

Vitamin D

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Background

Vitamin D is found in many dietary sources such as fish, eggs, fortified milk, and cod liver oil. The sun also contributes significantly to the daily production of vitamin D, and as little as 10 minutes of exposure is thought to be enough to prevent deficiencies. The term "vitamin D" refers to several different forms of this vitamin. Two forms are important in humans: ergocalciferol (vitamin D₂) and cholecalciferol (vitamin D₃). Vitamin D₂ is synthesized by plants. Vitamin D₃ is synthesized by humans in the skin when it is exposed to ultraviolet-B (UVB) rays from sunlight. Foods may be fortified with vitamin D₂ or D₃.

The major biologic function of vitamin D is to maintain normal blood levels of calcium and phosphorus. Vitamin D aids in the absorption of calcium, helping to form and maintain strong bones. Recently, research also suggests vitamin D may provide protection from osteoporosis, hypertension (high blood pressure), cancer, and several autoimmune diseases.

Rickets and osteomalacia are classic vitamin D deficiency diseases. In children, vitamin D deficiency causes rickets, which results in skeletal deformities. In adults, vitamin D deficiency can lead to osteomalacia, which results in muscular weakness in addition to weak bones. Populations who may be at a high risk for vitamin D deficiencies include the elderly, obese individuals, exclusively breastfed infants, and those who have limited sun exposure. Also, individuals who have fat malabsorption syndromes (e.g., cystic fibrosis) or inflammatory bowel disease (e.g., Crohn's disease) are at risk.

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Synonyms

1 alpha (OH) D₃, 19-nor-1, 1 alpha-hydroxyvitamin D₂, 1,25-DHCC, 1,25-dihydroxy-22-ovavitamin D(3), 1,25-dihydroxycholecalciferol, 1,25-dihydroxyvitamin D₃, 1,25-diOHC, 1,25(OH) 2D₃, 1-alpha-hydroxycholecalciferol,

22-oxacalcitriol (OCT), 25-dihydroxyvitamin D2, 25-dihydroxyvitamin D2, 19-nor-1, 25-HCC, 25-hydroxycholecalciferol, 25-hydroxyvitamin D3, 25-OHCC, 25-OHD3, activated 7-dehydrocholesterol, activated ergosterol, alfacalcidol, calcifediol, calcipotriene, calcipotriol, calcitriol, cholecalciferol, colecalciferol, dichysterol, dihydrotachysterol 2, dihydrotachysterol, ecocalcidiol, ED-21 (vitamin D analog), ED-71 (vitamin D analog), ergocalciferol, ergocalciferolum, hexafluoro-1,25dihydroxyvitamin D3, irradiated ergosterol, MC903, paracalcin, paricalcitol, viosterol, vitamin D2, vitamin D3.

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Evidence

These uses have been tested in humans or animals. Safety and effectiveness have not always been proven. Some of these conditions are potentially serious, and should be evaluated by a qualified healthcare provider.

Uses based on scientific evidence

Grade*

Familial hypophosphatemia

Familial hypophosphatemia (low blood levels of phosphate in the blood) is a rare inherited disorder that consists of impaired phosphate transport in the blood and diminished vitamin D metabolism in the kidneys. Familial hypophosphatemia is a form of rickets. Taking calcitriol or dihydrotachysterol by mouth along with phosphate supplements is effective for treating bone disorders in people with familial hypophosphatemia. Management should be under medical supervision.

A

Fanconi syndrome-related hypophosphatemia

Fanconi syndrome is a defect of the proximal tubules of the kidney, and is associated with renal tubular acidosis. Taking ergocalciferol orally is effective for treating hypophosphatemia associated with Fanconi syndrome.

A

Hyperparathyroidism due to low vitamin D levels

Some patients may develop secondary hyperparathyroidism due to low levels of vitamin D. The initial treatment for this type of hyperparathyroidism is vitamin D. For patients with primary or refractory hyperparathyroidism, surgical removal of the parathyroid glands is commonly recommended. Studies also suggest that vitamin D supplementation may reduce the incidence of hypoparathyroidism following surgery for primary hyperparathyroidism (partial or total removal of the parathyroid glands).

A

Hypocalcemia due to hypoparathyroidism

Hypoparathyroidism (low blood levels of parathyroid hormone) is rare, and is often due to surgical removal of the parathyroid glands. High oral doses of dihydrotachysterol (DHT), calcitriol, or ergocalciferol can assist in increasing serum calcium concentrations in people with hypoparathyroidism or pseudohypoparathyroidism.

A

Osteomalacia (adult rickets)

Adults with severe vitamin D deficiency lose bone mineral content ("hypomineralization") and experience bone pain, muscle weakness, and osteomalacia (soft bones). Osteomalacia may be found among elderly patients with vitamin D-deficient diets, individuals with decreased absorption of vitamin D, individuals with inadequate sun exposure (such as those living in latitudes with seasonal lack of sunlight), patients with gastric or intestinal surgery, patients with aluminum-induced bone disease, patients with chronic liver disease, or patients with kidney disease with renal osteodystrophy. Treatment for osteomalacia depends on the underlying cause of the disease and often includes pain control and orthopedic surgical intervention, as well as vitamin D and phosphate binding agents.

A

Psoriasis

A number of different approaches are used in the treatment of psoriasis skin plaques. Mild approaches include light therapy, stress reduction, moisturizers, or salicylic acid to remove scaly skin areas. For more severe cases, treatments may include UV-A light, psoralen plus UV-A light (PUVA), retinoids such as isotretinoin (Accutane), corticosteroids, or cyclosporine (Neoral®, Sandimmune®). The synthetic vitamin D3 analog calcipotriene (Dovonex®) appears to control skin cell growth and is used for moderately severe skin plaques, particularly for skin lesions resistant to other therapies or located on the face. Vitamin D3 (tacalcitol) ointment has been reported as being safe and well-tolerated. High doses of becocalcidiol (a vitamin D analog) used on the skin may be beneficial in the treatment of psoriasis.

A

Rickets

Rickets develop in children with vitamin D deficiency due to a vitamin D-deficient diet, a lack of sunlight, or both. Infants fed only breast milk (without supplemental vitamin D) may also develop rickets. Although now rare, partially due to the availability of vitamin D-fortified milk, there has been a recent increase in rickets among children in latitudes with periodic, seasonal lack of sunlight. Ergocalciferol or cholecalciferol is effective for treating vitamin D deficiency rickets. Calcitriol should be used in patients with renal (kidney) failure. Treatment should be under medical supervision.

A

Muscle weakness/pain

Vitamin D deficiency has been associated with muscle weakness and pain in both adults and children. Limited research has reported vitamin D deficiency in patients with low-back pain, and supplementation may reduce pain in many patients.

B

Osteoporosis (general)

Without sufficient vitamin D, inadequate calcium is absorbed and the resulting elevated parathyroid (PTH) secretion causes increased bone resorption. This may weaken bones and increase the risk of fracture. Vitamin D supplementation has been shown to slow bone loss and reduce fracture, particularly when taken with calcium.

B

Renal osteodystrophy

Renal osteodystrophy is a term that refers to all of the bone problems that occur in patients with chronic kidney failure. Oral calcifediol or ergocalciferol may help manage hypocalcemia and prevent renal osteodystrophy in people with chronic renal failure undergoing dialysis.

B

Anticonvulsant-induced osteomalacia

Supplementation with vitamin D2 has been reported to reduce seizure frequency in initial research. Further study is needed to confirm these results.

C

Breast cancer prevention

High-dose vitamin D supplementation may be associated with a slightly reduced risk of developing breast cancer. Additional study in this area is warranted.

C

Cancer prevention

Limited research suggests that synthetic vitamin D analogs may play a role in the treatment of human cancers. However, it remains unclear if vitamin D deficiency raises cancer risk, or if an increased intake of vitamin D is protective against some cancers. Until additional trials are conducted, it is premature to advise the use of regular vitamin D supplementation to prevent cancer.

C

Colorectal cancer

Data from a meta-analysis suggest that supplemental vitamin D may prevent the development of colorectal cancer. More research is needed in this area.

C

Corticosteroid-induced osteoporosis

Some evidence implies that steroids may impair vitamin D metabolism, further contributing to the loss of bone and development of osteoporosis associated with steroid medications. There is limited evidence that vitamin D may be beneficial to bone strength in patients taking long-term steroids.

C

Diabetes (type 1/type 2)

Type 1 diabetes : It has been reported that infants given calcitriol during the first year of life are less likely to develop type 1 diabetes than infants fed lesser amounts of vitamin D. Other related studies have suggested using cod liver oil as a source of vitamin D to reduce the incidence of type 1 diabetes. There is currently insufficient evidence to form a clear conclusion in this area. **Type 2 diabetes** : In recent studies, adults given vitamin D supplementation were shown to improve insulin sensitivity. Further research is needed to confirm these results.

C

Fall prevention

Multiple trials have found conflicting results for the effects of vitamin D in the prevention of falls. More studies are needed.

C

Hepatic osteodystrophy

Metabolic bone disease is common among patients with chronic liver disease, and osteoporosis accounts for the majority of cases. Varying degrees of calcium malabsorption may occur in patients with chronic liver disease due to malnutrition and vitamin D deficiency. Oral or injected vitamin D may play a role in the management of this condition.

C

High blood pressure (hypertension)

Low levels of vitamin D may play a role in the development of high blood pressure. It has been noted that blood pressure is often elevated under the following conditions: during the winter season, at a further distance from the equator, and in individuals with dark skin pigmentation (all of which are associated with lower production of vitamin D via sunlight). However, evidence is not clear, and a comparison with more proven methods to reduce blood pressure has not been conducted. Patients with elevated blood pressure should be managed by a licensed healthcare professional.

C

Hypertriglyceridemia

There is insufficient evidence in this area.

C

Immunomodulation

Preliminary human evidence suggests that vitamin D and its analogues, such as alfacalcidol, may act as immunomodulatory agents. More studies are needed to confirm these results.

C

Mortality reduction

Intake of vitamin D may be associated with a reduction in total mortality. Additional evidence is needed to confirm this association.

C

Multiple sclerosis (MS)

Scientists have detected MS rates to be lower in areas with greater sunlight and higher consumption of vitamin D rich fish. Preliminary research suggests that long-term vitamin D supplementation decreases the risk of MS; however, additional research is necessary before a firm conclusion can be reached.

C

Myelodysplastic syndrome

There is insufficient evidence in this area.

C

Osteogenesis imperfecta (OI)

OI is a genetic disease that consists of unusually fragile bones that break easily, often under loads that normal bones bear daily due to a malfunction in the body's production of collagen. Proper calcium and vitamin D intake is essential to maintaining strong bones.

C

Osteoporosis (cystic fibrosis patients)

Osteoporosis is common in patients with cystic fibrosis (due to fat malabsorption, which leads to a deficiency of fat-soluble vitamins such as vitamin D). Oral calcitriol administration appears to increase the absorption of calcium and decrease parathyroid concentrations.

C

Proximal myopathy

There is insufficient evidence in this area.

C

Rickets (hypophosphatemic vitamin D-resistant)

There are insufficient data to support a role of vitamin D in this condition.

C

Seasonal affective disorder (SAD)

Seasonal affective disorder (SAD) is a form of depression that occurs during the winter months, possibly due to reduced exposure to sunlight. In one study, vitamin D was found to be better than light therapy in the treatment of SAD. Further studies are necessary to confirm these findings.

C

Senile warts

In early study, senile warts have been treated with topical vitamin D3.

C

Skin pigmentation disorders (pigmented lesions)

Application of vitamin D3 ointment on the skin, in combination with intense pulsed-radio frequency, may be beneficial in the treatment of pigmented lesions associated with neurofibromatosis 1 (NF1).

C

Tooth retention

Oral bone and tooth loss are correlated with bone loss at non-oral sites. Research suggests that intake levels of calcium and vitamin D aimed at preventing osteoporosis may have a beneficial effect on tooth retention.

C

Vitamin D deficiency (infants and nursing mothers)

High-quality clinical trial evidence suggests that high doses of supplemental vitamin D provided to breast feeding mothers may improve the vitamin D status of both mother and child. More research is needed to confirm these findings.

C

Weight gain (postmenopausal)

Vitamin D supplementation (in combination with calcium) may have an effect on postmenopausal weight gain. Evidence suggests this may be particularly true in women consuming inadequate calcium and warrants further study.

C

Muscle strength

Oral cholecalciferol does not appear to increase muscle strength or improve physical performance in healthy older men who are not vitamin D deficient.

D

Prostate cancer

There is preliminary evidence based on laboratory and human studies that high-dose vitamin D may be beneficial in the treatment of prostate cancer. This area is under active investigation, but clear evidence of benefit is not yet available.

D

Key to grades

A Strong scientific evidence for this use

B Good scientific evidence for this use

C Unclear scientific evidence for this use

D Fair scientific evidence against this use (it may not work)

F Strong scientific evidence against this use (it likely does not work)

[Grading rationale](#)

Uses based on tradition or theory

The below uses are based on tradition or scientific theories. They often have not been thoroughly tested in humans, and safety and effectiveness have not always been proven. Some of these conditions are potentially serious, and should be evaluated by a qualified healthcare provider.

Actinic keratosis, Alzheimer's disease associated hip fractures, ankylosing spondylitis, autoimmune disorders, Graves disease, hyperparathyroidism in renal dialysis, hypocalcemia, hypocalcemic tetany, kidney transplant-related bone loss, metabolic disorders (metabolic syndrome), nervous system disorders (hemichorea), osteitis fibrosa in dialysis, rheumatoid arthritis, scleroderma, squamous cell carcinoma, systemic lupus erythematosus, vaginal disorders

(atrophy), vitiligo.

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Dosing

The below doses are based on scientific research, publications, traditional use, or expert opinion. Many herbs and supplements have not been thoroughly tested, and safety and effectiveness may not be proven. Brands may be made differently, with variable ingredients, even within the same brand. The below doses may not apply to all products. You should read product labels, and discuss doses with a qualified healthcare provider before starting therapy.

Adults (over 18 years old)

Vitamin D is included in most multivitamins, usually in strengths from 50 IU to 1,000 IU as softgels, capsules, tablets, and liquids. The Adequate Intake (AI) levels have been established by the U.S. Institute of Medicine of the National Academy of Sciences. Recommendations are: 5 micrograms (200 IU or International Units) daily for all individuals (males, female, pregnant/lactating women) under the age of 50 years-old. For all individuals from 50-70 years-old, 10 micrograms daily (400 IU) is recommended. For those who are over 70 years-old, 15 micrograms daily (600 IU) is suggested. Some authors have questioned whether the current recommended adequate levels are sufficient to meet physiological needs, particularly for individuals deprived of regular sun exposure. The upper limit (UL) for vitamin D has been recommended as 2,000 IU daily due to toxicities that can occur when taken in higher doses.

Not all doses have been found effective for conditions that have been studied. However, ergocalciferol has been used in an oral dose of 400 to 800 IU per day (sometimes higher doses are used in conjunction with calcium) for osteoporosis prevention and treatment.

Calcitriol has been used in an initial oral dose of 0.25 micrograms per day; dosing may be increased by 0.25 micrograms per day at four to eight week intervals in patients with hypocalcemia from chronic dialysis.

Dihydroxycholesterol has been used in an oral initial dose of 750 micrograms (0.75 milligrams) to 2.5 milligrams per day for several days for the treatment of hypoparathyroidism. A maintenance dose is typically 200 micrograms (0.2 milligrams) to 1 milligram per day. Ergocalciferol has also been used in an oral dose of 50,000 to 200,000 IU units daily concomitantly with calcium lactate 4 grams, six times per day.

Rickets may be treated gradually over several months or in a single day's dose. Gradual dosing may be 125-250 micrograms (5,000-10,000 IU) taken daily for two to three months, until recovery is well established and alkaline phosphatase blood concentration is close to normal limits. Single-day dosing may be 15,000

micrograms (600,000 IU) of vitamin D, taken by mouth divided into four to six doses. Intramuscular injection is also an alternative for single-day dosing. For resistant rickets, some authors suggest a higher dose of 12,000 to 500,000 IU per day, although this has not yet been proven effective.

Children (under 18 years old)

Adequate Intake (AI) levels have been established by the U.S. Institute of Medicine of the National Academy of Sciences. The recommendation from birth until 50 years old is 5 micrograms per day (200 IU or International Units per day). Children older than one year should not exceed the "upper limit" (UL) of 50 micrograms (2,000 IU) per day; children younger than one year should not exceed the UL of 25 micrograms (1,000 IU) per day. Vitamin D is possibly unsafe when used orally in excessive amounts, with adverse effects including hypercalcemia (high blood calcium levels). Some authors have questioned whether the current recommended adequate levels are sufficient to meet physiological needs, particularly for individuals deprived of regular sun exposure.

Not all doses have been found effective for conditions that have been studied. However, for hypoparathyroidism, ergocalciferol has been used orally in an initial dose of 8,000 units per kilogram per day for one to two weeks. For maintenance, a dose of 2,000 units per kilogram per day has been used.

Rickets may be treated gradually over several months or in a single day's dose. Based on one clinical trial, a single dose of 600,000 IU of oral vitamin D3 was comparable to a dose of 20,000 IU per day of oral vitamin D3 for 30 days. Gradual dosing may be 125-250 micrograms (5000-10,000 IU) taken daily for two to three months, until recovery is well established and alkaline phosphatase blood concentration is close to normal limits. Single-day dosing may be 15,000 micrograms (600,000 IU) of vitamin D, taken by mouth divided into 4-6 doses. Intramuscular injection is also an alternative for single-day dosing. For resistant rickets, some authors suggest a higher dose of 12,000 to 500,000 IU per day.

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Safety

The U.S. Food and Drug Administration does not strictly regulate herbs and supplements. There is no guarantee of strength, purity or safety of products, and effects may vary. You should always read product labels. If you have a medical condition, or are taking other drugs, herbs, or supplements, you should speak with a qualified healthcare provider before starting a new therapy. Consult a healthcare provider immediately if you experience side effects.

Allergies

Avoid or use caution with known hypersensitivity to vitamin D or any of its analogues and derivatives.

Side Effects and Warnings

Vitamin D is generally well tolerated in recommended "Adequate Intake (AI)" doses. One study found a greater likelihood of daytime sleepiness for patients given vitamin D analogues.

Vitamin D toxicity can result from regular excess intake of this vitamin, and may lead to hypercalcemia and excess bone loss. Individuals at particular risk include those with hyperparathyroidism, kidney disease, sarcoidosis, tuberculosis, or histoplasmosis. Chronic hypercalcemia may lead to serious or even life-threatening complications, and should be managed by a physician. Early symptoms of hypercalcemia may include nausea, vomiting, and anorexia (appetite/weight loss), followed by polyuria (excess urination), polydipsia (excess thirst), weakness, fatigue, somnolence, headache, dry mouth, metallic taste, vertigo, tinnitus (ear ringing), and ataxia (unsteadiness). Kidney function may become impaired, and metastatic calcifications (calcium deposition in organs throughout the body) may occur, particularly affecting the kidneys. Treatment involves stopping the intake of vitamin D or calcium, and lowering the calcium levels under strict medical supervision, with frequent monitoring of calcium levels. Acidification of urine and corticosteroids may be necessary.

Pregnancy and Breastfeeding

The recommended adequate intake for pregnant women is the same as for non-pregnant adults. Some authors have suggested that requirements during pregnancy may be greater than these amounts, particularly in sun-deprived individuals, although this has not been clearly established. Due to risks of vitamin D toxicity, any consideration of higher daily doses of vitamin D should be discussed with a physician.

Vitamin D is typically low in maternal milk, and to prevent deficiency and rickets in exclusively breastfed infants, supplementation may be necessary, starting within the first two months of life.

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Methodology

This patient information is based on a professional level monograph edited and peer-reviewed by contributors to the Natural Standard Research Collaboration (www.naturalstandard.com).

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