

# NAMS PRACTICE PEARL

## ***Should Vitamin D Supplements Be Prescribed Routinely for Midlife Women?***

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***Recommendations for vitamin D in midlife women include daily intakes of at least 600 IU to 800 IU daily to promote bone health. Although vitamin D supplements do not appear to benefit healthy women with normal vitamin D reserves, daily doses of 1,000 IU to 2,000 IU are safe and ensure adequate vitamin D levels in most women. This Practice Pearl will review updated knowledge and recommendations regarding the role of vitamin D in midlife and older women.***

Vitamin D and calcium are important for bone health, and supplements are routinely recommended for the prevention and treatment of osteoporosis. Observational studies have linked low vitamin D levels to many medical problems, including osteoporosis, frailty, falls, and inflammation, as well as neurologic, cardiovascular, and respiratory diseases.<sup>1</sup> Interest in the possible benefits of vitamin D supplements is evidenced by the publication of more than 200 meta-analyses of various effects of vitamin D since January 2021.

***Vitamin D physiology and deficiency.*** Vitamin D facilitates calcium absorption, especially in patients with very low intakes of calcium, and is necessary for the deposition of calcium into newly formed bone tissue. Severe deficiency of vitamin D results in rickets in children and osteomalacia in adults and is associated with impaired muscle function and weakness. Vitamin D receptors have been identified in most tissues and have been shown to have important regulatory roles in cell growth and inflammation. Sources of vitamin D include synthesis in the skin in response to sunlight as well some foods and supplements. A person's vitamin D status is assessed by measurement of serum 25-OH vitamin D (25(OH)D), with insufficiency defined as a value less than 20 ng/mL. Osteomalacia is seen infrequently and only with very low levels (<10 ng/mL). The Recommended Dietary Allowance (RDA) for vitamin D, set by the Institute of Medicine, is 600 IU per day in persons aged 1 to 70 years and 800 IU per day for persons aged 71 years and older. In the National Health and Nutrition Examination Survey, the overall prevalence of vitamin D insufficiency was 39.9%.<sup>2</sup> Older persons and those with severe obesity, malabsorption, serious liver or kidney disease, and who take certain medicines such as phenytoin that affect vitamin D metabolism are at higher risk of vitamin D deficiency.

**Vitamin D supplements.** Vitamin D<sub>3</sub> (cholecalciferol) is available in multiple doses. The effects of vitamin D<sub>3</sub> supplements on serum 25(OH)D levels depend on the person's baseline level. In persons with deficiency, vitamin D<sub>3</sub> 1,000 IU per day leads to an increase of 25(OH)D of about 10 ng/mL, but in adults with normal 25(OH)D values, it has only minimal effect on 25(OH)D levels, bone mineral density (BMD), or muscle strength. No adverse effects of doses up to 2,000 IU per day are known.

**Vitamin D effects on important health outcomes.** Although observational studies have consistently reported associations between low 25(OH)D and higher risk of cancer and cardiovascular disease, the VITamin D and OmegA-3 Trial (VITAL) did not show benefits of supplementation for these endpoints.<sup>3</sup> Meta-analyses that included the VITAL study results have shown no benefit of vitamin D supplements on the risks of cancer, depression, heart disease, diabetes, or death in the general population.<sup>4</sup> VITAL also showed no benefits of supplementation for BMD or falls.<sup>5-6</sup> A meta-analysis of randomized, controlled trials involving many thousands of community-dwelling older adults found no evidence that different doses of vitamin D, with or without calcium, reduced risks of falls or fractures, whereas intermittent doses of 4,000 IU per day or much larger were associated with an increased risk of falls and fractures.<sup>7</sup> Small studies in older adults with severe vitamin D deficiency have demonstrated reductions in fracture risk, improved muscle strength, and reduced fall risk, and one meta-analysis did observe reduced fracture risk in vitamin D-deficient adults.<sup>8</sup> On the basis of these studies, many organizations, including the US Preventive Services Task Force (USPSTF), have recommended against the routine use of vitamin D supplements in healthy adults.<sup>4</sup>

Unfortunately, these large studies, meta-analyses, and the USPSTF recommendations do not address the question of whether vitamin D supplements are useful in people with vitamin D deficiency, nor do they inform who should be screened to identify those who would benefit from supplements.<sup>9</sup> Supplementation with vitamin D in people at increased risk for deficiency should be individualized and guided by serum 25(OH)D levels. Women with osteoporosis do not need more vitamin D than other women, but supplements are recommended to ensure against deficiency and to minimize the risk of hypocalcemia associated with some osteoporosis medications.

**Vitamin D and COVID-19.** Vitamin D modulates immune responses and has been shown to reduce the risk and severity of viral respiratory infections. Observational studies evaluating the relationship between 25(OH)D levels and the risk or severity of COVID-19 infections have shown mixed results, with some showing no relationship, but other studies show more serious disease in patients with low levels. Low levels of vitamin D in a person could simply be a marker of being a sicker person. A meta-analysis of 20 studies demonstrated no statistical difference in mortality, intensive care unit admission rate, or need for ventilator support in patients with COVID-19 who had low versus high 25(OH)D levels.<sup>10</sup> Larger randomized trials of vitamin D in treating COVID-19 are ongoing.

**Pearls.** Although vitamin D supplementation is necessary to correct severe deficiency, healthy women do not need vitamin D supplements. The RDA for vitamin D is 600 IU to 800 IU daily. Daily intakes of 1,000 IU to 2,000 IU daily appear to be safe; doses more than 2,000 IU daily should be avoided for long-term use. For people with or at risk for osteoporosis or COVID-19,

daily intakes of 1,000 IU to 2,000 IU will usually ensure vitamin D adequacy. The management of persons at high risk for vitamin D deficiency needs to be individualized.

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## Disclosures

Dr. McClung reports Consultant/Advisory Board for Amgen.



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