# Assessment and management of vitamin D deficiency

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Vitamin D deficiency is associated with serious health problems that can be prevented with early detection and treatment. There is no universal screening recommendation for vitamin D deficiency but the nurse practitioner should be aware of risk factors associated with individuals who may require screening. Screening of at-risk individuals, diagnosis, and prompt treatment are key to preventing complications of vitamin D deficiency.

KEY WORDS: **vitamin D deficiency, vitamin D, bone health**


An estimated 1 in 5 persons (18%) in the United States has inadequate levels of vitamin D and 5% have vitamin D deficiency.[1] Vitamin D deficiency has a profound impact on bone health and implications for other aspects of health. Treatment for vitamin D deficiency is safe and inexpensive, but the condition often goes undiagnosed or untreated. This article provides an evidence-based approach to assessment, diagnosis, and treatment of vitamin D deficiency.

## Overview of vitamin D

Vitamin D is a fat-soluble vitamin essential for the intestinal absorption of calcium. Vitamin D contributes to many aspects of overall health and wellness including musculoskeletal, cardiovascular, neurologic, and immune system functions.[2] Vitamin D is synthesized by ultraviolet irradiation of 7-dehydrocholesterol in the skin.[3] Another source of vitamin D is from foods in the diet, many of which are fortified with vitamin D.[3]

The synthesized or ingested forms of vitamin D must be metabolized to achieve potency.[3] Vitamin D enters the bloodstream from the skin or intestine and then is concentrated in the liver. Vitamin D is hydroxylated to form 25-hydroxyvitamin D (25(OH)D), calcidiol. It is then transported from the liver to the kidney and transformed into active 1,25(OH)2D, calcitriol. The ac-

tivated form of vitamin D maintains normal plasma levels of calcium by increasing absorption from the intestine.[3] Additionally, calcitriol sensitizes bone to the resorptive actions of parathyroid hormone.[3]

### Vitamin D and bone health

There is a firmly established relationship between vitamin D, calcium, and bone health. Adequate levels of vitamin D are needed for calcium absorption from the intestines. Inadequate levels of calcium lead to disruption in the process of bone resorption and bone formation. Long-term adequate calcium levels are important to the prevention of osteoporosis and osteoporotic fractures in older adults.[4,5] Osteoporosis is a significant problem in the US primarily among postmenopausal women. There were approximately 2.3 million osteoporotic fractures in 2015, and it is projected that these fractures will increase to more than 3 million by 2025.[2,6] Nearly half of all women age 50 years and older will experience an osteoporotic fracture during their lifetime.[6] These fractures are associated with chronic pain and limited performance of activities of daily living over a lifetime. Hip fractures are a serious event associated with increased mortality and morbidity.[6]

Vitamin D deficiency can result in muscle weakness. Muscle weakness can affect balance and postural sway and could increase the risk for falls, and further increase in the risk for fractures.[2] However, studies on the effects of supplemental vitamin D on muscle strength and muscle function have had inconsistent results.[2] The USPSTF concludes that current evidence is insufficient to recommend daily vitamin D supplementation of greater than 400 IU for primary prevention of fractures in community-dwelling postmenopausal women without a history of osteoporotic fractures, osteoporosis, increased risk for falls, or vitamin D deficiency.[6]

### Vitamin D and other health benefits

The knowledge that vitamin D is essential to healthy function of several body systems and that many tissues have vitamin D receptors has prompted ongoing interest in investigating potential associations of vitamin D with other health outcomes. Prominent among these studies have been those looking at cancer and cardiovascular disease and, more recently, Covid-19.

Studies to date do not support that vitamin D inadequacy increases risk for cancer or that vitamin D supplementation decreases the risk for cancer.[7] Clinical trials suggest that although vitamin D supplements may not affect cancer risk, adequate or higher vitamin D levels might slightly reduce cancer mortality rates.[2]

Some observational studies have found associations between higher vitamin D levels and lower risks of cardiovascular disease incidence and related mortality, but overall, clinical trials have not demonstrated any risk reduction. Clinical studies have had mixed findings on the effects of vitamin D supplements on lowering blood cholesterol levels and high blood pressure.[2]

Vitamin D is known to play a role in the body's immune response, and thus it has been proposed that vitamin D deficiency may affect the body's susceptibility to viral infection. Although under active study, current data are insufficient to support a recommendation for or against the use of vitamin D supplementation to prevent or treat Covid-19.[8]

Other areas of study on the association of vitamin D and health outcomes have focused on depression, diabetes, and multiple sclerosis.[2] High-quality research with randomized controlled trials is needed to help us better understand if vitamin D supplementation can contribute to prevention and treatment of health conditions.

## Assessment

The USPSTF does not support universal population-based screening for vitamin D levels, noting there is insufficient evidence to determine benefit and harm of screening in asymptomatic adults.[7] The Endocrine Society and the American Association of Clinical Endocrinologists recommend screening for vitamin D deficiency in those individuals who are at risk.[9] Most individuals with vitamin D deficiency are asymptomatic so assessment for risk factors is essential in determining the need for screening.[2] Multiple risk factors have been identified with certain populations at particular risk for vitamin D deficiency.[1,2,9]

Individuals who have limited sun exposure are at risk for vitamin D deficiency. This includes those who are homebound, live in cold climates or northern latitudes, and consistently wear sunscreen or sun-protective clothing. Older adults and persons with dark skin tones synthesize less vitamin D from sunlight, increasing their risk for vitamin D deficiency. Individuals with Crohn's disease, celiac disease, and ulcerative colitis may have fat malabsorption and thus impaired vitamin D absorption.[7] Individuals who have had gastric bypass surgery are also at risk for vitamin D deficiency. Because vitamin D is sequestered in subcutaneous fat, persons who are obese (body mass index > 30 kg/m$^2$) may have lower 25(OH)D levels.[2,9] A low vitamin D dietary intake is associated with lower 25(OH)D levels. Very few foods naturally contain vitamin D, and fortified

foods provide most of the vitamin D in the US.[2] Most milk is fortified with 3 µg (120 IU) vitamin D per cup.[2] Some of the plant-based alternatives such as soy, almond, and oat milk are also fortified with vitamin D. Foods made from milk, cheese, and ice cream are usually not fortified. Fish such as trout, salmon, tuna, mackerel, and fish liver oils are natural sources of vitamin D. There are also small amounts of vitamin D in beef liver, cheese, mushrooms, and egg yolks.[2] Individuals who consume a vegan or ovo-vegetarian diet and those who have milk allergy or lactose intolerance may be at risk for deficiency unless they consume other vitamin D fortified foods or take a vitamin D supplement.[2]

Vitamin D levels may be affected by some medications. Orlistat can reduce the amount of vitamin D the body absorbs from both food and supplements. Because statins such as atorvastatin, lovastatin, and simvastatin reduce cholesterol synthesis, they may also reduce endogenous vitamin D synthesis as it is derived from cholesterol. Steroids such as prednisone and the anticonvulsants phenytoin and phenobarbital can impair vitamin D metabolism.[2]

Pregnant individuals with any of the described risk factors for vitamin D deficiency should be screened. Even more ideal is to assess risk factors during any prepregnancy counseling so a deficiency can be corrected prior to conception. Severe vitamin D deficiency in pregnancy has been associated with congenital rickets and fractures in the newborn.[10]

## Diagnosis

The diagnosis of vitamin D deficiency depends on the evaluation of blood levels of 25(OH)D. This is the preferred test for assessment of vitamin D status in at-risk individuals.[1,11] Measuring 1,25(OH)D levels will lead to erroneous results and misdiagnosis. Physical exam is generally unremarkable in vitamin D deficiency. The National Institutes of Health describes serum levels of 25(OH)D measured in either ng/mL or nmol/L.[1]

Levels of 20 ng/mL (50 nmol/L) or above are adequate for most individuals for bone and overall health. Levels of 12 ng/mL (30 nmol/L) to less than 20 ng/mL (50 nmol/L) are generally considered inadequate, whereas levels below 12 ng/mL (30 nmol/L) indicate vitamin D deficiency. Levels above 50 ng/mL (125 nmoL) may cause health problems.[2]

## Treatment

Sources of vitamin D include dietary intake, endogenous production from sun exposure, and vitamin D supplements.[12] Cholecalciferol (vitamin D3) is synthesized in the skin with exposure to sunlight.[12] Ergocalciferol (vitamin D2) is found in plants, fortified foods, and fatty fish. Dietary supplements can contain vitamin D2 or D3.

Adults with vitamin D deficiency should be treated with either vitamin D2 or vitamin D3, beginning with 50,000 IU weekly, or with 6,000 IU daily for 8 weeks to achieve a serum level of 25(OH)D 30 ng/mL or more. Patients who fail to achieve the therapeutic serum level after 8 weeks of treatment with good adherence should be referred to an endocrinologist for further evaluation. Once the target serum level of 25(OH)D 30 ng/mL or more is achieved, maintenance treatment consists of 1,500 IU to 2,000 IU vitamin D2 or vitamin D3 daily to sustain the therapeutic level. Alternatively, 50,000 IU of vitamin D2 once every other week may be prescribed and is effective in maintaining therapeutic serum levels.[13] Vitamin D2 and D3 are available over the counter in strengths up to 5,000 IU per capsule, with higher strengths available by prescription.[14]

Vitamin D is a fat-soluble vitamin that accumulates and is stored in fatty tissues, with less availability for distribution in the bloodstream. Obese patients require 2 to 3 times more vitamin D to correct vitamin D deficiency and to maintain therapeutic serum levels.[9]

Patients with malabsorption syndromes or who take certain medications that may affect vitamin D metabolism (anticonvulsants, glucocorticoids, and antiretrovirals) also require higher initial and maintenance doses. For these patients, initial treatment is 6,000 IU to 10,000 IU vitamin D2 or vitamin D3 daily for 8 weeks, with maintenance doses of 3,000 IU to 6,000 IU daily to maintain therapeutic serum levels of 25(OH)D 30 ng/mL or more.[9,13]

The potency of cholesterol-lowering statins may be reduced if taking high-dose vitamin D supplements because they compete with the same metabolizing enzyme. Because thiazide diuretics decrease urinary calcium excretion and vitamin D supplements increase intestinal calcium absorption, there is a risk for hypercalcemia when taken in combination.[2]

The recommendation of the Endocrine Society is that pregnant women should take a prenatal vitamin containing 400 IU vitamin D and an additional supplement of 1,000 IU vitamin D daily.[9] According to the American College of Obstetricians and Gynecologists (ACOG), evidence is insufficient to support routine supplementation with vitamin D other than the 400 IU in prenatal vitamins during pregnancy in women who are not at risk for vitamin D deficiency. ACOG recommends screening pregnant women who are at risk for vitamin D deficiency, and

treating those with identified vitamin D deficiency with 1,000 IU to 2,000 IU vitamin D daily, in addition to a prenatal vitamin containing 400 IU vitamin D.[10] During lactation, adequate serum vitamin D levels are necessary to ensure adequate calcium content of breast milk.[10] Lactating women require at least 600 IU vitamin D daily.[2,9] If the infant is not taking a vitamin D supplement of at least 400 IU daily, the lactating mother requires 4,000 IU to 6,000 IU vitamin D daily.[9,13]

## Patient education

Patient education should include information about dietary sources of vitamin D including fortified dairy products, fatty fish, and fish liver oils. Patient should be cautioned against excess or unprotected sun exposure as a source of vitamin D due to the increased risk for skin cancer. Vitamin D toxicity is rare but can occur when serum levels of vitamin D exceed 150 ng/mL and may lead to renal failure, arrhythmias, and death. Patients should be cautioned not to exceed the prescribed dose of the supplement and to keep the supplement out of reach of children. It is also important to educate patients about immediately reporting symptoms of vitamin D toxicity including nausea, weakness, confusion, anorexia, excessive thirst, frequent urination, or pain.[1] As well, patients should be educated about interactions among vitamin D supplements and other medications and supplements. Finally, patients should be advised to report all current and new medications to their healthcare provider.

The *Table* provides a summary of recommendations for the prevention and treatment of vitamin D deficiency.[9]

**Table.** Recommendations for prevention and treatment of vitamin D deficiency[9]

| Age/condition | Minimum recommended daily Intake | Maintenance upper limit | Recommended daily intake for patients at risk for deficiency | Upper limit for patients at risk for deficiency | Treatment of vitamin D deficiency | Maintenance after treatment for deficiency |
|---|---|---|---|---|---|---|
| Adolescent | 600 IU/day | 4,000 IU/day | 600–1,000 IU/day | 4,000 IU/day | 50,000 IU vit D2 or D3 once weekly, or 2,000 IU vit D2 or D3 daily for at least 6 weeks | 600–1,000 IU/day |
| Adult Age 19–50 | 600 IU/day | 4,000 IU/day | 1,500–2,000 IU/day | 10,000 IU/day | 50,000 IU vit D2 or D3 once weekly, or 6,000 IU vit D2 or D3 daily for 8 weeks | 1,500–2,000 IU/day |
| Older adult Age 51–70 | 600 IU/day | 4,000 IU/day | 1,500–2,000 IU/day | 10,000 IU/day | 50,000 IU vit D2 or D3 once weekly, or 6,000 IU vit D2 or D3 daily for 8 weeks | 1,500–2,000 IU/day |
| Older adult Age 70+ (American Geriatrics Society) | 800 IU/day | 4,000 IU/day | 1,500–2,000 IU/day | 10,000 IU/day | 50,000 IU vit D2 or D3 once weekly, or 6,000 IU vit D2 or D3 daily for 8 weeks | 1,500–2,000 IU/day |
| Pregnancy (ACOG 2011; Endocrine Society, 2011) | 600 IU/day | 4,000 IU/day | 1,000–2,000 IU/day | 4,000 IU/day | 1,000–2,000 IU/day | 1,000–2,000 IU/day (up to 4,000 IU/day) |
| Lactation Infant on vit D supplementation | 600 IU/day | 4,000 IU/day | 1,500–2,000 IU/day | 10,000 IU/day | No specific recommendation | |
| Lactation Infant not on vit D supplementation | 4,000–6,000 IU/day | 4,000 IU/day | 4,000–6,000 IU/day | 10,000 IU/day | No specific recommendation | |

### Evaluation and follow-up

Although healthy adults initiating vitamin D supplementation (600–800 IU daily) do not require an initial or follow-up serum 25(OH)D measurement after starting supplementation, patients treated specifically for serum 25(OH)D below 20 ng/mL (50 nmol/L) require a repeat 25(OH)D measurement approximately 3 to 4 months after initiating therapy.[9] The dose of vitamin D may require further adjustment and additional measurements of 25(OH)D. Follow-up 25(OH)D measurements should be made approximately 3 to 4 months after initiating maintenance therapy to confirm that the target level has been sustained.[9]

## Conclusion

Treatment of vitamin D deficiency is essential to bone health and important for overall health. Knowing the sources of vitamin D and recognition of at-risk populations is important. Assessment for sunlight exposure, dietary intake, vitamin D supplementation, and relevant medical conditions and medications is needed. Although universal screening is not recommended, screening those at risk is essential for diagnosis of vitamin D deficiency. Vitamin D deficiency should be corrected and normal levels maintained by following recognized supplement recommendations. Nurse practitioners can promote healthy behaviors to ensure adequate vitamin D and can treat vitamin D deficiency. Referral to an endocrinology specialist is needed when supplementation is not effective. ■

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