reports D 2 and D 3 content combined in one value.  
  
Food fortification [ edit ]  
  
Manufactured foods fortified with vitamin D include some fruit juices and fruit juice drinks, meal replacement energy bars, soy protein-based beverages, certain cheese and cheese products, flour products, infant formulas, many breakfast cereals, and milk.[140][141]  
  
In 2016 in the United States, the Food and Drug Administration (FDA) amended food additive regulations for milk fortification,[142] stating that vitamin D 3 levels not exceed 42 IU vitamin D per 100 g (400 IU per US quart) of dairy milk, 84 IU of vitamin D 2 per 100 g (800 IU per quart) of plant milks, and 89 IU per 100 g (800 IU per quart) in plant-based yogurts or in soy beverage products.[143][144][145] Plant milks are defined as beverages made from soy, almond, rice, among other plant sources intended as alternatives to dairy milk.[146][147]  
  
While some studies have found that vitamin D 3 raises 25(OH)D blood levels faster and remains active in the body longer,[148][149] others contend that vitamin D 2 sources are equally bioavailable and effective as D 3 for raising and sustaining 25(OH)D.[138][150][151]  
  
Food preparation [ edit ]  
  
Vitamin D content in typical foods is reduced variably by cooking. Boiled, fried and baked foods retained 69–89% of original vitamin D.[152]  
  
Recommended serum levels [ edit ]  
  
[153][154] > 75 50-74 25-49 Global vitamin D serum levels among adults (nmol/L).  
  
Recommendations on recommended 25(OH)D serum levels vary across authorities, and vary based on factors like age.[2] US labs generally report 25(OH)D levels in ng/mL.[155] Other countries often use nmol/L.[155] One ng/mL is approximately equal to 2.5 nmol/L.[156]  
  
A 2014 review concluded that the most advantageous serum levels for 25(OH)D for all outcomes appeared to be close to 30 ng/mL (75 nmol/L).[157] The optimal vitamin D levels are still controversial and another review concluded that ranges from 30 to 40 ng/mL (75 to 100 nmol/L) were to be recommended for athletes.[158] Part of the controversy is because numerous studies have found differences in serum levels of 25(OH)D between ethnic groups; studies point to genetic as well as environmental reasons behind these variations.[159] Supplementation to achieve these standard levels could cause harmful vascular calcification.[52]  
  
A 2012 meta-analysis showed that the risk of cardiovascular diseases increases when blood levels of vitamin D are lowest in a range of 8 to 24 ng/mL (20 to 60 nmol/L), although results among the studies analyzed were inconsistent.[160]  
  
In 2011 an IOM committee concluded a serum 25(OH)D level of 20 ng/mL (50 nmol/L) is needed for bone and overall health. The dietary reference intakes for vitamin D are chosen with a margin of safety and 'overshoot' the targeted serum value to ensure the specified levels of intake achieve the desired serum 25(OH)D levels in almost all persons. No contributions to serum 25(OH)D level are assumed from sun exposure and the recommendations are fully applicable to people with dark skin or negligible exposure to sunlight. The Institute found serum 25(OH)D concentrations above 30 ng/mL (75 nmol/L) are "not consistently associated with increased benefit". Serum 25(OH)D levels above 50 ng/mL (125 nmol/L) may be cause for concern. However, some people with serum 25(OH)D between 30 and 50 ng/mL (75 nmol/L-125 nmol/L) will also have inadequate vitamin D.[59]  
  
Excess [ edit ]  
  
Vitamin D toxicity is rare.[23] It is caused by supplementing with high doses of vitamin D rather than sunlight. The threshold for vitamin D toxicity has not been established; however, according to some research, the tolerable upper intake level (UL) is 4,000 IU/day for ages 9–71[161] (100 μg/day), while other research concludes that, in healthy adults, sustained intake of more than 50,000 IU/day (1250 μg) can produce overt toxicity after several months and can increase serum 25-hydroxyvitamin D levels to 150 ng/mL and greater.[23][162] Those with certain medical conditions, such as primary hyperparathyroidism,[163] are far more sensitive to vitamin D and develop hypercalcemia in response to any increase in vitamin D nutrition, while maternal hypercalcemia during pregnancy may increase fetal sensitivity to effects of vitamin D and lead to a syndrome of intellectual disability and facial deformities.[163][164]  
  
Idiopathic infantile hypercalcemia is caused by a mutation of the CYP24A1 gene, leading to a reduction in the degradation of vitamin D. Infants who have such a mutation have an increased sensitivity to vitamin D and in case of additional intake a risk of hypercalcaemia.[165][166] The disorder can continue into adulthood.[167]  
  
A review published in 2015 noted that adverse effects have been reported only at 25(OH)D serum concentrations above 200 nmol/L.[158]  
  
Published cases of toxicity involving hypercalcemia in which the vitamin D dose and the 25-hydroxy-vitamin D levels are known all involve an intake of ≥40,000 IU (1,000 μg) per day.[163]  
  
Those who are pregnant or breastfeeding should consult a doctor before taking a vitamin D supplement. The FDA advised manufacturers of liquid vitamin D supplements that droppers accompanying these products should be clearly and accurately marked for 400 international units (1 IU is the biological equivalent of 25 ng cholecalciferol/ergocalciferol). In addition, for products intended for infants, the FDA recommends the dropper hold no more than 400 IU.[168] For infants (birth to 12 months), the tolerable upper limit (maximum amount that can be tolerated without harm) is set at 25 μg/day (1,000 IU). One thousand micrograms per day in infants has produced toxicity within one month.[162] After being commissioned by the Canadian and American governments, the Institute of Medicine (IOM) as of 30 November 2010 , has increased the tolerable upper limit (UL) to 2,500 IU per day for ages 1–3 years, 3,000 IU per day for ages 4–8 years and 4,000 IU per day for ages 9–71+ years (including pregnant or lactating women).[161]  
  
Calcitriol itself is auto-regulated in a negative feedback cycle, and is also affected by parathyroid hormone, fibroblast growth factor 23, cytokines, calcium, and phosphate.[169]  
  
A study published in 2017 assessed the prevalence of high daily intake levels of supplemental vitamin D among adults ages 20+ in the United States, based on publicly available NHANES data from 1999 through 2014. It’s data shows the following:  
  
Over 18% of the population exceeds the NIH daily recommended allowance (RDA) of 600-800 IU, [170] by taking over 1000 IU, which suggests intentional supplement intake. [171]  
  
by taking over 1000 IU, which suggests intentional supplement intake. Over 3% of the population exceeds the NIH daily tolerable upper intake level (UL) of 4000 IU, [170] above which level the risk of toxic effects increases. [172] [171]  
  
above which level the risk of toxic effects increases. The percentage of the population taking over 1000 IU/day, as well as the percentage taking over 4000 IU/day, have both increased since 1999, according to trend analysis.[171]  
  
Effect of excess [ edit ]  
  
Vitamin D overdose causes hypercalcemia, which is a strong indication of vitamin D toxicity – this can be noted with an increase in urination and thirst. If hypercalcemia is not treated, it results in excess deposits of calcium in soft tissues and organs such as the kidneys, liver, and heart, resulting in pain and organ damage.[23][28][173]  
  
The main symptoms of vitamin D overdose are hypercalcemia including anorexia, nausea, and vomiting. These may be followed by polyuria, polydipsia, weakness, insomnia, nervousness, pruritus and ultimately kidney failure. Furthermore, proteinuria, urinary casts, azotemia, and metastatic calcification (especially in the kidneys) may develop.[162] Other symptoms of vitamin D toxicity include intellectual disability in young children, abnormal bone growth and formation, diarrhea, irritability, weight loss, and severe depression.[23][173]  
  
Vitamin D toxicity is treated by discontinuing vitamin D supplementation and restricting calcium intake. Kidney damage may be irreversible. Exposure to sunlight for extended periods of time does not normally cause vitamin D toxicity. The concentrations of vitamin D precursors produced in the skin reach an equilibrium, and any further vitamin D produced is degraded.[163]  
  
Biosynthesis [ edit ]  
  
Synthesis of vitamin D in nature is dependent on the presence of UV radiation and subsequent activation in the liver and in the kidneys. Many animals synthesize vitamin D 3 from 7-dehydrocholesterol, and many fungi synthesize vitamin D 2 from ergosterol.[174][138]  
  
Interactive pathway [ edit ]  
  
Click on icon in lower right corner to open.  
  
Click on genes, proteins and metabolites below to link to respective articles. [§ 1] [[ ]] ]] [[ ]] ]] [[ ]] ]] [[ ]] ]] [[ ]] ]] [[ ]] ]] [[ ]] ]] [[ ]] ]] [[ ]] ]] [[ ]] ]] [[ ]] ]] [[ ]] ]] [[ ]] ]] [[ ]] ]] [[ ]] ]] [[ ]] ]] [[ ]] ]] [[ ]] ]] [[ ]] ]] [[ ]] ]] [[ ]] ]] [[ ]] ]] [[File:|alt=Vitamin D Synthesis Pathway ( view edit )]] edit) Vitamin D Synthesis Pathway ( view ^ "VitaminDSynthesis\_WP1531". The interactive pathway map can be edited at WikiPathways:  
  
Photochemistry [ edit ]  
  
The photochemistry of vitamin D biosynthesis in animal and fungi  
  
The transformation that converts 7-dehydrocholesterol to vitamin D 3 occurs in two steps.[175][176] First, 7-dehydrocholesterol is photolyzed by ultraviolet light in a 6-electron conrotatory ring-opening electrocyclic reaction; the product is previtamin D 3 . Second, previtamin D 3 spontaneously isomerizes to vitamin D 3 (cholecalciferol) in an antarafacial sigmatropic [1,7] hydride shift. At room temperature, the transformation of previtamin D 3 to vitamin D 3 in an organic solvent takes about 12 days to complete. The conversion of previtamin D 3 to vitamin D 3 in the skin is about 10 times faster than in an organic solvent.[177]  
  
The conversion from ergosterol to vitamin D 2 follows a similar procedure, forming previtamin D 2 by photolysis, which isomerizes to vitamin D 2 (ergocalciferol).[178] The transformation of previtamin D 2 to vitamin D 2 in methanol has a rate comparable to that of previtamin D 3 . The process is faster in white button mushrooms.[138]: fig. 3  
  
Synthesis in the skin [ edit ]  
  
In the epidermal strata of the skin, vitamin D production is greatest in the stratum basale (colored red in the illustration) and stratum spinosum (colored light brown).  
  
Vitamin D 3 is produced photochemically from 7-dehydrocholesterol in the skin of most vertebrate animals, including humans.[179] The precursor of vitamin D 3 , 7-dehydrocholesterol is produced in relatively large quantities. 7-Dehydrocholesterol reacts with UVB light at wavelengths of 290–315 nm.[180] These wavelengths are present in sunlight, as well as in the light emitted by the UV lamps in tanning beds (which produce ultraviolet primarily in the UVA spectrum, but typically produce 4% to 10% of the total UV emissions as UVB, some tanning beds can use only separate UVB light bulbs specifically for vitamin production). Exposure to light through windows is insufficient because glass almost completely blocks UVB light.[181]  
  
Adequate amounts of vitamin D can be produced with moderate sun exposure to the face, arms and legs (for those with the least melanin), averaging 5–30 minutes twice per week, or approximately 25% of the time for minimal sunburn. The darker the skin, and the weaker the sunlight, the more minutes of exposure are needed. Vitamin-D overdose is impossible from UV exposure: the skin reaches an equilibrium where the vitamin degrades as fast as it is created.[23][182]  
  
The skin consists of two primary layers: the inner layer called the dermis, and the outer, thinner epidermis. Vitamin D is produced in the keratinocytes of two innermost strata of the epidermis, the stratum basale and stratum spinosum, which also are able to produce calcitriol and express the VDR.[183]  
  
Evolution [ edit ]  
  
Vitamin D can be synthesized only by a photochemical process. Its production from sterols would have started very early in the evolution of life around the origin of photosynthesis, possibly helping to prevent DNA damage by absorbing UVB, making vitamin D an inactive end product. The familiar vitamin D endocrine machinery containing vitamin D receptor (VDR), various CYP450 enzymes for activation and inactivation, and a vitamin D binding protein (DBP) is found in vertebrates only. Primitive marine vertebrates are thought to absorb calcium from the ocean into their skeletons and eat plankton rich in vitamin D, although the function in those without a calcified cartilage is unclear.[184] Phytoplankton in the ocean (such as coccolithophore and Emiliania huxleyi) have been photosynthesizing vitamin D for more than 500 million years.  
  
Land vertebrates required another source of vitamin D other than plants for their calcified skeletons. They had to either ingest it or be exposed to sunlight to photosynthesize it in their skin.[174][177] Land vertebrates have been photosynthesizing vitamin D for more than 350 million years.[185]  
  
In birds and fur-bearing mammals, fur or feathers block UV rays from reaching the skin. Instead, vitamin D is created from oily secretions of the skin deposited onto the feathers or fur, and is obtained orally during grooming.[186] However, some animals, such as the naked mole-rat, are naturally cholecalciferol-deficient, as serum 25-OH vitamin D levels are undetectable.[187] Dogs and cats are practically incapable of vitamin D synthesis due to high activity of 7-dehydrocholesterol reductase, but they do get them from prey animals.[188]  
  
Industrial synthesis [ edit ]  
  
Vitamin D 3 (cholecalciferol) is produced industrially by exposing 7-dehydrocholesterol to UVB and UVC light, followed by purification.[189][138] The 7-dehydrocholesterol is a natural substance in fish organs, especially the liver,[190] or in wool grease (lanolin) from sheep. Vitamin D 2 (ergocalciferol) is produced in a similar way using ergosterol from yeast or mushrooms as a starting material.[189][138]  
  
Mechanism of action [ edit ]  
  
Metabolic activation [ edit ]  
  
Kidney hydroxylation of calcifediol to calcitriol  
  
Vitamin D is carried via the blood to the liver, where it is converted into the prohormone calcifediol. Circulating calcifediol may then be converted into calcitriol – the biologically active form of vitamin D – in the kidneys.[191]  
  
Whether synthesized in the skin or ingested, vitamin D is hydroxylated in the liver at position 25 (upper right of the molecule) to form 25-hydroxycholecalciferol (calcifediol or 25(OH)D).[4] This reaction is catalyzed by the microsomal enzyme vitamin D 25-hydroxylase, the product of the CYP2R1 human gene, and expressed by hepatocytes.[192] Once made, the product is released into the plasma, where it is bound to an α-globulin carrier protein named the vitamin D-binding protein.[193]  
  
Calcifediol is transported to the proximal tubules of the kidneys, where it is hydroxylated at the 1-α position (lower right of the molecule) to form calcitriol (1,25-dihydroxycholecalciferol, 1,25(OH) 2 D).[1] The conversion of calcifediol to calcitriol is catalyzed by the enzyme 25-hydroxyvitamin D 3 1-alpha-hydroxylase, which is the product of the CYP27B1 human gene.[1] The activity of CYP27B1 is increased by parathyroid hormone, and also by low calcium or phosphate.[1]  
  
Following the final converting step in the kidney, calcitriol is released into the circulation. By binding to vitamin D-binding protein, calcitriol is transported throughout the body, including to the intestine, kidneys, and bones.[16] Calcitriol is the most potent natural ligand of the vitamin D receptor, which mediates most of the physiological actions of vitamin D.[1][191]  
  
In addition to the kidneys, calcitriol is also synthesized by certain other cells, including monocyte-macrophages in the immune system. When synthesized by monocyte-macrophages, calcitriol acts locally as a cytokine, modulating body defenses against microbial invaders by stimulating the innate immune system.[191]  
  
Inactivation [ edit ]  
  
The activity of calcifediol and calcitriol can be reduced by hydroxylation at position 24 by vitamin D3 24-hydroxylase, forming secalciferol and calcitetrol, respectively.[4]  
  
Difference between substrates [ edit ]  
  
Vitamin D 2 (ergocalciferol) and vitamin D 3 (cholecalciferol) share a similar mechanism of action as outlined above.[4] Metabolites produced by vitamin D 2 are named with an er- or ergo- prefix to differentiate them from the D 3 -based counterparts (sometimes with a chole- prefix).[15]  
  
Metabolites produced from vitamin D 2 tend to bind less well to the vitamin D-binding protein. [4]  
  
D tend to bind less well to the vitamin D-binding protein. Vitamin D 3 can alternatively be hydroxylated to calcifediol by sterol 27-hydroxylase (CYP27A1), but vitamin D 2 cannot. [4]  
  
D can alternatively be hydroxylated to calcifediol by sterol 27-hydroxylase (CYP27A1), but vitamin D cannot. Ergocalciferol can be directly hydroxylated at position 24 by CYP27A1.[4] This hydroxylation also leads to a greater degree of inactivation: the activity of calcitriol decreases to 60% of original after 24-hydroxylation,[194] whereas ercalcitriol undergoes a 10-fold decrease in activity on conversion to ercalcitetrol.[195]  
  
It is disputed whether these differences lead to a measurable drop in efficacy (see § Food fortification).  
  
Intracellular mechanisms [ edit ]  
  
Calcitriol enters the target cell and binds to the vitamin D receptor in the cytoplasm. This activated receptor enters the nucleus and binds to vitamin D response elements (VDRE) which are specific DNA sequences on genes.[1] Transcription of these genes is stimulated and produces greater levels of the proteins which mediate the effects of vitamin D.[4]  
  
Some reactions of the cell to calcitriol appear to be too fast for the classical VDRE transcription pathway, leading to the discovery of various non-genomic actions of vitamin D. The membrane-bound PDIA3 likely serves as an alternate receptor in this pathway.[196] The classical VDR may still play a role.[197]  
  
History [ edit ]  
  
Vitamin D was discovered in 1922 following on from previous research.[198] American researchers Elmer McCollum and Marguerite Davis in 1914[10] discovered a substance in cod liver oil which later was called "vitamin A". British doctor Edward Mellanby noticed dogs that were fed cod liver oil did not develop rickets and concluded vitamin A, or a closely associated factor, could prevent the disease. In 1922, Elmer McCollum tested modified cod liver oil in which the vitamin A had been destroyed.[10] The modified oil cured the sick dogs, so McCollum concluded the factor in cod liver oil which cured rickets was distinct from vitamin A. He called it vitamin D because it was the fourth vitamin to be named.[199][200] It was not initially realized that, unlike other vitamins, vitamin D can be synthesised by humans through exposure to UV light.  
  
In 1925,[10] it was established that when 7-dehydrocholesterol is irradiated with light, a form of a fat-soluble vitamin is produced (now known as D 3 ). Alfred Fabian Hess stated: "Light equals vitamin D."[201] Adolf Windaus, at the University of Göttingen in Germany, received the Nobel Prize in Chemistry in 1928 for his work on the constitution of sterols and their connection with vitamins.[202] In 1929, a group at NIMR in Hampstead, London, were working on the structure of vitamin D, which was still unknown, as well as the structure of steroids. A meeting took place with J.B.S. Haldane, J.D. Bernal, and Dorothy Crowfoot to discuss possible structures, which contributed to bringing a team together. X-ray crystallography demonstrated the sterol molecules were flat, not as proposed by the German team led by Windaus. In 1932, Otto Rosenheim and Harold King published a paper putting forward structures for sterols and bile acids which found immediate acceptance.[203] The informal academic collaboration between the team members Robert Benedict Bourdillon, Otto Rosenheim, Harold King, and Kenneth Callow was very productive and led to the isolation and characterization of vitamin D.[204] At this time, the policy of the Medical Research Council was not to patent discoveries, believing the results of medical research should be open to everybody. In the 1930s, Windaus clarified further the chemical structure of vitamin D.[205]  
  
In 1923, American biochemist Harry Steenbock at the University of Wisconsin demonstrated that irradiation by ultraviolet light increased the vitamin D content of foods and other organic materials.[206] After irradiating rodent food, Steenbock discovered the rodents were cured of rickets. A vitamin D deficiency is a known cause of rickets. Using US$300 of his own money, Steenbock patented his invention. His irradiation technique was used for foodstuffs, most notably for milk. By the expiration of his patent in 1945, rickets had been all but eliminated in the US.[207]  
  
In 1969, after studying nuclear fragments of intestinal cells, a specific binding protein for vitamin D called the vitamin D receptor was identified by Mark Haussler and Tony Norman.[208] In 1971–72, the further metabolism of vitamin D to active forms was discovered. In the liver, vitamin D was found to be converted to calcifediol. Calcifediol is then converted by the kidneys to calcitriol, the biologically active form of vitamin D. Calcitriol circulates as a hormone in the blood, regulating the concentration of calcium and phosphate in the bloodstream and promoting the healthy growth and remodeling of bone. The vitamin D metabolites, calcifediol and calcitriol, were identified by competing teams led by Michael F. Holick in the laboratory of Hector DeLuca and by Tony Norman and colleagues.[8][9][209] The photosynthesis of vitamin D3 in skin via previtamin D3 and its subsequent metabolism was described by Michael Holick and his colleagues in 1980.[210]  
  
Research [ edit ]  
  
There is conflicting evidence about the benefits of interventions with vitamin D,[211] one view purporting an intake of 4,000–12,000 IU/day from sun exposure with concomitant serum 25-hydroxyvitamin D levels of 40 to 80 ng/mL,[212] while another view is that serum concentrations above 50 ng/mL are not plausible.[54][212]  
  
The United States National Institutes of Health Office of Dietary Supplements established a Vitamin D Initiative in 2014 to track current research and provide education to consumers.[213] In their 2020 update it was recognized that a growing body of research suggests that vitamin D might play some role in the prevention and treatment of types 1 and 2 diabetes, glucose intolerance, hypertension, multiple sclerosis, and other medical conditions. However, it was concluded that the available evidence was either inadequate or too contradictory to confirm the effectiveness of vitamin D on those conditions, save for the more positive findings on bone health.[2]  
  
Some preliminary studies link low vitamin D levels with disease later in life.[214] One meta-analysis found a decrease in mortality in elderly people.[11] Another meta-analysis covering over 350,000 people concluded that vitamin D supplementation in unselected community-dwelling individuals does not reduce skeletal (total fracture) or non-skeletal outcomes (myocardial infarction, ischemic heart disease, stroke, cerebrovascular disease, cancer) by more than 15%, and that further research trials with similar design are unlikely to change these conclusions.[13] A 2019 meta-analysis found that a small increase in risk of stroke when calcium supplements were added to vitamin D.[215] Evidence as of 2013 is insufficient to determine whether vitamin D affects the risk of cancer.[216]  
  
As of April 2021 the US National Institutes of Health state there is insufficient evidence to recommend for or against using vitamin D supplementation to prevent or treat COVID-19.[217] The UK National Institute for Health and Care Excellence (NICE) does not recommend to offer a vitamin D supplement to people solely to prevent or treat COVID‑19.[218][219] Both organizations included recommendations to continue the previous established recommendations on vitamin D supplementation for other reasons, such as bone and muscle health, as applicable. Both organizations noted that more people may require supplementation due to lower amounts of sun exposure during the pandemic.[217][218]  
  
Several systematic reviews and meta-analyses of multiple studies have described the associations of vitamin D deficiency with adverse outcomes in COVID-19.[220][221][222][223][224][225] In the largest analysis, with data from 76 observational studies including almost two million adults, vitamin D deficiency or insufficiency significantly increased the susceptibility to becoming infected with COVID-19 and having severe COVID-19, with odds ratios of 1.5 and 1.9 respectively, but these findings had high risk of bias and heterogeneity. A two-fold greater mortality was found, but this analysis was less robust.[225] These findings confirm smaller, earlier analyses,[221][222][223][224] one of which, in reporting that people with COVID-19 tend to have lower 25(OH)D levels than healthy subjects, stated that the trend for associations with health outcomes was limited by the low quality of the studies and by the possibility of reverse causality mechanisms.[223]  
  
A meta-analysis of three studies on the effect of oral vitamin D or calcifediol supplementation indicated a lower intensive care unit (ICU) admission rate (odds ratio: 0.36) compared to those without supplementation, but without a change in mortality.[226] A Cochrane review, also of three studies, found the evidence for the effectiveness of vitamin D supplementation for the treatment of COVID-19 to be very uncertain.[227] They found there was substantial clinical and methodological heterogeneity in the three studies that were included, mainly because of different supplementation strategies, vitamin D formulations (one using calcifediol), pre-treatment status and reported outcomes.[227] Another meta-analysis stated that the use of high doses of vitamin D in people with COVID-19 is not based on solid evidence although calcifediol supplementation may have a protective effect on ICU admissions.[223]  
  
References [ edit ]  
  
  
https://ods.od.nih.gov/factsheets/VitaminD-HealthProfessional/  
TITLE: Health Professional Fact Sheet  
META DESCRIPTION: Vitamin D overview for health professionals. Research health effects, dosing, sources, deficiency symptoms, side effects, and interactions here.  
META KEYWORDS: vitamin d, calcium, vitamin d and calcium, calcium and vitamin d, vitamin d2, vitamin d3, d2, d3, dietary supplement, calcidiol, calcitriol, hydroxyvitamin d, dihidroxyvitamin d, bone health, recommended intakes, ergocalciferol, cholecalciferol, vitamin d deficiency, food sources, vitamin d and health,   
H1: Vitamin D,   
H2: Table of Contents, Introduction, Recommended Intakes, Sources of Vitamin D, Vitamin D Intakes and Status, Vitamin D Deficiency, Groups at Risk of Vitamin D Inadequacy, Vitamin D and Health, Health Risks from Excessive Vitamin D, Interactions with Medications, Vitamin D and Healthful Diets, References, Disclaimer,   
BOLD/STRONG: Updated:,   
Health Information  
,   
Programs & Activities  
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Grants & Funding  
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Italic: : This is a fact sheet intended for health professionals. For a reader-friendly overview of Vitamin D, see our, For information on vitamin D and COVID-19, see Dietary Supplements in the Time of COVID-19., Serum concentrations of 25(OH)D and health, Food, Sun exposure, Dietary supplements, Breastfed infants, Older adults, People with limited sun exposure, People with dark skin, People with conditions that limit fat absorption, People with obesity or who have undergone gastric bypass surgery, Bone health and osteoporosis, Cancer, increased, Cardiovascular disease, Depression, Multiple sclerosis, Type 2 diabetes, Weight loss, Orlistat, Statins, Steroids, Thiazide diuretics, Dietary Guidelines for Americans, Dietary Guidelines for Americans, MyPlate., Dietary Guidelines for Americans,   
TEXT: This is a fact sheet intended for health professionals. For a reader-friendly overview of Vitamin D, see our consumer fact sheet on Vitamin D.  
  
For information on vitamin D and COVID-19, see Dietary Supplements in the Time of COVID-19.  
  
Introduction  
  
Vitamin D (also referred to as "calciferol") is a fat-soluble vitamin that is naturally present in a few foods, added to others, and available as a dietary supplement. It is also produced endogenously when ultraviolet (UV) rays from sunlight strike the skin and trigger vitamin D synthesis.  
  
Vitamin D obtained from sun exposure, foods, and supplements is biologically inert and must undergo two hydroxylations in the body for activation. The first hydroxylation, which occurs in the liver, converts vitamin D to 25-hydroxyvitamin D [25(OH)D], also known as "calcidiol." The second hydroxylation occurs primarily in the kidney and forms the physiologically active 1,25-dihydroxyvitamin D [1,25(OH)2D], also known as "calcitriol" [1].  
  
Vitamin D promotes calcium absorption in the gut and maintains adequate serum calcium and phosphate concentrations to enable normal bone mineralization and to prevent hypocalcemic tetany (involuntary contraction of muscles, leading to cramps and spasms). It is also needed for bone growth and bone remodeling by osteoblasts and osteoclasts [1-3]. Without sufficient vitamin D, bones can become thin, brittle, or misshapen. Vitamin D sufficiency prevents rickets in children and osteomalacia in adults. Together with calcium, vitamin D also helps protect older adults from osteoporosis.  
  
Vitamin D has other roles in the body, including reduction of inflammation as well as modulation of such processes as cell growth, neuromuscular and immune function, and glucose metabolism [1-3]. Many genes encoding proteins that regulate cell proliferation, differentiation, and apoptosis are modulated in part by vitamin D. Many tissues have vitamin D receptors, and some convert 25(OH)D to 1,25(OH)2D.  
  
In foods and dietary supplements, vitamin D has two main forms, D 2 (ergocalciferol) and D 3 (cholecalciferol), that differ chemically only in their side-chain structures. Both forms are well absorbed in the small intestine. Absorption occurs by simple passive diffusion and by a mechanism that involves intestinal membrane carrier proteins [4]. The concurrent presence of fat in the gut enhances vitamin D absorption, but some vitamin D is absorbed even without dietary fat. Neither aging nor obesity alters vitamin D absorption from the gut [4].  
  
Serum concentration of 25(OH)D is currently the main indicator of vitamin D status. It reflects vitamin D produced endogenously and that obtained from foods and supplements [1]. In serum, 25(OH)D has a fairly long circulating half-life of 15 days [1]. Serum concentrations of 25(OH)D are reported in both nanomoles per liter (nmol/L) and nanograms per milliliter (ng/mL). One nmol/L is equal to 0.4 ng/mL, and 1 ng/mL is equal to 2.5 nmol/L.  
  
Assessing vitamin D status by measuring serum 25(OH)D concentrations is complicated by the considerable variability of the available assays (the two most common ones involve antibodies or chromatography) used by laboratories that conduct the analyses [5,6]. As a result, a finding can be falsely low or falsely high, depending on the assay used and the laboratory. The international Vitamin D Standardization Program has developed procedures for standardizing the laboratory measurement of 25(OH)D to improve clinical and public health practice [5,7-10].  
  
In contrast to 25(OH)D, circulating 1,25(OH)2D is generally not a good indicator of vitamin D status because it has a short half-life measured in hours, and serum levels are tightly regulated by parathyroid hormone, calcium, and phosphate [1]. Levels of 1,25(OH)2D do not typically decrease until vitamin D deficiency is severe [2].  
  
Serum concentrations of 25(OH)D and health  
  
Although 25(OH)D functions as a biomarker of exposure, the extent to which 25(OH)D levels also serve as a biomarker of effect on the body (i.e., relating to health status or outcomes) is not clear [1,3].  
  
Researchers have not definitively identified serum concentrations of 25(OH)D associated with deficiency (e.g., rickets), adequacy for bone health, and overall health. After reviewing data on vitamin D needs, an expert committee of the Food and Nutrition Board (FNB) at the National Academies of Sciences, Engineering, and Medicine (NASEM) concluded that people are at risk of vitamin D deficiency at serum 25(OH)D concentrations less than 30 nmol/L (12 ng/mL; see Table 1 for definitions of "deficiency" and "inadequacy") [1]. Some people are potentially at risk of inadequacy at 30 to 50 nmol/L (12–20 ng/mL). Levels of 50 nmol/L (20 ng/mL) or more are sufficient for most people. In contrast, the Endocrine Society stated that, for clinical practice, a serum 25(OH)D concentration of more than 75 nmol/L (30 ng/mL) is necessary to maximize the effect of vitamin D on calcium, bone, and muscle metabolism [11,12]. The FNB committee also noted that serum concentrations greater than 125 nmol/L (50 ng/mL) can be associated with adverse effects [1] (Table 1).  
  
Table 1: Serum 25-Hydroxyvitamin D [25(OH)D] Concentrations and Health [1] nmol/L\* ng/mL\* Health status <30 <12 Associated with vitamin D deficiency, which can lead to rickets in infants and children and osteomalacia in adults 30 to <50 12 to <20 Generally considered inadequate for bone and overall health in healthy individuals ≥50 ≥20 Generally considered adequate for bone and overall health in healthy individuals >125 >50 Linked to potential adverse effects, particularly at >150 nmol/L (>60 ng/mL)  
  
\*Serum concentrations of 25(OH)D are reported in both nanomoles per liter (nmol/L) and nanograms per milliliter (ng/mL). One nmol/L = 0.4 ng/mL, and 1 ng/mL = 2.5 nmol/L.  
  
Optimal serum concentrations of 25(OH)D for bone and general health have not been established because they are likely to vary by stage of life, by race and ethnicity, and with each physiological measure used [1,13,14]. In addition, although 25(OH)D levels rise in response to increased vitamin D intake, the relationship is nonlinear [1]. The amount of increase varies, for example, by baseline serum levels and duration of supplementation.  
  
Recommended Intakes  
  
Intake recommendations for vitamin D and other nutrients are provided in the Dietary Reference Intakes (DRIs) developed by expert committees of NASEM [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:  
  
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.  
  
An FNB committee established RDAs for vitamin D to indicate daily intakes sufficient to maintain bone health and normal calcium metabolism in healthy people. RDAs for vitamin D are listed in both micrograms (mcg) and international units (IU); 1 mcg vitamin D is equal to 40 IU (Table 2). Even though sunlight is a major source of vitamin D for some people, the FNB based the vitamin D RDAs on the assumption that people receive minimal sun exposure [1]. For infants, the FNB committee developed AIs based on the amount of vitamin D that maintains serum 25(OH)D levels above 20 ng/mL (50 nmol/L) and supports bone development.  
  
Table 2: Recommended Dietary Allowances (RDAs) for Vitamin D [1] Age Male Female Pregnancy Lactation 0-12 months\* 10 mcg  
  
(400 IU) 10 mcg  
  
(400 IU) 1–13 years 15 mcg  
  
(600 IU) 15 mcg  
  
(600 IU) 14–18 years 15 mcg  
  
(600 IU) 15 mcg  
  
(600 IU) 15 mcg  
  
(600 IU) 15 mcg  
  
(600 IU) 19–50 years 15 mcg  
  
(600 IU) 15 mcg  
  
(600 IU) 15 mcg  
  
(600 IU) 15 mcg  
  
(600 IU) 51–70 years 15 mcg  
  
(600 IU) 15 mcg  
  
(600 IU) >70 years 20 mcg  
  
(800 IU) 20 mcg  
  
(800 IU)  
  
\*Adequate Intake (AI)  
  
Many other countries around the world and some professional societies have somewhat different guidelines for vitamin D intakes [15]. These differences are a result of an incomplete understanding of the biology and clinical implications of vitamin D, different purposes for the guidelines (e.g., for public health in a healthy population or for clinical practice), and/or the use in some guidelines of observational studies in addition to randomized clinical trials to establish recommendations [9,15]. The Endocrine Society states, for example, that to maintain serum 25(OH)D levels above 75 nmol/L (30 ng/mL), adults might need at least 37.5 to 50 mcg (1,500–2,000 IU)/day of supplemental vitamin D, and children and adolescents might need at least 25 mcg (1,000 IU)/day [11]. In contrast, the United Kingdom government recommends intakes of 10 mcg (400 IU)/day for its citizens aged 4 years and older [16].  
  
Sources of Vitamin D  
  
Food  
  
Few foods naturally contain vitamin D. The flesh of fatty fish (such as trout, salmon, tuna, and mackerel) and fish liver oils are among the best sources [17,1]. An animal’s diet affects the amount of vitamin D in its tissues. Beef liver, egg yolks, and cheese have small amounts of vitamin D, primarily in the form of vitamin D 3 and its metabolite 25(OH)D 3 . Mushrooms provide variable amounts of vitamin D 2 [17]. Some mushrooms available on the market have been treated with UV light to increase their levels of vitamin D 2 . In addition, the Food and Drug Administration (FDA) has approved UV-treated mushroom powder as a food additive for use as a source of vitamin D 2 in food products [18]. Very limited evidence suggests no substantial differences in the bioavailability of vitamin D from various foods [19].  
  
Animal-based foods typically provide some vitamin D in the form of 25(OH)D in addition to vitamin D 3 . The impact of this form on vitamin D status is an emerging area of research. Studies show that 25(OH)D appears to be approximately five times more potent than the parent vitamin for raising serum 25(OH)D concentrations [17,20,21]. One study found that when the 25(OH)D content of beef, pork, chicken, turkey, and eggs is taken into account, the total amount of vitamin D in the food is 2 to 18 times higher than the amount in the parent vitamin alone, depending on the food [20].  
  
Fortified foods provide most of the vitamin D in American diets [1,22]. For example, almost all of the U.S. milk supply is voluntarily fortified with about 3 mcg/cup (120 IU), usually in the form of vitamin D 3 [23]. In Canada, milk must be fortified with 0.88–1.0 mcg/100 mL (35–40 IU), and the required amount for margarine is at least 13.25 mcg/100 g (530 IU). Other dairy products made from milk, such as cheese and ice cream, are not usually fortified in the United States or Canada. Plant milk alternatives (such as beverages made from soy, almond, or oats) are often fortified with similar amounts of vitamin D to those in fortified cow's milk (about 3 mcg [120 IU]/cup); the Nutrition Facts label lists the actual amount [24]. Ready-to-eat breakfast cereals often contain added vitamin D, as do some brands of orange juice, yogurt, margarine, and other food products.  
  
The United States mandates the fortification of infant formula with 1–2.5 mcg/100 kcal (40–100 IU) vitamin D; 1–2 mcg/100 kcal (40–80 IU) is the required amount in Canada [1].  
  
A variety of foods and their vitamin D levels per serving are listed in Table 3.  
  
Table 3: Vitamin D Content of Selected Foods [25] Food Micrograms  
  
(mcg) per  
  
serving International  
  
Units (IU)  
  
per serving Percent DV\* Cod liver oil, 1 tablespoon 34.0 1,360 170 Trout (rainbow), farmed, cooked, 3 ounces 16.2 645 81 Salmon (sockeye), cooked, 3 ounces 14.2 570 71 Mushrooms, white, raw, sliced, exposed to UV light, ½ cup 9.2 366 46 Milk, 2% milkfat, vitamin D fortified, 1 cup 2.9 120 15 Soy, almond, and oat milks, vitamin D fortified, various brands, 1 cup 2.5-3.6 100-144 13-18 Ready-to-eat cereal, fortified with 10% of the DV for vitamin D, 1 serving 2.0 80 10 Sardines (Atlantic), canned in oil, drained, 2 sardines 1.2 46 6 Egg, 1 large, scrambled\*\* 1.1 44 6 Liver, beef, braised, 3 ounces 1.0 42 5 Tuna fish (light), canned in water, drained, 3 ounces 1.0 40 5 Cheese, cheddar, 1.5 ounce 0.4 17 2 Mushrooms, portabella, raw, diced, ½ cup 0.1 4 1 Chicken breast, roasted, 3 ounces 0.1 4 1 Beef, ground, 90% lean, broiled, 3 ounces 0 1.7 0 Broccoli, raw, chopped, ½ cup 0 0 0 Carrots, raw, chopped, ½ cup 0 0 0 Almonds, dry roasted, 1 ounce 0 0 0 Apple, large 0 0 0 Banana, large 0 0 0 Rice, brown, long-grain, cooked, 1 cup 0 0 0 Whole wheat bread, 1 slice 0 0 0 Lentils, boiled, ½ cup 0 0 0 Sunflower seeds, roasted, ½ cup 0 0 0 Edamame, shelled, cooked, ½ cup 0 0 0  
  
\* DV = Daily Value. The 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 vitamin D is 20 mcg (800 IU) for adults and children aged 4 years and older [ 26 ]. The labels must list vitamin D content in mcg per serving and have the option of also listing the amount in IUs in parentheses. 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.\*\* Vitamin D is in the yolk.  
  
The U.S. Department of Agriculture’s (USDA’s) FoodData Central lists the nutrient content of many foods and provides a comprehensive list of foods containing vitamin D arranged by nutrient content and by food name. However, FoodData Central does not include the amounts of 25(OH)D in foods.  
  
Sun exposure  
  
Most people in the world meet at least some of their vitamin D needs through exposure to sunlight [1]. Type B UV (UVB) radiation with a wavelength of approximately 290–320 nanometers penetrates uncovered skin and converts cutaneous 7-dehydrocholesterol to previtamin D 3 , which in turn becomes vitamin D 3 . Season, time of day, length of day, cloud cover, smog, skin melanin content, and sunscreen are among the factors that affect UV radiation exposure and vitamin D synthesis. Older people and people with dark skin are less able to produce vitamin D from sunlight [1]. UVB radiation does not penetrate glass, so exposure to sunshine indoors through a window does not produce vitamin D [27].  
  
The factors that affect UV radiation exposure, individual responsiveness, and uncertainties about the amount of sun exposure needed to maintain adequate vitamin D levels make it difficult to provide guidelines on how much sun exposure is required for sufficient vitamin D synthesis [15,28]. Some expert bodies and vitamin D researchers suggest, for example, that approximately 5–30 minutes of sun exposure, particularly between 10 a.m. and 4 p.m., either daily or at least twice a week to the face, arms, hands, and legs without sunscreen usually leads to sufficient vitamin D synthesis [13,15,28]. Moderate use of commercial tanning beds that emit 2% to 6% UVB radiation is also effective [13,29].  
  
But despite the importance of the sun for vitamin D synthesis, limiting skin exposure to sunlight and UV radiation from tanning beds is prudent [28]. UV radiation is a carcinogen, and UV exposure is the most preventable cause of skin cancer. Federal agencies and national organizations advise taking photoprotective measures to reduce the risk of skin cancer, including using sunscreen with a sun protection factor (SPF) of 15 or higher, whenever people are exposed to the sun [28,30]. Sunscreens with an SPF of 8 or more appear to block vitamin D-producing UV rays. In practice, however, people usually do not apply sufficient amounts of sunscreen, cover all sun-exposed skin, or reapply sunscreen regularly. Their skin probably synthesizes some vitamin D, even with typically applied sunscreen amounts [1,28].  
  
Dietary supplements  
  
Dietary supplements can contain vitamins D 2 or D 3 . Vitamin D 2 is manufactured using UV irradiation of ergosterol in yeast, and vitamin D 3 is typically produced with irradiation of 7-dehydrocholesterol from lanolin obtained from the wool of sheep [13,31]. An animal-free version of vitamin D3 sourced from lichen is also available [32]. People who avoid all animal-sourced products can contact dietary supplement manufacturers to ask about their sourcing and processing techniques.  
  
Both vitamins D2 and D3 raise serum 25(OH)D levels, and they seem to have equivalent ability to cure rickets [4]. In addition, most steps in the metabolism and actions of vitamins D 2 and D 3 are identical. However, most evidence indicates that vitamin D 3 increases serum 25(OH)D levels to a greater extent and maintains these higher levels longer than vitamin D 2 , even though both forms are well absorbed in the gut [33-36].  
  
Some studies have used dietary supplements containing the 25(OH)D 3 form of vitamin D. Per equivalent microgram dose, 25(OH)D 3 is three to five times as potent as vitamin D 3 [37,38]. However, no 25(OH)D 3 dietary supplements appear to be available to consumers on the U.S. market at this time [32].  
  
Vitamin D Intakes and Status  
  
Most people in the United States consume less than recommended amounts of vitamin D. An analysis of data from the 2015–2016 National Health and Nutrition Examination Survey (NHANES) found that average daily vitamin D intakes from foods and beverages were 5.1 mcg (204 IU) in men, 4.2 mcg (168 IU) in women, and 4.9 mcg (196 IU) in children aged 2–19 years [39]. In fact, 2013–2016 NHANES data showed that 92% of men, more than 97% of women, and 94% of people aged 1 year and older ingested less than the EAR of 10 mcg (400 IU) of vitamin D from food and beverages [40].  
  
The analysis of 2015–2016 data also showed that 28% of all individuals aged 2 years and older in the United States took a dietary supplement containing vitamin D [39]. In addition, 26% of participants aged 2–5 years and 14% of those aged 6–11 years took supplements; rates increased with age from 10% of those aged 12–19 years to 49% of men and 59% of women aged 60 and older. Total vitamin D intakes were three times higher with supplement use than with diet alone; the mean intake from foods and beverages alone for individuals aged 2 and older was 4.8 mcg (192 IU) but increased to 19.9 mcg (796 IU) when dietary supplements were included.  
  
Some people take very high doses of vitamin D supplements. In 2013–2014, an estimated 3.2% of the U.S. adult population took supplements containing 100 mcg (4,000 IU) or more vitamin D [41].  
  
One might expect a large proportion of the U.S. population to have vitamin D inadequacy on the basis of vitamin D intakes from foods, beverages, and even dietary supplements. However, comparing vitamin D intakes to serum 25(OH)D levels is problematic. One reason is that sun exposure affects vitamin D status, so serum 25(OH)D levels are usually higher than would be predicted on the basis of vitamin D dietary intakes alone [1]. Another reason is that animal foods contain some 25(OH)D. This form of vitamin D is not included in intake surveys and is considerably more potent than vitamins D 2 or D 3 at raising serum 25(OH)D levels [42].  
  
An analysis of NHANES 2011–2014 data on serum 25(OH)D levels found that most people in the United States aged 1 year and older had sufficient vitamin D intakes according to the FNB thresholds [43]. However, 18% were at risk of inadequacy (levels of 30–49 nmol/L [12–19.6 ng/mL]), and 5% were at risk of deficiency (levels below 30 nmol/L [12 ng/mL]). Four percent had levels higher than 125 nmol/L (50 ng/mL). Proportions at risk of deficiency were lowest among children aged 1–5 years (0.5%), peaked at 7.6% in adults aged 20–39 years, and fell to 2.9% among adults aged 60 years and older; patterns were similar for risks of inadequacy. Rates of deficiency varied by race and ethnicity: 17.5% of non-Hispanic Blacks were at risk of vitamin D deficiency, as were 7.6% of non-Hispanic Asians, 5.9% of Hispanics, and 2.1% of non-Hispanic White people. Again, the pattern was similar for the risk of inadequacy. Vitamin D status in the United States remained stable in the decade between 2003–2004 and 2013–2014.  
  
Vitamin D Deficiency  
  
People can develop vitamin D deficiency when usual intakes are lower over time than recommended levels, exposure to sunlight is limited, the kidneys cannot convert 25(OH)D to its active form, or absorption of vitamin D from the digestive tract is inadequate. Diets low in vitamin D are more common in people who have milk allergy or lactose intolerance and those who consume an ovo-vegetarian or vegan diet [1].  
  
In children, vitamin D deficiency is manifested as rickets, a disease characterized by a failure of bone tissue to become properly mineralized, resulting in soft bones and skeletal deformities [44]. In addition to bone deformities and pain, severe rickets can cause failure to thrive, developmental delay, hypocalcemic seizures, tetanic spasms, cardiomyopathy, and dental abnormalities [45,46].  
  
Prolonged exclusive breastfeeding without vitamin D supplementation can cause rickets in infants, and, in the United States, rickets is most common among breastfed Black infants and children [47]. In one Minnesota county, the incidence rate of rickets in children younger than 3 years in the decade beginning in 2000 was 24.1 per 100,000 [48]. Rickets occurred mainly in Black children who were breastfed longer, were born with low birthweight, weighed less, and were shorter than other children. The incidence rate of rickets in the infants and children (younger than 7) seen by 2,325 pediatricians throughout Canada was 2.9 per 100,000 in 2002–2004, and almost all patients with rickets had been breastfed [49].  
  
The fortification of milk (a good source of calcium) and other staples, such as breakfast cereals and margarine, with vitamin D beginning in the 1930s along with the use of cod liver oil made rickets rare in the United States [28,50]. However, the incidence of rickets is increasing globally, even in the United States and Europe, especially among immigrants from African, Middle-Eastern, and Asian countries [51]. Possible explanations for this increase include genetic differences in vitamin D metabolism, dietary preferences, and behaviors that lead to less sun exposure [45,46].  
  
In adults and adolescents, vitamin D deficiency can lead to osteomalacia, in which existing bone is incompletely or defectively mineralized during the remodeling process, resulting in weak bones [46]. Signs and symptoms of osteomalacia are similar to those of rickets and include bone deformities and pain, hypocalcemic seizures, tetanic spasms, and dental abnormalities [45].  
  
Screening for vitamin D status is becoming a more common part of the routine laboratory bloodwork ordered by primary-care physicians, irrespective of any indications for this practice [6,52-54]. No studies have examined whether such screening for vitamin D deficiency results in improved health outcomes [55]. The U.S. Preventive Services Task Force (USPSTF) found insufficient evidence to assess the benefits and harms of screening for vitamin D deficiency in asymptomatic adults [6]. It added that no national professional organization recommends population screening for vitamin D deficiency.  
  
Groups at Risk of Vitamin D Inadequacy  
  
Obtaining sufficient vitamin D from natural (nonfortified) food sources alone is difficult. For many people, consuming vitamin D-fortified foods and exposing themselves to some sunlight are essential for maintaining a healthy vitamin D status. However, some groups might need dietary supplements to meet their vitamin D requirements. The following groups are among those most likely to have inadequate vitamin D status.  
  
Breastfed infants  
  
Consumption of human milk alone does not ordinarily enable infants to meet vitamin D requirements, because it provides less than 0.6 to 2.0 mcg/L (25 to 78 IU/L) [1,56,57]. The vitamin D content of human milk is related to the mother’s vitamin D status; studies suggest that the breastmilk of mothers who take daily supplements containing at least 50 mcg (2,000 IU) vitamin D 3 have higher levels of the nutrient [57,58].  
  
Although UVB exposure can produce vitamin D in infants, the American Academy of Pediatrics (AAP) advises parents to keep infants younger than 6 months out of direct sunlight, dress them in protective clothing and hats, and apply sunscreen on small areas of exposed skin when sun exposure is unavoidable [59]. The AAP recommends 10 mcg (400 IU)/day vitamin D supplements for exclusively and partially breastfed infants starting shortly after birth and lasting until they are weaned and consume at least 1,000 mL/day vitamin D-fortified formula or whole milk [57]. The AAP also recommends 10 mcg (400 IU)/day supplemental vitamin D for all infants who are not breastfed and ingest less than 1,000 mL/day vitamin D-fortified formula or milk. An analysis of NHANES 2009–2016 data found that only 20.5% of breastfed infants and 31.1% of infants who were not breastfed ingested these recommended amounts of supplements [60].  
  
Older adults  
  
Older adults are at increased risk of developing vitamin D insufficiency, partly because the skin's ability to synthesize vitamin D declines with age [1,61]. In addition, older adults are likely to spend more time than younger people indoors, and they might have inadequate dietary intakes of the vitamin [1].  
  
People with limited sun exposure  
  
Homebound individuals; people who wear long robes, dresses, or head coverings for religious reasons; and people with occupations that limit sun exposure are among the groups that are unlikely to obtain adequate amounts of vitamin D from sunlight [62]. The use of sunscreen also limits vitamin D synthesis from sunlight. However, because the extent and frequency of sunscreen use are unknown, the role that sunscreen may play in reducing vitamin D synthesis is unclear [1].  
  
People with dark skin  
  
Greater amounts of the pigment melanin in the epidermal layer of the skin result in darker skin and reduce the skin’s ability to produce vitamin D from sunlight [1]. Black Americans, for example, typically have lower serum 25(OH)D levels than White Americans. However, whether these lower levels in persons with dark skin have significant health consequences is not clear [14]. Those of African American ancestry, for example, have lower rates of bone fracture and osteoporosis than do Whites (see the section below on bone health and osteoporosis).  
  
People with conditions that limit fat absorption  
  
Because vitamin D is fat soluble, its absorption depends on the gut’s ability to absorb dietary fat [4]. Fat malabsorption is associated with medical conditions that include some forms of liver disease, cystic fibrosis, celiac disease, Crohn’s disease, and ulcerative colitis [1,63]. In addition to having an increased risk of vitamin D deficiency, people with these conditions might not eat certain foods, such as dairy products (many of which are fortified with vitamin D), or eat only small amounts of these foods. Individuals who have difficulty absorbing dietary fat might therefore require vitamin D supplementation [63].  
  
People with obesity or who have undergone gastric bypass surgery  
  
Individuals with a body mass index (BMI) of 30 or more have lower serum 25(OH)D levels than individuals without obesity. Obesity does not affect the skin’s capacity to synthesize vitamin D. However, greater amounts of subcutaneous fat sequester more of the vitamin [1]. People with obesity might need greater intakes of vitamin D to achieve 25(OH)D levels similar to those of people with normal weight [1,64,65].  
  
Individuals with obesity who have undergone gastric bypass surgery can also become vitamin D deficient. In this procedure, part of the upper small intestine, where vitamin D is absorbed, is bypassed, and vitamin D that is mobilized into the bloodstream from fat stores might not raise 25(OH)D to adequate levels over time [66,67]. Various expert groups—including the American Association of Metabolic and Bariatric Surgery, The Obesity Society, and the British Obesity and Metabolic Surgery Society—have developed guidelines on vitamin D screening, monitoring, and replacement before and after bariatric surgery [66,68]  
  
Vitamin D and Health  
  
The FNB committee that established DRIs for vitamin D found that the evidence was inadequate or too contradictory to conclude that the vitamin had any effect on a long list of potential health outcomes (e.g., on resistance to chronic diseases or functional measures), except for measures related to bone health. Similarly, in a review of data from nearly 250 studies published between 2009 and 2013, the Agency for Healthcare Research and Quality concluded that no relationship could be firmly established between vitamin D and health outcomes other than bone health [69]. However, because research has been conducted on vitamin D and numerous health outcomes, this section focuses on seven diseases, conditions, and interventions in which vitamin D might be involved: bone health and osteoporosis, cancer, cardiovascular disease (CVD), depression, multiple sclerosis (MS), type 2 diabetes, and weight loss.  
  
Most of the studies described in this section measured serum 25(OH)D levels using various methods that were not standardized by comparing them to the best methods. Use of unstandardized 25(OH)D measures can raise questions about the accuracy of the results and about the validity of conclusions drawn from studies that use such measures and, especially, from meta-analyses that pool data from many studies that use different unstandardized measures [5,9,70]. More information about assay standardization is available from the Vitamin D Standardization Program webpage.  
  
Bone health and osteoporosis  
  
Bone is constantly being remodeled. However, as people age—and particularly in women during menopause—bone breakdown rates overtake rates of bone building. Over time, bone density can decline, and osteoporosis can eventually develop [71].  
  
More than 53 million adults in the United States have or are at risk of developing osteoporosis, which is characterized by low bone mass and structural deterioration of bone tissue that increases bone fragility and the risk of bone fractures [72]. About 2.3 million osteoporotic fractures occurred in the United States in 2015 [73]. Osteoporosis is, in part, a long-term effect of calcium and/or vitamin D insufficiency, in contrast to rickets and osteomalacia, which result from vitamin D deficiency. Osteoporosis is most often associated with inadequate calcium intakes, but insufficient vitamin D intakes contribute to osteoporosis by reducing calcium absorption [1].  
  
Bone health also depends on support from the surrounding muscles to assist with balance and postural sway and thereby reduce the risk of falling. Vitamin D is also needed for the normal development and growth of muscle fibers. In addition, inadequate vitamin D levels can adversely affect muscle strength and lead to muscle weakness and pain (myopathy) [1].  
  
Most trials of the effects of vitamin D supplements on bone health also included calcium supplements, so isolating the effects of each nutrient is difficult. In addition, studies provided different amounts of nutrients and used different dosing schedules.  
  
Clinical trial evidence on older adults  
  
Among postmenopausal women and older men, many clinical trials have shown that supplements of both vitamin D and calcium result in small increases in bone mineral density throughout the skeleton [1,74]. They also help reduce fracture rates in institutionalized older people. However, the evidence on the impact of vitamin D and calcium supplements on fractures in community-dwelling individuals is inconsistent.  
  
The USPSTF evaluated 11 randomized clinical trials of vitamin D and/or calcium supplementation in a total of 51,419 healthy, community-dwelling adults aged 50 years and older who did not have osteoporosis, vitamin D deficiency, or prior fractures [75,76]. It concluded that the current evidence was insufficient to evaluate the benefits and harms of supplementation to prevent fractures. In addition, the USPSTF recommended against supplementation with 10 mcg (400 IU) or less of vitamin D and 1,000 mg or less of calcium to prevent fractures in this population, but it could not determine the balance of benefits and harms from higher doses.  
  
The USPSTF also reviewed the seven published studies on the effects of vitamin D supplementation (two of them also included calcium supplementation) on the risk of falls in community-dwelling adults aged 65 years or older who did not have osteoporosis or vitamin D deficiency. It concluded "with moderate certainty" that vitamin D supplementation does not reduce the numbers of falls or injuries, such as fractures, resulting from falls [77,78]. Another recent systematic review also found that vitamin D and calcium supplements had no beneficial effects on fractures, falls, or bone mineral density [79,80]. In contrast, a meta-analysis of 6 trials in 49,282 older adults found that daily vitamin D (10 or 20 mcg [400 IU or 800 IU]/day) and calcium (800 or 1,200 mg/day) supplementation for a mean of 5.9 years reduced the risk of any fracture by 6% and of hip fracture by 16% [81].  
  
One systematic review and meta-analysis of 11 randomized, controlled trials published through 2018 of vitamin D supplementation alone (10–20 mcg [400–800 IU]/day or more at least every week or as rarely as once a year) for 9 months to 5 years found that the supplements provided no protection from fractures in 34,243 older adults [81].  
  
Vitamin D supplements for bone health in minority populations  
  
Bone mineral density, bone mass, and fracture risk are correlated with serum 25(OH)D levels in White Americans and Mexican Americans, but not in Black Americans [14,82]. Factors such as adiposity, skin pigmentation, vitamin D binding protein polymorphisms, and genetics contribute to differences in 25(OH)D levels between Black and White Americans.  
  
One clinical trial randomized 260 Black women aged 60 years and older (mean age 68.2 years) to receive 60 to 120 mcg (2,400 to 4,800 IU) per day vitamin D 3 supplementation to maintain serum 25(OH)D levels above 75 nmol/L (30 ng/mL) for 3 years [83]. The results showed no association between 25(OH)D levels or vitamin D dose and the risk of falling in the 184 participants who completed the study. In fact, Black Americans might have a greater risk than White Americans of falls and fractures with daily vitamin D intakes of 50 mcg (2,000 IU) or more [14]. Furthermore, the bone health of older Black American women does not appear to benefit from raising serum 25(OH)D levels beyond 50 nmol/L (20 ng/mL) [83].  
  
Vitamin D supplements and muscle function  
  
Studies examining the effects of supplemental vitamin D on muscle strength and on rate of decline in muscle function have had inconsistent results [55]. One recent clinical trial, for example, randomized 78 frail and near-frail adults aged 65 years and older to receive 20 mcg (800 IU) vitamin D 3 , 10 mcg 25(OH)D, or placebo daily for 6 months. The groups showed no significant differences in measures of muscle strength or performance [84]. Another study randomized 100 community-dwelling men and women aged 60 years and older (most were White) with serum 25(OH)D levels of 50 nmol/L (20 ng/ml) or less to 800 IU vitamin D 3 or placebo for 1 year [85]. Participants in the treatment group whose serum 25(OH)D level was less than 70 nmol/L (28 ng/ml) after 4 months received an additional 800 IU/day vitamin D 3 . Despite increasing serum 25(OH)D levels to an average of more than 80 nmol/L (32 ng/ml), vitamin D supplementation did not affect lower-extremity power, strength, or lean mass.  
  
Conclusions about vitamin D supplements and bone health  
  
All adults should consume recommended amounts of vitamin D and calcium from foods and supplements if needed. Older women and men should consult their healthcare providers about their needs for both nutrients as part of an overall plan to maintain bone health and to prevent or treat osteoporosis.  
  
Cancer  
  
Laboratory and animal studies suggest that vitamin D might inhibit carcinogenesis and slow tumor progression by, for example, promoting cell differentiation and inhibiting metastasis. Vitamin D might also have anti-inflammatory, immunomodulatory, proapoptotic, and antiangiogenic effects [1,86]. Observational studies and clinical trials provide mixed evidence on whether vitamin D intakes or serum levels affect cancer incidence, progression, or mortality risk.  
  
Total cancer incidence and mortality  
  
Some observational studies show associations between low serum levels of 25(OH)D and increased risks of cancer incidence and death. In a meta-analysis of 16 prospective cohort studies in a total of 137,567 participants who had 8,345 diagnoses of cancer, 5,755 participants died from cancer [87]. A 50 nmol/L (20 ng/mL) increase in 25(OH)D levels was associated with an 11% reduction in total cancer incidence rates and, in women but not men, a 24% reduction in cancer mortality rates. A meta-analysis of prospective studies that evaluated the association between serum 25(OH)D levels and cancer incidence (8 studies) or cancer mortality (16 studies) found that cancer risk decreased by 7% and cancer mortality rates decreased by 2% with each 20 nmol/L (8 ng/mL) increase in serum 25(OH)D levels [88]. Importantly, not all observational studies found higher vitamin D status to be beneficial, and the studies varied considerably in study populations, baseline comorbidities, and measurement of vitamin D levels.  
  
Clinical trial evidence provides some support for the observational findings. For example, three meta-analyses of clinical trial evidence found that vitamin D supplementation does not affect cancer incidence but does significantly reduce total cancer mortality rates by 12–13% [89-91]. In the most recent meta-analysis, 10 randomized clinical trials (including the Vitamin D and Omega-3 Trial [VITAL] trial described below) that included 6,537 cancer cases provided 10 to 50 mcg (400 to 2,000 IU) vitamin D 3 daily (six trials) or 500 mcg (20,000 IU)/week to 12,500 mcg (500,000 IU)/year boluses of vitamin D 3 (four trials) [90]. The study reports included 3–10 years of followup data. The vitamin D supplements were associated with serum 25(OH)D levels of 54 to 135 nmol/L (21.6 to 54 ng/mL). Vitamin D supplementation reduced cancer mortality rates by 13%, and most of the benefit occurred with daily supplementation.  
  
The largest clinical trial, VITAL, to investigate the effects of vitamin D supplementation on the primary prevention of cancer in the general population gave 50 mcg (2,000 IU)/day vitamin D 3 supplements with or without 1,000 mg/day marine omega-3 fatty acids or a placebo for a median of 5.3 years [92]. The study included 25,871 men aged 50 years and older and women aged 55 years and older who had no history of cancer, and most had adequate serum 25(OH)D levels at baseline. Rates of breast, prostate, and colorectal cancer did not differ significantly between the vitamin D and placebo groups. However, normal-weight participants had greater reductions in cancer incidence and mortality rates than those with overweight or obesity.  
  
A few studies have examined the effect of vitamin D supplementation on specific cancers. Below are brief descriptions of studies of vitamin D and its association with, or effect on, breast, colorectal, lung, pancreatic, and prostate cancers.  
  
Breast cancer  
  
Some observational studies support an inverse association between 25(OH)D levels and breast cancer risk and mortality, but others do not [93-96]. The Women's Health Initiative clinical trial randomized 36,282 postmenopausal women to receive 400 IU vitamin D 3 plus 1,000 mg calcium daily or a placebo for a mean of 7 years [97]. The vitamin D 3 and calcium supplements did not reduce breast cancer incidence, and 25(OH)D levels at the start of the study were not associated with breast cancer risk [98].  
  
In a subsequent investigation for 4.9 years after the study's end, women who had taken the vitamin D and calcium supplements (many of whom continued to take them) had an 18% lower risk of in situ (noninvasive) breast cancer [99]. However, women with vitamin D intakes higher than 15 mcg (600 IU)/day at the start of the trial and who received the supplements experienced a 28% increased risk of invasive (but not in situ) breast cancer.  
  
Colorectal cancer  
  
A large case-control study included 5,706 individuals who developed colorectal cancer and whose 25(OH)D levels were assessed a median of 5.5 years from blood draw to cancer diagnosis and 7,105 matched controls [100]. The results showed an association between 25(OH)D levels lower than 30 nmol/L (12 ng/mL) and a 31% higher colorectal cancer risk. Levels of 75 to less than 87.5 nmol/L (30 to less than 35 ng/mL) and 87.5 to less than 100 nmol/L (35 to less than 40 ng/mL) were associated with a 19% and 27% lower risk, respectively. The association was substantially stronger in women.  
  
In the Women's Health Initiative clinical trial (described above), vitamin D 3 and calcium supplements had no effect on rates of colorectal cancer. In a subsequent investigation for 4.9 years after the study's end, women who had taken the vitamin D and calcium supplements (many of whom continued to take them) still had the same colorectal cancer risk as those who received placebo [99].  
  
Another study included 2,259 healthy individuals aged 45 to 75 years who had had one or more serrated polyps (precursor lesions to colorectal cancer) that had been removed [101]. These participants were randomized to take 25 mcg (1,000 IU) vitamin D 3 , 1,200 mg calcium, both supplements, or a placebo daily for 3–5 years, followed by an additional 3–5 years of observation after participants stopped the treatment. Vitamin D alone did not significantly affect the development of new serrated polyps, but the combination of vitamin D with calcium increased the risk almost fourfold. The VITAL trial found no association between vitamin D supplementation and the risk of colorectal adenomas or serrated polyps [102].  
  
Lung cancer  
  
A study of cohorts that included 5,313 participants who developed lung cancer and 5,313 matched controls found no association between serum 25(OH)D levels and risk of subsequent lung cancer, even when the investigators analyzed the data by sex, age, race and ethnicity, and smoking status [103].  
  
Pancreatic cancer  
  
One study comparing 738 men who developed pancreatic cancer to 738 matched controls found no relationship between serum 25(OH)D levels and risk of pancreatic cancer [104]. Another study that compared 200 male smokers in Finland with pancreatic cancer to 400 matched controls found that participants in the highest quintile of 25(OH)D levels (more than 65.5 nmol/L [26.2 ng/mL]) had a threefold greater risk of developing pancreatic cancer over 16.7 years than those in the lowest quintile (less than 32 nmol/L [12.8 ng/mL]) [105]. An investigation that pooled data from 10 studies of cancer in 12,205 men and women found that concentrations of 25(OH)D greater than 75 nmol/L (30 ng/mL) but less than 100 nmol/L (40 ng/mL) did not reduce the risk of pancreatic cancer. However, the results did show an increased risk of pancreatic cancer with 25(OH)D levels of 100 nmol/L (40 ng/mL) or above [106].  
  
Prostate cancer  
  
Research to date provides mixed evidence on whether levels of 25(OH)D are associated with the development of prostate cancer. Several studies published in 2014 suggested that high levels of 25(OH)D might increase the risk of prostate cancer. For example, a meta-analysis of 21 studies that included 11,941 men with prostate cancer and 13,870 controls found a 17% higher risk of prostate cancer for participants with higher levels of 25(OH)D [107]. What constituted a "higher" level varied by study but was typically at least 75 nmol/L (30 ng/mL). In a cohort of 4,733 men, of which 1,731 had prostate cancer, those with 25(OH)D levels of 45–70 nmol/L (18–28 ng/mL) had a significantly lower risk of the disease than men with either lower or higher values [108]. This U-shaped association was most pronounced for men with the most aggressive forms of prostate cancer. A case-control analysis of 1,695 cases of prostate cancer and 1,682 controls found no associations between 25(OH)D levels and prostate cancer risk [109]. However, higher serum 25(OH)D levels (at a cut point of 75 nmol/L [30 ng/mL]) were linked to a modestly higher risk of slow-growth prostate cancer and a more substantial lower risk of aggressive disease.  
  
Since 2014, however, several published studies and meta-analyses have found no relationship between 25(OH)D levels and prostate cancer risk [110,111]. For example, an analysis was conducted of 19 prospective studies that provided data on prediagnostic levels of 25(OH)D for 13,462 men who developed prostate cancer and 20,261 control participants [112]. Vitamin D deficiency or insufficiency did not increase the risk of prostate cancer, and higher 25(OH)D concentrations were not associated with a lower risk.  
  
Several studies have examined whether levels of 25(OH)D in men with prostate cancer are associated with a lower risk of death from the disease or from any cause. One study included 1,119 men treated for prostate cancer whose plasma 25(OH)D levels were measured 4.9 to 8.6 years after their diagnosis. Among the 198 participants who died (41 deaths were due to prostate cancer), 25(OH)D levels were not associated with risk of death from prostate cancer or any cause [113]. However, a meta-analysis of 7 cohort studies that included 7,808 men with prostate cancer found higher 25(OH)D levels to be significantly associated with lower mortality rates from prostate cancer or any other cause [114]. A dose-response analysis found that each 20 nmol/L [8 ng/mL] increase in 25(OH)D was associated with a 9% lower risk of both all-cause and prostate cancer-specific mortality.  
  
For men with prostate cancer, whether vitamin D supplementation lengthens cancer-related survival is not clear. A meta-analysis of 3 randomized controlled trials in 1,273 men with prostate cancer found no significant differences in total mortality rates between those receiving vitamin D supplementation (from 10 mcg [400 IU]/day for 28 days to 45 mcg [1,800 IU] given in three doses total at 2-week intervals) and those receiving a placebo [115].  
  
Conclusions about vitamin D and cancer  
  
The USPSTF stated that, due to insufficient evidence, it was unable to assess the balance of benefits and harms of supplemental vitamin D to prevent cancer [116]. Taken together, studies to date do not indicate that vitamin D with or without calcium supplementation reduces the incidence of cancer, but adequate or higher 25(OH)D levels might reduce cancer mortality rates. Further research is needed to determine whether vitamin D inadequacy increases cancer risk, whether greater exposure to the nutrient can prevent cancer, and whether some individuals could have an increased risk of cancer because of their vitamin D status over time.  
  
Cardiovascular disease  
  
Vitamin D helps regulate the renin-angiotensin-aldosterone system (and thereby blood pressure), vascular cell growth, and inflammatory and fibrotic pathways [117]. Vitamin D deficiency is associated with vascular dysfunction, arterial stiffening, left ventricular hypertrophy, and hyperlipidemia [118]. For these reasons, vitamin D has been linked to heart health and risk of CVD.  
  
Observational studies support an association between higher serum 25(OH)D levels and a lower risk of CVD incidence and mortality. For example, a meta-analysis included 34 observational studies that followed 180,667 participants (mean age greater than 50 years) for 1.3 to more than 32 years. The results showed that baseline serum 25(OH)D levels were inversely associated with total number of CVD events (including myocardial infarction, ischemic heart disease, heart failure, and stroke) and mortality risk [119]. Overall, the risk of CVD events was 10% lower for each 25 nmol/L (10 ng/mL) increase in serum 25(OH)D.  
  
Another large observational study that followed 247,574 adults from Denmark for 0–7 years found that levels of 25(OH)D that were low (about 12.5 nmol/L [5 ng/mL]) and high (about 125 nmol/L [50 ng/mL]) were associated with a greater risk of mortality from CVD, stroke, and acute myocardial infarction [120]. Other meta-analyses of prospective studies have found associations between lower vitamin D status measured by serum 25(OH)D levels or vitamin D intakes and an increased risk of ischemic stroke, ischemic heart disease, myocardial infarction, and early death [121,122].  
  
In contrast to the observational studies, clinical trials have provided little support for the hypothesis that supplemental vitamin D reduces the risk of CVD or CVD mortality. For example, a 3-year trial in New Zealand randomized 5,110 adults (mean age 65.9 years) to a single dose of 5,000 mcg (200,000 IU) vitamin D 3 followed by 2,500 mcg (100,000 IU) each month or a placebo for a median of 3.3 years [123]. Vitamin D supplementation had no effect on the incidence rate of myocardial infarction, angina, heart failure, arrhythmia, arteriosclerosis, stroke, venous thrombosis, or death from CVD. Similarly, the VITAL clinical trial described above found that vitamin D supplements did not significantly decrease rates of heart attacks, strokes, coronary revascularization, or deaths from cardiovascular causes [92]. Moreover, the effects did not vary by baseline serum 25(OH)D levels or whether participants took the trial’s omega-3 supplement in addition to vitamin D.  
  
However, another clinical trial designed to investigate bone fracture risk found that 800 IU/day vitamin D 3 (with or without calcium) or a placebo in 5,292 adults aged 70 years and older for a median of 6.2 years offered protection from cardiac failure, but not myocardial infarction or stroke [124].  
  
High serum cholesterol levels and hypertension are two of the main risk factors for CVD. The data on supplemental vitamin D and cholesterol levels are mixed, as shown in one meta-analysis of 41 clinical trials in a total of 3,434 participants (mean age 55 years). The results of this analysis showed that 0.5 mcg (20 IU) to 214 mcg (8,570 IU)/day vitamin D supplementation (mean of 2,795 IU) for 6 weeks to 3 years reduced serum total cholesterol, low-density lipoprotein cholesterol, and triglyceride levels, but not high-density lipoprotein cholesterol levels [125].  
  
Studies of the effects of vitamin D supplements on hypertension have also had mixed findings. In one meta-analysis of 46 clinical trials that included 4,541 participants, vitamin D supplements (typically 40 mcg [1,600 IU]/day or less) for a minimum of 4 weeks had no significant effects on systolic or diastolic blood pressure [126]. In contrast, another meta-analysis of 30 clinical trials in 4,744 participants (mean age 54.5 years) that administered 5 mcg (200 IU) to 300 mcg (12,000 IU)/day vitamin D 3 for a mean of 5.6 months showed that more than 20 mcg (800 IU)/day significantly reduced systolic and diastolic blood pressure in normal-weight participants who had hypertension [127]. However, more than 20 mcg (800 IU)/day vitamin D 3 , when taken with calcium supplements, significantly increased blood pressure in participants with overweight and obesity. Another meta-analysis of genetic studies in 146,581 participants (primarily adults) found that a low vitamin D status increased blood pressure and hypertension risk in people with genetic variants associated with low endogenous production of 25(OH)D [128].  
  
Overall, clinical trials show that vitamin D supplementation does not reduce CVD risk, even for people with low 25(OH)D status (below 20 nmol/L [12 ng/mL]) at baseline [92,123].  
  
Depression  
  
Vitamin D is involved in various brain processes, and vitamin D receptors are present on neurons and glia in areas of the brain thought to be involved in the pathophysiology of depression [129].  
  
A systematic review and meta-analysis of 14 observational studies that included a total of 31,424 adults (mean age ranging from 27.5 to 77 years) found an association between deficient or low levels of 25(OH)D and depression [129].  
  
Clinical trials, however, do not support these findings. For example, a meta-analysis of 9 trials with a total of 4,923 adult participants diagnosed with depression or depressive symptoms found no significant reduction in symptoms after supplementation with vitamin D [130]. The trials administered different amounts of vitamin D (ranging from 10 mcg [400 IU]/day to 1,000 mcg [40,000 IU]/week). They also had different study durations (5 days to 5 years), mean participant ages (range, 22 years to 75 years), and baseline 25(OH)D levels; furthermore, some but not all studies administered concurrent antidepressant medications.  
  
Three trials conducted since that meta-analysis also found no effect of vitamin D supplementation on depressive symptoms. One trial included 206 adults (mean age 52 years) who were randomized to take a bolus dose of 2,500 mcg (100,000 IU) vitamin D 3 followed by 500 mcg (20,000 IU)/week or a placebo for 4 months [131]. Most participants had minimal or mild depression, had a low mean baseline 25(OH) level of 33.8 nmol/L (13.5 ng/mL), and were not taking antidepressants. The second trial included 155 adults aged 60–80 years who had clinically relevant depressive symptoms, no major depressive disorder, and serum 25(OH)D levels less than 50 to 70 nmol/L (20 to 28 ng/mL) depending on the season; in addition, they were not taking antidepressants [132,133]. Participants were randomized to take either 30 mcg (1,200 IU)/day vitamin D 3 or a placebo for 1 year. In the VITAL trial described above, 16,657 men and women 50 years of age and older with no history of depression and 1,696 with an increased risk of recurrent depression (that had not been medically treated for the past 2 years) were randomized to take 50 mcg (2,000 IU)/day vitamin D 3 (with or without fish oil) or a placebo for a median of 5.3 years [134]. The groups showed no significant differences in the incidence and recurrent rates of depression, clinically relevant depressive symptoms, or changes in mood scores.  
  
Overall, clinical trials did not find that vitamin D supplements helped prevent or treat depressive symptoms or mild depression, especially in middle-aged to older adults who were not taking prescription antidepressants. No studies have evaluated whether vitamin D supplements may benefit individuals under medical care for clinical depression who have low or deficient 25(OH)D levels and are taking antidepressant medication.  
  
Multiple sclerosis  
  
MS is an autoimmune disease of the central nervous system that damages the myelin sheath surrounding and protecting nerve cells in the brain and spinal cord. This damage hinders or blocks messages between the brain and body, leading to clinical features, such as vision loss, motor weakness, spasticity, ataxia, tremor, sensory loss, and cognitive impairment [135,136]. Some people with MS eventually lose the ability to write, speak, or walk.  
  
The geographical distribution of MS around the world is unequal. Few people near the equator develop the disease, whereas the prevalence is higher further north and south. This uneven distribution has led to speculation that lower vitamin D levels in people who have less sunlight exposure might predispose them to the disease [136].  
  
Many epidemiological and genetic studies have shown an association between MS and low 25(OH)D levels before and after the disease begins [136]. Observational studies suggest that adequate vitamin D levels might reduce the risk of contracting MS and, once MS is present, decrease the risk of relapse and slow the disease's progression [137]. One study, for example, tested 25(OH)D levels in 1,092 women in Finland an average of 9 years before their MS diagnosis and compared their outcomes with those of 2,123 similar women who did not develop MS [138]. More than half the women who developed MS had deficient or insufficient vitamin D levels. Women with 25(OH)D levels of less than 30 nmol/L (12 ng/mL) had a 43% higher MS risk than women with levels of 50 nmol/L (20 ng/mL) or higher. Among the women with two or more serum 25(OH)D samples taken before diagnosis (which reduced random measurement variation), a 50 nmol/L increase in 25(OH)D was associated with a 41% reduced risk of MS, and 25(OH)D levels less than 30 nmol/L were associated with an MS risk that was twice as high as levels of 50 nmol/L or higher.  
  
Two earlier prospective studies of similar design—one in the United States with 444 non-Hispanic White individuals [139] and the other with 576 individuals in northern Sweden [140]—found that levels of 25(OH)D greater than 99.1 nmol/L (39.6 ng/mL) and at least 75 nmol/L (30 ng/mL), respectively, were associated with a 61–62% lower risk of MS.  
  
No clinical trials have examined whether vitamin D supplementation can prevent the onset of MS, but several have investigated whether supplemental vitamin D can help manage the disease. A 2018 Cochrane review analyzed 12 such trials that had a total of 933 participants with MS; the reviewers judged all of these trials to be of low quality [136]. Overall, vitamin D supplementation, when compared with placebo administration, had no effect on relevant clinical outcomes, such as recurrent relapse or worsened disability.  
  
Experts have reached no firm consensus on whether vitamin D can help prevent MS given the lack of clinical trial evidence [141]. In addition, studies have not consistently shown that vitamin D supplementation tempers the signs and symptoms of active MS or reduces rates of relapse.  
  
Type 2 diabetes  
  
Vitamin D plays a role in glucose metabolism. It stimulates insulin secretion via the vitamin D receptor on pancreatic beta cells and reduces peripheral insulin resistance through vitamin D receptors in the muscles and liver [142]. Vitamin D might be involved in the pathophysiology of type 2 diabetes through its effects on glucose metabolism and insulin signaling as well as its ability to reduce inflammation and improve pancreatic beta-cell function [143,144].  
  
Observational studies have linked lower serum 25(OH)D levels to an increased risk of diabetes, but their results might have been confounded by the fact that many participants were overweight or had obesity and were therefore more predisposed to developing diabetes and having lower 25(OH)D levels [1]. A review of 71 observational studies in adults with and without type 2 diabetes from 16 countries found a significant inverse relationship between vitamin D status and blood sugar levels in participants who did and did not have diabetes [145].  
  
In contrast to observational studies, clinical trials provide little support for the benefits of vitamin D supplementation for glucose homeostasis. One trial included 65 adult men and women (mean age 32 years) with overweight or obesity who were otherwise healthy, did not have diabetes, and had low serum vitamin D levels (at or below 50 nmol/L [20 ng/mL]) [146]. The investigators randomly assigned participants to receive either a bolus oral dose of 2,500 mcg (100,000 IU) vitamin D 3 followed by 100 mcg (4,000 IU)/day or a placebo for 16 weeks. In the 54 participants who completed the study, vitamin D supplementation did not improve insulin sensitivity or insulin secretion in comparison with placebo.  
  
One systematic review and meta-analysis evaluated 35 clinical trials that included 43,407 adults with normal glucose tolerance, prediabetes, or type 2 diabetes who received a median of 83 mcg (3,332 IU)/day vitamin D supplements or placebo for a median of 16 weeks [147]. Vitamin D had no significant effects on glucose homeostasis, insulin secretion or resistance, or hemoglobin A1c levels (a measure of average blood sugar levels over the previous 2–3 months), irrespective of the study population, vitamin D dose, or trial quality.  
  
Several trials have investigated whether vitamin D supplementation can prevent the transition from prediabetes to diabetes in patients with adequate 25(OH)D levels, and all have had negative results. In a trial in Norway, 511 men and women aged 25–80 years (mean age 62 years) with prediabetes received 500 mcg (20,000 IU) vitamin D 3 or a placebo each week for 5 years [148]. The results showed no significant differences in rates of progression to type 2 diabetes; in serum glucose, insulin, or hemoglobin A1c levels; or in measures of insulin resistance. At baseline, participants had an adequate mean serum 25(OH)D level of 60 nmol/L (24 ng/mL).  
  
The largest trial to date of vitamin D supplements for diabetes prevention randomized 2,423 men and women aged 25 years and older (mean age 60 years) with prediabetes and overweight or obesity (mean BMI of 32.1) to 100 mcg (4,000 IU)/day vitamin D 3 or placebo for a median of 2.5 years [144]. Most participants (78%) had adequate serum levels of vitamin D at baseline (at least 50 nmol/L [20 ng/mL]). Vitamin D did not significantly prevent the development of diabetes in comparison with placebo. However, a post hoc analysis showed a 62% lower incidence of diabetes among participants with low baseline serum 25(OH)D levels (less than 30 nmol/L [12 ng/mL]) who took the vitamin D supplement than among those who took the placebo [144,149].  
  
Studies have also assessed the value of vitamin D supplementation for managing diabetes, and they have found that the vitamin offers limited benefits. One meta-analysis of 20 clinical trials compared the effects of 0.5 mcg (20 IU)/day to 1,250 mcg (50,000 IU)/week vitamin D supplementation for 2–6 months with those of placebo on glycemic control in 2,703 adults from around the world who had diabetes [142]. The vitamin D reduced insulin resistance to a small but significant degree, especially in people taking more than 50 mcg (2,000 IU)/day who were vitamin D deficient at baseline, had good glycemic control, did not have obesity, and were of Middle Eastern ethnicity. However, the supplementation had no significant effects on fasting blood glucose, hemoglobin A1c, or fasting insulin levels.  
  
Clinical trials to date provide little evidence that vitamin D supplementation helps maintain glucose homeostasis, reduces the risk of progression from prediabetes to type 2 diabetes, or helps manage the disease, particularly in vitamin D-replete individuals.  
  
Weight loss  
  
Observational studies indicate that greater body weights are associated with lower vitamin D status, and individuals with obesity frequently have marginal or deficient circulating 25(OH)D levels [150]. However, clinical trials do not support a cause-and-effect relationship between vitamin D and weight loss.  
  
A systematic review and meta-analysis of 15 weight-loss intervention studies that used caloric restriction, exercise, or both, but not necessarily vitamin D supplementation or other treatments, found that people who lost weight had significantly greater increases in serum 25(OH)D levels than those who maintained their weight [151]. In another study, 10 mcg (400 IU)/day vitamin D and 1,000 mg/day calcium supplementation slightly, but significantly, reduced weight gain amounts in comparison with placebo in postmenopausal women, especially those with a baseline total calcium intake of less than 1,200 mg/day [152]. However, a meta-analysis of 12 vitamin D supplementation trials (including 5 in which body composition measurements were primary outcomes) found that vitamin D supplements without calorie restriction did not affect body weight or fat mass when the results were compared with those of placebo [153].  
  
Overall, the available research suggests that consuming higher amounts of vitamin D or taking vitamin D supplements does not promote weight loss.  
  
Health Risks from Excessive Vitamin D  
  
Excess amounts of vitamin D are toxic. Because vitamin D increases calcium absorption in the gastrointestinal tract, vitamin D toxicity results in marked hypercalcemia (total calcium greater than 11.1 mg/dL, beyond the normal range of 8.4 to 10.2 mg/dL), hypercalciuria, and high serum 25(OH)D levels (typically greater than 375 nmol/l [150 ng/mL]) [154]. Hypercalcemia, in turn, can lead to nausea, vomiting, muscle weakness, neuropsychiatric disturbances, pain, loss of appetite, dehydration, polyuria, excessive thirst, and kidney stones.  
  
In extreme cases, vitamin D toxicity causes renal failure, calcification of soft tissues throughout the body (including in coronary vessels and heart valves), cardiac arrhythmias, and even death. Vitamin D toxicity has been caused by consumption of dietary supplements that contained excessive vitamin D amounts because of manufacturing errors, that were taken inappropriately or in excessive amounts, or that were incorrectly prescribed by physicians, [154-156].  
  
Experts do not believe that excessive sun exposure results in vitamin D toxicity because thermal activation of previtamin D 3 in the skin gives rise to various non-vitamin D forms that limit formation of vitamin D 3 . Some vitamin D 3 is also converted to nonactive forms [1]. However, frequent use of tanning beds, which provide artificial UV radiation, can lead to 25(OH)D levels well above 375–500 nmol/L (150–200 ng/mL) [157-159].  
  
The combination of high intakes of calcium (about 2,100 mg/day from food and supplements) with moderate amounts of vitamin D (about 19 mcg [765 IU]/day from food and supplements) increased the risk of kidney stones by 17% over 7 years among 36,282 postmenopausal women who were randomly assigned to take 1,000 mg/day calcium and 10 mcg (400 IU)/day vitamin D or a placebo [160]. However, other, shorter (from 24 weeks to 5 years) clinical trials of vitamin D supplementation alone or with calcium in adults found greater risks of hypercalcemia and hypercalciuria, but not of kidney stones [161,162].  
  
The FNB established ULs for vitamin D in 2010 (Table 4) [1]. While acknowledging that signs and symptoms of toxicity are unlikely at daily intakes below 250 mcg (10,000 IU), the FNB noted that even vitamin D intakes lower than the ULs might have adverse health effects over time. The FNB recommended avoiding serum 25(OH)D levels above approximately 125–150 nmol/L (50–60 ng/mL), and it found that even lower serum levels (approximately 75–120 nmol/L [30–48 ng/mL]) are associated with increases in rates of all-cause mortality, risk of cancer at some sites (e.g., pancreas), risk of cardiovascular events, and number of falls and fractures among older adults.  
  
Table 4: Tolerable Upper Intake Levels (ULs) for Vitamin D [1] Age Male Female Pregnancy Lactation 0-6 months 25 mcg (1,000 IU) 25 mcg (1,000 IU) 7–12 months 38 mcg (1,500 IU) 38 mcg (1,500 IU) 1–3 years 63 mcg (2,500 IU) 63 mcg (2,500 IU) 4–8 years 75 mcg (3,000 IU) 75 mcg (3,000 IU) 9–18 years 100 mcg (4,000 IU) 100 mcg (4,000 IU) 100 mcg (4,000 IU) 100 mcg (4,000 IU) 19+ years 100 mcg (4,000 IU) 100 mcg (4,000 IU) 100 mcg (4,000 IU) 100 mcg (4,000 IU)  
  
Interactions with Medications  
  
Vitamin D supplements may interact with several types of medications. A few examples are provided below. Individuals taking these and other medications on a regular basis should discuss their vitamin D intakes and status with their healthcare providers.  
  
Orlistat  
  
The weight-loss drug orlistat (Xenical® and alli®), together with a reduced-fat diet, can reduce the absorption of vitamin D from food and supplements, leading to lower 25(OH)D levels [163-166].  
  
Statins  
  
Statin medications reduce cholesterol synthesis. Because endogenous vitamin D is derived from cholesterol, statins may also reduce vitamin D synthesis [166]. In addition, high intakes of vitamin D, especially from supplements, might reduce the potency of atorvastatin (Lipitor®), lovastatin (Altoprev® and Mevacor®), and simvastatin (FloLipid™ and Zocor®), because these statins and vitamin D appear to compete for the same metabolizing enzyme [166-169].  
  
Steroids  
  
Corticosteroid medications, such as prednisone (Deltasone®, Rayos®, and Sterapred®), are often prescribed to reduce inflammation. These medications can reduce calcium absorption and impair vitamin D metabolism [170-172]. In the NHANES 2001–2006 survey, 25(OH)D deficiency (less than 25 nmol/L [10 ng/mL]) was more than twice as common among children and adults who reported oral steroid use (11%) than in nonusers (5%) [173].  
  
Thiazide diuretics  
  
Thiazide diuretics (e.g., Hygroton®, Lozol®, and Microzide®) decrease urinary calcium excretion. The combination of these diuretics with vitamin D supplements (which increase intestinal calcium absorption) might lead to hypercalcemia, especially among older adults and individuals with compromised renal function or hyperparathyroidism [166,174,175].  
  
Vitamin D 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 and the U.S. Department of Agriculture's MyPlate.  
  
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. Milk, many ready-to-eat cereals, and some brands of yogurt and orange juice are fortified with vitamin D. Cheese naturally contains small amounts of vitamin D. Vitamin D is added to some margarines.  
  
Includes a variety of protein foods such as lean meats; poultry; eggs; seafood; beans, peas, and lentils; nuts and seeds; and soy products. Fatty fish, such as salmon, tuna, and mackerel, are very good sources of vitamin D. Beef liver and egg yolks have small amounts of vitamin D.  
  
Limits foods and beverages higher in added sugars, saturated fat, and sodium.  
  
  
  
Limits alcoholic beverages.  
  
  
  
Stays within your daily calorie needs.  
  
  
https://www.hsph.harvard.edu/nutritionsource/vitamin-d/  
TITLE: Vitamin D  
META DESCRIPTION: For most people, the best way to get enough vitamin D is taking a supplement because it is hard to eat enough through food. Learn more.  
META KEYWORDS:   
H1: Vitamin D,   
H2: Explore:, Explore Other Vitamins and Minerals, Support The Nutrition Source,   
BOLD/STRONG: RDA:, UL:,  ,  ,  ,  , Multiple Sclerosis  
, Type 1 Diabetes  
, Flu and the Common Cold  
, Tuberculosis  
, Other Autoimmune Conditions  
,  , Deficiency, Toxicity,   
Italic: : RDA:, UL:,  ,  ,  ,  , Multiple Sclerosis  
, Type 1 Diabetes  
, Flu and the Common Cold  
, Tuberculosis  
, Other A, utoimmune Conditions  
, Archives of Internal Medicine, Deficiency, Toxicity,  , New England Journal of Medicine., Archives of pediatrics & adolescent medicine, The Journal of steroid biochemistry and molecular biology, Archives of Disease in Childhood, The Journal of pediatrics, Pediatrics, The Journal of Clinical Endocrinology & Metabolism, Jama, Annals of internal medicine, Journal of Bone and Mineral Research, Archives of internal medicine, Cochrane Database of Systematic Reviews, Jama, Journal of the American Geriatrics Society, Archives of internal medicine, BMJ, Jama, International journal of epidemiology, Annals of epidemiology, JNCI: Journal of the National Cancer Institute, Alimentary pharmacology & therapeutics, Journal of the National Cancer Institute, American journal of preventive medicine, Journal of Bone and Mineral Research, American journal of epidemiology, Nutrition and cancer, Cancer Epidemiology and Prevention Biomarkers, The Journal of steroid biochemistry and molecular biology, Archives of Internal Medicine, Cancer causes & control, Cancer Epidemiology and Prevention Biomarkers, New England Journal of Medicine, JNCI: Journal of the National Cancer Institute, N Engl J Med, N Engl J Med, New England Journal of Medicine, Annals of Oncology, J Clin Endocrinol Metab, Circulation research, Molecular aspects of medicine, Archives of internal medicine, Journal of Clinical Endocrinology & Metabolism, Stroke, Circulation, Archives of internal medicine, The Journal of Clinical Endocrinology & Metabolism, Endocrinol Metab Clin North Am, Diabetes care, N Engl J Med, European journal of neurology, International Journal of Environmental Studies, Neurology, Jama, Neurology, Neurology, JAMA neurology, JAMA neurology, InSeminars in neurology, The Lancet, The Lancet, American journal of epidemiology, Epidemiology & Infection, Epidemiology & Infection, Archives of internal medicine, American journal of clinical nutrition, BMJ, Nature medicine, International journal of epidemiology, Nutrition reviews, Archives of internal medicine, Archives of Internal Medicine, The American journal of clinical nutrition, Proceedings of the Nutrition Society, Am J Clin Nutr, N Engl J Med, BMJ, Last reviewed January 2022,   
TEXT: Vitamin D is both a nutrient we eat and a hormone our bodies make. It is a fat-soluble vitamin that has long been known to help the body absorb and retain calcium and phosphorus; both are critical for building bone. Also, laboratory studies show that vitamin D can reduce cancer cell growth, help control infections and reduce inflammation. Many of the body’s organs and tissues have receptors for vitamin D, which suggest important roles beyond bone health, and scientists are actively investigating other possible functions.  
  
Few foods naturally contain vitamin D, though some foods are fortified with the vitamin. For most people, the best way to get enough vitamin D is taking a supplement because it is hard to eat enough through food. Vitamin D supplements are available in two forms: vitamin D2 (“ergocalciferol” or pre-vitamin D) and vitamin D3 (“cholecalciferol”). Both are also naturally occurring forms that are produced in the presence of the sun’s ultraviolet-B (UVB) rays, hence its nickname, “the sunshine vitamin,” but D2 is produced in plants and fungi and D3 in animals, including humans. Vitamin D production in the skin is the primary natural source of vitamin D, but many people have insufficient levels because they live in places where sunlight is limited in winter, or because they have limited sun exposure due to being inside much of the time. Also, people with darker skin tend to have lower blood levels of vitamin D because the pigment (melanin) acts like a shade, reducing production of vitamin D (and also reducing damaging effects of sunlight on skin, including skin cancer).  
  
Recommended Amounts  
  
The Recommended Dietary Allowance for vitamin D provides the daily amount needed to maintain healthy bones and normal calcium metabolism in healthy people. It assumes minimal sun exposure.  
  
RDA: The Recommended Dietary Allowance for adults 19 years and older is 600 IU (15 mcg) daily for men and women, and for adults >70 years it is 800 IU (20 mcg) daily.  
  
UL: The Tolerable Upper Intake Level is the maximum daily intake unlikely to cause harmful effects on health. The UL for vitamin D for adults and children ages 9+ is 4,000 IU (100 mcg).  
  
Many people may not be meeting the minimum requirement for the vitamin. NHANES data found that the median intake of vitamin D from food and supplements in women ages 51 to 71 years was 308 IU daily, but only 140 IU from food alone (including fortified products). [1] Worldwide, an estimated 1 billion people have inadequate levels of vitamin D in their blood, and deficiencies can be found in all ethnicities and age groups. [2-4] In industrialized countries, doctors are seeing the resurgence of rickets, the bone-weakening disease that had been largely eradicated through vitamin D fortification. [5-7] There is scientific debate about how much vitamin D people need each day and what the optimal serum levels should be to prevent disease. The Institute of Medicine (IOM) released in November 2010 recommendations increasing the daily vitamin D intake for children and adults in the U.S. and Canada, to 600 IU per day. [1] The report also increased the upper limit from 2,000 to 4,000 IU per day. Although some groups such as The Endocrine Society recommend 1,500 to 2,000 IU daily to reach adequate serum levels of vitamin D, the IOM felt there was not enough evidence to establish a cause and effect link with vitamin D and health benefits other than for bone health. Since that time, new evidence has supported other benefits of consuming an adequate amount of vitamin D, although there is still not consensus on the amount considered to be adequate.  
  
Vitamin D and Health  
  
The role of vitamin D in disease prevention is a popular area of research, but clear answers about the benefit of taking amounts beyond the RDA are not conclusive. Although observational studies see a strong connection with lower rates of certain diseases in populations that live in sunnier climates or have higher serum levels of vitamin D, clinical trials that give people vitamin D supplements to affect a particular disease are still inconclusive. This may be due to different study designs, differences in the absorption rates of vitamin D in different populations, and different dosages given to participants. Learn more about the research on vitamin D and specific health conditions and diseases:  
  
Bone health and muscle strength Several studies link low vitamin D blood levels with an increased risk of fractures in older adults, and they suggest that vitamin D supplementation may prevent such fractures—as long as it is taken in a high enough dose. [8-12] A meta-analysis of 12 randomized controlled trials that included more than 42,000 people 65+ years of age, most of them women, looked at vitamin D supplementation with or without calcium, and with calcium or a placebo. Researchers found that higher intakes of vitamin D supplements—about 500-800 IU per day—reduced hip and non-spine fractures by about 20%, while lower intakes (400 IU or less) failed to offer any fracture prevention benefit. [12] A systematic review looked at the effect of vitamin D supplements taken with or without calcium on the prevention of hip fractures (primary outcome) and fractures of any type (secondary outcome) in older men and postmenopausal women 65+ years of age. It included 53 clinical trials with 91,791 participants who lived independently or in a nursing home or hospital. It did not find a strong association between vitamin D supplements alone and prevention of fractures of any type. However, it did find a small protective effect from all types of fractures when vitamin D was taken with calcium. All of the trials used vitamin D supplements containing 800 IU or less. [13] Vitamin D may also help increase muscle strength, which in turn helps to prevent falls, a common problem that leads to substantial disability and death in older people. [14–16] A combined analysis of multiple studies found that taking 700 to 1,000 IU of vitamin D per day lowered the risk of falls by 19%, but taking 200 to 600 IU per day did not offer any such protection. [17] Though taking 800-1,000 IU daily may have benefit for bone health in older adults, it is important to be cautious of very high dosage supplements. A clinical trial that gave women 70+ years of age a once-yearly dosage of vitamin D at 500,000 IU for five years caused a 15% increased risk of falls and a 26% higher fracture risk than women who received a placebo. [18] It was speculated that super-saturating the body with a very high dose given infrequently may have actually promoted lower blood levels of the active form of vitamin D that might not have occurred with smaller, more frequent doses. [13]  
  
Cancer Nearly 30 years ago, researchers noticed an intriguing relationship between colon cancer deaths and geographic location: People who lived at higher latitudes, such as in the northern U.S., had higher rates of death from colon cancer than people who lived closer to the equator. [19] Many scientific hypotheses about vitamin D and disease stem from studies that have compared solar radiation and disease rates in different countries. These studies can be a good starting point for other research but don’t provide the most definitive information. The sun’s UVB rays are weaker at higher latitudes, and in turn, people’s vitamin D blood levels in these locales tend to be lower. This led to the hypothesis that low vitamin D levels might somehow increase colon cancer risk. [3] Animal and laboratory studies have found that vitamin D can inhibit the development of tumors and slow the growth of existing tumors including those from the breast, ovary, colon, prostate, and brain. In humans, epidemiological studies show that higher serum levels of vitamin D are associated with substantially lower rates of colon, pancreatic, prostate, and other cancers, with the evidence strongest for colorectal cancer. [20-32] However, clinical trials have not found a consistent association: The Women’s Health Initiative trial, which followed roughly 36,000 women for an average of seven years, failed to find any reduction in colon or breast cancer risk in women who received daily supplements of 400 IU of vitamin D and 1,000 mg of calcium, compared with those who received a placebo. [33,34] Limitations of the study were suggested: 1) the relatively low dose of vitamin D given, 2) some people in the placebo group decided on their own to take extra calcium and vitamin D supplements, minimizing the differences between the placebo group and the supplement group, and 3) about one-third of the women assigned to vitamin D did not take their supplements. 4) seven years may be too short to expect a reduction in cancer risk. [35,36] A large clinical trial called the VITamin D and OmegA-3 TriaL (VITAL) followed 25,871 men and women 50+ years of age free of any cancers at the start of the study who took either a 2,000 IU vitamin D supplement or placebo daily for a median of five years. [37] The findings did not show significantly different rates of breast, prostate, and colorectal cancer between the vitamin D and placebo groups. The authors noted that a longer follow-up period would be necessary to better assess potential effects of supplementation, as many cancers take at least 5-10 years to develop. Although vitamin D does not seem to be a major factor in reducing cancer incidence, evidence including that from randomized trials suggests that having higher vitamin D status may improve survival if one develops cancer. In the VITAL trial, a lower death rate from cancer was observed in those assigned to take vitamin D, and this benefit seemed to increase over time since starting on vitamin D. A meta-analysis of randomized trials of vitamin D, which included the VITAL study, found a 13% statistically significant lower risk of cancer mortality in those assigned to vitamin D compared to placebo. [38] These findings are consistent with observational data, which suggest that vitamin D may have a stronger effect on cancer progression than for incidence.  
  
Heart disease  
  
The heart is basically a large muscle, and like skeletal muscle, it has receptors for vitamin D. [39] Immune and inflammatory cells that play a role in cardiovascular disease conditions like atherosclerosis are regulated by vitamin D. [40] The vitamin also helps to keep arteries flexible and relaxed, which in turn helps to control high blood pressure. [41] In the Health Professionals Follow-up Study nearly 50,000 healthy men were followed for 10 years. [42] Those who had the lowest levels of vitamin D were twice as likely to have a heart attack as men who had the highest levels. Meta-analyses of epidemiological studies have found that people with the lowest serum levels of vitamin D had a significantly increased risk of strokes and any heart disease event compared with those with the highest levels. [40;43-46] However, taking vitamin D supplements has not been found to reduce cardiovascular risk. A meta-analysis of 51 clinical trials did not demonstrate that vitamin D supplementation lowered the risk of heart attack, stroke, or deaths from cardiovascular disease. [47] The VITamin D and OmegA-3 TriaL (VITAL) came to the same conclusion; it followed 25,871 men and women free of cardiovascular disease who took either a 2,000 IU vitamin D supplement or placebo daily for a median of five years. No association was found between taking the supplements and a lower risk of major cardiovascular events (heart attack, stroke, or death from cardiovascular causes) compared with the placebo. [37]  
  
Type 2 diabetes  
  
Vitamin D deficiency may negatively affect the biochemical pathways that lead to the development of Type 2 diabetes (T2DM), including impairment of beta cell function in the pancreas, insulin resistance, and inflammation. Prospective observational studies have shown that higher vitamin D blood levels are associated with lower rates of T2DM. [48] More than 83,000 women without diabetes at baseline were followed in the Nurses’ Health Study for the development of T2DM. Vitamin D and calcium intakes from diet and supplements were assessed throughout the 20-year study. [49] The authors found that when comparing the women with the highest intakes of vitamin D from supplements with women with the lowest intakes, there was a 13% lower risk of developing T2DM. The effect was even stronger when vitamin D was combined with calcium: there was a 33% lower risk of T2DM in women when comparing the highest intakes of calcium and vitamin D from supplements (>1,200 mg, >800 IU daily) with the lowest intakes (<600 mg, 400 IU). A randomized clinical trial gave 2,423 adults who had prediabetes either 4000 IU of vitamin D or a placebo daily for two years. The majority of participants did not have vitamin D deficiency at the start of the study. At two years, vitamin D blood levels in the supplement versus placebo group was 54.3 ng/mL versus 28.2 ng/mL, respectively, but no significant differences were observed in rates of T2DM at the 2.5 year follow-up. [50] The authors noted that a lack of effect of vitamin D may have been due to the majority of participants having vitamin D blood levels in a normal range of greater than 20 ng/mL, which is considered an acceptable level to reduce health risks. Notably, among the participants who had the lowest blood levels of vitamin D at the beginning of the study, vitamin D supplementation did reduce risk of diabetes. This is consistent with the important concept that taking additional vitamin D may not benefit those who already have adequate blood levels, but those with initially low blood levels may benefit.  
  
Immune function Vitamin D’s role in regulating the immune system has led scientists to explore two parallel research paths: Does vitamin D deficiency contribute to the development of multiple sclerosis, type 1 diabetes, and other so-called “autoimmune” diseases, where the body’s immune system attacks its own organs and tissues? And could vitamin D supplements help boost our body’s defenses to fight infectious disease, such as tuberculosis and seasonal flu? Multiple Sclerosis  
  
The rate of multiple sclerosis (MS) is increasing in both developed and developing countries, with an unclear cause. However, a person’s genetic background plus environmental factors including inadequate vitamin D and UVB exposure have been identified to increase risk. [51] Vitamin D was first proposed over 40 years ago as having a role in MS given observations at the time including that rates of MS were much higher far north (or far south) of the equator than in sunnier climates, and that geographic regions with diets high in fish had lower rates of MS. [52] A prospective study of dietary intake of vitamin D found women with daily intake above 400 IU had a 40% lower risk of MS. [53] In a study among healthy young adults in the US, white men and women with the highest vitamin D serum levels had a 62% lower risk of developing MS than those with the lowest vitamin D levels. [54] The study didn’t find this effect among black men and women, possibly because there were fewer black study participants and most of them had low vitamin D levels, making it harder to find any link between vitamin D and MS if one exists. Another prospective study in young adults from Sweden also found a 61% lower risk of MS with higher serum vitamin D levels; [55] and a prospective study among young Finnish women found that low serum vitamin D levels were associated with a 43% increased risk of MS. [56] In prospective studies of persons with MS, higher vitamin D levels have been associated with reduced disease activity and progression. [57,58] While several clinical trials are underway to examine vitamin D as a treatment in persons with MS, there are no clinical trials aimed at prevention of MS, likely because MS is a rare disease and the trial would need to be large and of long duration. Collectively, the current evidence suggests that low vitamin D may have a causal role in MS and if so, approximately 40% of cases may be prevented by correcting vitamin D insufficiency. [59] This conclusion has been strengthened substantially by recent evidence that genetically determined low levels of vitamin D predict higher risk of multiple sclerosis. Type 1 Diabetes  
  
Type 1 diabetes (T1D) is another disease that varies with geography—a child in Finland is about 400 times more likely to develop T1D than a child in Venezuela. [60] While this may largely be due to genetic differences, some studies suggest that T1D rates are lower in sunnier areas. Early evidence suggesting that vitamin D may play a role in T1D comes from a 30-year study that followed more than 10,000 Finnish children from birth: Children who regularly received vitamin D supplements during infancy had a nearly 90% lower risk of developing type 1 diabetes than those who did not receive supplements. [61] However, multiple studies examining the association between dietary vitamin D or trials supplementing children at high risk for T1D with vitamin D have produced mixed and inconclusive results [62] Approximately 40% of T1D cases begin in adulthood. A prospective study among healthy young adults in the US found that white individuals with the highest levels of serum vitamin D had a 44% lower risk of developing T1D in adulthood than those with the lowest levels. [63] No randomized controlled trials on vitamin D and adult onset T1D have been conducted, and it is not clear that they would be possible to conduct. More research is needed in this area. Flu and the Common Cold  
  
The flu virus wreaks the most havoc in the winter, abating in the summer months. This seasonality led a British doctor to hypothesize that a sunlight-related “seasonal stimulus” triggered influenza outbreaks. [64] More than 20 years after this initial hypothesis, several scientists published a paper suggesting that vitamin D may be the seasonal stimulus. [65] Among the evidence they cite: Vitamin D levels are lowest in the winter months. [65] The active form of vitamin D tempers the damaging inflammatory response of some white blood cells, while it also boosts immune cells’ production of microbe-fighting proteins. [65] Children who have vitamin D-deficiency rickets are more likely to get respiratory infections, while children exposed to sunlight seem to have fewer respiratory infections. [65] Adults who have low vitamin D levels are more likely to report having had a recent cough, cold, or upper respiratory tract infection. [66]  
  
A randomized controlled trial in Japanese school children tested whether taking daily vitamin D supplements would prevent seasonal flu. [67] The trial followed nearly 340 children for four months during the height of the winter flu season. Half of the study participants received pills that contained 1,200 IU of vitamin D; the other half received placebo pills. Researchers found that type A influenza rates in the vitamin D group were about 40% lower than in the placebo group; there was no significant difference in type B influenza rates. Although randomized controlled trials exploring the potential of vitamin D to prevent other acute respiratory infections have yielded mixed results, a large meta-analysis of individual participant data indicated that daily or weekly vitamin D supplementation lowers risk of acute respiratory infections. [68] This effect was particularly prominent for very deficient individuals. The findings from this large meta-analysis have raised the possibility that low vitamin D levels may also increase risk of or severity of novel coronavirus 2019 (COVID-19) infection. Although there is no direct evidence on this issue because this such a new disease, avoiding low levels of vitamin D makes sense for this and other reasons. Thus, if there is reason to believe that levels might be low, such as having darker skin or limited sun exposure, taking a supplement of 1000 or 2000 IU per day is reasonable. This amount is now part of many standard multiple vitamin supplements and inexpensive. More research is needed before we can definitively say that vitamin D protects against the flu and other acute respiratory infections. Even if vitamin D has some benefit, don’t skip your flu shot. And when it comes to limiting risk of COVID-19, it is important to practice careful social distancing and hand washing. Tuberculosis  
  
Before the advent of antibiotics, sunlight and sun lamps were part of the standard treatment for tuberculosis (TB). [69] More recent research suggests that the “sunshine vitamin” may be linked to TB risk. Several case-control studies, when analyzed together, suggest that people diagnosed with tuberculosis have lower vitamin D levels than healthy people of similar age and other characteristics. [70] Such studies do not follow individuals over time, so they cannot tell us whether vitamin D deficiency led to the increased TB risk or whether taking vitamin D supplements would prevent TB. There are also genetic differences in the receptor that binds vitamin D, and these differences may influence TB risk. [71] Again, more research is needed. Other Autoimmune Conditions  
  
The Vitamin D and Omega 3 trial (VITAL), a randomized double-blind placebo-controlled trial following more than 25,000 men and women ages 50 and older, found that taking vitamin D supplements (2,000 IU/day) for five years, or vitamin D supplements with marine omega-3 fatty acids (1,000 mg/day), reduced the incidence of autoimmune diseases by about 22%, compared with a placebo. Autoimmune conditions observed included rheumatoid arthritis, psoriasis, polymyalgia rheumatica, and autoimmune thyroid diseases (Hashimoto’s thyroiditis, Graves’ disease). [78] The doses in these supplements are widely available and generally well-tolerated. The authors recommended additional trials to test the effectiveness of these supplements in younger populations and those at high risk of developing autoimmune diseases.  
  
Risk of premature death  
  
A promising report in the Archives of Internal Medicine suggests that taking vitamin D supplements may reduce overall mortality rates: A combined analysis of multiple studies found that taking modest levels of vitamin D supplements was associated with a statistically significant 7% reduction in mortality from any cause. [72] The analysis looked at the findings from 18 randomized controlled trials that enrolled a total of nearly 60,000 study participants; most of the study participants took between 400 and 800 IU of vitamin D per day for an average of five years. Keep in mind that this analysis has several limitations, chief among them the fact that the studies it included were not designed to explore mortality in general, or explore specific causes of death. A recent meta-analysis suggests that this reduction in mortality is driven mostly by a reduction in cancer mortality. [38] More research is needed before any broad claims can be made about vitamin D and mortality. [73]  
  
Food Sources  
  
Few foods are naturally rich in vitamin D3. The best sources are the flesh of fatty fish and fish liver oils. Smaller amounts are found in egg yolks, cheese, and beef liver. Certain mushrooms contain some vitamin D2; in addition some commercially sold mushrooms contain higher amounts of D2 due to intentionally being exposed to high amounts of ultraviolet light. Many foods and supplements are fortified with vitamin D like dairy products and cereals.  
  
Cod liver oil  
  
Salmon  
  
Swordfish  
  
Tuna fish  
  
Orange juice fortified with vitamin D  
  
Dairy and plant milks fortified with vitamin D  
  
Sardines  
  
Beef liver  
  
Egg yolk  
  
Fortified cereals  
  
Is There a Difference Between Vitamin D3 and Vitamin D2 Supplements? If you purchase vitamin D supplements, you may see two different forms: vitamin D2 and vitamin D3. Vitamin D2 is made from plants and is found in fortified foods and some supplements. Vitamin D3 is naturally produced in the human body and is found in animal foods. There is ongoing debate whether vitamin D3 “cholecalciferol” is better than vitamin D2 “ergocalciferol” at increasing blood levels of the vitamin. A meta-analysis of randomized controlled trials that compared the effects of vitamin D2 and D3 supplements on blood levels found that D3 supplements tended to raise blood concentrations of the vitamin more and sustained those levels longer than D2. [74,75] Some experts cite vitamin D3 as the preferred form as it is naturally produced in the body and found in most foods that naturally contain the vitamin.  
  
Ultraviolet Light  
  
Vitamin D3 can be formed when a chemical reaction occurs in human skin, when a steroid called 7-dehydrocholesterol is broken down by the sun’s UVB light or so-called “tanning” rays. The amount of the vitamin absorbed can vary widely. The following are conditions that decrease exposure to UVB light and therefore lessen vitamin D absorption:  
  
Use of sunscreen; correctly applied sunscreen can reduce vitamin D absorption by more than 90%. [76]  
  
Wearing full clothing that covers the skin.  
  
Spending limited time outdoors.  
  
Darker skin tones due to having higher amounts of the pigment melanin, which acts as a type of natural sunscreen. [77]  
  
Older ages when there is a decrease in 7-dehydrocholesterol levels and changes in skin, and a population that is likely to spend more time indoors.  
  
Certain seasons and living in northern latitudes above the equator where UVB light is weaker. [76] In the northern hemisphere, people who live in Boston (U.S.), Edmonton (Canada), and Bergen (Norway) can’t make enough vitamin D from the sun for 4, 5, and 6 months out of the year, respectively. [76] In the southern hemisphere, residents of Buenos Aires (Argentina) and Cape Town (South Africa) make far less vitamin D from the sun during their winter months (June through August) than they can during their spring and summer months. [76] The body stores vitamin D from summer sun exposure, but it must last for many months. By late winter, many people in these higher-latitude locales are deficient. [77]  
  
Note that because ultraviolet rays can cause skin cancer, it is important to avoid excessive sun exposure and in general, tanning beds should not be used.  
  
Signs of Deficiency and Toxicity  
  
Deficiency  
  
Vitamin D deficiency may occur from a lack in the diet, poor absorption, or having a metabolic need for higher amounts. If one is not eating enough vitamin D and does not receive enough ultraviolet sun exposure over an extended period (see section above), a deficiency may arise. People who cannot tolerate or do not eat milk, eggs, and fish, such as those with a lactose intolerance or who follow a vegan diet, are at higher risk for a deficiency. Other people at high risk of vitamin D deficiency include:  
  
People with inflammatory bowel disease (ulcerative colitis, Crohn’s disease) or other conditions that disrupt the normal digestion of fat. Vitamin D is a fat-soluble vitamin that depends on the gut’s ability to absorb dietary fat.  
  
People who are obese tend to have lower blood vitamin D levels. Vitamin D accumulates in excess fat tissues but is not easily available for use by the body when needed. Higher doses of vitamin D supplementation may be needed to achieve a desirable blood level. Conversely, blood levels of vitamin D rise when obese people lose weight.  
  
People who have undergone gastric bypass surgery, which typically removes the upper part of the small intestine where vitamin D is absorbed.  
  
Conditions resulting from prolonged vitamin D deficiency:  
  
Rickets: A condition in infants and children of soft bones and skeletal deformities caused by failure of bone tissue to harden.  
  
Osteomalacia: A condition in adults of weak and softened bones that can be reversed with supplementation. This is different than osteoporosis, in which the bones are porous and brittle and the condition is irreversible.  
  
Toxicity  
  
Vitamin D toxicity most often occurs from taking supplements. The low amounts of the vitamin found in food are unlikely to reach a toxic level, and a high amount of sun exposure does not lead to toxicity because excess heat on the skin prevents D3 from forming. It is advised to not take daily vitamin D supplements containing more than 4,000 IU unless monitored under the supervision of your doctor.  
  
Symptoms of toxicity:  
  
Anorexia  
  
Weight loss  
  
Irregular heart beat  
  
Hardening of blood vessels and tissues due to increased blood levels of calcium, potentially leading to damage of the heart and kidneys  
  
Did You Know?  
  
Catching the sun’s rays in a sunny office or driving in a car unfortunately won’t help to obtain vitamin D as window glass completely blocks UVB ultraviolet light.  
  
Last reviewed January 2022  
  
Terms of Use  
  
The contents of this website are for educational purposes and are not intended to offer personal medical advice. You should seek the advice of your physician or other qualified health provider with any questions you may have regarding a medical condition. Never disregard professional medical advice or delay in seeking it because of something you have read on this website. The Nutrition Source does not recommend or endorse any products.  
  
  
https://www.nhs.uk/conditions/vitamins-and-minerals/vitamin-d/  
TITLE: Vitamin D  
META DESCRIPTION: Find out about vitamin D, including what it does, how much you need, and how to ensure you get enough.  
META KEYWORDS:   
H1:   
Vitamin D  
   
 -   
 Vitamins and minerals  
   
  
,   
H2: Contents, Good sources of vitamin D, How much vitamin D do I need?, Should I take a vitamin D supplement?, What happens if I take too much vitamin D?, Support links,   
BOLD/STRONG: Vitamin D helps regulate the amount of calcium and phosphate in the body.,   
Italic: :   
TEXT: Vitamin D helps regulate the amount of calcium and phosphate in the body. These nutrients are needed to keep bones, teeth and muscles healthy. A lack of vitamin D can lead to bone deformities such as rickets in children, and bone pain caused by a condition called osteomalacia in adults. Government advice is that everyone should consider taking a daily vitamin D supplement during the autumn and winter. People at high risk of not getting enough vitamin D, all children aged 1 to 4, and all babies (unless they're having more than 500ml of infant formula a day) should take a daily supplement throughout the year.  
  
Information: There have been some reports about vitamin D reducing the risk of coronavirus (COVID-19). But there is currently not enough evidence to support taking vitamin D solely to prevent or treat COVID-19.  
  
Good sources of vitamin D From about late March/early April to the end of September, most people should be able to make all the vitamin D they need from sunlight. The body creates vitamin D from direct sunlight on the skin when outdoors. But between October and early March we do not make enough vitamin D from sunlight. Read more about vitamin D and sunlight. Vitamin D is also found in a small number of foods. Sources include: oily fish – such as salmon, sardines, herring and mackerel  
  
red meat  
  
liver  
  
egg yolks  
  
fortified foods – such as some fat spreads and breakfast cereals Another source of vitamin D is dietary supplements. In the UK, cows' milk is generally not a good source of vitamin D because it is not fortified, as it is in some other countries.  
  
How much vitamin D do I need? From about late March/early April to the end of September, the majority of people should be able to make all the vitamin D they need from sunlight on their skin. Children from the age of 1 year and adults need 10 micrograms of vitamin D a day. This includes pregnant and breastfeeding women, and people at risk of vitamin D deficiency. Babies up to the age of 1 year need 8.5 to 10 micrograms of vitamin D a day. A microgram is 1,000 times smaller than a milligram (mg). The word microgram is sometimes written with the Greek symbol μ followed by the letter g (μg). Sometimes the amount of vitamin D is expressed as International Units (IU). 1 microgram of vitamin D is equal to 40 IU. So 10 micrograms of vitamin D is equal to 400 IU.  
  
Should I take a vitamin D supplement? Advice for adults and children over 4 years old During the autumn and winter, you need to get vitamin D from your diet because the sun is not strong enough for the body to make vitamin D. But since it's difficult for people to get enough vitamin D from food alone, everyone (including pregnant and breastfeeding women) should consider taking a daily supplement containing 10 micrograms of vitamin D during the autumn and winter. Between late March/early April to the end of September, most people can make all the vitamin D they need through sunlight on their skin and from a balanced diet. You may choose not to take a vitamin D supplement during these months. People at risk of vitamin D deficiency Some people will not make enough vitamin D from sunlight because they have very little or no sunshine exposure. The Department of Health and Social Care recommends that adults and children over 4 take a daily supplement containing 10 micrograms of vitamin D throughout the year if they: are not often outdoors – for example, if they're frail or housebound  
  
are in an institution like a care home  
  
usually wear clothes that cover up most of their skin when outdoors If you have dark skin – for example you have an African, African-Caribbean or south Asian background – you may also not make enough vitamin D from sunlight. You should consider taking a daily supplement containing 10 micrograms of vitamin D throughout the year. Advice for infants and young children The Department of Health and Social Care recommends that babies from birth to 1 year of age should have a daily supplement containing 8.5 to 10 micrograms of vitamin D throughout the year if they are: breastfed  
  
formula-fed and are having less than 500ml (about a pint) of infant formula a day, as infant formula is already fortified with vitamin D Children aged 1 to 4 years old should be given a daily supplement containing 10 micrograms of vitamin D throughout the year. You can buy vitamin D supplements or vitamin drops containing vitamin D (for under 5s) at most pharmacies and supermarkets. Women and children who qualify for the Healthy Start scheme can get free supplements containing vitamin D. See the Healthy Start website for more information.  
  
What happens if I take too much vitamin D? Taking too many vitamin D supplements over a long period of time can cause too much calcium to build up in the body (hypercalcaemia). This can weaken the bones and damage the kidneys and the heart. If you choose to take vitamin D supplements, 10 micrograms a day will be enough for most people. Do not take more than 100 micrograms (4,000 IU) of vitamin D a day as it could be harmful. This applies to adults, including pregnant and breastfeeding women and the elderly, and children aged 11 to 17 years. Children aged 1 to 10 years should not have more than 50 micrograms (2,000 IU) a day. Infants under 12 months should not have more than 25 micrograms (1,000 IU) a day. Some people have medical conditions that mean they may not be able to safely take as much. If in doubt, you should consult your doctor. If your doctor has recommended you take a different amount of vitamin D, you should follow their advice. You cannot overdose on vitamin D through exposure to sunlight. But always remember to cover up or protect your skin if you're out in the sun for long periods to reduce the risk of skin damage and skin cancer.  
  
  
https://www.mayoclinic.org/drugs-supplements-vitamin-d/art-20363792  
TITLE: Vitamin D  
META DESCRIPTION:   
META KEYWORDS:   
H1: Vitamin D,   
H2: COVID-19: Advice, updates and vaccine options,   
  
Appointments at Mayo Clinic  
  
, Vitamin D, From Mayo Clinic to your inbox  
 , Advertisement, Other Topics in Patient Care & Health Info, Mayo Clinic Footer,   
BOLD/STRONG: Featured conditions, Cancer., Cognitive health., Inherited bone disorders., Multiple sclerosis., Osteomalacia., Osteoporosis., Psoriasis., Rickets., Aluminum., Anticonvulsants., Atorvastatin (Lipitor)., Calcipotriene (Dovonex, Sorilux)., Cholestyramine (Prevalite)., Cytochrome P-450 3A4 (CYP3A4) substrates., Digoxin (Lanoxin)., Diltiazem (Cardizem, Tiazac, others)., Orlistat (Xenical, Alli)., Thiazide diuretics., Steroids., Stimulant laxatives., Verapamil (Verelan, Calan SR)., Advertising & Sponsorship, Privacy Policy, Notice of Privacy Practices,   
Italic: : Products and services,   
TEXT: Vitamin D By Mayo Clinic Staff  
  
Overview  
  
Vitamin D is a nutrient your body needs for building and maintaining healthy bones. That's because your body can only absorb calcium, the primary component of bone, when vitamin D is present. Vitamin D also regulates many other cellular functions in your body. Its anti-inflammatory, antioxidant and neuroprotective properties support immune health, muscle function and brain cell activity.  
  
Vitamin D isn't naturally found in many foods, but you can get it from fortified milk, fortified cereal, and fatty fish such as salmon, mackerel and sardines. Your body also makes vitamin D when direct sunlight converts a chemical in your skin into an active form of the vitamin (calciferol).  
  
The amount of vitamin D your skin makes depends on many factors, including the time of day, season, latitude and your skin pigmentation. Depending on where you live and your lifestyle, vitamin D production might decrease or be completely absent during the winter months. Sunscreen, while important to prevent skin cancer, also can decrease vitamin D production.  
  
Many older adults don't get regular exposure to sunlight and have trouble absorbing vitamin D. If your doctor suspects you're not getting enough vitamin D, a simple blood test can check the levels of this vitamin in your blood.  
  
Taking a multivitamin with vitamin D may help improve bone health. The recommended daily amount of vitamin D is 400 international units (IU) for children up to age 12 months, 600 IU for people ages 1 to 70 years, and 800 IU for people over 70 years.  
  
Evidence  
  
Research on vitamin D use for specific conditions shows:  
  
Cancer. Findings on the benefits of vitamin D for cancer prevention are mixed. More studies are needed to determine whether vitamin D supplementation may reduce the risk of certain cancers.  
  
Findings on the benefits of vitamin D for cancer prevention are mixed. More studies are needed to determine whether vitamin D supplementation may reduce the risk of certain cancers. Cognitive health. Research shows that low levels of vitamin D in the blood are associated with cognitive decline. However, more studies are needed to determine the benefits of vitamin D supplementation for cognitive health.  
  
Research shows that low levels of vitamin D in the blood are associated with cognitive decline. However, more studies are needed to determine the benefits of vitamin D supplementation for cognitive health. Inherited bone disorders. Vitamin D supplements can be used to help treat inherited disorders resulting from an inability to absorb or process vitamin D, such as familial hypophosphatemia.  
  
Vitamin D supplements can be used to help treat inherited disorders resulting from an inability to absorb or process vitamin D, such as familial hypophosphatemia. Multiple sclerosis. Research suggests that long-term vitamin D supplementation reduces the risk of multiple sclerosis.  
  
Research suggests that long-term vitamin D supplementation reduces the risk of multiple sclerosis. Osteomalacia. Vitamin D supplements are used to treat adults with severe vitamin D deficiency, resulting in loss of bone mineral content, bone pain, muscle weakness and soft bones (osteomalacia).  
  
Vitamin D supplements are used to treat adults with severe vitamin D deficiency, resulting in loss of bone mineral content, bone pain, muscle weakness and soft bones (osteomalacia). Osteoporosis. Studies suggest that people who get enough vitamin D and calcium in their diets can slow bone mineral loss, help prevent osteoporosis and reduce bone fractures. Ask your doctor if you need a calcium and vitamin D supplement to prevent or treat osteoporosis.  
  
Studies suggest that people who get enough vitamin D and calcium in their diets can slow bone mineral loss, help prevent osteoporosis and reduce bone fractures. Ask your doctor if you need a calcium and vitamin D supplement to prevent or treat osteoporosis. Psoriasis. Applying vitamin D or a topical preparation that contains a vitamin D compound called calcipotriene to the skin can treat plaque-type psoriasis in some people.  
  
Applying vitamin D or a topical preparation that contains a vitamin D compound called calcipotriene to the skin can treat plaque-type psoriasis in some people. Rickets. This rare condition develops in children with vitamin D deficiency. Supplementing with vitamin D can prevent and treat the problem.  
  
Our take  
  
Generally safe  
  
Without vitamin D your bones can become soft, thin and brittle. Insufficient vitamin D is also connected to osteoporosis. If you don't get enough vitamin D through sunlight or dietary sources, you might need vitamin D supplements.  
  
Safety and side effects  
  
Taken in appropriate doses, vitamin D is generally considered safe.  
  
However, taking too much vitamin D in the form of supplements can be harmful. Children age 9 years and older, adults, and pregnant and breastfeeding women who take more than 4,000 IU a day of vitamin D might experience:  
  
Nausea and vomiting  
  
Poor appetite and weight loss  
  
Constipation  
  
Weakness  
  
Confusion and disorientation  
  
Heart rhythm problems  
  
Kidney stones and kidney damage  
  
Interactions  
  
Possible interactions include:  
  
Aluminum. Taking vitamin D and aluminum-containing phosphate binders, which may be used to treat high serum phosphate levels in people with chronic kidney disease, might cause harmful levels of aluminum in people with kidney failure in the long term.  
  
Taking vitamin D and aluminum-containing phosphate binders, which may be used to treat high serum phosphate levels in people with chronic kidney disease, might cause harmful levels of aluminum in people with kidney failure in the long term. Anticonvulsants. The anticonvulsants phenobarbital and phenytoin (Dilantin, Phenytek) increase the breakdown of vitamin D and reduce calcium absorption.  
  
The anticonvulsants phenobarbital and phenytoin (Dilantin, Phenytek) increase the breakdown of vitamin D and reduce calcium absorption. Atorvastatin (Lipitor). Taking vitamin D might affect the way your body processes this cholesterol drug.  
  
Taking vitamin D might affect the way your body processes this cholesterol drug. Calcipotriene (Dovonex, Sorilux). Don't take vitamin D with this psoriasis drug. The combination might increase the risk of too much calcium in the blood (hypercalcemia).  
  
Don't take vitamin D with this psoriasis drug. The combination might increase the risk of too much calcium in the blood (hypercalcemia). Cholestyramine (Prevalite). Taking vitamin D with this cholesterol-lowering drug can reduce your absorption of vitamin D.  
  
Taking vitamin D with this cholesterol-lowering drug can reduce your absorption of vitamin D. Cytochrome P-450 3A4 (CYP3A4) substrates. Use vitamin D cautiously if you're taking drugs processed by these enzymes.  
  
Use vitamin D cautiously if you're taking drugs processed by these enzymes. Digoxin (Lanoxin). Avoid taking high doses of vitamin D with this heart medication. High doses of vitamin D can cause hypercalcemia, which increases the risk of fatal heart problems with digoxin.  
  
Avoid taking high doses of vitamin D with this heart medication. High doses of vitamin D can cause hypercalcemia, which increases the risk of fatal heart problems with digoxin. Diltiazem (Cardizem, Tiazac, others). Avoid taking high doses of vitamin D with this blood pressure drug. High doses of vitamin D can cause hypercalcemia, which might reduce the drug's effectiveness.  
  
Avoid taking high doses of vitamin D with this blood pressure drug. High doses of vitamin D can cause hypercalcemia, which might reduce the drug's effectiveness. Orlistat (Xenical, Alli). Taking this weight-loss drug can reduce your absorption of vitamin D.  
  
Taking this weight-loss drug can reduce your absorption of vitamin D. Thiazide diuretics. Taking these blood pressure drugs with vitamin D increases your risk of hypercalcemia.  
  
Taking these blood pressure drugs with vitamin D increases your risk of hypercalcemia. Steroids. Taking steroid mediations such as prednisone can reduce calcium absorption and impair your body's processing of vitamin D.  
  
Taking steroid mediations such as prednisone can reduce calcium absorption and impair your body's processing of vitamin D. Stimulant laxatives. Long-term use of high doses of stimulant laxatives can reduce vitamin D and calcium absorption.  
  
Long-term use of high doses of stimulant laxatives can reduce vitamin D and calcium absorption. Verapamil (Verelan, Calan SR). Taking high doses of vitamin D with this blood pressure drug can cause hypercalcemia, and might also reduce the effectiveness of verapamil.  
  
There is a problem with information submitted for this request. Review/update the information highlighted below and resubmit the form. From Mayo Clinic to your inbox Sign up for free, and stay up to date on research advancements, health tips and current health topics, like COVID-19, plus expertise on managing health. Email ErrorEmail field is required ErrorInclude a valid email address Learn more about Mayo Clinic’s use of data. To provide you with the most relevant and helpful information, and understand which information is beneficial, we may combine your email and website usage information with other information we have about you. If you are a Mayo Clinic patient, this could include protected health information. If we combine this information with your protected health information, we will treat all of that information as protected health information and will only use or disclose that information as set forth in our notice of privacy practices. You may opt-out of email communications at any time by clicking on the unsubscribe link in the e-mail. Subscribe! Thank you for subscribing Our Housecall e-newsletter will keep you up-to-date on the latest health information. Sorry something went wrong with your subscription Please, try again in a couple of minutes Retry  
  
  
  
  
  
  
https://www.medicalnewstoday.com/articles/161618  
TITLE: Vitamin D: Benefits, deficiency, sources, and dosage  
META DESCRIPTION: The body produces vitamin D in response to sun exposure. Vitamin D is important to bone development and immune support.  
META KEYWORDS:   
H1: What are the health benefits of vitamin D?,   
H2: Roles of vitamin D in the body, Deficiency, Symptoms, Vitamin D in infants, Vitamin D in pregnancy, Sources of vitamin D, Dosage, Risks, Summary, Latest news,   
BOLD/STRONG: Skin color:, Lack of sun exposure:, Breastfeeding:, Older adults:, Those with conditions that limit fat absorption:, People with obesity:, People following a gastric bypass:,   
Italic: : et al, et al, et al, et al, et al, et al, et al, et al, et al, et al, et al, et al, et al., et al, et al, et al, et al.,   
TEXT: The human body produces vitamin D as a response to sun exposure. A person can also boost their vitamin D intake through certain foods or supplements. Vitamin D is essential for maintaining healthy bones and teeth. It also plays many other important roles in the body, including regulating inflammation and immune function. Despite its name, vitamin D is not a vitamin but a hormone or prohormone. In this article, we look at the benefits of vitamin D, what happens to the body when people do not get enough, and how to boost vitamin D intake.  
  
Roles of vitamin D in the body Share on Pinterest Mateo Arias/EyeEm/Getty Images Vitamin D plays a critical role in many bodily functions. Healthy bones Vitamin D promotes intestinal calcium absorption and helps maintain adequate blood levels of calcium and phosphorus, which is necessary for healthy bone mineralization. Vitamin D deficiency in children can cause rickets, leading to a bowlegged appearance due to the softening of the bones. Similarly, in adults, vitamin D deficiency manifests as osteomalacia or a softening of the bones. Osteomalacia results in poor bone density and muscular weakness. Long-term vitamin D deficiency can also present as osteoporosis. Immune function An adequate intake of vitamin D may support good immune function and reduce the risk of autoimmune diseases. Researchers suggest that vitamin D plays an important role in immune function. They believe there may be a link between long-term vitamin D deficiency and the development of autoimmune conditions, such as diabetes, asthma, and rheumatoid arthritis, but more research is necessary to confirm the link. While test-tube studies have shown vitamin D to have a positive effect on the immune response of human cells, researchers are yet to replicate these findings in controlled human trials.  
  
Deficiency Although the body can create vitamin D, some people are more likely to be at risk of a deficiency than others. Factors that can influence this include: Skin color: Pigmentation in the skin reduces the body’s ability to absorb ultraviolet B (UVB) rays from the sun. Absorbing sunlight is essential for the skin to produce vitamin D.  
  
Pigmentation in the skin reduces the body’s ability to absorb ultraviolet B (UVB) rays from the sun. Absorbing sunlight is essential for the skin to produce vitamin D. Lack of sun exposure: People who live in northern latitudes or areas of high pollution , work night shifts, or are homebound should aim to consume vitamin D from food sources whenever possible.  
  
People who live in northern latitudes or areas of , work night shifts, or are homebound should aim to consume vitamin D from food sources whenever possible. Breastfeeding: The American Academy of Pediatrics recommends that all breastfed infants receive 400 international units (IU) per day of oral vitamin D.  
  
The American Academy of Pediatrics recommends that all breastfed infants receive (IU) per day of oral vitamin D. Older adults: The skin’s ability to synthesize vitamin D decreases with age. Older adults may also spend more time indoors.  
  
The skin’s ability to synthesize vitamin D with age. Older adults may also spend more time indoors. Those with conditions that limit fat absorption: Vitamin D is fat-soluble, meaning intake is dependent on the gut absorbing dietary fats. Conditions that limit fat absorption can decrease vitamin D intake from the diet.  
  
Vitamin D is fat-soluble, meaning intake is dependent on the gut absorbing dietary fats. Conditions that limit fat absorption can decrease vitamin D intake from the diet. People with obesity: High levels of body fat can limit the body’s ability to absorb vitamin D from the skin.  
  
High levels of body fat can limit the body’s ability to absorb vitamin D from the skin. People following a gastric bypass: This surgery bypasses a part of the upper intestine that absorbs large amounts of vitamin D. This bypass can cause a deficiency. Read more on vitamin D deficiency.  
  
Symptoms The majority of people with a vitamin D deficiency do not present with symptoms. However, a chronic deficiency may cause hypocalcemia, a calcium deficiency disease, and hyperparathyroidism, where the parathyroid glands create a hormone imbalance that raises the blood calcium levels. These conditions can lead to secondary symptoms including: bone fragility, especially in older adults  
  
osteoporosis  
  
bone pain  
  
fatigue  
  
muscle twitching  
  
muscle weakness  
  
myalgias, or muscle pain  
  
arthralgias, or joint stiffness If Vitamin D deficiency continues for long periods, it may result in complications, such as: cardiovascular conditions  
  
autoimmune problems  
  
neurological diseases  
  
infections  
  
pregnancy complications  
  
certain cancers, including breast, prostate, and colon  
  
Vitamin D in infants Infancy and childhood is a period of rapid growth bone growth. Due to this, it is essential for infants to get adequate amounts of vitamin D. Chronic vitamin D deficiency can cause rickets, which is a softening of bone tissues that can lead to the malformation of bones and joints. Vitamin D deficiency also has links to high blood pressure and hypertension in children. A 2018 study found a possible connection between low vitamin D levels and arterial wall stiffness in children. The American Academy of Allergy Asthma and Immunology (AAAAI) suggests a connection between low vitamin D exposure and an increased risk of allergic sensitization. For example, children who live closer to the equator have lower rates of admission to the hospital for allergies and fewer prescriptions for epinephrine auto-injectors, or EpiPens. They are also less likely to have a peanut allergy.  
  
Sources of vitamin D People can often get the majority of their vitamin D intake from sunlight exposure. However, people at risk of developing vitamin D deficiency, and many other people, cannot solely rely on sunlight exposure for vitamin D production. During the winter months, when the sun is not as strong, everyone can benefit from vitamin D supplements. The following foods are a source of vitamin D: fatty fish, such as salmon, mackerel, and tuna  
  
egg yolks  
  
cheese  
  
beef liver  
  
mushrooms  
  
fortified milk  
  
fortified cereals and juices  
  
Dosage People can measure vitamin D intake in micrograms (mcg) or international units (IU). One mcg of vitamin D is equal to 40 IU. The recommended daily intakes of vitamin D are as follows: Demographic Recommended daily intake Infants 0-12 months 400 IU (10 mcg) Children 1-18 years 600 IU (15 mcg) Adults up to 70 years 600 IU (15 mcg) Adults over 70 years 800 IU (20 mcg) Pregnant or lactating women 600 IU (15 mcg) Learn how to get more vitamin D from the sun here.  
  
Risks The upper limit that healthcare professionals recommend for vitamin D is 4,000 IU per day for an adult. However, the National Institutes of Health (NIH) reports that vitamin D toxicity is unlikely at intakes under 10,000 IU per day. Vitamin D toxicity is typically the result of inappropriate supplement dosing and prescription errors. Excessive vitamin D consumption can lead to hypercalcemia, or an excessively high blood calcium level. This can lead to calcification of bones and the hardening of blood vessels, kidneys, lungs, and heart tissues. Hypercalcemia can be life threatening and requires immediate medical attention. The most common symptoms of excessive vitamin D include headaches and nausea. However, too much vitamin D can also lead to the following: loss of appetite  
  
dry mouth  
  
a metallic taste  
  
vomiting  
  
constipation  
  
diarrhea Excessive vitamin D usually occurs from accidental overconsumption and prescription errors. If someone is taking supplements, they should choose their brand carefully, as the Food and Drug Administration (FDA) does not monitor the safety or purity of supplements the same way it does pharmaceuticals. A complete diet and regular eating pattern are most important in disease prevention and good health. It is better to eat a diet with various nutrients than to concentrate on only a few nutrients.  
  
  
https://dlang.org/  
TITLE: D Programming Language  
META DESCRIPTION: D is a general-purpose programming language with static typing, systems-level access, and C-like syntax.  
META KEYWORDS: D programming language,   
H1:   
H2: Support the D language, Fast code, fast.,   
BOLD/STRONG: D, D Programming Language,   
Italic: : and,   
TEXT: Got a brief example illustrating D?  
  
Submit your code to the digitalmars.D forum specifying "[your code here]" in the subject.  
  
Upon approval it will be showcased here on a random schedule.  
  
  
https://bg.wikipedia.org/wiki/%D0%92%D0%B8%D1%82%D0%B0%D0%BC%D0%B8%D0%BD\_D  
TITLE: Витамин D – Уикипедия  
META DESCRIPTION:   
META KEYWORDS:   
H1: Витамин D,   
H2: Източници[редактиране | редактиране на кода], Навигация,   
BOLD/STRONG: Витамин D, а, б,   
Italic: : а, б, Mayo Clinic Proceedings, The Journal of Nutrition, The American Journal of Clinical Nutrition, {{{journal}}}, The American Journal of Clinical Nutrition, Тази статия, свързана с биохимия, все още е мъниче. Помогнете на Уикипедия, като я редактирате и разширите.,   
TEXT: 3 . Структурна формула на витамин D  
  
Витамин D е витамин, който се съдържа в рибеното масло, яйцата и черния дроб. Недостигът му през детска възраст води до болестта рахит (изкривяване на кости и крайници). Двете му главни форми са D 2 и D 3 . Разтворим е в мазнини. За хората най-важните форми на този витамин са витамин D 3 (холекалциферол) и витамин D 2 (ергокалциферол).[1] Те могат да се приемат както чрез храната, така и като добавки.[1][2][3] Най-големият естествен източник на витамин D е синтезът на холекалциферол в кожата от холестерола чрез химична реакция, зависеща от излагането на слънчеви лъчи (в частност, на UVB лъчи). Ергокалциферолът може да се набавя само от храната. Препоръчителният ежедневен прием на витамина за хора на възраст от 1 до 70 години (включително бременни и кърмещи жени) е 15 mg холекалциферол.[4] Храни, от които може да се набави витамин D, са: мазни (тлъсти) риби, като сьомга, риба тон, скумрия; някои рибни консерви (риба тон, сардини); рибен хайвер; яйца и по-конкретно яйчен жълтък; гъби (печурка, манатарка); овесени ядки; портокалов сок; млечни продукти (краве масло, сирене, прясно и кисело мляко).[5]  
  
Дефицитът на витамин D води до намалена абсорбция на калций, магнезий и фосфор.[6] В резултат от това, продължителният дефицит на витамин D има отрицателен ефект върху костната минерализация. При бебета и деца, такъв дефицит се проявява като рахит – състояние, характеризиращо се с костни деформации и забавяне на растежа. Недостатъчната минерализация на костите води до омекване. Резултатът е деформации на черепа, гръдния кош, изкривяване на костите на крайниците и др.