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Vitamin D Supplements Review (Including Calcium, Vitamin K, Magnesium, and Boron)

Find the Best Vitamin D Supplement. Tests and Reviews of Popular Vitamin D Supplements & CL's *Top Picks*.

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Latest Update: Vitamin D for Diabetic Nerve Pain?

Summary

- **What does vitamin D do?** There are many reasons to make sure you're getting sufficient vitamin D: These include improved bone health, reduced risk of heart attack and stroke, reduced risk of asthma and allergy, reduced inflammation, and perhaps others. Not surprisingly, over given periods of time there are fewer deaths among people who have the right amount of vitamin D compared to those who have too little or too much. For details, see What It Does >>

- **How much vitamin D do I need?** You may already get enough vitamin D from the sun (about 15 minutes to the face, arms, and hands at least twice a week without sunscreen) and the foods you normally eat. If you're not sure, get your blood level checked by your doctor. A total serum 25-hydroxyvitamin D level of at least 20 ng/mL is considered "sufficient," although there may be additional benefit to being in the 25 to 35 ng/mL range. Don't exceed 39 ng/mL. Be aware that people who are Black generally have lower total vitamin D levels than whites, but new research suggests these lower levels may be sufficient for Blacks. For details see How Much Do You Need and How Much is Too Much? >>

- **What form of vitamin D is best?** Vitamin D_2 or D_3 will raise your vitamin D level, but D_3 is preferable as it may raise levels more effectively over time and is less likely to cause erroneously low vitamin D blood test results.

- **How much vitamin D should I take?** For every 1 ng/mL increase, you'll need to get an additional 100 IU of vitamin D per day (obese individuals may require double the amount). For example, if your blood level is 18 ng/mL, taking 400 IU of vitamin D daily (or 800 IU if you are obese) should get you to about 22 ng/mL. It can take 6 weeks to reach the peak. Keep taking the vitamin D to stay at that level. For details, see What to Consider When Using >>

- **When to take vitamin D:** Take vitamin D supplements with your biggest meal of the day (the one that contains most fats and oils) as this can increase absorption by as much as 50%! For details, see Take Vitamin D with Food >>

- ***Top Picks* for vitamin D:** Choose a supplement that has been Approved by ConsumerLab.com in the table below because not all supplements live up to their ingredient claims (See What CL Found). Also, see CL's ***Top Picks*** for those offering the best value, dose, and convenience.

- **Don't overdo it! Vitamin D safety and side effects:** Studies show that people with the highest levels of vitamin D actually tend to have more bone fractures, fall more frequently, sleep less well, and die sooner than those with lower, but sufficient, levels. If your level is over 20 ng/mL, you probably don't need a supplement. If your level is above 35 ng/mL, taking a supplement may be doing more harm than good, so consider cutting back. For details see How Much Do You Need and How Much is Too Much? >>

What It Is:

Vitamin D is a fat-soluble vitamin. There are two major forms of vitamin D found in food and supplements: D_2 (ergocalciferol) and D_3 (cholecalciferol). Both vitamin D_2 and D_3 appear to be absorbed with equal efficiency, and both can raise levels of 25-hydroxyvitamin D (also known as calcifediol or calcidiol), which is the prehormone form of vitamin D and a clinical measure of vitamin D status. However, there is evidence that D_3 may be more efficient at raising 25-hydroxyvitamin D levels than D_2 (see "D_2 or D_3?"). There is also evidence that calcifediol can raise 25-hydroxyvitamin D levels more efficiently than D_3 (see "D_3 or calcifediol?"). Be aware, however, that calcifediol is only sold as a prescription drug in the U.S., as is also the case with the active hormone form of vitamin D, calcitriol. However, calcifediol can be found in animal-based foods, as it is present in animal muscle and adipose (fat) tissue.

Vitamin D_3 is produced naturally in human skin exposed to ultraviolet B light and occurs in some animal products, such as cod liver oil, and, in smaller amounts, in other fatty (oily) fish such as herrings, mackerel, sardines, and salmon. Vitamin D_3 is the most common form used in dietary supplements and is the form generally used to fortify foods such as milk (which naturally contains a small amount of vitamin D_3). Vitamin D_3 is made by the conversion of cholesterol compounds, such as 7-dehydroxycholesterol from lanolin found in sheep's wool. Vitamin D_2 is made by the conversion of a sterol found in plants and yeast. Vitamin D_2 is used in some dietary supplements.

See ConsumerTips™ for more information about the two forms of vitamin D and dosing.

(See separate reviews of Calcium and Vitamin K, which are also used in bone health).

What It Does:

Bone and fractures

Vitamin D regulates the amount of calcium and phosphorus in the body, partly by controlling their levels of absorption. Vitamin D treats and prevents rickets in children and osteomalacia (bone softening) in adults. However, as discussed below, benefits of vitamin D supplementation on bone appear generally limited to people deficient in vitamin D, i.e., having blood levels below 20 ng/mL. A study of 81 vitamin D trials went so far as to conclude that "vitamin D supplementation does not prevent fractures or falls, or have clinically meaningful effects on bone mineral density" -- but this study did not analyze results according to the vitamin D status of trial participants and the study authors acknowledged that "trials in individuals with marked vitamin D deficiency... might produce different results." (Bolland, Lancet Diab & Endocrin 2018).

In children:

Given to breast-fed infants, vitamin D may help increase **bone density**.

In girls ages 9 to 13, regular supplementation with calcium and vitamin D has been shown to significantly increase bone density and bone strength (measured in arms and legs) compared to placebo (Greene, Osteoporosis Int 2011). Similarly, in girls ages 10 to 17, supplementation with vitamin D for one year significantly improved bone mineral density in their hips. This effect was not seen among boys of the same age (Al-Shaar, Bone 2013). It is notable, however, that 83% of the girls and 80% of the boys in this study in Lebanon were deficient in vitamin D (below 20 ng/mL) to start. In fact, 34% of the girls started with levels below 10 ng/mL. Two different doses of vitamin D_3 were used in the study, a low dose (1,400 IU) or a high dose (14,000 IU), each given weekly. Interestingly, greater improvements were seen with the lower dose, although the differences were not statistically significant.

One study suggests that children whose mothers supplement with high-dose vitamin D during pregnancy may have a reduced risk of **tooth enamel defects** (but not dental carries, i.e., cavities) (see the Pregnancy section for details).

In adults:

Taken with calcium, vitamin D can help **decrease post-menopausal bone loss and prevent osteoporosis** (loss of bone density), as well as improve **tooth retention** in the elderly. *However, if a person's blood level of vitamin D is already close to or above 20 ng/mL, taking a vitamin D supplement provides no further bone benefit.* This was demonstrated in a placebo-controlled study of a group of white, postmenopausal women in New York with an average vitamin D level above 20 ng/mL (but below 30 ng/mL). Taking 4,000 IU of vitamin D_3 daily for 6 months did not reduce bone loss in these women (based on measurements of bone turnover markers which occur in the

blood) (Aloia, J Clin Endocrin Metab 2013). In the same study, some of the women were given high-dose calcium supplementation (1,200 mg from calcium carbonate, as 600 mg twice a day). Those who received the calcium showed signs of reduced bone loss during the study -- regardless of whether they received the vitamin D

supplement. This benefit is likely due to the fact that the women, on average, were not getting the recommended daily intake of calcium before supplementation (their average intake was 900 mg, while the recommended daily intake for women their age is 1,200 mg). It is possible that a lower dose of calcium would also have been beneficial, as well as safer: Too much calcium from supplements has been associated with a higher risk of kidney stones and stroke (see Calcium Review -- Concerns and Cautions).

In a study among older women (average age 67) with blood levels of vitamin D averaging 19 mg/mL, daily doses of vitamin D ranging from 400 IU to 4,800 IU were not associated with a significant effect on bone mineral density compared to placebo. During the study, all of the women maintained a total calcium intake of 1,200 mg per day from food and/or calcium supplements (Smith, J Intern Med 2018). (Another analysis of the same study, discussed in the Muscle, Balance and Falls section below, found that the rate of falls was lowest in women who achieved vitamin D blood levels of 32-38 ng/mL after supplementation — but women with higher blood levels had the highest rate of falls.)

Another placebo-controlled study in post-menopausal women compared the effectiveness of 800 IU of vitamin D_3 daily (400 IU twice a day) to the same daily dose plus an additional 20,000 IU twice a week. Both groups also received 1,000 mg of calcium daily (500 mg twice a day from calcium carbonate). After one year, bone mineral density was unchanged or slightly improved in both groups. Markers of bone turnover (bone loss) in blood serum were also reduced in both groups, but the *higher dose was actually less efficient at reducing bone turnover*, contrary to what the researchers had expected (Grimnes, Osteoporos Int 2012).

Similarly, a study of postmenopausal women in Wisconsin found no beneficial effect on bone mineral density from giving vitamin D at low-dose (800 IU daily) or high-dose (800 IU daily plus 50,000 IU twice monthly) for 1 year, compared to placebo. There was also no beneficial effect on muscle function, muscle mass, or falls, and only a small effect on calcium absorption. Women in the study started with a median vitamin D blood level of 21 ng/mL and, during the study, averaged 19, 28, and 56 ng/mL, respectively, in the placebo, low-, and high-dose groups. The women in this study had adequate calcium intake. The researchers concluded that the findings did not support "experts' recommendations" to maintain levels of 30 ng/mL or higher in postmenopausal women, but did support the Institute of Medicine's recommended level of at least 20 ng/mL (Hansen, JAMA 2015).

A study in the U.S. among 687 older men and women (average age 63) with sufficient blood levels of vitamin D, most of whom had some degree of bone loss, showed that taking 2,000 IU of vitamin D3 daily for two years did not increase bone mineral density or improve bone structure compared to placebo. Supplementation increased average blood levels of vitamin D from 27 ng/mL to 39 ng/mL. Calcium intakes were not reported, but 17% of the participants reported using a calcium supplement and, among these, there was less bone mineral density loss in the neck of the femur if they were taking vitamin D versus placebo but there was no benefit in whole body bone mineral density (LeBoff, J Bone Miner Res 2020).

Although not all studies have shown a benefit of vitamin D supplementation in reducing **fractures**, a review of several studies concluded that supplementation with 800 IU or more of vitamin D was "somewhat favorable" in the prevention of hip fracture and any nonvertebral fracture in people 65 years of age or older.[39] Most notably, it found a 30% reduction in hip fracture among people taking 792 to 2,000 IU of vitamin D per day compared to those taking no vitamin D or small amounts (up to 360 IU per day). The review also suggested that vitamin D blood levels above 24 ng/mL are most beneficial for reducing the risk of both hip and nonvertebral fractures, and frequent dosing of vitamin D (such as daily or weekly) is more beneficial than annual dosing. Similarly, a large study of men aged 70 to 97 years in Sydney, Australia found that those with vitamin D levels between 24 and 29 ng/mL were least likely to suffer bone fractures. In comparison to this group, men with lower levels (at or below

14.4 ng/mL) and higher levels (above 29.2 ng/mL) were, respectively, 3.5 and 2.7 times as likely to experience a fracture — suggesting a potential risk from too little, as well as too much, vitamin D in the body (Bleicher, J Bone and Min Res 2014).

Middle-aged and older women who follow a vegan diet and do not supplement with calcium and vitamin D were found to have *three times the risk* of **hip fracture** compared to women who are not vegetarians, while women who follow a vegan diet but take supplemental calcium and vitamin D did not have an increased risk, according to a large study of men and women age 42 or older. No association between calcium and vitamin D supplementation and hip fracture risk was found in men who follow a vegan diet (Thorpe, Am J Clin Nutr 2021). (See the Calcium Supplements Review for more details.)

Be aware that vitamin D deficiency may impede **healing from fractures**, as was reported in a 44-year-old man in the Netherlands whose femoral (thighbone) fracture failed to heal four years after the initial injury despite multiple surgeries to properly set the bone. He was found to have severe vitamin D deficiency (25(OH)D of 4 ng/mL) and diagnosed with hyperparathyroidism due to vitamin D deficiency and low dietary calcium intake. He was given weekly injections of 50,000 IU of vitamin D for six weeks, after which he took 400 IU of oral vitamin D and 500 mg of calcium daily. Eight months after supplementation began, his vitamin D levels were sufficient (24 ng/mL) and his fracture healed (Moonen, Nutrition 2021).

In healing fractures, improving one's vitamin D level alone is insufficient if calcium intake is inadequate, as shown in a study in the Netherlands of 32 postmenopausal women (average age 65) with wrist fractures who had low levels of vitamin D (average 25(OH)D of 17 ng/mL) and inadequate intake of calcium (average 715 mg per day, compared to the 1,200 mg per day recommended for women in this age group). They were divided into three groups and given one oral dose of either 30,000 IU or 75,000 IU of vitamin D, which was repeated six weeks later, or no vitamin supplementation. None of the groups received calcium supplementation. Despite increasing their levels to 20 ng/mL and 23 ng/mL, respectively, their fractures healed no better than those in women who did not receive vitamin D. In fact, the higher dose of vitamin D (equivalent to 1,800 IU per day) resulted in *poorer* bone healing than in the control group. (As noted elsewhere in this Review, large single doses of vitamin D have been shown to be detrimental.) There were no differences in self-reported pain or function between the lower and higher dose groups or the control group. (Heyer, J Bone Miner Res 2021).

Vitamin D may reduce **aging of bones**. Compared to bone samples from the hips of people with vitamin D blood levels of 20 ng/mL or higher, bone from those with levels below 20 ng/mL (i.e., deficient in vitamin D) were found to be more brittle (over-mineralized) on the inside while thicker and under-mineralized on the outside. When physically tested, bone from vitamin D-deficient people was 22% more likely to crack and the cracks were longer compared to bone from people not deficient in vitamin D. The researchers believe that osteoclast cells, which normally keep bone healthy, cannot get through the thick, under-mineralized outer layer of bone formed in vitamin D-deficient people and, as a result, areas of bone under this layer continue to age and over-mineralize even as the overall bone mineral content progressively decreases (Busse, Sci Transl Med 2013).

Vitamin D levels below 10 ng/mL (severe deficiency) were associated with more severe **lumbosacral disc degeneration** and **low back pain** among 232 postmenopausal women in China compared to those with levels of 30 ng/mL. There was no significant difference in disc degeneration between those with levels of 10 - 30 ng/mL versus levels above 30 ng/mL, leading the researchers to speculate that only extremely low vitamin D levels affect disc degeneration. However, those with levels between 10 - 30 ng/mL were more likely to have moderate to severe low back pain, and other predictors of back pain were smoking, higher BMI (body mass index), lack of vitamin D supplementation, and osteoporosis (Xu, Menopause 2020).

Muscle, balance, and falls

In older adults:

A review of 13 studies found that vitamin D supplements (800 to 1,000 IU daily) may improve balance and muscle strength, but not gait, among older adults.[30] *The benefits of taking vitamin D, however, may depend on whether or not a person has insufficient levels to start. Too much vitamin D may even have negative effects, including increasing the risk of falls that result in fractures.*

A placebo-controlled, six-month study among older men and women (average age 73) in Lebanon with low skeletal muscle mass who also had very low blood levels of vitamin D (averaging 10 ng/mL) found that increasing blood levels of vitamin D to 28 ng/mL (by giving 10,000 IU of vitamin D three times a week -- a high dose) significantly increased muscle mass in the arms and legs, although it did not increase hand-grip strength. The increase in muscle mass was greater in normal-weight individuals than in those who were obese (Hajj, Arch Osteoporos 2018).

One of the best studies of vitamin D and falls focused on women with insufficient levels of vitamin D (blood levels less than 20 ng/mL) who had not taken vitamin D supplements and were getting only about 120 IU daily of vitamin D from their diets. They were divided into groups given 400 IU, 800 IU, 1,600 IU, 3,200 IU, 4,000 IU, or 4,800 IU of vitamin D_3 or a placebo. Over the course of one year, 58% of those given the placebo had fallen, but those given 1,600 to 3,200 IU of vitamin D_3 had the lowest rate of falls — just 30%. Those given lower or higher doses did not fall significantly less than the placebo group. Women ending with blood levels of 32-38 ng/mL had the lowest rate of falls (21%), while the highest rate of falls (72%) was among those with levels of 38 to 46 ng/mL. In short, those who received enough vitamin D to correct insufficiencies but remained under 40 ng/mL fared best (Smith, J Steroid Biochem Mol Biol 2017). The researchers suggested that the current upper limit on vitamin D intake of 4,000 IU daily should be lowered to 2,000 IU to reduce the risk of falls. Similarly, a study in Denmark among women with hyperparathyroidism and low vitamin D levels (averaging 12.4 ng/mL) found that giving 2,800 IU of vitamin D_3 daily for 3 months increased vitamin D levels to 36 ng/mL and lowered the elevated parathyroid hormone levels but *reduced* maximal handgrip strength by 9%, knee flexion strength by 13%, and *slowed performance* on a "Timed Up and Go" test as compared to results for women given placebo. The researchers cautioned against relatively high daily doses of vitamin D in treating vitamin D insufficiency (Bislev, Calcif Tissue Int 2018). Additional analysis of data from this study suggested that the loss in muscle strength could be due to a "direct detrimental effect" of moderately high doses of vitamin D on skeletal muscles. In contrast to women given placebo, the women supplemented with vitamin D developed increased blood levels of several compounds associated with muscle breakdown (carnitine, choline, and urea), as well as a tendency towards increased serum levels of TMAO and urinary creatinine, which can also occur with muscle breakdown (Bislev, Nutrients 2020).

A study among 688 older men and women (average age 77) with elevated fall risk (e.g., balance or walking problems or a history of falls) and 25(OH) vitamin D blood levels averaging 22 ng/mL found that doses of 1,000 IU or higher (2,000 or 4,000 IU) taken daily for two years did not prevent falls compared with 200 IU. In fact, those who took 1,000 IU or more had an 87% increased risk of a serious fall (resulting in fracture or dislocation) and 148% increased risk of a fall requiring hospitalization compared to those who took just 200 IU per day (whose blood levels rose, on average, to 27 ng/mL vs 32, 35, and 48 6 ng/mL, respectively, for the 1,000, 2,000, and 4,000 IU groups). A major contributor to the findings was an unusually high rate of adverse events in the 2,000 and 4,000 IU groups during the first year of the study (Appel, Ann Intern Med 2020). Further analysis of data from the same study showed that participants who took 1,000 IU or more of vitamin D were also 166% more likely to have a first-time fall resulting in a fracture, although not more likely to have a greater number of falls, compared to those taking 200 IU per day or not taking vitamin D at all (Wanigatunga, J Am Geriatr Soc 2021).

A small study of women aged 65 years and older with somewhat limited mobility found that those given a capsule of 4,000 IU of vitamin D_3 daily after breakfast for 4 months experienced a 10% increase in muscle fiber size (measured at the thigh) compared to those given placebo (Ceglia, J Clin Endocrin Metab 2013). The supplemented group also experienced a 30% increase in vitamin D receptors in muscle cells, suggesting an

effect on muscle metabolism and/or function. There was no effect, however, on physical functioning (balance, walking, rising) or knee extension power — although the study did not involve increased exercise. The women chosen for the study had moderately low vitamin D levels (mean of 18.5 ng/mL) which rose in the supplemented group to 32 ng/mL. (Note: 4,000 IU per day is a large dose at the Tolerable Upper Intake Level; however, absorption was probably somewhat reduced as the vitamin was taken after breakfast rather than with a larger meal).

A 9-month study in younger postmenopausal Brazilian women (ages 50 to 65) known to be deficient in vitamin D (averaging 15 ng/mL) and with a history of falls found that a daily dose of 1,000 IU (given as liquid drops) increased the average level to 27.5 ng/mL and was associated with a 25.3% increase in muscle strength of the lower limbs, as demonstrated by chair rising test, but no increase in handgrip strength. Although there was no exercise component of the study, women receiving the vitamin D maintained lean mass (muscle) while women in the placebo group lost lean mass (Cangussu, Osteoporos Int 2015). It was separately reported that the rate of falls during the study was 46% higher for those receiving placebo rather than vitamin D, and the researchers calculated that, after adjusting for variables, the risk of a fall was actually 90% greater in the placebo group and the risk of recurrent falls was 180% greater (Cangussu, N Am Menopause Soc Meeting Abstract 2015, p. 67). Similarly, giving 800 IU of vitamin D daily to postmenopausal women in Turkey who were deficient in vitamin D (average level of 10 ng/mL) resulted in small but statistically significant increases in muscle strength in the hamstring and quadriceps. In contrast, women in the study who were, instead, given a single, very high dose (300,000 IU) of vitamin D did not have a statistically significant improvement despite a greater rise in their vitamin D levels even through the end of the 12 week study (Apaydin, BMC Endocr Disor 2018).

In contrast, a study in women aged 70 and older who were at risk for bone fracture showed an *increase* in falls and fractures among those given an extremely high, single, annual dose (500,000 IU) of vitamin D3.[10] This unexpected finding may have resulted from unusual effects of the extreme dose.[11] A *higher* rate of falls with higher-dose vitamin D3 was also found in a study of community-dwelling men and women 70 years of age and older with a prior fall -- 58% of whom were vitamin D deficient (i.e., blood levels under 20 ng/mL) (Bischoff-Ferrari, 2016). The study compared a monthly dose of 24,000 IU of vitamin D (equivalent to 800 IU per day) to two higher doses: 60,000 IU or 24,000 IU with 300 mcg of calcifediol — a vitamin D metabolite which is 2 to 3 times more potent than vitamin D3 (Jetter, Bone 2014). Although the higher-doses raised vitamin D levels more than the lower dose, they had no benefit on lower extremity function and were each associated with an *increased* risk of falls over the course of a year (about 66% fell) compared with the lower dose (47.9% fell). Seniors who were not deficient in vitamin D but were given 60,000 IU per month experienced the most falls, and people whose levels reached 44.7 - 98.9 ng/mL had nearly *twice as many falls* as those whose levels reached 21.3 to 30.3 ng/mL.

Too high a dose of vitamin D may actually weaken leg muscles, as shown in a one-year study of overweight and obese women (with a mean vitamin D blood levels of 21.4 ng/mL) given 2,000 IU of vitamin D3 per day or placebo in conjunction with a reduced calorie diet and moderate to vigorous aerobic activity. Over the course of the year, *leg strength significantly decreased in the vitamin D group* (-2.5 pounds decrease in lifting weight) while it increased slightly in the placebo group (+1.8 pounds). There were no significant differences between the groups in changes in lean body mass or bone mineral density of the spine and femoral neck (Mason, JAGS 2016). The same study found no benefit on weight loss between the groups, as reported earlier (see "Weight loss control" below). Mean vitamin D levels in the treated group rose by 13.6 ng/mL to 35 ng/mL while it fell in the untreated group b 1.3 ng/mL to 20.1 ng/mL -- which is still above the cut-off for insufficiency (under 20 ng/mL).

In a study among homebound older adults, more than half of whom had insufficient (< 20 ng/mL) blood levels of vitamin D and had reported having fallen in the previous year, a monthly dose of 100,000 IU vitamin D3 taken for 5 months increased vitamin D blood levels to sufficient levels in all but one person, and reduced the number of falls over the 5 months by approximately half, compared to placebo. One weakness of the study, however, is that the researchers knew who received the vitamin D3 and who received a placebo (Houston, J Am Geriatrics Soc 2015).

A large observational study among older men in England suggests that having very low blood levels of vitamin D may increase the risk of **orthostatic hypotension (low blood pressure when standing)**, a condition that is

associated with an increased risk of falls and fractures (Mol, J Am Med Dir Assoc 2019; Hamrefors, PLoS One 2016). The study, among 3,620 men (average age 69), found that vitamin D deficiency (< 10 ng/mL) was associated with a 51% increased risk of orthostatic hypotension. Vitamin D levels were measured as total vitamin D (25OHD2 plus 25OHD3) (Gilani, Age Ageing 2020). However, giving vitamin D (1,000, 2,000, or 4,000 IU daily) to older adults with orthostatic hypotension did not help reduce orthostatic symptoms (such as lightheadedness, dizziness, seeing spots, imbalance, headache, etc.) compared to taking 200 IU of vitamin D3 daily. The study participants had vitamin D levels ranging from 10 to 29 ng/mL (Juraschek, Circulation 2021). Interestingly, a preliminary study in teenage girls with orthostatic instability suggested a possible benefit of vitamin D supplementation.

Several studies have shown that vitamin D supplementation in older women who already have sufficient levels of vitamin D (at least 20 ng/mL) does not improve balance or strength:

- A study of women aged 70 to 80 in Finland who generally had sufficient vitamin D levels (averaging 25 ng/mL), showed that taking vitamin D3 (800 IU daily) for 2 years did not reduce falls, injuries from falls, or physical functioning. In fact, compared to those given placebo, the women who received vitamin D actually showed a decline in a "get up and go" test. Average blood levels of vitamin D rose to 37 ng/mL among those receiving vitamin D. In the study, some of the women were enrolled in physical training classes once or twice week and performed exercises at home (5 to 15 minutes) on the other days. Compared to women who did not train, the exercisers experienced less than half the number of injurious falls and injured fallers, although there was no decrease in the number of falls. The exercisers also showed improved muscle strength, balance and mobility, although exercisers treated with vitamin D showed smaller benefits than exercisers receiving placebo. Vitamin D did have a small effect on reducing bone loss in the hip and increasing bone density in the lower leg, but this did not translate into other benefits (Uusi-Rasi, JAMA Intern Med 2015).

- A year-long study in Norway among postmenopausal women (ages 50 to 80) with generally sufficient blood levels of vitamin D (averaging about 25 ng/mL) and osteopenia (reduced bone density) or osteoporosis, found that neither high-dose vitamin D supplementation (800 IU D3 daily + 20,000 IU twice weekly) nor supplementation with a lower dose (800 IU D3 daily + placebo), improved muscular strength, balance or quality of life (Grimnes, Clin Endocrinol (Oxf) 2017). Women in both the high and lower-dose groups also took 1,000 mg of calcium daily.

- A 3-year study among older African-American women (average age 68) who were generally not vitamin D deficient found that increasing blood levels of vitamin D to an average of 47 ng/mL with high-dose vitamin D supplementation (3,600 IU median daily dose) *did not* decrease the risk of falls compared to women who took a placebo and maintained an average blood level of 21 ng/mL (Aloia, J Am Geriatr Soc 2019).

- A large, 5-year, placebo-controlled study in Australia found that monthly, high-dose (60,000 IU) vitamin D3 did *not* reduce the risk and incidence of falls among men and women ages 60 to 84, most of whom already had more than adequate blood levels of vitamin D at the beginning of study. If fact, there was a 25% *increased* risk of falls among normal-weight participants (BMI < 25 kg/m^2) given vitamin compared to those who were overweight or obese (BMI > 25 kg/m^2). The researchers speculated that people with less body fat (where vitamin can be stored) may have higher circulating levels of vitamin D when taking high doses compared to those with more body fat (Waterhouse, J Cachexia Sarcopenia Muscle 2021).

The bottom line from these studies appears to be that vitamin D may increase muscle mass in older individuals with very low levels of vitamin D. It may also help may help with balance and reduce falls in women with insufficient levels of vitamin D (below 20 ng/mL), but may do little or have negative effects in women with already sufficient

levels. In older men, vitamin D deficiency may increase the risk of orthostatic hypotension, which is a risk factor for falls and fractures, but it is not known if vitamin D supplementation helps prevent falls due to this condition. Not surprisingly, exercise can be extremely effective in reducing the risk of injury from falls.

In younger adults:
A review of seven clinical trials (from 2010 to 2013) in healthy adults aged 18 to 40 concluded that vitamin D supplementation increased upper and lower limb strength. It is important to note that the vast majority of subjects in these studies were deficient in vitamin D (average blood level was only 12.3 ng/mL), many of whom were in India, where deficiency is more common than in the U.S. High doses (2,000 IU per day to 60,000 IU per week) were used in the studies, which lasted 4 weeks to 6 months. It is not clear whether these results are relevant to a population with adequate levels of vitamin D. As noted in the review, vitamin D receptors are found on skeletal muscle and these receptors are involved in protein synthesis within the muscle, possibly explaining these findings (and those for older individuals -- discussed above) (Tomlinson, J Sci and Med in Sport 2015).

However, not all studies have found a benefit in younger adults with low or deficient blood levels of vitamin D. A study in Estonia among 39 previously untrained men (average age 23) with low blood levels of vitamin D (averaging 14 ng/mL as 25(OH)D) who began a strength training program (3 sessions per week, supplementing with 20 grams of whey protein after each session), taking 8,000 IU (200 mcg) of vitamin D3 daily for three months did not increase training-induced gains in muscle strength or lean body mass compared to strength training plus placebo, despite raising average blood levels to 57 ng/mL 25(OH)D. In fact, men who took the placebo (and had low blood levels of vitamin D throughout training) had greater gains in muscle strength in two of the seven strength exercises performed (chest press and seated row) compared to those who took vitamin D. The researchers suggested that benefits might only occur in people with severe deficiency (< 10 ng/mL) and the very high dose vitamin D given may actually *block* the activity of vitamin D receptors (as pointed out by other researchers) (Savolainen, Eur J Appl Physiol 2021).

No increase in muscle strength occurred in a placebo-controlled study of slightly older, active adults (average age 44) in Japan, although lean body mass (i.e., muscle) increased by 1 lb. Participants were initially deficient in vitamin D and were given 420 IU (10.5 mcg) of vitamin D3 daily, raising blood levels from an average of 13 ng/mL to 24 ng/mL (Sun, Ann Nutr Metab 2019).

Two small studies of U.S. professional football players found associations between lower levels of vitamin D and injuries. A study of players on the Pittsburgh Steelers found that the mean vitamin D level among players who suffered a muscle injury was 19.9 ng/mL, while players with no muscle injury had a mean level of 24.7 ng/mL (Shindle, AOSSM 2011 abstract p. 56). A study of players on the New York Giants found vitamin D levels significantly lower in those with at least one bone fracture when compared with levels in those with no fractures after accounting for the number of seasons played. In addition, players who were released during the preseason because of either injury or poor performance had significantly lower vitamin D levels (62% were below 20 ng/mL) than did players who played in the regular season (11% were below 20 ng/mL) (Maroon, Am J Sports Med 2015). (The team names were not disclosed in the studies, but were identified in a Wall Street Journal article).

In children and adolescents:
Orthostatic intolerance (OI), which can cause dizziness or fainting upon standing, can affect children and adolescents. OI includes conditions such as orthostatic hypotension, vasovagal syndrome, and postural tachycardia syndrome (POTS). A small study among teenage girls (average age 16) with OI and vitamin D levels averaging 22 ng/mL (i.e., at the lower end of adequate) found that taking 2,000 to 5,000 IU of vitamin D daily for two months increased vitamin D levels to 41 ng/mL on average and increased the amount of time the girls could

tolerate standing on head-up tilt by about 15 minutes. Heart rate variability when standing on tilt was also increased after vitamin D treatment, which suggests the body was under less stress. Baroreflex sensitivity, a measure of how well the heart rate adapts to changes in blood pressure, also improved after supplementation

with vitamin D. However, the study did not include a control group, so it's not possible to conclude that vitamin D supplementation improves OI (Shaltout, Hypertension 2020). As noted earlier, very low levels of vitamin D have been associated with orthostatic hypotension (a form of OI) in older men.

Benign Paroxysmal Positional Vertigo (BPPV)

BPPV is a common form of vertigo that is caused by displacement of calcium carbonate crystals (otoliths) within the inner ear. There is a hypothesis that vitamin D deficiency may reduce the density of these crystals, increasing the risk of their displacement, and a study in England found that BPPV was more common in months when levels of vitamin D (measured as 25-hydroxyvitamin D) are lower (March, April and May). A preliminary study among 10 women in Portugal with a history of BPPV and generally low vitamin D blood levels evaluated the effect of giving vitamin D on BPPV episodes. Half the women were given 5,000 IU of vitamin D daily if their starting levels were below 20 ng/mL, or 800 IU per day (given as a single monthly dose) if their levels were 20 ng/mL or higher. Over 12 months, the vitamin D blood levels in these women rose to an average of 32.1 ng/mL and none experienced BPPV. The other women did not receive vitamin D and each experienced 1 to 3 episodes of BPPV, suggesting a possible protective role of vitamin D supplementation against recurrence of BPPV (Matos Carniero de Sousa, Hear Bal Comm 2019).

Further evidence of a protective role of supplementation was provided by a larger study among 957 people in South Korea (average age 62) recently treated (with a repositioning maneuver) for BPPV. In the study, people in the intervention group were evaluated for serum levels of vitamin D at baseline, and those with levels less than 20 ng/mL were given 400 IU of vitamin D and 500 mg of calcium carbonate twice daily for 12 months. People in the observation group were not evaluated for vitamin D status or given supplementation. Both groups were followed for about one year, although data was considered for any person who had been followed up for at least one month. People in the intervention group had a 24% lower rate of BPPV recurrence compared to those in the observation group, with greatest benefit seen for patients in the treatment group who had been vitamin D deficient (25-hydroxyvitamin D levels <10 ng/mL) (Jeong, Neurology 2020). *It appears that supplementation with vitamin D, with or without calcium, may reduce recurrent episodes of BPPV in people who have low levels of vitamin D*.

Overactive bladder and urinary incontinence

Low blood levels of vitamin D have been associated with higher risk of overactive bladder (OAB) (i.e., suffering from urinary urgency or frequency with or without incontinence) (Yoo, BJU Int 2018), possibly explained by the role of vitamin D in muscle function (Parker-Autry, Int Urogynecol J 2012). A small study in Jordan, for example, found that people with severe vitamin D deficiency (below 10 ng/mL) were *32 times more likely* to have overactive bladder symptoms than people with levels above 30 ng/mL. No rigorous studies have been conducted to determine if vitamin D is beneficial in OAB, but the same Jordanian researchers gave vitamin D (50,000 IU weekly for 4 to 8 weeks) with encouragement to increase dietary calcium intake to 13 people with OAB (11 of whom had vitamin D levels below 20 ng/mL) in whom drug therapies had not been successful. The vast majority of these patients reported improvements in nighttime and daytime urinary symptoms, although it is impossible to evaluate the clinical significance of these results as there was no placebo or other scientific control (Abdul-Razzak, Neurourology and Urodynamic, 2019). A study among 56 women (average age 60) with urgency urinary incontinence found that, overall, vitamin D supplementation (50,000 IU weekly for three months) *did not* improve bladder symptoms, pelvic floor muscle function, or functional status compared to placebo, although it should be noted that most of the women who took vitamin D had sufficient blood levels before supplementation. A sub-group analysis found a significant decrease in the number of incontinence episodes per day among Black women who took vitamin D compared to placebo (-63% vs. -22%). During the study, average blood levels of vitamin D increased from 21 ng/mL to 58 ng/mL among those who took vitamin D (Markland, J Am Geriatr Soc 2019).

Statin drugs and vitamin D

If you use a statin medication for cholesterol-lowering, it may very helpful to maintain sufficient blood levels of vitamin D for the following reasons:

Statins may work better when vitamin D is adequate:

A 6-month, placebo-controlled study in China among people with high cholesterol and treated with statin drugs found that taking 2,000 IU of vitamin D_3 tablets significantly improved cholesterol levels. Approximately half the people in the study began with vitamin D blood levels below 20 ng/mL (i.e., vitamin D deficient) and about another quarter had levels between 20 and 30 ng/mL. Mean vitamin D blood levels increased by 17.1 ng/mL in the treated group and by 2.4 ng/mL in the placebo group (due to increased sun exposure because the study ended in June). Compared to the placebo group, which experienced slight improvements in cholesterol levels, total cholesterol levels in the treated group fell by an additional 22.1 ng/mL, triglycerides fell by 28.2 mg/dL, LDL ("bad") cholesterol fell by 20.2 mg/dL, and HDL ("good") cholesterol increased by 8.2 mg/dL. Improvements were greater when excluding those who began the study with vitamin D levels of 30 ng/mL or higher (no analysis was reported of just those who had been vitamin D deficient). The researchers noted that these results with vitamin D may be limited to statin-treated patients (Qin, Clin Nutr 2015).

Note — Giving high-dose vitamin D to people who are *not* deficient may slightly *increase* cholesterol levels (see Concerns and Cautions).

Statin-related muscle pain less likely with when vitamin D is adequate:

The risk of developing muscle pain (myalgia) and inflammation (myositis) while taking cholesterol-lowering statin drugs appears to be greater when people have lower levels of vitamin D (and keep in mind that severe vitamin D deficiency itself -- regardless of statin use -- can cause bone pain and muscle weakness). A study found that, among statin users, the average vitamin D level among those without myalgia was 34.9 ng/mL, while the average among those with myalgia was 28.4 ng/mL (Michalska-Kasiczak, Int J Cardiol 2015). A small study of people who suffered muscle pain while on statins and had generally blood levels of vitamin D averaging 22 to 23 ng/mL evaluated the effects of giving very large weekly doses of vitamin D_2, ranging from 50,000 to 100,000 IU, with a goal of boosting vitamin D levels to 50 to 80 ng/mL. The researchers concluded that 88% to 95% of patients were able to tolerate statins without muscle pain at various time points in the study, although these percentages ignore those who had dropped out at earlier points due to renewed muscle pain. Over two years, 44 of the 146 patients (30%) experienced myalgia-myositis and stopped statin treatment, and 70% were symptom free. The study was not double-blind, lower doses were not tried, and, likely for ethical reasons, there was no control group (i.e., patients not given vitamin D but restarted on statins) (Khayznikov, N Am J Med Sci 2015). As noted in Concerns and Cautions, the dosage of vitamin D used in this study is very high and could be associated long-term safety risks. However, based on the evidence, it would seem worthwhile to make sure you have adequate vitamin D levels if taking a statin.

Statin-related decline in exercise performance is blunted when vitamin D is adequate:

While statins can lessen improvements in cardiorespiratory fitness that normally occur with exercise as well as reduce the content of mitochondria (i.e., the "energy powerhouses") in muscle cells, vitamin D adequacy may lessen these negative effects. A study in India among 28 people with type 2 diabetes who were vitamin D deficient (averaging about 10 ng/mL) found that, after 12 weeks of performing moderate aerobic exercise, those given simvastatin (40 mg daily) had an 8.4% decrease in cardiovascular fitness, but if also given vitamin D (60,000 IU weekly — which is a very high dose), the decrease was only 0.6%. Skeletal muscle mitochondrial content decreased 3.6% with simvastatin but improved 12.1% if vitamin D was also given. Vitamin D alone, without simvastatin, increased cardiovascular fitness and mitochondrial content by 7.1% and 16.7%, respectively (Singla, J Diabetes 2017).

More vitamin D is needed to raise blood levels when taking a statin:

A review of clinical trials in which vitamin D was given to people aged 60 and over with low vitamin D levels found that statin users had a 21.4% smaller increase in vitamin D blood levels than people not using statins (Bischoff-Ferrari, JAGS 2017). It would seem advisable to use a slightly higher than normal dose of vitamin D if you are taking a statin.

Vitamin D levels may increase or decrease depending on the statin:
In small clinical trials, certain statin medications have been shown to increase blood levels of vitamin D, while other stains have been shown to have little effect or to slightly decrease blood levels of vitamin D — possibly due to enzymes involved in metabolizing these drugs or whether the drugs are more soluble in fats or water. **Rosuvastatin (Crestor)** was shown to increase 25(OH)D levels by 22.3 ng/mL and 1,25-dihydroxyvitamin D (the active form) by 3.7 pg/dL when taken daily for 8 weeks (Yavuz, Cardiovasc Drugs Ther 2009), although not all studies have found a large an impact. This was also seen in a separate study by the same research group in which rosuvastatin (10 mg/day) taken daily for two months increased 25(OH)D blood levels by about 23 ng/mL (from 11.8 to 35.2 ng/mL); however, the same study found that **fluvastatin (Lescol XL)**, taken at a dose of 80 mg per day, had *no effect* on vitamin D levels (Ertugrul, Cardiovasc Ther 2011).

Atorvastatin (Lipitor) appears to have a more modest effect on vitamin D levels, although results from clinical trials have been inconsistent. A study in Spain found that either a low (10 mg to 20 mg) or higher (40 mg to 80 mg) daily doses of atorvastatin for one year led to modest increases in 25(OH)D blood levels (about 3 ng/mL) (Perez-Castrillon, Am J Cardiol 2007). However, a study in India found that atorvastatin (10 mg/day) taken for six months caused a small but significant reduction in 25(OH)D blood levels (about 2 ng/mL), while those taking rosuvastatin (5 mg/day) showed an increase in 25(OH)D levels, although the increase was modest (about 2 ng/mL) compared to the studies described above. The researchers noted that atorvastatin is a stronger inducer (i.e. it enhances activity) of an enzyme (CYP3A4) involved in the breakdown of 25(OH)D, possibly explaining the reduction (Patwardhan, Indian J Pharmacol 2020).

There is some evidence that 20 to 80 mg of **lovastatin (Mevacor)** daily increases 25(OH)D blood levels, while it seems that **simvastatin (Zocor)** either increases or has little effect on vitamin D levels (Gupta, Atherosclerosis 2011).

Back pain
A study among overweight and obese adults in Australia with back pain who also were deficient in vitamin D (levels below 20 ng/mL) found that high-dose vitamin D significantly reduced back pain among those who were *severely deficient* (levels below 12 ng/mL), but not among those with levels above 12 ng/mL. Vitamin D was given as an initial 100,000 IU dose followed by 4,000 IU per day for 16 weeks, boosting levels, on average, by 22 ng/mL (Brady, J Ster Biochem Mol Biol 2018). [Note: Obese individuals require larger doses of vitamin D to raise levels.]

Rheumatoid arthritis
Low levels of vitamin D are associated with a higher risk of developing **rheumatoid arthritis** and may be associated with more significant disease severity and progression. These associations do not prove a cause-and-effect relationship.

A study in China found the mean level of serum vitamin D in men and women with rheumatoid arthritis to be 17.2 ng/mL, while it was 23.2 ng/mL in a matched control group of healthy individuals. Among the patients with arthritis, lower vitamin D levels were associated with higher rates of swollen joint, tender joint, joint pain, and morning stiffness, as well as osteopenia and osteoporosis (Hong Rheumatology 2014).

A study in France among 643 people with early rheumatoid arthritis found that disease activity and severity was worse at baseline for those with vitamin D deficiency (<10 ng/mL) compared to those with higher levels. Vitamin D deficiency was also associated with a 70% greater chance of functional disability at 6 months, as well as 90%

greater chance of radiographic progression and erosion progression at 12 months (Mouterde, J Rheumatol 2020).

Osteoarthritis (worn joints)

Giving vitamin D_3 to people with painful osteoarthritis of the knee was *not* found to improve symptoms nor slow progression of the disease more than giving a placebo, according to a two-year study in Boston (McAlindon, JAMA 2013). In fact, throughout the study, those given vitamin D were more likely to report using non-steroidal anti-inflammatory drugs (e.g., ibuprofen) than patients given placebo. However, most patients who participated in the study were *not deficient* in vitamin D to begin with -- the average starting blood level of 22.7 ng/mL. Vitamin D was given at an initial dose of 2,000 IU daily and then adjusted, primarily upward, to achieve levels over 36 ng/mL. Only the subset of people who began the study deficient in vitamin D (levels below 15 ng/mL) experienced improvement taking vitamin D, although this improvement could not be considered statistically significant due to the small size of this group.

Similarly, a large three-year study among people aged 50 years and older in the UK with knee osteoarthritis given 800 IU daily of vitamin D3 showed no benefit compared to placebo with regard to progressive narrowing of the joint space, mobility, function, or pain. The average starting blood level of vitamin D was just slightly above 20 ng/mL, with half the individuals under that amount and, therefore, deficient in vitamin D. However, unlike the study above, further analysis did not show better results for those who started the study deficient in vitamin D compared to those who were not (Arden, Osteoarth Cartilge 2016).

A two-year study in Australia found that knee joint pain decreased by 36% in a group treated with vitamin D_3 (50,000 IU per month: equal to 1,667 IU per day) but this was not found to be statistically significant because pain declined 26% among those given placebo. Both groups lost knee cartilage volume during the study but the loss was slightly less in the vitamin D group -- although not to a significant degree. Unlike the Boston study above, many patients in this study were deficient in vitamin D, with a mean level of 17.5 ng/mL, which, by the end of the study, was over 24 ng/mL in 79% of those treated with vitamin D and 43% of those receiving placebo. Although not an original endpoint of the study, there was a statistically significant improvement in joint function for the vitamin D group compared to placebo. Interestingly, while improvements plateaued in the placebo group after 1 year, symptoms continued to improve in the vitamin D group through the second year (Jin, JAMA, 2016). A later analysis of the same two-year study looked at the effects of vitamin D supplementation on **foot pain and related disability**, which is common in people with knee osteoarthritis and associated with more severe knee pain. The analysis showed modest improvements in foot pain and disability in the vitamin D treatment group that maintained blood levels of 20 to 30 ng/mL. Although small, these improvements were, statistically, significantly better than the general lack of improvement seen in the placebo group as well as in those in the treatment group who did not maintain blood levels of at least 20 ng/mL (Tu, Arthritis Care Res (Hoboken) 2020).

These studies suggest that vitamin D supplementation does not benefit osteoarthritis of the knee in people not deficient in vitamin D, while the evidence is mixed on whether it may help those who are deficient in vitamin D.

Cardiovascular disease, blood pressure, and cholesterol

As discussed below, several studies have shown increased risk of cardiovascular disease associated with lower blood levels of vitamin D (i.e., lower than 15 to 20 ng/mL). Studies in which vitamin D has been given to such people with low levels have shown cardiovascular benefits (e.g., small improvements in blood pressure, cholesterol, arterial stiffness) with regular, moderate doses (600 to 1,000 IU), but generally less benefit and even side effects with higher doses (2,000 IU daily or 100,000 IU monthly or quarterly). There appears to be no cardiovascular benefit giving high-dose vitamin D to people with blood levels already above 15 to 20 ng/mL.

A major study (the VITAL study) of a cross-section of middle-aged Americans given 2,000 IU of vitamin D daily for a median of 5.3 years found no overall reduction in cardiovascular events (heart attack, stroke, or death from

cardiovascular causes) relative to placebo. However, participants were *not deficient in vitamin D* — the average starting blood level was 30.8 ng/mL, which increased to over 40 ng/mL among those given vitamin D during the study (Manson, NEJM 2018).

Similarly, a study in England gave 2,000 or 4,000 IU of vitamin D, or a placebo, daily for one year to over 300 generally healthy older people with average vitamin D blood levels of 20 ng/mL -- about 10% of whom were already taking 400 IU of vitamin D or more daily. Although blood levels of vitamin D more than doubled, there was no significant effect on blood pressure, heart rate, arterial stiffness, echocardiogram measures, cardiac function, or blood levels of prohormone that regulates blood pressure (Tomson, J Am Heart Assoc 2017).

On the other hand, an earlier analysis of two large studies showed that men who consumed 600 IU or more per day of vitamin D from foods and supplements were 16% less likely to have **cardiovascular disease and stroke** over a period of approximately 20 years compared to men consuming less than 100 IU per day. The same association was not seen among women; the reason for this is unclear but one possible explanation given is that women may need higher intake of vitamin D because they tend to have a higher percentage of body fat than men and vitamin D is fat soluble. In addition, vitamin D intake during the study period, which ended in 2006, may have been too low to produce meaningful differences.[21]

Research has found that men with low levels of vitamin D in the blood (15 ng/mL and lower) are at increased risk for **heart attack** compared to those with levels at 30 ng/mL and higher, even after adjusting for other risk factors and physical activity. Similarly, in a study lasting about 6 years, adults with vitamin D levels below 30 ng/mL were more likely like to suffer from **hypertension**, **coronary artery disease**, **cardiomyopathy**, and **diabetes** than those with higher levels.[32] In fact, after adjusting for other factors, the **risk of death** from all causes was 164% higher among those with the lower levels of vitamin D. The researchers note that 71% of people in the study (involving over 10,000 people in Kansas) had serum vitamin D levels below 30 ng/mL — the mean was 24.1 ng/mL. Among those with levels below 30 ng/mL, the risk of death was reduced if a vitamin D supplement was being taken; however, there was no such additional advantage with supplementation for those with levels already above 30 ng/mL. The researchers did not analyze the results by further subgroups of vitamin D level. A study that followed 230,000 men and women (average age 48) in the southwest U.S. for 5 years applied different vitamin D level subgroupings and found that the risk of cardiovascular disease was 35% higher for those with vitamin D levels below 15 ng/mL (9% of the studied population) compared to those with higher levels (Muhlestein, Circulation 2015). Although the apparent benefit of avoiding vitamin D deficiency appears dramatic, there is potential downside from much higher levels (see How Much Do You Need and "How Much is Too Much?" for more about mortality rates and vitamin D).

Research suggests that long-term, high-dose vitamin D supplementation does *not* improve mortality rates, and may *worsen* certain outcomes, in **people with chronic heart failure**, despite modest improvements in heart output reported in one study. In that trial, 163 people in the UK with chronic heart failure (less than half the normal ventricular output) were given high-dose (4,000 IU) vitamin D_3 or placebo daily for 1 year, with the primary goal of increasing walking distance in a 6-minute test. All of the patients started the study with vitamin D levels below 20 ng/mL. Among those given vitamin D, blood levels of vitamin D generally rose to about 50 ng/mL, however, there was no increase in walking distance -- which actually *decreased by 4%*, while it increased by 4% among those given placebo. Those taking vitamin D did, however, experience a modest but statistically greater improvement in heart output (left ventricular ejection fraction increased from 25.6% at baseline to 33.3%, while, in the placebo group, it increased from 26.5% at baseline to only 27.9%) (Witte, J Am Coll Cardiol 2016). [ConsumerLab.com Comment: The high dose given in this study caused patients to achieve unusually high vitamin D blood levels -- levels associated with *increased falls* in other studies, possibly explaining the reduction in walking distance despite improved heart output. A lower but still higher than normal dose (e.g., 2,000 IU) could have achieved vitamin D sufficiency and may have improved heart output *as well as* improved walking distance.]

A placebo-controlled study in Germany among 400 people with advanced heart failure and low blood levels of vitamin D found that 4,000 IU of vitamin D given daily for three years increased median blood levels of 25(OH)D from 14 ng/mL to 37 ng/mL but did not reduce mortality and increased the need for mechanical circulatory support (MCS) implants (used to manage reduced heart output) and hospitalization (Zittermann, Eur Heart J 2017). Researchers followed the participants for an additional three years after supplementation ended (during which blood levels of vitamin D would have likely decreased) and found that those previously treated with vitamin D were no longer at increased risk of requiring an MCS implant or hospitalization, further suggesting that high-dose supplementation had a detrimental effect (Zittermann, ESC Heart Failure 2020).

Low levels of vitamin D are generally associated with **elevated blood pressure**. However, studies have, at best, only shown a modest reduction in blood pressure when vitamin D is given. A comprehensive review of 46 trials concluded that vitamin D is ineffective for lowering blood pressure, regardless of starting levels of vitamin D in the blood, and should not be used as antihypertensive agent -- although most patients with hypertension in the analyzed studies were also being treated with antihypertensive medication, possibly obscuring an effect of vitamin D (Beveridge, JAMA Intern Med 2015). One trial which found no effect was conducted among adults age 70 and older with systolic hypertension. The participants, most of whom were also taking anti-hypertension medication, were given 100,000 IU of vitamin D3 every three months (equaling 1,100 IU per day) for one year, raising the mean vitamin D blood level from 18 ng/mL to 28 ng/mL. Vitamin D supplementation failed to improve hypertension or other measures of cardiovascular health, including cholesterol levels (Witham, JAMA 2013). However, another placebo-controlled study using a dose of 2,000 IU of vitamin D3 daily for 6 months found that those receiving vitamin D supplementation experienced reductions in systolic and diastolic blood pressures of, respectively, 6.2 mm Hg and 4.2 mm Hg compared to those not receiving vitamin D. People in the study were all taking nifedipine (a calcium channel blocker). Among those receiving vitamin D, mean vitamin D blood levels rose from 19.4 ng/mL to 34.1 ng/mL (Chen, Atherosclerosis 2014).

Be aware that one study found vitamin D deficiency to be associated with *low blood pressure* upon standing (known as orthostatic hypotension) in older men (see Muscle, balance and falls for details).

A 12-week study in Iran of overweight and obese premenopausal women found that daily supplementation for 12 weeks with 1,000 IU vitamin D3 increased HDL ("good") **cholesterol** by 7%. However, total cholesterol increased 1.7% and there was also a 4% increase in LDL ("bad") cholesterol — although it contained less ApoB, suggesting less plaque-forming ability. Interestingly, **body fat** decreased by 9.6% (about 6 lbs), although total body weight was unchanged.[31] A larger and longer (2 year) study in the U.S. found that postmenopausal women given 400 IU of vitamin D3 and 1,000 mg of calcium (from calcium carbonate), taken in two divided doses daily, experienced a 4.5 mg/dL decrease in LDL cholesterol compared to those who received a placebo. Vitamin D blood levels rose to a mean of 24.3 ng/mL among the supplemented women compared to 18.2 ng/mL in the placebo group. Although there was no statistically significant effect of taking the supplement on total cholesterol, HDL, or triglycerides, the researchers did find that women with higher blood levels of vitamin D tended to have higher levels of HDL and lower levels of both triglycerides and LDL (Schnatz, Menopause 2014).

A small study of obese adolescents given a monthly dose of 100,000 IU of vitamin D3 for 3 months (averaging 3,333 IU per day) showed no improvement in arterial function and insulin and glucose levels, and increases of 32% and 9%, respectively, in triglycerides and total cholesterol. A weakness of the study was that few participants had been deficient in vitamin D (below 20 ng/mL), with the average starting level of 22 ng/mL, which increased to 35 ng/mL (Javed, Pediatric Obesity 2015). A large placebo-controlled study giving 100,000 IU of vitamin D3 monthly to older adults (average age of 66), for approximately 3 years found no reduction in cardiovascular events even among a subgroup who started the study deficient in vitamin D (blood levels below 20 ng/mL) (Scragg, JAMA Cardio 2017). However, a 16-week study among overweight African-Americans with vitamin D deficiency (blood levels averaging about 15 ng/mL), found that high doses of vitamin D (60,000 IU or 120,000 IU given once-a-month -- each of which raised levels to about 35 ng/mL) improved (i.e., reduced) arterial stiffness by

about 8 to 10%. A lower dose (18,000 IU per month) did not have this effect despite raising the levels to an average to 23 ng/mL. The study did not assess effects on cardiovascular disease (Raed, PLOSOne 2017).

Diabetes, insulin resistance and glucose control

Maintaining a vitamin D level of at least 25 or 26 ng/mL or moderately higher may reduce insulin resistance and may improve blood sugar control in people at risk for or with diabetes, although not all studies have found a benefit. There is preliminary evidence that vitamin D supplementation might modestly reduce the pain of peripheral neuropathy in people with type 2 diabetes and low blood levels of vitamin D.

Risk of type 1 diabetes

Higher serum levels of vitamin D — up to a point -- have been associated with a lower risk of developing **type 1 diabetes** (i.e., requiring insulin). In a study of two thousand people on active duty in the military, those with vitamin D levels between 24 and 31 ng/mL had the lowest risk of being diagnosed with type 1 diabetes. Compared to this group, the risk of diabetes was more than 2.5 times as great among those with levels between 17 and 24 ng/mL, and the risk was more than 3.5 times as great among those with levels below 17 ng/mL. No risk reduction was associated with levels above 31 ng/mL — in fact, the risk of diabetes was slightly higher for those with levels above 31 ng/mL than those with levels between 24 and 31 ng/mL (Gorham, Diabetologia 2012).

Observational data suggests that dietary intake of vitamin D is associated with lower risk of developing type 1 diabetes (Hypponen, Lancet 2001). It has been suggested that to reduce the risk of type 1 diabetes, infants and children receive supplemental vitamin D if they have limited sun exposure, live in northern areas, are exclusively breastfed, or are dark skinned (Harris, J Nutr 2005).

Insulin resistance and prediabetes

Obesity itself is a major risk factor for insulin resistance, but too little vitamin D may increase the risk. A study found that obese individuals with vitamin D blood levels below 20 ng/mL were 12 times more likely to be insulin resistant than obese individuals with sufficient levels of vitamin D (Kabadi, Diabetes Care 2012) . In addition, a study of overweight and obese women who were not diabetic found that vitamin D blood levels of at least 26 ng/mL appear to be needed for normal glucose metabolism in both Black and white women, and those with this amount of vitamin D had lower body fat, blood glucose, insulin and triglyceride levels than women with lower levels of vitamin D (Sorkin, JN 2014).

Furthermore, a study of 115 overweight older adults in Lebanon with low average blood levels of vitamin D (10 ng/mL) but who did not have diabetes (although 14 were considered to be pre-diabetic) found that 10,000 IU of vitamin D3 taken three times per week for six months modestly reduced insulin resistance (as measured by HOMA-IR) from an average of 2.63 to 2.4, and decreased fasting blood sugar levels, compared to placebo (Hajj, J Nutr Health Aging 2018). However, a placebo-controlled trial among 64 men and women in Ireland with prediabetes and low blood levels of vitamin D found that high-dose vitamin D (3,000 IU daily for six months) *did not* improve blood sugar control or insulin function despite increasing vitamin D blood levels from an average of 12 ng/mL to 40 ng/mL (Wallace, Am J Clin Nutr 2019).

Maintaining adequate blood levels of vitamin D may also have a beneficial effect on blood sugar and insulin levels in healthy people who are not overweight: A study among 81 healthy men and women in Japan, most of whom had low or deficient blood levels of vitamin D (average blood level 13 ng/mL) found that, compared to placebo, 420 IU of vitamin D3 taken daily for one year increased average blood levels of vitamin D to an average of 24 ng/mL, decreased fasting blood glucose (from an average of 88.3 mg/dL to 85.3 mg/dL), and improved insulin resistance values (as measured by HOMA-IR) from 1.17 to 0.84 (Sun, Nutr Res 2016).

One study found the risk of developing type 2 diabetes was 43% lower among individuals with vitamin D levels over 25 ng/mL compared to those with levels under 14 ng/mL (Mitri, Eur J Clin Nutr 2011).

A study in India among men and women with prediabetes and very low blood levels of vitamin D (averaging 10 ng/mL) found that oral supplementation with 60,000 IU of vitamin D3 after breakfast once a week (equivalent to about 2,140 IU daily) for three months improved insulin sensitivity (measured by the insulin sensitivity (OGIS) index) compared to placebo. However, there were no improvements in the insulin-sensitivity check index (QUICKI), HOMA-IR, nor in fasting or post-meal blood sugar levels compared to placebo. Interestingly, average vitamin D blood levels in those who took vitamin D increased to 52 ng/mL, which is above the level at which the risk of adverse effects may increase (Ahmed, Cureus 2020).

Supplementing people at risk of type 2 diabetes who are not deficient in vitamin D does not reduce the incidence of type 2 diabetes, as was shown in a large, placebo-controlled 2.5 year study in which people with pre-diabetes took 4,000 IU of vitamin D daily, raising the average level from 27.7 ng/mL to 54.3 ng/mL. However, among the subgroup of people who started the study with vitamin D levels below 12 ng/mL, those given vitamin D were *62% less likely* to develop type 2 diabetes than those given placebo — a major difference (Pittas, NEJM 2019). A placebo-controlled study among older men and women at high risk of diabetes or newly diagnosed type 2 diabetes with vitamin D levels averaging 21 ng/mL (45% of whom were below 20 ng/mL, i.e., vitamin D deficient) found that supplementation for 6 months with 5,000 IU daily of vitamin D significantly improved peripheral (i.e., in muscles) insulin sensitivity although not hepatic sensitivity, i.e., there was no improvement in insulin secretion, glucose levels, or HbA1C (Lemieux, Eur J Endocrin 2019).

In people with type 2 diabetes

Among people with type 2 diabetes with vitamin D levels of 20 ng/mL or higher, vitamin D supplementation may not provide benefit (Mitri, Eur J Clin Nutr 2011). In fact, a large U.S.-based trial found that giving high-dose vitamin D (4,000 IU daily) for 48 weeks to people with stable type 2 diabetes who were not vitamin D deficient (average starting level was 27 ng/mL) did not improve any measure of blood sugar control (Angellotti, J Endocrine Society 2018). Also see "Depression" below for more about type 2 diabetes and vitamin D.)

A study in Indonesia among 68 men and women (average age 65) with type 2 diabetes and low 25(OH)D levels of vitamin D (average 15 ng/mL) who also had **peripheral neuropathy** (nerve damage resulting in pain, numbness, burning, tingling and other sensations in the hands and feet) found that 125 mcg (5,000 IU) of vitamin D taken daily for eight weeks in addition to standard treatment (pregabalin, gabapentin, or amitriptyline) *modestly* reduced self-reported *overall pain* scores (- 3.34 vs -2.37 points on a 10-point scale) compared to standard treatment alone. However, both groups experienced similar reductions in burning pain (an average reduction of about 10 points on a 100-point scale), and vitamin D did not reduce tingling, electric shock pain or numbness and did not improve sleep quality, general activity scores, or mood compared to standard treatment alone. Blood levels increased to an average of 40 ng/mL among those given vitamin D but remained low (18 ng/mL) in the others (Pinzon, J Pain Res 2021). More research is needed to confirm any benefit, as the study did not include a placebo control.

A study in Denmark found that both high and low vitamin D levels are associated with a form of nerve damage called **cardiovascular autonomic neuropathy (CAN)** in people with type 1 and type 2 diabetes. CAN affects heart rate and blood vessel function and may cause low blood pressure on standing and exercise intolerance. Patients with CAN have a greater chance of having a heart attack and lower chance of surviving one. The findings suggest that beneficial effects of vitamin D are restricted to a specific serum range (around 20 ng/mL to 50 ng/mL) and both too low and too high levels are detrimental to the autonomic nervous system (Hansen, Diabetic Med 2016).This may help explain similar associations found between vitamin D levels and falls as well as mortality.

Gestational diabetes

Supplementation with a combination vitamin D and calcium may improve blood sugar control in pregnant women with **gestational diabetes**. In a six-week study of 56 women with gestational diabetes (at 24 to 28 weeks

gestation), those who received 1,000 mg calcium per day, plus 50,000 IU of vitamin D3 at the beginning of the study and another 50,000 IU at week 3, had significantly lower fasting blood glucose levels compared to those given placebo (respectively, a 0.89 mmol/l reduction versus a 0.26 mmol/l increase), lower serum insulin levels

(-13.55 vs. +9.17 pmol/l), and a significant increase in insulin sensitivity (+0.02 vs -0.002) (Asemi, Diabetologia 2014).

Non-alcoholic fatty liver disease (NAFLD):

Low levels of vitamin D have been associated with non-alcoholic fatty liver disease -- the accumulation of fat in the liver (also called hepatic steatosis) which can lead to inflammation, scarring and cirrhosis (Elaides, Aliment Pharmacol Ther 2013). NAFLD affects approximately 30% of Americans. A preliminary study in 40 women and men with significant liver fat accumulation and insufficient blood levels of vitamin D (averaging 11.8 ng/mL) found that with a weekly dose of 20,000 IU of vitamin D3 (equivalent to about 2,857 IU per day), liver fattiness decreased by approximately 5% after only four weeks; while vitamin levels rose to an average of about 35 ng/mL. A weakness of this study, however, is that it did not include a control group (Papaostoli, J Gastrointestin Liver Dis 2016). A study of adults with NAFLD with vitamin D blood levels below 30 ng/mL given 2,000 IU of vitamin D daily for six months found that levels rose above 30 ng/mL in most (75%) of those who did not have liver inflammation but in only 15% of those with inflammation (known as steatohepatitis). Only those whose levels increased showed significant improvements in plasma ALT levels (an indicator of liver function) and HOMA-IR scores (an assessment of insulin resistance). Higher doses of vitamin D may be necessary to sufficiently raise vitamin D levels in such people (Dasarathy, J of Nutr 2017).

Inflammation

Raising low levels of vitamin D may also reduce inflammation in the body. In a study of blood from thousands of adult Americans, levels of C-reactive protein (CRP), a marker of inflammation, decreased as vitamin D levels increased to just below 21 ng/mL[28] However, there was no further benefit when vitamin D levels reached and exceeded 21 ng/mL. In fact, after adjusting for cardiovascular risk factors, it was found that CRP levels slowly but progressively *increased* at that point, *suggesting a slight inflammatory action of vitamin D* at these higher levels. The results seem to reinforce the importance of maintaining a plasma vitamin D level of at least 20 ng/mL and suggest some potential downside of higher levels of vitamin D.

Somewhat similar conclusions were drawn from a well-controlled, 1-year study of vitamin D in adults aged 60 to 84 years in Australia. Starting with vitamin D levels of about 17 ng/mL, people were given monthly dose of vitamin D of 30,000 IU (equal to 1,000 IU/day), 60,000 IU, or a placebo. At 1 year, there were no significant differences in levels of inflammatory biomarkers in the treated groups versus placebo — except for a slight increase in a pro-inflammatory marker (IL-6) in the higher-dosed group, half of whom achieved vitamin D blood levels of 30 ng/mL or higher. The researchers note that this may suggest a detrimental effect of higher vitamin D levels (Waterhouse, Br J Nutr 2015).

Vitamin D appears to accelerate the resolution of inflammatory responses during **tuberculosis** therapy.[42] In a study in London, patients given very large doses of vitamin D3 (100,000 IU every 2 weeks) along with standard antibiotic therapy had less inflammation, and their infections cleared 13 days earlier on average, than patients who did not receive vitamin D. It is important to note, however, the very high prevalence of profound vitamin D deficiency in the studied population -- more than half the patients had levels of vitamin D below 8 ng/mL prior to therapy. Added vitamin D may not yield the same benefits for patients who already have sufficient levels of vitamin D.

Asthma

Moderate doses of vitamin D may improve symptoms of asthma in children as well as in adults with uncontrolled asthma. However, improvements seem to be limited to those with very low vitamin D levels, e.g. less than 10

ng/mL.

A review of medical studies published from 1950 to 2009 that looked at, among other variables, vitamin D intake and asthma, suggested that vitamin D deficiency may be linked to airway inflammation, decreased lung function and poor asthma control. The researchers conducting the review hypothesized that vitamin D supplementation may lead to improved asthma control, although this cannot be established as many of the studies were not specifically designed to test the effects of vitamin D supplementation on patients with asthma (Urashima, Am J Clin Nutr 2010). A clinical study published in 2014 tested whether high-dose vitamin D supplementation reduced treatment failures among adults with asthma already receiving an inhaled corticosteroid (ciclesonide) and a bronchodilator (levalbuterol). Vitamin D supplementation (4,000 IU per day after an initial 100,000 IU dose) did not lead to a statistically significant reduction in initial treatment failures compared to those receiving a placebo supplement. However, during the 28-week study, the group receiving vitamin D was 20% less likely to have a treatment failure and 37% less likely to have an exacerbation of symptoms. It is possible that more significant results may have been obtained if the study did not have certain weaknesses: Half the patients started the study with vitamin D levels above 20 ng/mL and, therefore, were not vitamin D deficient and might not benefit from additional vitamin D; and, because of the very high dosage used in the study, many of these people may have achieved unusually high blood levels of vitamin D which other studies suggest may counter beneficial effects of vitamin D (Castro, JAMA 2014). Further analysis of this group found no benefit regarding colds -- see Denlinger study, below). A small pilot study (not placebo-controlled) tested a lower dose (a daily capsule of 2,000 IU of vitamin D3) for 12 weeks in asthmatic people age 65 and older in Philadelphia. Prior to initiation of therapy, it found that mean vitamin D levels in the blood were significantly lower (19.0 ng/mL) in those with uncontrolled asthma compared to those with well-controlled symptoms (25.7 ng/mL). Self-reported symptoms of asthma decreased significantly after 12 weeks of vitamin D treatment only in patients who had uncontrolled asthma, although clinical measurements of airflow remained unchanged. The researchers note that vitamin D receptors are present in the smooth muscle of the bronchi and vitamin D has been shown to play a role in modulating the immune system (Columbo, Allergy, Asthma, & Clin Immun 2014).

A study in Japan among schoolchildren with asthma found that giving them each 800 IU of vitamin D daily for two months led to significantly greater improvements in asthma control than did giving a placebo. This improvement remained significant even four months after discontinuing vitamin D, at which point 34% of those who had received placebo had difficulty breathing compared to only 15% of those who had received vitamin D. Interestingly, the children in both groups had had relatively high levels of vitamin D (around 30 ng/mL) before the trial began and few were vitamin D deficient (Tachimoto, Allergy 2016). In contrast, a placebo-controlled study among 192 children with asthma in the U.S. aged 6 to 16 years (most of whom had vitamin D levels above 20 ng/mL) found that giving very high-dose vitamin D (4,000 IU daily) for 48 weeks did not reduce the number of days until the next severe asthma exacerbation or lead to reductions in their use of an inhaled steroid (fluticasone) (Forno, JAMA 2020). Furthermore, analysis of additional data from the study showed that supplementing with vitamin D did not reduce the immune response (based on antibody levels) to dust mites or cockroaches — two common triggers of year-round asthma attacks (Rosser, J Allergy Clin Immunol 2021).

A review in 2016 of seven clinical trials (ranging in length from 4 months to one year -- including the Castro and Tachimoto studies noted above) investigating the effects of vitamin D supplementation in children or adults with asthma (most of whom had mild to moderate asthma and used their regular asthma medications as needed) found that oral vitamin D supplementation (average daily dose 900 IU vitamin D3, although some participants received additional, larger doses in some trials) reduced the average number of attacks per year requiring treatment with oral steroid medication from 0.44 to 0.22, and reduced the risk of hospitalization from asthma attacks from 6% to about 3%. However, measures of lung function (such as forced expiratory volume, or FEV1) were not improved (Martineau, Cochrane Database Syst Rev 2016). Due to lack of data, the researchers were not able to assess whether the improvements would be limited to those who were deficient in vitamin D before supplementation, or whether those with more severe asthma would benefit. A later review of studies similarly

found that vitamin D supplementation reduces the rates of asthma exacerbations requiring treatment with systemic corticosteroids. *However*, it found that these protective effects were only seen among people with very low vitamin D levels (less than 10 ng/mL) prior to vitamin D treatment and not in people with higher levels

(Jolliffee, Lancet Respir Med, 2017).

COPD (Chronic obstructive pulmonary disease)

Several studies have shown that high-dose vitamin D may reduce exacerbations in adults with COPD and/or asthma who also have low blood levels of vitamin D, but it does not appear to be beneficial in those who already have sufficient levels.

A placebo-controlled study in the UK of 240 people with COPD found that taking vitamin D3 (120,000 IU orally every 2 months — equal to 2,000 IU per day) significantly reduced the risk of having moderate or severe exacerbations among those who began the study deficient in vitamin D (blood levels below 20 ng/mL). This benefit was not found for those who began the study with sufficient levels of vitamin D. Vitamin D did not reduce the risk of upper respiratory infection among any group. (Martineau, Lancet Resp Med 2014).

A study in Belgium found that vitamin D supplementation (100,000 IU every 4 weeks) significantly reduced exacerbations of COPD but only among patients starting with vitamin D levels less than 10 ng/mL (Lehouck, Ann Intern Med 2012). Similarly, a study in New Zealand among 775 older men and women (average age 67) with **asthma and/or COPD** found that, overall, vitamin D3 supplementation (initial oral dose of 200,000 IU followed by 100,000 IU monthly for more than three years) did not reduce the risk of exacerbations (use of oral corticosteroids more than 20 days) compared to placebo, except in those who began the study with deficient blood levels of vitamin D (< 10 ng/mL) (Camargo, Nutrients 2021).

Allergies

Higher serum vitamin D levels are associated with a reduced risk of allergy in children and adolescents, but not in adults. Preliminary evidence suggests that giving vitamin D to pregnant women may reduce infants' risk of allergic sensitivity and supplementing people with low levels of vitamin D may help reduce some symptoms of allergy.

A review of data from a nationwide study of over 6,000 individuals showed that, for children and adolescents, allergic sensitization was more common in those with serum vitamin D of less than 15 ng/mL compared to those with 30 ng/mL or greater for 11 out of 17 allergens. Results were adjusted for potentially confounding factors like time spent on indoor activities. The strongest associations were for allergy to oak (5 times the risk), peanut (2.4 times the risk), and ragweed (1.8 times the risk). There was also increased risk of allergy to dog, cockroach, mite, shrimp, ryegrass, Bermuda grass, birch and thistle. In adults, there was no consistent association between allergy and vitamin D levels.[19]

Giving vitamin D daily to infants (as well as to their mothers while pregnant) *reduces infants' risk of allergic sensitivity to dust mites* and *reduces visits to the doctor for **asthma** during the infancy*. This was shown in a study in New Zealand in which pregnant women were given 1,000 IU or 2,000 IU of vitamin D during the last 3 months of pregnancy and their newborn infants were then given, respectively, 400 IU or 800 IU for 6 months. Another group of mothers and infants received placebo. During the first 18 months of life, 11% of infants in the placebo group saw a doctor for asthma, compared to 0% who received the lower dose of vitamin D and 4% who received the higher dose. Virtually all of the infants were breastfed at birth, although 47% began infant formula prior to age six months. The researchers noted that other studies have shown that sensitization to dust mites is associated with increased risk of childhood asthma (Grant, Allergy 2016).

A double-blind study among 68 men and women (average age 29) in Iran with seasonal allergies (allergic rhinitis) with generally low average blood levels of vitamin D (14.4 ng/mL) found that those who took 50,000 IU of vitamin

D3 once per week for two months in addition to the antihistamine medication cetirizine (Zyrtec, Aller-Tec) had significant decreases in self-reported nasal itching, sneezing, runny nose and post-nasal drip compared to those who took cetirizine with a placebo. There was no improvement in eye redness and itching. Among those who took vitamin D, average blood levels of vitamin D increased to 24 ng/mL while levels remained relatively unchanged (15 ng/mL) in those who did not take vitamin D (Bakhshaee, Eur Arch Otorhinolaryngol 2019).

Chronic Hives (Urticaria)

Chronic hives or urticaria is characterized by the recurring appearance of hives and welts. A 12-week, placebo-controlled study among 120 people with chronic urticaria in India who were deficient in vitamin D (average blood level of 14 ng/mL) found that a 60,000 IU dose of vitamin D3 taken every two weeks (averaging 4,286 IU per day) significantly reduced disease severity and levels of inflammatory cytokines in the blood. Need for antihistamine medication also decreased. Blood levels of vitamin D increased to an average 29.5 ng/mL among those taking it. The researchers attribute the improvement to vitamin D's action as an immunoregulatory hormone (Mony, Clinica Chimica Acta, 2020). [Note, it is preferable to take lower doses of vitamin D daily or weekly than a large dose less often, although this is used in some clinical trials, like this one, to ensure compliance.]

Eczema

*Some research shows that taking vitamin D reduces **eczema (atopic dermatitis)** severity in people with moderate to severe disease and low or borderline low levels of vitamin D when used along with standard treatment.*

Achieving or maintaining a vitamin D blood level of at least 20 ng/mL was associated with a significant reduction in the severity of eczema (atopic dermatitis) in comparison to levels below 20 ng/mL in a study of 58 children and adults in Mexico with moderate to severe eczema who were also given standard treatment (topical steroid, soap substitute, and emollient). Levels of 30 ng/mL or higher provided no further benefit (Sanchez-Armendariz, Int J Dermatol 2018). A study in Egypt among 86 children and adolescents with severe eczema found that taking 1,600 IU of vitamin D3 daily for three months in addition to applying 1% hydrocortisone cream twice daily moderately reduced eczema severity compared to using hydrocortisone cream alone. The percentage of people who achieved at least 75% improvement in eczema severity was significantly higher in the vitamin D group than the placebo group (39% vs 7%). In those who took vitamin D, average blood levels of vitamin D increased from 22.8 ng/mL to 36.11 ng/mL, while levels in the placebo group did not significantly change from the baseline value of about 25 ng/mL (Mansour, Pharmacol Res Perspect 2020).

Psoriasis

Vitamin D supplementation was found to improve psoriasis in a study among 45 patients with mild, **chronic, plaque psoriasis** in Thailand who had not responded satisfactorily to other treatments and generally had low vitamin D levels. A statistically significant improvement in symptoms relative to placebo was seen at 3 months. Improvements with vitamin D continued through 6 months, but the difference from placebo at that point fell slightly short of statistical significance. Patients were given 60,000 IU of vitamin D2 (as three 20,000 IU capsules) every 2 weeks (averaging 4,286 IU/day) for 6 months. At the start of the study, just over one-fourth of patients had vitamin D levels below 20 ng/mL, with an average level of 24 ng/mL and, by the end of the study, none of the vitamin D-treated patients were below 20 ng/mL, compared to 44% in the placebo group (an increase, due to seasonality), although vitamin D only raised levels, on average, by about 3 ng/mL — a surprisingly small increase considering the large dose. The researchers noted that vitamin D deficiency appears to be several times higher among those with psoriasis than in the general Thai population (Disphanurat, Derm Res Prac 2019).

Fibromyalgia

Fibromyalgia is a common syndrome in which a person has long-term, body-wide pain and tenderness in the joints, muscles, tendons, and other soft tissues. Some, but not all, studies suggest improvements in symptoms of fibromyalgia with vitamin D supplementation, and it would seem worthwhile to raise vitamin D levels if not already at least 20 to 24 ng/mL.

One randomized controlled study found that increasing vitamin D blood levels from a mean of 19 ng/mL to about 50 ng/mL was associated with a modest decrease in fibromyalgia pain (a 20-point decrease on a 100-point scale). The study involved 30 adults (mostly women) in Austria with fibromyalgia. Most of the participants started the study with vitamin D levels below 24 ng/mL and were given 2,400 IU of vitamin D_3 daily, while those starting with levels between 24 ng/mL and 32 ng/mL were given 1,200 IU daily. Treatment continued for 20 weeks or until vitamin D levels reached 48 ng/mL (levels in several patients went as high as 55 to 93 ng/mL). Twenty-four weeks after supplementation ended, pain returned to the original level in the group (Wepner, Pain 2013).

A study in Mexico among 80 women (average age 51) with mild to moderate fibromyalgia found that weekly supplementation with 50,000 IU of vitamin D3 for 12 weeks did not improve function or measures of fatigue, pain, anxiety or depression compared to placebo. However, 95% of those who received vitamin D were not deficient in vitamin D to start (levels were 20 ng/mL or higher, and were raised to an average of 51.8 ng/mL) and those in the placebo group who had levels below 20 ng/mL were also given vitamin D (for ethical reasons), bringing their average level up to 20 ng/mL. Symptoms scores dropped almost equally in both groups. It does not seem possible to draw a valid conclusion from this study regarding the benefit of vitamin D in treating women with fibromyalgia (Lozano-Plato, Clin Rheumatol 2021).

Insomnia

Although insomnia can occur in people with vitamin D deficiency, the evidence that vitamin D supplementation improves sleep in people with low blood levels of vitamin D is mixed. In addition, supplementation with high doses of vitamin D may decrease the quality of sleep.

Vitamin D supplementation was shown to decrease the amount of time it took to fall asleep by an average of about 10 minutes, and increase the duration of sleep by about a half-hour, in U.S. veterans with chronic pain whose 25(OH)D blood levels increased from an average of 18 ng/mL to 26 ng/mL with supplementation. However, this study did not include a placebo group, and it's not known if the improvement in sleep was a direct result of supplementation, or due to a decrease in pain that also occurred, limiting the significance of the findings (Romano, Curr Pharm Des 2020).

A placebo-controlled study in Norway among 189 men and women (average age 51) with low 25(OH)D blood levels (average 14 ng/mL) found that increasing blood levels to an average of 34 ng/mL with vitamin D3 supplementation did *not* increase sleep duration, or reduce symptoms of daytime sleepiness or insomnia, compared to placebo, even among those who reported having insomnia before supplementation. Vitamin D3 was given for four months starting with a single, high oral dose of 100,000 IU followed by a once weekly dose of 20,000 IU — equivalent to 2,857 IU per day (Larsen, Sleep Med 2021).

Some research suggests that high-dose vitamin D supplementation may interfere with melatonin production, and some but not all studies suggest that having blood levels over 32 ng/mL may worsen sleep quality (see Concerns and Cautions).

Restless legs syndrome

A three-month, placebo-controlled trial among 22 men and women with restless legs syndrome found that increasing average vitamin D blood levels from 19 ng/mL to 36 ng/mL with high-dose vitamin D supplementation (50,000 IU once a week) did *not* decrease the severity of the symptoms of RLS (Wali, Sleep Breath 2018).

Headache

Low blood levels (under 20 ng/mL) of vitamin D have been associated with a higher risk of frequent headaches and a moderate increase in migraine episodes, although it has not yet been determined whether supplementing with vitamin D provides these benefits. A study among 2,601 middle-aged men in Finland found those who had

the lowest blood levels of vitamin D (under 12 ng/mL or below) were *twice as likely* to report **frequent headaches** than men with higher blood levels. About 15% of men with the lowest levels (less than 12 ng/mL) had headaches at least weekly, while the percentage was only 8% among men with levels of 12 to 16 ng/mL, 16 to 22 ng/mL, or above 22 ng/mL (Virtanen, Scientific Reports 2016). The researchers noted that vitamin D deficiency has also been associated with chronic tension-type headache, perhaps by causing musculoskeletal pain. A study in Korea among 157 men and women (average age 37) with **migraine** found that headaches occurred 20% more frequently in those who were deficient in vitamin D (< 20 ng/mL) than those who were not deficient, regardless of gender, type of migraine (chronic, episodic, with or without aura), and factors such as depression, anxiety and sleep quality. However, vitamin D deficiency was not associated with the severity of migraine episodes (Song, J Clin Neurol 2018).

Lupus

A preliminary study suggests that raising low vitamin D levels with supplementation provides beneficial immunological effects in patients with **systemic lupus erythematosus (SLE)**. Giving 100,000 IU of vitamin D3 (weekly for a month and then monthly) along with regular therapy to SLE patients with generally low vitamin D levels (averaging 19 ng/mL) raised vitamin D blood levels to 42 ng/mL after 6 months of therapy, during which patients experienced no flare ups and experienced an increase in regulatory T cells and decreases in memory B cells, effector T cells, and anti-DNA antibodies (Terrier, Arth Res & Ther 2012).

Crohn's disease

Some, but not all, research suggests that people with Crohn's disease tend to have lower blood levels of vitamin D, and that lower levels of vitamin D may be associated with disease severity (Weisshof, Curr Opin Clin Nutr Metab Care 2015). A small study among people with mild to moderate Crohn's disease and insufficient blood levels of vitamin D found that increasing average blood levels of vitamin D from 16 ng/mL to 40 ng/mL over 24 weeks decreased average Crohn's disease activity index (CDAI) scores by 112 points (from 230 to 118 points on a scale of 0 to 600 points) but did not increase bone density compared to baseline. Participants started at a dose of 1,000 IU of vitamin D3 per day for the first week, and this dose was increased to 5,000 IU per day for most participants in order to reach a blood level of 40 ng/mL. Most participants did not have adequate calcium intake at the beginning of the trial, but average total calcium intake from diet and supplements increased from 879 mg to 1,153 mg over the course of the study (Yang, Clin Transl Gastroenterol 2013).

Irritable bowel syndrome (IBS)

A study in the UK among 135 men and women (average age 29) with mild to moderate IBS, most of whom also had low or deficient blood levels of vitamin D, found that 3,000 IU (75 mcg) of vitamin D3 taken as a sublingual spray (by BetterYou Ltd, which funded the study) daily for three months did *not* reduce symptom severity or improve quality of life compared to placebo, despite increasing average blood levels of vitamin D from 19 ng/mL to 37 ng/mL (Williams, Eur J Nutr 2021).

Menstrual pain and Premenstrual Syndrome (PMS)

A small study of women with primary dysmenorrhea (**painful menstrual cramping**) and a mean vitamin D blood level of 27 ng/mL found that giving a single high dose (300,000 IU) of vitamin D3 reduced pain by 41% during the next two menstrual periods. None of the women who received vitamin D needed anti-inflammatory medicine to manage menstrual pain during the two months, whereas 40% of those taking placebo used it at least once.[29] A concern, however, is that high dose vitamin D has been shown to increase the risk of falls and fractures — at least in the elderly (as noted above) and the dose given works out to 5,000 IU vitamin D per day, more than the Tolerable Upper Intake Level of 4,000 IU per day (see Concerns and Cautions).

A study among extremely vitamin D deficient (< 10 ng/mL) adolescent and young women (ages 15 — 21) with self-reported severe or extremely severe emotional and cognitive symptoms associated with premenstrual syndrome found that high-dose supplementation (an initial dose of 200,000 IU followed by 25,000 I.U. every two

weeks) with liquid vitamin D3 (*Dibase®*, Abiogen Pharma, Italy) for four months significantly reduced these symptoms: Mean scores of "irritability" decreased from 130 to 70, "crying easily" decreased from 41 to 30, sadness decreased from "51 to 31" and "disturbed relationships" decreased from 150 to 70 compared to the

beginning of treatment. Those who took a placebo had a significant reduction only in "irritability" (from 128 to 119). (Tartagni, J Pediatr Adolesc Gynecol 2015). It should be noted that the dosing may have been unnecessarily high as blood levels rose to 35 to 60 ng/mL.

Polycystic Ovary Syndrome (PCOS)

A randomized, placebo-controlled study in Jordan among 58 overweight women with vitamin D deficiency and PCOS (average age 24) found that taking 50,000 IU of vitamin D_3 once weekly for 12 weeks increased 25(OH)D levels from 12.5 ng/mL at baseline to 50.2 ng/mL. Compared to placebo, women supplemented with vitamin D showed decreased levels of parathyroid hormone and testosterone, increased levels of sex hormone binding globulin, and reduced severity of hirsutism (male-patten hair growth in women). Ovarian volume, which is often increased in women with PCOS, returned to normal for 24% of women given vitamin D compared to none of the women given placebo. Also, a greater percentage of women given vitamin D experienced regular menstrual cycles compared to placebo (93% vs 10%) (Al-Bayyari, Clin Nutr 2020). The researchers did not determine if these improvements increased fertility.

Uterine fibroids

A study of women ages 35 to 49 found that those with vitamin D levels above 20 ng/mL were 32% less likely to have had uterine fibroids than those with lower levels. Similarly, women who reported getting at least one hour per day of sun exposure (weather permitting), were 40% less likely to have had fibroids than women reporting less sun exposure (Baird, Epidemiology 2013). The risk of fibroids appeared to continue to decrease as vitamin D levels approached 35 ng/mL. Possibly explaining these findings are laboratory studies showing that vitamin D in its active form inhibits the overproduction of tissue by uterine muscle cells -- the cause of fibroids. The study was conducted in Washington, D.C. in the late 1990s and only 10% of Black women and 50% of white women had vitamin D levels above 20 ng/mL. Fibroids are the leading reason for hysterectomy in the U.S.

Early menopause

Adequate intake of vitamin D from the diet is associated with a lower risk of early menopause (i.e., menopause before age 45). Early menopause is of concern because it is associated with higher risk of cardiovascular disease, osteoporosis, and other conditions. A study of more than 80,000 women found that those who had the highest intakes of vitamin D from foods (528 IU per day -- equivalent to that found in 2.5 cups of milk per day) had a 17% lower risk of early menopause than women with the lowest intakes from food (148 IU per day) after adjusting for age, smoking and other factors. The association between intake of vitamin D from foods and reduced risk of early menopause was strongest when vitamin D was obtained from dairy foods, as opposed to non-dairy foods, although the reason for this is not clear. Intake of vitamin D from supplements was not associated with a reduced risk — and high intake of calcium from supplements (particularly 900 mg or more per day) was actually associated with an increased risk of early menopause (Purdue-Smith, Am J Clin Nutr 2017).

Erectile dysfunction

Vitamin D plays a role in endothelial function and in the production of nitric oxide, which are important for proper erectile function (Andrukhova, Mol Endocrinol 2014; Molinari Cell Physiol Biochem 2011). A study in Turkey among 111 men with erectile dysfunction and low blood levels of vitamin D (average 14 ng/mL, measured as 25(OH)D) found that those who took 4,000 IU (100 mcg) of vitamin D3 in addition to 5 mg of tadalafil (Cialis) once daily for three months had greater improvements in erectile function (an increase of about 13 points vs 5.5 points on a 30-point scale) and increased sexual desire (an increase of about 2.4 points vs 1.5 points on a 10-point scale) compared to those who took tadalafil alone. Both groups had similar improvements in orgasmic function, and sexual and overall satisfaction. In those who took vitamin D, average blood levels increased to 35 ng/mL, while there was no significant change in vitamin D levels among those who did not take vitamin D

(Demirci, Urol Int 2021).

Pregnancy

As described below, an adequate vitamin D level during pregnancy is associated with better infant growth and decreased risk of pre-term labor, pre-eclampsia, and gestational diabetes. Supplementing with vitamin D to correct deficiency has also been shown to reduce health risks to the mother, improve bone mineral density in children as they grow, and possibly reduce the risk of tooth defects in children. However, high-dose vitamin D during pregnancy does not seem to reduce the risk of pre-term birth, NICU admission, or neonatal infection or improve motor or cognitive development in children, although it might reduce the risk of pregnancy loss.

Vitamin D levels in the blood of pregnant women are associated with **infant growth**. A study in the U.S. found that the birth weight and head circumference of babies rose with increasing vitamin D levels up to 15 ng/mL (Gernand, J Clin Endocrin & Metab 2012). Mothers with levels of 15 ng/mL or greater gave birth to newborns 46 grams (0.1 lb) heavier and with head circumferences 0.13 cm larger, on average, than those of mothers with vitamin D levels less than 15 ng/mL. A level of 15 ng/mL or greater in the first trimester was also associated with half the risk of an infant being small for its gestational age.

Having sufficient blood levels of vitamin D during pregnancy is also associated with a decreased risk of **gestational diabetes** (diabetes developing in pregnant women). A study among 8,468 women in China found that, among those who had 25(OH)D blood levels of 20 to 30 ng/mL (measured before 20 weeks gestation), 9.73% developed gestational diabetes compared to 12% among those with blood levels below 20 ng/mL (Yue, Nutr Metab (Lond) 2020).

A study in India evaluated the effect of giving pregnant women large doses of vitamin D. Those with already sufficient levels (above 20 ng/mL) were given a single dose of 60,000 IU D_3 at week 20 of their pregnancy (averaging about 400 IU per day over the duration of their pregnancy), and those with insufficient (10 to 20 ng/mL) or deficient (<10 ng/mL) levels were given a monthly dose of 120,000 IU twice or four times, respectively, raising the average blood level of the entire group to 32 ng/mL. In another group of women who were not given vitamin D (average vitamin D level of 18.4 ng/mL), 44% developed **pre-term labor, pre-eclampsia, and/or gestational diabetes**, in contrast to 20.3% of the women given vitamin D. The non-treated group also had babies with a lower average birth weight (5.28 lbs) than did those given vitamin D (5.72 lbs) (Sablok, Clin Endocrinol 2015). The researchers note that lower-dose daily preparations may have been preferable to the large monthly doses but were not available.

A study in the U.S. among 392 pregnant women who, on average, already had sufficient levels of vitamin D, found that supplementing with 3,000 IU of vitamin D daily during pregnancy did *not* reduce the risk of preterm birth, low birth weight, NICU admission, respiratory distress, or infection in the infant compared to not supplementing. However, **pregnancy loss** was significantly lower and infants' **Apgar scores** (reflecting their general condition at birth) were significantly higher among women who supplemented with vitamin D compared to those who did not (Persad, Am J Obstet Gynecol 2021).

Giving expectant mothers high-dose vitamin D appears to reduce the risk of **tooth enamel defects** in their children. At age six, the children in Denmark of mothers who were given vitamin D3 (2,400 IU plus another 400 IU per day) from the 24th week of pregnancy to one week postpartum had a 50% lower risk of enamel defects in baby and permanent teeth compared to children of mothers given 400 IU per day (Note: The recommended daily allowance for pregnant women is 600 IU per day). Interestingly, the women were generally not deficient in vitamin D prior to supplementation, having average blood levels of about 30 ng/mL, which increased to 43 ng/mL at one week postpartum in those who took the higher dose of vitamin D but decreased slightly to 28 ng/mL in those who took the lower dose. However, there was no association between high-dose vitamin D supplementation and the risk of cavities (Norrisgaard, JAMA Pediatr 2019).

The same study found that children of the mothers given high-dose vitamin D had greater whole body **bone mineral density** at age 6 than those of mothers given only 400 IU. However, this only held true for children of

mothers who, prior to the study, had vitamin D levels *below 30 ng/mL* (an arbitrary breakpoint for analysis). There was no bone benefit from giving high-dose vitamin D to women whose levels were already sufficient. In fact, an accompanying editorial noted that giving vitamin D to women with levels above 50 ng/mL is associated with ***decreased growth*** of offspring (Holmlund-Suila, JAMA Ped 2020). The researchers noted that starting vitamin D earlier in pregnancy may have additional benefit because bone growth centers begin in the first trimester (Brustad, JAMA Ped 2020).

Further analysis of results from this same trial did *not* find benefits from prenatal high-dose vitamin D in children by age 6 with regard to motor, language, or cognitive development, nor reduced emotional or behavioral problems in comparison to those of mothers given 400 IU daily. The average blood level of vitamin D prior to high-dose supplementation was 30.6 ng/mL, with only 14% of the women having levels less than 20 ng/mL. (Sass, JAMA Netw Open 2020).

Respiratory infection, colds, and influenza

Vitamin D may be effective in reducing respiratory infections in people who do not already have adequate levels (20 ng/mL) of vitamin D (which is most common in the winter and spring) and when vitamin D is given daily, not in extremely large periodic doses.

In healthy adults with generally sufficient vitamin D levels (averaging 29 ng/mL), monthly supplementation of high dose vitamin D3 (100,000 IU) resulted in no reduction in the number of **upper respiratory infections (colds)**, the severity or duration of such infections, nor the number of days of missed work, compared to a similar group of people given placebo (Murdoch, JAMA 2012). Among those receiving the supplement, vitamin D levels averaged over 48 ng/mL throughout the study. The researchers commented that vitamin D supplementation may have been helpful had the population been vitamin D deficient, citing a study in which vitamin D supplementation was associated with a 50% reduction in **acute respiratory infections** among Mongolian schoolchildren who had an average vitamin D level below 10 ng/mL (Camargo, Pediatrics 2012).

Similarly, a five-year, placebo-controlled study among 15,373 people in Australia ages 60 to 84 found that monthly, high-dose (60,000 IU) vitamin D3 did not reduce the risk of developing an acute respiratory infection. However, blood levels of vitamin D measured during the study averaged 46 ng/mL in the vitamin D group and 31 ng/mL in the placebo group, indicating that people in both groups had more than adequate levels (Pham, Lancet Diabetes Endocrinol 2021).

A study in London found that periodic high doses of vitamin D *increased the risk and duration of respiratory infections*. The study was conducted among 194 older residents of group homes and 46 of their caregivers (average age was 67 years). Sixty-four percent of subjects began the study with blood levels below 20 ng/mL (92% were below 30 ng/mL). During the study, all residents were given 400 IU of vitamin D3 daily and more than half were given an additional 96,000 IU every two months -- for a total dose averaging 2,000 IU per day. (A subgroup of caregivers was given what also averaged to 2,000 IU per day, but as 120,000 IU every two months.) Over one year, those who received the large doses of vitamin D were 48% more likely to develop an upper respiratory infection than those who did not receive the large doses, and these infections lasted longer (7 days vs. 5 days, respectively). The researchers note that other studies have found that relatively low-dose vitamin D has been shown to offer protection against upper respiratory infection and that intermittent large doses have not. Interestingly, those receiving large doses had an average level of 34 ng/mL at the end of the study (2 months after the last large dose), while those who did not receive large doses (most of whom received just 400 IU daily) and had fewer respiratory infections ended the study with levels averaging 24 ng/mL (Martineau, Thorax 2015).

Similarly, a placebo-controlled study in people with mild to moderate asthma found that giving high-dose vitamin D (100,000 IU initial dose and 4,000 IU daily for 28-weeks) did not decrease the risk of developing a cold. In fact, with this vitamin D supplementation (which raised the mean vitamin D level to 42 ng/mL), the risk of a developing

a cold was found to be *40% higher* among those who reached vitamin D blood levels of 30 ng/mL or higher, and *70% higher* among those who were African-American (Denlinger, Am J Resp and Crit Care Med 2015. Also see Castro study, above, for effects on asthma control in this same group.)

In contrast the above studies in adults, a study in Sweden found vitamin D supplementation to be quite helpful. The double-blind study was conducted in adults with frequent upper respiratory infections in whom vitamin D levels tended to be low (half had levels below 20 ng/mL). Many also had immunodeficiencies. Vitamin D3 (4,000 IU) or placebo was taken daily for one year. Although benefits were not seen until after 3 months, over the full course of the year vitamin D reduced the risk of infection by 36% and the total number of respiratory tract infections by 28% relative to placebo (Bergman BMC Res Notes, 2015). An earlier analysis of the same study additionally showed that vitamin D resulted in reductions of 50% in positive bacterial cultures and 60% in antibiotic consumption (Bergman, BMJ Open 2012).

A study among older men and women (average age 81) in a long-term care facility with average vitamin D blood levels of about 23 ng/mL who, each month, received either high dose (100,000 IU) or a lower dose (which was either 12,000 IU monthly or 400 IU to 1,000 IU daily as part of standard care) found that over the course of a year, those who received high dose vitamin D_3 had a 40% lower incidence of acute respiratory infections compared to those who received the low dose. However, the high dose patients were also more than twice as likely to experience a fall (although not a fracture) during the study period (Ginde, J Am Geriatr Soc 2016) — a finding in line with other research showing that high dose vitamin D may weaken legs and increase the risk of falls (See "Muscle, balance and falls" for more about this).

Respiratory infections tend to be seasonal events, occurring more often in winter/spring than summer/fall. Some research has found that antimicrobial activity in the airway varies with seasons, being *less active* in winter/spring than summer/fall. This might contribute to increased respiratory infections in the winter/spring. Low levels of vitamin D have been associated with reduced antimicrobial activity in the airway. A study of 40 people (average age 28) with low levels of 25-hydroxy vitamin D showed that taking 1,000 IU of vitamin D3 daily for 90 days (during the winter and spring) corrected for seasonal differences in antimicrobial activity of the airway (Buonfiglio, Nutrients 2020). This suggests that supplementation with vitamin D during the winter/spring months might reduce the risk of respiratory infection.

Researchers in Japan studied the effect of vitamin D_3 supplements (1,200 IU per day from December through March) on the incidence of seasonal **influenza A** in school children. Influenza A infection occurred in 18.6% of children in a placebo group versus 10.8% of children who received the supplement -- a 42% reduction in risk among those taking the supplement. The reduction was more prominent among children who had not been taking other vitamin D supplements. Influenza infection was not reduced among a subgroup of asthmatic children but those who became infected were significantly less likely to have an asthmatic attack if they had received vitamin D than if they had not. Supplementation did not affect the incidence of influenza B (which is less common than influenza A and is not seasonal).[14]

An analysis of 25 studies of vitamin D for cold and flu (including many of the studies noted above) concluded that vitamin D supplementation protected against acute respiratory tract infection, but the patients most likely to benefit were very deficient (blood levels of vitamin D below 10 ng/mL) and receiving daily or weekly doses rather than less frequent, large doses. Giving vitamin D reduced the risk of infection by 42% in people with levels below 10 ng/mL, and by 70% if dosing was daily or weekly. For those with levels above 10 ng/mL, the risk reduction with giving vitamin D was only statistically significant when given daily or weekly, resulting in a 25% reduction in risk of infection (Martineau, BMJ 2017).

Adequate vitamin D levels were associated with a lower risk of **pneumonia** in a study of men and women ages 53 to 73 in Finland which followed them for an average of nine years (Aregbesola, J Epid Comm Hlth 2013).

Compared to adults with vitamin D levels above 20 ng/mL, the likelihood of being hospitalized with pneumonia was 40% higher among those with levels below 20 ng/mL but above 13.5 ng/mL, and 140% higher among those with levels below 13.5 ng/mL, after adjusting for other factors which might predict pneumonia. The researchers found that a low vitamin D level was almost as strong a risk factor for pneumonia as smoking.

COVID-19:

Most, but not all, studies have linked adequate levels of vitamin D in people who develop COVID-19 with less severe disease, decreased need for intensive care and ventilation, and a lower risk of death. Preliminary research suggests that supplementing with moderate to high vitamin D when vitamin D levels are low (about 20 ng/mL or lower) may improve prognosis in people hospitalized with COVID-19, but extremely high single doses have not been shown to help. There appears to be an increased risk of COVID-19 in people with very high levels of vitamin D.

How vitamin D may work

As noted elsewhere, vitamin D is an immunomodulatory hormone that may help reduce respiratory infections and is required in certain steps of the body's immune response to fight the replication of viruses such as SARS-CoV-2 (Berry, Brit J Nutr 2011). Vitamin D has been theorized as helping to prevent a damaging "cytokine storm" in the lungs of COVID-19 patients. Another theory, based on the analysis of lung tissue of COVID-19 patients, suggests that vitamin D might prevent a "bradykinin storm" by preventing bradykinin levels in the lungs from getting too high and causing the fluid leakage from the blood vessels in the lungs (Garvin, Elife 2020).

Reduced risk of coronavirus infection

Three studies linked low levels of vitamin D to a higher risk of SARS-CoV-2 infection.

A study among 392 healthcare workers (average age 41) in the U.K. who had previously shown symptoms of COVID-19 found that the presence of SARS-CoV-2 antibodies (confirming that infection had occurred) was more common in those who were vitamin D deficient (25(OH)D <12 ng/mL) than those who were not vitamin D deficient (72% vs. 51%), suggesting that vitamin D deficiency may increase susceptibility to SARS-CoV-2. Men of Black, Asian, or ethnic minority groups were particularly affected, with SARS-CoV-2 antibodies detected in 94% of those who were vitamin D deficient compared to only 53% of those who were not deficient (Faniyi, medRxiv 2020 - preprint).

A study in Chicago found that people who were likely to be deficient in vitamin D (determined from previous vitamin D testing, such as having a level below 20 ng/mL and/or a history of lack of supplementation) were *77% more likely to test positive* for coronavirus than those expected to be vitamin D sufficient after controlling for demographic and other variables. The researchers concluded that "vitamin D deficiency that is not sufficiently treated is associated with COVID-19 risk." (Meltzer, JAMA Netw Open 2020). A subsequent study by these researchers did not show a significantly lower likelihood of testing positive at levels of 40 ng/mg or greater compared to levels of 30-39 or 20-29 ng/mL in the studied population; however, specifically among Black individuals, the likelihood of testing positive was lower at levels at or above 40 ng/mL than at 30-39 ng/mL, although oddly, the likelihood of testing positive at or above 40 ng/mL was not significantly different from that at 20-29 ng/mL (Meltzer, JAMA Netw Open 2021).

Similarly, a study in Israel found that people with vitamin D levels below 30 ng/mL were 45% more likely to test positive for SARS-CoV-2 as well as 95% more likely to be hospitalized for it after adjusting for demographic and other variables. The 30 ng/mL level was arbitrarily selected for the analyses and a look at the study data shows greater clustering of positive test results at levels below 20 ng/mL (Merzon, medRxiv 2020).

Be aware that high levels of vitamin D have been associated with *increased* risk of COVID-19.

Reduced severity of disease, need for intervention, and death

Low levels of vitamin D have also been associated with more severe respiratory symptoms and higher risk of death from COVID-19 in some, but not all, studies.

A study in Germany among 185 people (average age 60) with COVID-19 found that those with blood levels of vitamin D (total 25(OH)D) below 12 ng/mL when they became ill were approximately *six times as likely to require invasive mechanical ventilation* and *15 times as likely to die* from COVID-19 compared to those with blood levels above 12 ng/mL, even after adjusting for age, gender, and underlying health conditions (Radujkovic, Nutrients 2020).

Additionally, a study among 20 hospitalized COVID-19 patients in New Orleans, found that 84.6% of the COVID-19 patients in the ICU (intensive care unit) had blood levels of vitamin D of less than 30 ng/mL vs. 57.1% of COVID-19 patients who did not require intensive care, although the difference did not reach statistical significance, possibly due to the small size of the study. All of the COVID-19 ICU patients under 75 years of age had vitamin D blood levels below 30 ng/mL, and among these, 64.6% had levels below 20 ng/mL and 27% had levels below 10 ng/mL. The researchers noted that vitamin D insufficiency is more prevalent in African Americans, the elderly, and those with conditions such as high blood pressure and diabetes, all of whom are at higher risk for more severe outcomes from COVID-19 (Lau, medRxiv 2020 -- preprint).

A study among 144 people (median age 66) in Boston and New York hospitalized with COVID-19 found that those with 25(OH)D levels at least 30 ng/mL had significantly lower rates of death compared to those with levels less than 30 ng/mL (9.2% vs. 25.3%, respectively). It is important to note that 30 ng/mL was arbitrarily selected as the threshold value for the primary analyses but "similar findings were obtained ... with a threshold of 20 [ng/mL]". That is, levels of at least 30 ng/mL were not necessarily better than levels of at least 20 ng/mL (Angelidi, Mayo Clin Proc 2021).

A review of the records of 42 people (average age 65) hospitalized in southern Italy for acute respiratory failure due to COVID-19 showed an association between severe vitamin D deficiency (blood levels of 25(OH)D <10 ng/mL) and a higher risk of mortality. Patients with severe vitamin D deficiency had a 50% probability of dying by day 10 compared to a 5% probability of dying among those with 25(OH)D levels at least 10 ng/mL, suggesting that severe vitamin D deficiency may worsen prognosis of patients with COVID-19 (Carpagnano, J Endocrinol Invest 2020).

A study among 235 adults (average age 59) treated for COVID-19 in a hospital in Iran found that those with 25(OH)D levels of less than 30 ng/mL were 59% more likely to have a severe or critical case compared to those with levels of 30 ng/mL or more (Maghbooli, PLoS One 2020). [Note: This study is currently under review due to the publisher's concerns as to whether the statistical analyses used can support the authors' conclusions, the number of patients whose diagnosis was not laboratory confirmed, and other issues.] Blood levels of vitamin D were also found to be an independent predictor of mortality in a study of hospitalized COVID-19 patients in Turkey, where average 25(OH)D levels among those who died was only 10 ng/mL compared to 19 ng/mL in those who survived (Karahan, J Nutr Health Aging 2020).

Interestingly, a study in Italy that focused on COVID-19 patients taking doses of vitamin D equivalent to 800 IU or higher per day (mean intake 1,800 IU daily) during the prior 3 months (and excluding those taking lower doses) showed no lower risk of hospitalization or in-hospital mortality compared with those who did *not* take vitamin D supplements, despite almost three-fold higher blood levels of vitamin D (32.9 ng/mL vs 11.3 ng/mL, respectively) (Cereda, Nutrition 2020).

Treatment of COVID-19 patients

As described below, there have been several preliminary reports suggesting benefits from giving patients hospitalized with COVID-19 vitamin D or a form of vitamin D (calcifediol), although it remains uncertain what dose is most effective, and any benefit seems to be limited to only those who are vitamin D deficient.

A review of medical records of elderly residents of a nursing home in France showed that survival at one month after COVID-19 diagnosis was 86% greater for those who had been given a high-dose (80,000 IU) vitamin D in the previous month or in the week following diagnosis compared to those who did not receive supplementation (Annweiler, J Steroid Biochem Mol Biol 2020). It should be stressed that these patients were given vitamin D due to high frequency of vitamin D deficiency (not as COVID-19 treatment) and that more frequent (daily or weekly) use of lower dose vitamin D to treat deficiency is preferable whenever possible (see How Much Is Too Much).

A preliminary analysis of patients admitted to a hospital system in northeastern England (where vitamin D deficiency is common) found a 35% higher prevalence of vitamin D deficiency in COVID-19 patients requiring intensive care compared to those managed in medical wards. Deficiency was promptly treated, which may partially explain why fatality rates did not differ by initial vitamin D level (Panagiotou, letter in Clin Endocrinol (Oxf) 2020).

A study in Spain among 76 people hospitalized with COVID-19 infection (all of whom were given hydroxychloroquine and azithromycin) found that those also given 532 mcg of calcifediol (a 25-hydroxylated form of vitamin D) on the day of admission followed by 266 mcg of calcifediol on day 3 and day 7 of hospitalization had a lower risk of being admitted to the ICU for complications compared to those not given calcifediol (2% with calcifediol vs 50% without), as well as a lower risk of death compared to those not given calcifediol (0 deaths with calcifediol vs 2 deaths without) (Castillo, J Steroid Biochem Mol Biol 2020). Bear in mind that the people included in this study were probably vitamin D deficient, as average levels of 25(OH)D in Córdoba, Spain, where the study was conducted, is about 16 ng/mL. It remains unknown if calcifediol would be beneficial in people with adequate levels of vitamin D. Furthermore, the dose of calcifediol used in this study was very high. Prescribed doses of calcifediol (for its approved indications) are typically much lower (about 30 to 60 mcg per day) than those used in this study. Excessive intake of vitamin D in any form, including as calcifediol, can increase the risk of hypercalcemia (see Concerns and Cautions). Finally, calcifediol is a prescription medicine in the U.S. and is not available in supplements.

A study in India among people diagnosed with mild or asymptomatic COVID-19 found that 62% achieved SARS-CoV-2 negativity after 14 days of high-dose vitamin D treatment compared to just 20.8% in a control group. Vitamin D was given as 60,000 IU daily for 7 days, followed 60,000 IU either daily or once weekly for another week (depending on blood levels of vitamin D after the first week). Blood levels of vitamin D were increased from 8.6 ng/mL to 51.7 ng/mL after 14 days for those in the vitamin D group (Rastogi, Postgrad Med J 2020).

A study in Singapore among 43 men and women age 50 or older hospitalized with COVID-19 found that those who were started on a daily oral dose of vitamin D3 (1,000 IU), magnesium (150 mg) and vitamin B12 (500 mcg) within the first day of hospitalization and continued for up to 14 days were about 71% less likely to require oxygen therapy and further intensive care compared to those not receiving the supplements. However, blood levels of vitamin D, magnesium and B12 were not measured, so it's not known if any of the patients were deficient before supplementation (Tan, Nutrition 2020).

In contrast, a study in Brazil among 232 people (average age 56) with severe COVID-19 found that a single oral dose of 200,000 IU of vitamin D3 did *not* shorten length of hospital stay or reduce mortality, admission to ICU, or need for mechanical ventilation compared to placebo, despite increasing blood levels of vitamin D to 30 ng/mL or more in 87% of the supplemented patients. Although not all patients included in this study were vitamin D deficient at baseline, a subgroup analysis found no benefit even among patients who were vitamin D deficient.

However, vitamin D3 was not given until about 10 days after symptom onset, which may have been too late to provide any significant benefit (Murai, medRxiv preprint 2020 and Murai, JAMA 2021).

Ear infection (Otitis media)

Among children ages 1 to 5 years with a history of recurrent ear infections, those with higher blood levels of vitamin D had a decreased risk of developing *un*complicated ear infections (acute otitis media) during a 6-month study including wintertime. However, the study found that higher vitamin D levels did not reduce the risk of *complicated* ear infections (e.g., ear drum rupture). In fact, rates of complicated infections were actually higher at vitamin D levels above 30 and 40 ng/mL than at lower levels, leading the researchers to speculate that these higher vitamin D levels potentially foster certain bacterial infection in the ear. The study also found that giving 1,000 IU daily for 4 months raised vitamin levels from about 26 ng/mL to 37 ng/mL, while levels fell to about 19 ng/mL in children receiving placebo (due to reduced sun exposure in winter). Although the children receiving vitamin D experienced significantly fewer episodes of uncomplicated ear infections, there was no significant reduction in complicated infections (Marchisio, Pediatr Infect Dis J 2013). It would seem best for children to follow the recommendations for vitamin D outlined in the Summary above.

Hearing loss

An analysis of health data of 1,123 older people (average age 76) found that hearing loss of speech-frequency and low-frequency (low-pitch) sounds was about twice as great for those with low levels of vitamin D (total 25(OH)D < 20 ng/mL) compared to those with levels of 30 ng/mL or more, although there was no increased risk for those with levels between 20 ng/mL and 29 ng/mL. There was no association between vitamin D levels and the odds of high-frequency hearing loss, which is the most common form of hearing loss (Szeto, Am J Clin Nutr 2020). Note that this analysis only showed association and does not establish cause-and-effect relationships.

Depression & Mood

Lower levels of vitamin D have been associated with a higher risk and severity of depression in some but not all studies; however, there is little evidence that taking vitamin D reduces the risk of depression or improves mood. An possible exception is in people with type 2 diabetes.

A study in Italy showed that older women with low vitamin D levels (below 20 ng/mL) were twice as likely to develop depressive mood as those with higher levels. Older men with low levels were 60% more likely to develop depressive mood (Milaneschi, J Clin Endocrinol Metab 2010). Data from the same study showed that those who were severely vitamin D deficient (below 10 ng/mL) were approximately 60% more likely than those with vitamin D levels above 30 ng/mL to experience substantial cognitive decline, although there was no such association with attention level (Llewellyn, Arch Intern Med 2010).

A 3-year study found the risk of depression was 21% lower among women (aged 50 to 79) who reported total daily vitamin D intake (from foods and supplements) of at least 800 IU compared to women with intake of less than 100 IU. Excluding women with evidence of depression at the beginning of the study, a 20% lower risk of depression was seen with intake of just 400 IU or more per day from *foods*, but there was no reduced risk from supplements alone (Bertone-Johnson, Am J Clin Nutr 2011).

However, not all research has found an association between vitamin D levels and risk of depression. A 5-year study among Puerto Rican adults living in the Boston area (average age 57) found that those with vitamin D deficiency (25(OH)D less than 12 ng/mL) were no more likely to report symptoms of depression than those with adequate vitamin D levels (20 ng/mL or more). The researchers noted that the inconsistent findings across studies regarding the association between vitamin D levels and depression may be due to differences in study designs, study populations, cutoffs used for evaluating vitamin D status, and assessment of depression (Sahasrabudhe, J Nutr 2020).

On the other hand, a 6-month pilot study in the U.S. suggested that high-dose vitamin D (50,000 IU of vitamin D2 per week) significantly improved mood in women with type 2 diabetes who had serious depressive symptoms. Mean serum blood levels of vitamin D increased from 18.8 ng/mL to 37.5 ng/mL during the intervention. The study also showed a modest improvement in systolic blood pressure and a slight decrease in weight. Although promising, *the study had no control group* (Penckofer, Abstract from ADA Scientific Sessions 2013).

A study among 64 men and women in Iran with type 2 diabetes and mild to moderate depression who had generally low blood levels of vitamin D also found that 4,000 IU of vitamin D3 taken daily for three months decreased symptoms of depression by an average of 27.6%, which was significantly greater than among those given a placebo who experienced an average 10.8% decrease in symptoms. Average blood levels of vitamin D increased in the treated group from 15 ng/mL to 32 ng/mL. Those who took vitamin D also showed modest improvements relative to the placebo group in HbA1c (- 0.5% vs - 0.07%) and blood insulin levels (- 0.7 vs 0.1 mU/L), although there were no significant changes in fasting blood sugar or cholesterol levels (Omidian, Diabetes Metab Syndr 2019).

Meanwhile, a placebo-controlled study in which 50,000 IU of vitamin D3 was given monthly over autumn and winter to pre-menopausal women who were not depressed, nor, in general, deficient in vitamin D (starting levels averaged 25 ng/mL), showed *no impact* on mood, anxiety, or depressive symptoms (Choukri, J Nutri Sci 2018). Furthermore, a placebo-controlled study in Denmark among 62 men and women diagnosed with mild, moderate or severe depression found that daily supplementation with 70 mcg of D3 (2,800 IU) for six months did not improve depression scores - even among those who were deficient in vitamin D (< 10 ng/mL) before supplementation. Average blood levels of vitamin D rose from 17 ng/mL to 39 ng/mL during the study (Hansen, BMC Res Notes 2019).

A year-long, placebo-controlled study among 151 older men and women (average age 67) in the Netherlands with moderate depression and somewhat low average blood levels of vitamin D (18 ng/mL) also failed to find a benefit. Among those who took vitamin D (1,200 IU per day) and maintained a calcium intake from foods and/or supplements of approximately 1,000 mg per day, vitamin D blood levels increased to 34 ng/mL, but there were no significant improvements in symptoms of depression or anxiety, and no improvements in physical and cognitive function compared to those who took a placebo and whose average blood levels of vitamin D remained relatively low (average 17 ng/mL) (de Koning, Am J Clin Nutr 2019).

A 5-year study involving more than 18,000 adults in Massachusetts aged 50 and older with no history of depression found that 2,000 IU daily of vitamin D3 did not result in statistically significant differences in the rate of occurrence of depression. However, the individuals enrolled in the study were generally not vitamin D deficient, with a mean 25-hydoxyvitamin D level of 30.8 ng/mL and nearly 90% having levels at or above 20 ng/mL. About half of each group was also supplemented with 1 gram daily of highly-concentrated fish oil, which also had no effect on the occurrence of depression (Okereke, JAMA 2020).

Alzheimer's disease, dementia, memory and cognitive decline

Studies indicate that maintaining a vitamin D level of at least 20 ng/mL may be helpful in reducing the risk of developing Alzheimer's disease. Supplementing with vitamin D also seems to modestly improve cognition in older individuals with mild cognitive impairment who are vitamin D deficient, but it does not appear to boost cognitive performance in adults who are not cognitively impaired.

A study that followed 1,658 older adults in the U.S. for a mean period of 5.6 years found that the risk of developing dementia was increased for people with starting blood levels of vitamin D below 20 ng/mL. All participants were relatively healthy at the start of the study. People who began the study with a level of 10 ng/mL up to 20 ng/mL were 53% and 69% more likely to develop **dementia and Alzheimer's disease**, respectively, than those with starting levels of 20 ng/mL and above; and people with levels below 10 ng/mL were 125% and 122%

more likely to develop dementia and Alzheimer's disease, respectively, than those starting with levels of 20 ng/mL or above. While the study suggests that higher levels of vitamin D may be beneficial, it did not test whether raising a person's vitamin D level reduces the risk of dementia. However, as the researchers note, it clarifies that having a level above approximately 20 ng/mL is unlikely to further reduce the risk of developing dementia (Littlejohns, Neurology 2014).

Similarly, a study among 916 healthy older men and women in France (average age 73) who were followed for an average of 11.4 years found that those starting with vitamin D levels below 20 ng/mL had *nearly triple the risk of developing Alzheimer's disease* during the study than those starting with levels at or above 20 ng/mL. In addition, those who began the study with vitamin D blood levels below 10 ng/mL also had significantly faster rates of cognitive decline, and were more likely to have high cholesterol and triglycerides than those with levels at or above 10 ng/mL (Feart, Alzheimer's & Dementia 2017). Another study that followed older, ethnically diverse adults in California for a mean period of 4.8 years found that rates of decline in two areas of cognitive functioning — episodic memory (word list learning) and executive functioning — were greater among those starting with vitamin D levels below 20 ng/mL than those starting with levels of 20 ng/mL and above. Decline in these two areas are strongly associated with Alzheimer's dementia. Vitamin D status was not associated with rates of decline in two other cognitive areas: semantic memory (object naming and picture association) and visuospatial ability. The average starting level of vitamin D among the participants was 19.2 ng/mL (Miller, JAMA Neurol 2015)

A study in France among women 75 years of age and older found those with higher intakes of vitamin D from their diets were least likely to develop Alzheimer's disease over a seven-year study period. Women consuming more than 3,108 IU of vitamin D per week (444 IU per day) were 77% less likely to develop Alzheimer's disease than those with lower vitamin D intake. There was, however, no association between vitamin D intake and the risk of developing other types of dementia. The study excluded women who had taken vitamin D supplements (Annweiler, J Gerontol A Biol Sci Med 2012).

A 12-month, placebo-controlled clinical trial in China among 181 older individuals with **mild cognitive impairment (MCI)** found that vitamin D supplementation (400 IU daily, taken with or after a meal) resulted in modest but statistically significantly improvements in cognitive functioning shown in verbal and performance tasks. The vitamin D and placebo groups each started with average vitamin D levels of about 19 ng/mL, which increased to 23.4 ng/mL in the vitamin D group. Total cholesterol levels also decreased modestly in the vitamin D group relative to the placebo group, driven by decreases in triglycerides and, unexpectedly, HDL ("good") cholesterol (Note: Vitamin D has had mixed effects on cholesterol levels, and high doses may even increase total cholesterol) (Hu, J Neurol Neurosurg Psychiatry 2018).

Another study in China among 183 older people (average age 67) with MCI found that taking 800 IU of vitamin D daily for 12 months modestly improved overall cognitive function based on the full-scale intelligence quotient (FSIQ) score. People given vitamin D showed a 1.81% increase in FSIQ score, while those given placebo showed a 3.28% *decrease* in FSIQ score. People in the vitamin D group also showed improvements in some verbal measures (such as vocabulary and short-term verbal memory) and non-verbal measures (such as visuoconstructional ability and ability to interpret social situations) based on the Wechsler Adult Intelligence Scale-Revised score compared to those given placebo. Blood levels of vitamin D_3 increased from 19.07 ng/mL to 23.38 ng/mL for people in the vitamin D group. Interestingly, vitamin D also *increased* telomere length (measured in the DNA of white blood cells), which may be of potential benefit, as decreased telomere length may be a factor in predicting progression of cognitive decline (Yang, J Alzheimer's Dis 2020).

However, high-dose vitamin D supplementation for four months did *not* improve **cognitive functioning in healthy middle-aged and older adults** in Norway with low blood levels of vitamin D (average level of 13.6 ng/mL). Participants in the placebo-controlled study were given a starting dose of 100,000 IU of vitamin D followed by

20,000 IU taken weekly, boosting average levels to 35.6 ng/mL (Jorde, J Neurologic Sci 2018).

Parkinson's disease

A study from Finland suggested that higher vitamin D status provides protection against Parkinson's disease. People with the highest vitamin D levels (above 20 ng/mL) had a 65% lower risk of developing Parkinson disease than those with the lowest vitamin D levels (below 10 ng/mL).

Multiple sclerosis

Although research suggests that vitamin D deficiency is a risk factor for developing multiple sclerosis, it is not clear that supplementing with vitamin D reduces the risk. An FDA review concluded that, in healthy people, there is "no credible evidence of a relationship between intake of vitamin D and a reduced risk of MS" (FDA Constituent Update 2018). There is mixed evidence as to whether vitamin D levels of pregnant mothers correlate with MS risk in their children, but one study (in Finland) found that the risk of MS as an adult was 90 percent higher in children of mothers who were significantly deficient in vitamin D (levels less than 12.02 ng/mL) compared with the children of mothers with levels between 12.02 ng/mL and 20.03 ng/mL (Munger, JAMA Neurol 2016).

Autism Spectrum Disorder

Low blood levels of vitamin D have been associated with increased risk of autism spectrum disorder. Preliminary clinical research suggests that vitamin D given to children with autism spectrum disorder and vitamin D deficiency may improve symptoms. There is no evidence that vitamin D improves symptoms of autism in children who already have adequate levels of vitamin D.

A study in the Netherlands found that children whose mothers had very low vitamin D blood levels (< 10 ng/mL) during pregnancy (measured during the fifth month of gestation) were *3.8 times* as likely to have autistic traits by age six than those whose mothers had sufficient vitamin D levels (20 ng/mL). Even with levels between 10 and 19 ng/mL, there was a 75% higher risk, although this was not deemed statistically significant (Vinkhuyze, Mol Psychiatry 2016). The researchers noted that vitamin D is involved in the production of the neurotransmitter serotonin, which may play a role in certain autistic characteristics.

Similarly, a study in China found that infants with very low levels of vitamin D at birth were more likely to have autism spectrum disorder on follow up at age 3 than those with moderate levels. The average level in autistic children was just 7 ng/mL compared to 16 ng/mL in non-autistic children. It was predicted that the lowest risk of autism was among babies with a blood level of 19.2 ng/mL, as risk was seen to increase above this level (Wu, J Bone Mineral Res 2017).

In 2016, researchers in Egypt reported an association between lower blood levels of vitamin D and higher severity of autism symptoms. They also reported that treating children with autism spectrum disorder (ages 3 to 10) with high-dose vitamin D (about 5,000 IU daily, as drops) for four months resulted in a reduction in symptoms, while there was no change among children given placebo drops (Saad, J Child Psychol Psychiatry 2016). ***However, irregularities later discovered in how the data was collected and analyzed led the editors of the journal in which the report was published to retract it in 2019, stating they "... no longer have confidence in the findings reported in the original paper." (Editors, J Child Psychol Psychiatry 2019)***.

A placebo-controlled trial in Iran among 43 children with autism spectrum disorder (ages 3 to 13, average age 9), most of whom were vitamin D deficient at the beginning of the study, found that giving 300 IU/kg of vitamin D daily (up to a maximum dose of 6,000 IU/day) for 15 weeks increased the average blood level of vitamin D from just 8.19 ng/mL to 39.10 ng/mL and modestly reduced autism severity based on the childhood autism rating scale (CARS) and autism treatment evaluation checklist (ATEC), which focus on various symptoms and skills. However, supplementing with vitamin D did not improve aberrant behaviors such as irritability, hyperactivity, social withdrawal, and inappropriate speech. Note that the dose given was extremely high, particularly for

children. Lower doses would be safer and still able to treat deficiency (Javadfar, Nutrition 2020).

Executive functioning and cognitive performance

Executive functioning refers to the set of mental skills that help you get things done, like planning and strategic thinking. Maintaining a sufficient level of vitamin D appears to be associated with better executive functioning, according to a study in Norwegian adolescents. The study found that adolescents with low vitamin D blood levels (below 20 ng/mL) scored worse on tests of executive functioning and were more likely to report attention issues than those with higher levels. It also found that giving 1,520 IU (or 38 mcg) of vitamin D_3 daily for three months (which increased average vitamin D blood levels from 17.6 ng/mL to 24.8 ng/mL) improved performance on the most demanding executive functioning tasks -- although not on easier tasks (Grung, Scan J Psychol 2017). A preliminary study among Norwegian men also suggests a positive association between vitamin D blood levels of 20 ng/mL and above and better executive functioning (Hansen, Percept Motor Skills 2011).

A one-year study among 42 postmenopausal women in New Jersey who were overweight or obese found that a daily dose of 2,000 IU of vitamin D resulted in better performance in visual and working memory and learning than 600 IU or 4,000 IU. The 4,000 IU dose seemed to negatively impact reaction time, as that group had a slower reaction time than the 600 IU group. The average starting vitamin D blood level was 22.6 ng/mL, increasing to 30.2, 36, and 40.8 ng/mL, respectively, in the 600, 2,000, and 4,000 IU groups (Castle, J Gerontol Series A 2019). Note: Obese people tend to require larger doses of vitamin D to raise blood levels than people who are not overweight.

Weight control

Vitamin D does not appear to play a role in weight control. Raising blood levels of vitamin D from an average of 13 ng/mL to 24 ng/mL increased lean body mass (muscle) by about 1 lb. (as noted earlier) but did *not* decrease BMI or body fat in healthy in active men and women in Japan who supplemented with 420 IU of vitamin D for one year (Sun, Ann Nutr Metab 2019).

Similarly, a 12-month study found that taking vitamin D_3 had no overall effect on weight or fat loss in overweight or obese postmenopausal women consuming a reduced calorie diet and following a program of 45 minutes of aerobic 5 days per week (Mason, Am J Clin Nutr 2014). Regardless of whether they took 2,000 IU vitamin D_3 daily or a placebo, women lost an average 16 lbs. (Note: The 2,000 IU dose of vitamin D is fairly high for regular daily use, particularly in this study in which average vitamin D blood levels were above 20 ng/mL to start. Seven percent of the women taking vitamin D achieved levels above 50 ng/mL, which is potentially harmful. In fact, a subsequent analysis of this study found that those who received vitamin D *lost* strength in their leg muscles -- see "Muscle, balance, and falls" above.) Interestingly, among the vitamin D-treated women, those who achieved blood levels greater than 32 ng/mL lost more weight than those whose levels remained below 32 ng/mL (19 lbs vs. 12 lbs) and had greater reductions in their waistlines (3.5 inches vs. 2.2 inches) and body fat. *However, it may just be that vitamin D levels in the blood rose more in women who lost more fat*, due to the fact that vitamin D is fat soluble and stored within fat; indeed, an earlier study by the same researchers showed that weight loss raises vitamin D levels (Mason, Am J Clin Nutr 2011).

Frailty

A study found that older women (69 years and older) whose vitamin D levels were not between 20 and 29.9 ng/mL had a greater risk of being frail.[18] Frail individuals were those experiencing at least three of the following criteria: weight loss, weakness, exhaustion, slowness, and low physical activity. The risk of frailty was increased by 47% among those with vitamin D levels below 15 ng/mL, 24% among those with levels below 20 ng/mL, and 32% among those with levels above 29.9 ng/mL. An average of 4.5 years after these measurements were made, those originally not frail but whose blood levels had been below 20 ng/mL were 21% more likely to have become frail or died. These findings correspond with the 2010 report from the Institute of Medicine (IOM) indicating that 20 ng/mL is a sufficient level for vitamin D and that levels above 30 ng/mL may be associated with certain

risks.[17]

Cancer

All types

Studies generally show that having vitamin D serum levels above 20 ng/mL are associated with lower risk of various cancers and levels of up to 39 ng/mL may reduce the risk of death from cancer. Limited evidence suggests that vitamin D supplementation may reduce pain and possibly fatigue in patients with advanced cancer and low levels of vitamin D.

A major study (the VITAL study) of a cross-section of middle-aged Americans given 2,000 IU of vitamin D daily for median of 5.3 years found no overall reduction in invasive cancers and death from cancer relative to placebo, although few participants were vitamin D deficient: The average starting blood level was 30.8 ng/mL and increased to over 40 ng/mL with vitamin D supplementation. *However*, when excluding the first two years of the study, the rate of *death* from cancer was found to be 25% lower with vitamin D than with placebo. As noted in the study, the results are consistent with other studies: While supplementing with vitamin D may not reduce the overall incidence of cancer, it may decrease tumor invasiveness and the propensity to metastasize (Manson, NEJM 2018).

A secondary analysis of results from the VITAL study found that vitamin D modestly reduced the risk of *advanced cancer* (i.e., cancer that was metastatic or fatal) compared to placebo. Advanced cancer occurred in 2.1% of people in the placebo groups compared to 1.7% of people in the vitamin D group (17% reduction). When results were analyzed based on BMI of the people in the study, the incidence of advanced cancer was reduced by 38% for those with a normal BMI (BMI <25) but not for those who were overweight (BMI 25 to <30) or obese (BMI 30 or more) (Chandler, JAMA Netw Open 2020).

Other studies have not demonstrated a reduction in cancers from taking vitamin D supplements. For example, a large 4-year placebo-controlled study of post-menopausal women in rural Nebraska found that giving 2,000 IU daily of vitamin D3 and 1,500 mg of calcium (as 3 doses of 500 mg) did not significantly lower the risk of cancer. However, a weakness of this study is that the women were generally not deficient in vitamin D to start — their blood serum levels averaged 32 ng/mL (rising to 44 ng/mL in the treatment group). In fact, most of the women (including those in the placebo group) were already taking vitamin D supplements before the study and were allowed to continue during the study, with average daily intake of around 800 IU (Lappe, JAMA 2017). Similarly, a study of more than 5,000 older adults in New Zealand found that giving high-dose vitamin D (200,000 IU followed by monthly doses of 100,000 IU) for 2.5 to 4.2 years had no impact on cancer incidence compared to placebo treatment. However, most people did not start the study deficient in vitamin D (average blood level was 26.5 ng/mL). Vitamin D treatment raised levels by more than 20 ng/mL (Scragg, JAMA Oncology 2018).

An unusual report published in 2016 suggests that, for white women aged 55 years and older, vitamin D levels at or above 40 ng/mL, as compared to levels below 20 ng/mL, are associated with greater than a 65% reduction in risk of all invasive cancers combined, excluding skin cancer. This study, however, has several weaknesses including the fact that it was based on pooled data from two unrelated studies, one of which, run by the group GrassrootsHealth (which derives revenue from vitamin D home tests), was based entirely on a self-selected group of women who chose to maintain relatively high levels of vitamin D and self-reported their health status via a questionnaire. While the data indicated much lower rates of cancers (predominantly breast cancer) at increasing mean levels of vitamin D, the greatest decrease was seen as mean levels increased from below 20 ng/mL into the high 30s with no significant benefit indicated above that level. In addition, potential adverse effects were not assessed (McDonnell, PLOS ONE 2016).

A small but well-controlled study among 150 palliative care cancer patients with low levels of vitamin D (25(OH)D of 20 ng/mL or less) showed that those given 4,000 IU of vitamin D3 oil drops daily for 12 weeks increased their

dose of fentanyl (an opioid pain medicine) at a slower rate compared to those receiving placebo (about 0.56 mcg *less* fentanyl/hour per week), suggesting modestly reduced pain. Patients receiving vitamin D also reported less fatigue as measured by the Edmonton Symptom Assessment System (ESAS) scale, although not on a different scale. There was no between-group difference in antibiotic use or quality of life. Average 25(OH)D increased from about 14 ng/mL to 32 ng/mL among those in the vitamin D group (Frankling, Cancers 2021).

Colorectal cancer

A moderately decreased risk of developing **colorectal cancers**, specifically, has been demonstrated with higher vitamin D levels as well as with higher vitamin D intakes (Ma, J Clin Oncol 2011). An analysis of data from two large studies of health professionals found higher vitamin D levels to be associated with a much lower risk of developing a subtype of colorectal cancer in which there is extensive immune cell infiltration within the tumor — perhaps explained by vitamin D's effects on the immune system. Compared to people with the lowest vitamin D blood levels (around 19 ng/mL), those with mid-range levels (around 27.9 ng/mL) had only 33% of the risk of developing this type of tumor, and those with the highest vitamin D levels (around 37.4 ng/mL) had just 10% of the risk (Song, Gut 2015). A review of 17 studies compared the risk of colorectal cancer in people with varying blood levels. It found that, compared to those having levels of 20 to <25 ng/mL, the risk was 31% *higher* when levels were below 12 ng/mL, but 19% *lower* at 30 to <35 ng/mL and 27% *lower* at 35 to <40 ng/mL, although there was no statistically significant risk reduction at 40 ng/mL or greater (McCullough, J Natl Cancer Inst 2018).

In seeming contrast to this, a large, multi-year study in the U.S. found that daily supplementation with vitamin D3 (1,000 IU) and/or calcium (1,200 mg) did not reduce the risk of developing new precancerous colorectal polyps (adenomas) among people who had adenomas removed in the past. There was no statistically significant difference in the occurrence of adenomas between those who were or were not given the supplements. However, the vast majority of subjects began the study with adequate blood levels of vitamin D (averaging 24 to 25 ng/mL); in fact, anyone with a level below 12 ng/mL was excluded from the study (Baron, NEJM 2015). These findings, therefore, may not apply to people with vitamin D levels which are inadequate, i.e., under 20 ng/mL. In fact, a large study that followed men and women in the U.S. and Canada with previously untreated advanced or metastatic colorectal cancer for a median of 5.6 years found that those who started chemotherapy with vitamin D blood levels of at least 24.1 ng/mL were 19% less likely to have disease progression and 34% less likely to die in comparison to those who were deficient in vitamin D (< 10.8 ng/mL) at the start of treatment (Yuan, Clin Cancer Res 2019).

Breast cancer

A study of 1,666 women (average age 59) with **breast cancer** found that those with higher vitamin D blood levels around the time of diagnosis had the highest overall survival rates over an average 7 years of follow up. Nineteen percent of women with the lowest levels of vitamin D (under 17 ng/mL) died during the follow up period, while only about 14% died among those with higher levels. After accounting for differences in tumors and treatments, it was calculated that women with vitamin D levels of 17 to 25 ng/mL and those with more than 25 ng/mL were, respectively, 22% and 28% less likely to have died than women with the lowest levels. The reduction in risk associated with vitamin D was greatest for premenopausal women. Women with lowest blood levels of vitamin D at the time of diagnosis were more likely to have the most advanced-staged tumors (Yao, JAMA Oncol 2016).

Somewhat similarly, an analysis in 2014 of five clinical studies found that women who had the highest vitamin D blood levels at the time of breast cancer diagnosis were twice as likely to survive during the studies (which lasted 5 to 20 years) as women with the lowest vitamin D levels (Mohr, Anticancer Research 2014). Due to differences in the studies analyzed, the "low" vitamin D groups included women with less than 14 to 30 ng/mL of vitamin D while the "high" groups included those with more than 22 to 32.4 ng/mL.

While this association between vitamin D levels and mortality with breast cancer is not proven to be "cause-and-effect," there is no scientific reason to believe that breast cancer would cause a decrease in vitamin D, suggesting

a likely beneficial effect of vitamin D.

This potential beneficial link between vitamin D and breast cancer was somewhat strengthened by analysis of a study which gave 2,000 IU daily to overweight or obese postmenopausal women in the hope that it would aid weight loss during dieting -- although it did not (see Mason 2014 study in "Weight control" above). It was found that women whose vitamin D levels increased the most or to at least 32 ng/mL had the greatest reduction in blood estrogens, which are a known risk factor for breast cancer (Mason, Menopause 2016). However, *most of the reduction in blood estrogens appeared to be due to dieting itself*, with estrogen levels falling, on average, by about 14.5% among women who didn't receive vitamin D compared to about 19.5% among those who did.

An analysis of data pooled from three studies concluded that higher vitamin D blood levels "... were associated with a dose-response decrease in breast cancer risk with concentrations ≥ 60 ng/mL being most protective." *However*, this is a potentially unsafe level and the conclusion is dubious. The analysis was primarily based on data from just one of the studies, known as the GrassrootsHealth study, which, unlike the other two, was not randomized nor placebo-controlled and was based on self-reported health information from a self-selected group of people interested in vitamin D. Not surprisingly, it was also the only study that had a significant number of participants with vitamin D levels higher than 40 ng/mL (McDonnell, PLOS One 2018).

A randomized, placebo-controlled study in Canada among 80 women with newly diagnosed invasive breast cancer and generally sufficient blood levels of vitamin D (average 29 ng/mL) found that high-dose vitamin D3 (40,000 IU) taken daily for two to six weeks before breast cancer surgery *did not* slow tumor growth. Blood levels increased to about 98.5 ng/mL (an *extremely* high level) in those who took high-dose vitamin D, and decreased somewhat, to 25 ng/mL, in those who did not. Women who took high-dose vitamin D also experienced more fatigue than those who took a placebo, although no serious adverse effects were reported (Arnaout, Breast Cancer Res Treat 2019).

Bladder cancer

A study in Spain found that lower levels of vitamin D in the blood were associated with higher risks of **bladder cancer**. Compared to people with vitamin D levels of 30 ng/mL or above, the risk of bladder cancer was 83% higher among those with levels under 10 ng/mL, 67% higher among those with levels of 10 up to 15 ng/mL, and 63% higher among those with levels of 15 up to 20 ng/mL. There was no statistically significant difference in risk, however, between those with levels of 20 up to 30 ng/mL compared to those above 30 ng/mL. (Amaral, JNCI 2012). Even greater increases were found with the risk of *metastatic* bladder cancer.

Pancreatic cancer

Laboratory studies suggest that vitamin D may inhibit **pancreatic cancer** cell growth and a review of five large epidemiologic studies concluded that higher levels of serum vitamin D were associated with a lower risk of developing pancreatic cancer.[27] Compared to people whose serum vitamin D levels were less than 20 ng/mL, the risk of developing pancreatic cancer over the following 12 to 18 years was 25% lower among those with levels of 20 mg to 29 ng/mL, and 29% lower among those with levels above 30 ng/mL.

Prostate cancer

Vitamin D inhibits **prostate cancer** cells in laboratory studies. Whether or not vitamin D supplementation actually reduces the risk of prostate cancer is not known, but some studies do suggest an association between vitamin D levels and prostate cancer risk. For example, a large study in the U.S. found that *both low and high* vitamin D concentrations in the blood to be associated with increased risk of prostate cancer, particularly high-grade prostate cancer. The middle "sweet spot" associated with the lowest risk (about half the risk of the higher or lower levels) was between 23 ng/mL and 29 ng/mL, leading the researchers to write that the optimal range "for prostate cancer prevention may be narrow" Kristal, Canc Epi Biomark. Prev 2014. This finding is somewhat

consistent with a smaller study of men in Chicago undergoing radical prostatectomy (due to indications of possible cancer), in which those found *not* to have advanced cancer had a median blood level of 27.0 ng/mL, which was only slightly higher than that of men *with* advanced cancer (22.7 ng/mL). However, the study found that men with advanced cancer were more likely to be Black, and the Black men were more likely to have lower levels of vitamin D (as seen in other studies), so when the results were analyzed just among Blacks or among whites, there was no longer an association between vitamin D levels and advanced prostate cancer (Nyame, J Clin Oncol 2016).

A study of men aged 40 to 79 in the U.S. undergoing their first prostate biopsy for potential cancer, found that, in African American men, having a vitamin D level below 20 ng/mL was associated with increased odds of the biopsy showing prostate cancer. In addition, among both European American and African American men, having a level below 12 ng/mL was associated with a higher grade and stage of prostate cancer (Murphy, Clin Cancer Res, 2014).

A study of male smokers in Finland concluded that "men with higher vitamin D blood levels are at increased risk of developing prostate cancer," but this assertion has been called misleading since the risk increased only among men with calcium intakes of 1,338 mg per day or greater — an intake that substantially exceeds the recommended intake for adult men (1,000 mg). Increased calcium intake itself is a potential risk factor for prostate cancer.[33, 34]

Skin cancer A study of people with **melanoma** in whom lesions had recently been removed found no difference in disease-free *survival* with or without vitamin D supplementation (100,000 IU every 50 days) over a course of three years, despite that fact that half the participants started the study with a vitamin D level of 18 ng/mL or lower (Johansson, Nutrients 2021). It should also be noted that taking single, very-high doses of vitamin D (as was used in this study) has been associated with adverse effects, and in many cases, taking lower, daily doses may be preferable.

In summary, to potentially reduce the risk of cancer, it would seem reasonable to maintain a vitamin D level above 20 ng/mL and, to reduce the risk of death from cancer, into the upper 30's, but not necessarily higher. For prostate cancer, the "sweet spot" may be more limited -- to between 23 ng/mL and 29 ng/mL, while for colorectal cancer it may be higher — up to 39 ng/mL. Vitamin D supplementation does not appear to increase survival rates amount people being treated for cancer, but having a blood level of at least 24 ng/mL at the start of treatment for advanced or metastatic colorectal cancer is associated with increased survival rates.

Overall mortality

A review of studies involving vitamin D concluded that supplementation with vitamin D_3 reduced overall mortality among older adults significantly by 11%, while vitamin D_2 had no overall effect (Chowdhury, BMJ 2014). The review also found that, in the U.S., about 13% of all deaths could be attributable to "suboptimal" vitamin D levels, which is even greater than the risk of death associated with physical inactivity. The review did not define exactly when, or how much, vitamin D is most effective, but you can find sensible guidelines in the Summary, above.

A study that followed more than 300,000 healthy adults in the UK for a median of 8.9 years found that the risk of dying during that period decreased as vitamin D blood levels increased to 24 ng/mL (or to 19 ng/mL for death from cancer) and then leveled off (Fan, J Clin Endocrinol Metab 2020).

Similarly, a study that followed 1,970 European men (ages 40 to 79) for an average of 12.3 years found that those with vitamin D blood levels (i.e., *total* 25-hydroxyvitamin D levels) less than 9.3 ng/mL (i.e., severely deficient) had an 83% increased mortality risk compared to those with highest levels (Antonio, eECE 2020).

On a similar note, an analysis of data from 3,509 patients recovering from noncardiac surgery at the Cleveland

Clinic found that those with higher levels of vitamin D in their blood were less likely to experience serious post-operative complications, including death (Turan, Anesth Analg 2014). In fact, compared to the level of complications in patients with serum vitamin D levels below 13 ng/mL, the risk of having serious complications

fell to 65% when vitamin D levels were between 13 to 20 ng/mL, to 53% at levels between 20 and 27 ng/mL, and to 44% at levels between 27 and 36 ng/mL. Interestingly, at levels above 36 ng/mL, the relative odds of complications did not fall further and rose slightly, to 49%, consistent with other studies that have shown a reversal in benefits with vitamin D levels above approximately 35 ng/mL. The researchers suggest a trial be conducted in which vitamin D supplementation is given preoperatively.

Quality Concerns and Tests Performed:

Like other supplements, neither the FDA nor any other federal or state agency routinely tests calcium or vitamin D supplements for quality prior to sale. However, quality issues can include the following:

- **Labeled Amount** Does the product really contain the labeled amount of vitamin D (and other key listed ingredients such as calcium, magnesium, boron, and vitamin K)?
- **Purity** Vitamin D supplements for bone health often include calcium as an ingredient. Calcium may potentially be contaminated with heavy metals such as lead, arsenic and cadmium. In children, infants, and fetuses, even low levels of lead can adversely affect neurobehavioral development and cognitive function. In adults, lead at somewhat higher levels can cause elevated blood pressure, anemia, and adversely affect the nervous and reproductive systems. Lead is of particular concern during pregnancy as the mother can deliver it to the fetus. Arsenic is a carcinogen and can damage organs. Cadmium is a probable carcinogen (i.e., cancer-causing agent), can be toxic to the kidneys, can soften the bones, causing bone pain, and may affect fetal development.
- **Ability to Break Apart for Absorption** For a tablet to be most useful, it must fully disintegrate prior to leaving the stomach, delivering its contents for absorption in the gut. Some tablets are not properly made and can pass through your body completely or partially intact, depriving you of its ingredients. Remnants of such products are sometimes found in the stool. This happens, for example, when a tablet is too tightly compressed (too "hard") or is too thickly coated.

ConsumerLab.com, as part of its mission to independently evaluate products that affect health, wellness, and nutrition, purchased vitamin D supplements (some including calcium, boron, magnesium, and/or vitamin K) sold in the U.S. and Canada and tested them to determine whether they 1) possessed the claimed amount and form of vitamin D, calcium, magnesium, boron, and vitamin K, 2) were able to disintegrate fully to be available for absorption and, 3) if they contained 250 mg of minerals per daily dosage and/or whole herbs, were free from unacceptable levels of lead, cadmium, and arsenic (see Testing Methods and Passing Score).

What CL Found:

Most products contained their listed amounts of vitamin D and other key ingredients but the following two did not and, therefore, were Not Approved. These failures were each confirmed in a second independent laboratory.

- *Natural Vitality Natural Calm Plus Calcium - Raspberry-Lemon Flavor* contained its claimed amounts of calcium and magnesium, but contained a bit less vitamin D than claimed (22.1 IU instead of 35 IU) and more than double its listed amount of boron (198.5 mcg instead of 88.3 mcg) per teaspoon of powder. Although this suggests a quality control problem, these discrepancies do not pose a safety issue as the listed amounts are relatively small to start: The daily requirement for vitamin D is 400 IU to 800 IU, and although there is no daily requirement for boron -- because it is not essential -- most people get about 1,000 mcg to 10,0000 mcg from their diets and the daily Tolerable Upper Intake Level for adults is even

higher: 17,000 to 20,000 mcg (National Academies). (Note: In 2017 CL tested a magnesium-only version of *Natural Calm* of the same flavor and it passed testing.)

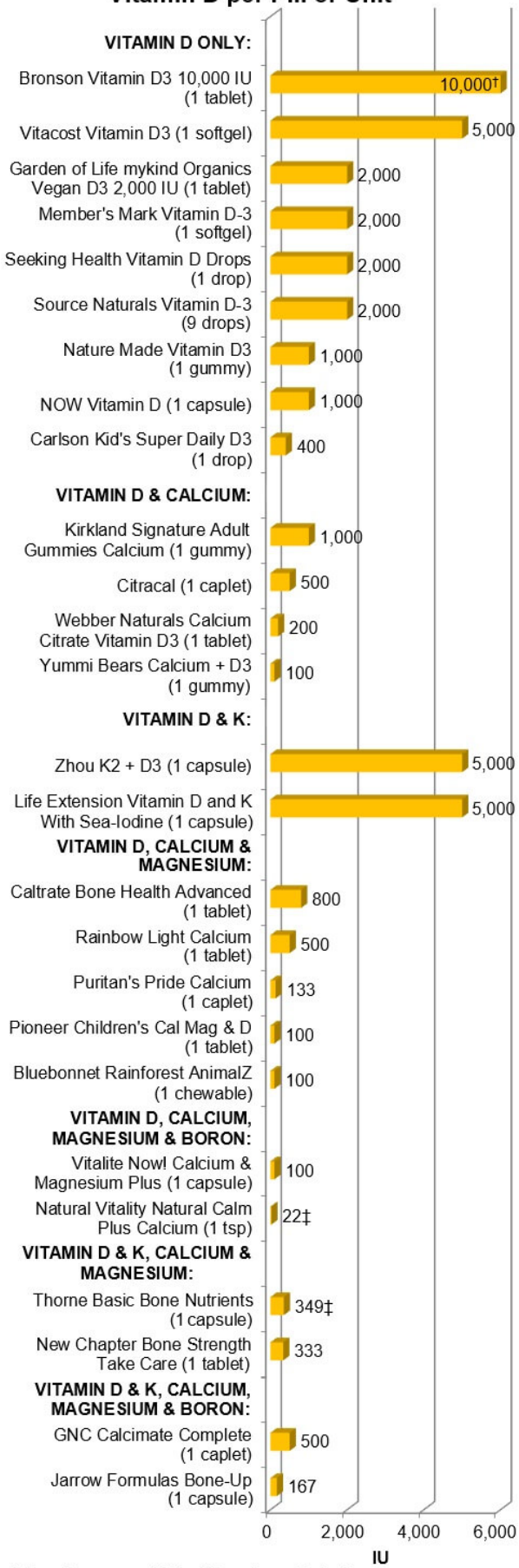
- *Thorne Basic Bone Nutrients* contained its claimed amounts of calcium and magnesium, but only 69.7% of its claimed vitamin D (348.5 IU vs. 500 IU) and just 2.2% of its vitamin K (1 mcg versus 45 mcg). *These are major discrepancies, particularly for vitamin K, indicating that one should not rely on this product for either of these nutrients.*

Nineteen of the 21 products that ConsumerLab.com selected for testing met all quality criteria, as did four products tested through ConsumerLab.com's voluntary Quality Certification Program. These products were found to contain their claimed amounts of vitamin D as well as calcium, boron, and vitamin K, none was contaminated with heavy metals, and all tablets and caplets disintegrated properly.

Vitamin D per pill or teaspoon

Be aware that the amount of vitamin D in a single pill, teaspoon of powder, or liquid serving of a supplement varied tremendously across products, from as little as 22.1 IU (Natural Vitality Natural Calm) to as much as 10,000 IU in *Bronson Vitamin D3 10,000 IU*. Most products provide 100 IU to 2,000 IU of vitamin D per unit, which is more in line with what are safe and effective doses to boost vitamin D intake to recommended levels — 600 IU except 800 IU for adults over 70 years of age and 400 IU for infants under 1 year of age.

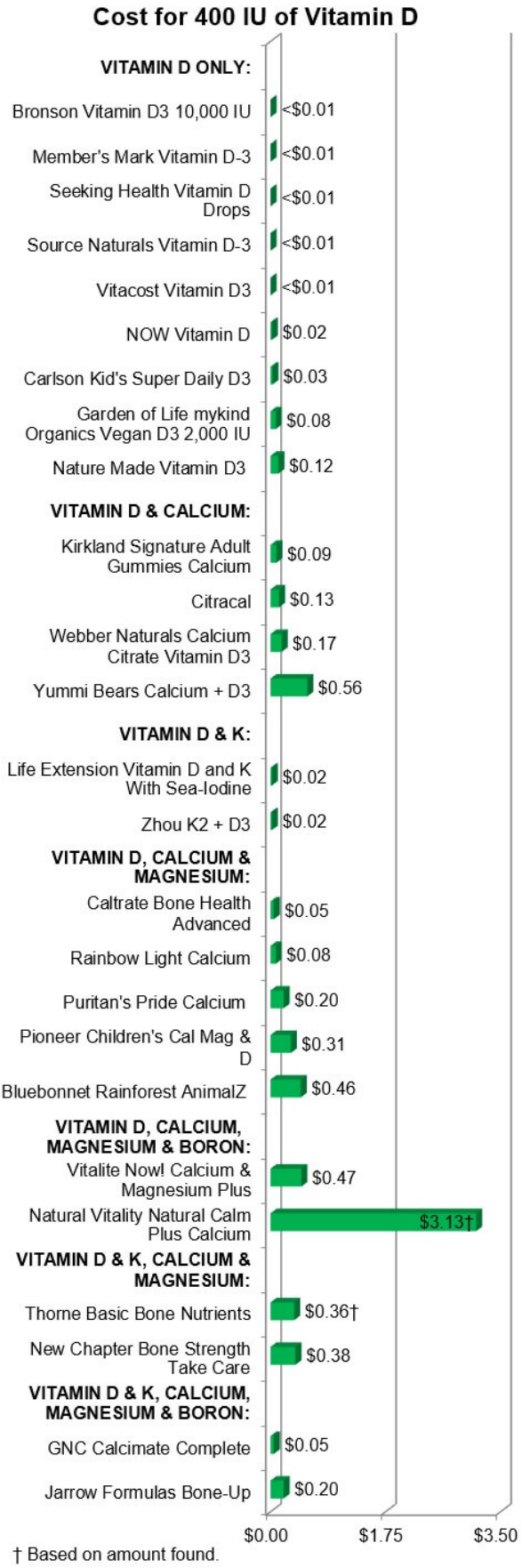
Vitamin D per Pill or Unit*



* Based on amount listed if confirmed in testing.
† Contains a much greater amount of vitamin D than other products. Data shown does not conform to same scale.
‡ Based on amount found.

Cost

Vitamin D itself is a very inexpensive ingredient, with 400 IU costing less than a penny from some products, as calculated and shown in the graph below. If you are just seeking vitamin D at a dose of even 2,000 IU, you can get it for about a dime or less. Extra ingredients and special formulations, such as gummies, chewables, powders can raise the cost significantly, although liquid drops tend to be more reasonably priced per dose.



Top Picks:

Among Approved products, ConsumerLab.com chose several as ***Top Picks*** (see below). To be a CL *Top Pick*, a Vitamin D supplement had to pass ConsumerLab's tests of quality, provide a reasonable dose, and offer good value (i.e., a favorable price). In combination products, amounts of other ingredients were also considered.

Keep in mind that unless your blood level of vitamin D (25-hydroxy vitamin D) is under 20 ng/mL, you may not need a supplement and most children and adults require only 600 IU of vitamin D per day (800 IU if you're over 70). The established daily Tolerable Upper Intake Level (the "upper limit") for adults is 4,000 IU per day and there are risks from getting too much vitamin D — it's probably best not to take more than 2,000 IU per day (see How Much Is Too Much and Cautions and Concerns for more information).

For combination products, be aware that most adults need a total of 1,000 to 1,200 mg of calcium, 90 to 120 mcg of vitamin K, and 310 to 420 mg magnesium from their total daily diets, which likely is already providing most or all of this. Some supplements provide much more of these other ingredients than you need. As to boron, it is not clear if you need it, but products that include a few thousand micrograms (i.e., a few milligrams) are safe.

Vitamin D Only:

- *Overall* Top Pick: ***Source Naturals Vitamin D-3*** liquid drops. This is an excellent choice because you can easily adjust your dose to suit your current needs and those of other family members. One drop provides 222 IU of vitamin D3 for just a fraction of a cent. If you need a higher dose, you can get 2,000 IU from 9 drops (which is the suggested daily serving size on the label) at a cost of just 2 cents. The drops have a mild lemon-orange flavor and can be added to food or beverages — preferably consumed as part of a meal containing fats or oils to aid vitamin D absorption (as would be the case with any vitamin D supplement). If you have trouble using the dropper and are prone to squeeze out more drops than you need, consider one of the other liquids which have special tops that pour out drops.

  As vitamin D supplements can slowly lose potency after they are opened, consider refrigerating your vitamin D supplement (to slow the loss) if you won't use it up before its listed expiration date (usually about 2 years from the date of manufacture). One bottle of *Source Naturals* provides 695 servings (each serving consisting of 9 drops providing 2,000 IU), so if you are only using, for example, 3 drops (667 IU) daily, a bottle could potentially last for more than five years.

- Low-Dose: Again, ***Source Naturals Vitamin D-3*** liquid drops, since you can get as little as 222 IU by taking just one drop, costing a fraction of a cent. ***Carlson Kid's Super Daily D3*** is another very good choice, providing 400 IU per drop — which is 2/3 of the daily requirement for most adults and children and 100% of that for infants. The *Carlson* drops have no taste at all and the cost is 3 cents per drop. One bottle provides enough 400 IU daily doses for an entire year.

- Moderate Dose: Again, ***Source Naturals Vitamin D-3*** is a good choice to get hundreds of IUs of vitamin D3 at little cost.

- High Dose: If you want 2,000 IU, you can consider the liquids discussed above or *Seeking Health Vitamin D Drops*, which is just as inexpensive as *Source Naturals* but provides 2,000 IU in a *single* drop, for 2 cents, as opposed to 9 drops with *Source Naturals* -- so be careful not take more than one drop of *Seeking Health*. Alternatively, you can take a single softgel of **Member's Mark [Sam's Club] Vitamin D-3 2000 IU** — each costs just 2 cents.

- Very High Dose: ***Vitacost Vitamin D3*** medium sized softgels each provide 5,000 IU of vitamin D for just 3

cents each. *Be aware that these exceed the safe Tolerable Upper Intake Level for vitamin D of 4,000 IU.*

- Extremely High Dose: ***Bronson Vitamin D3 10,000 IU.*** Each capsule provides *10,000 IU* of vitamin D3 for 6 cents. This is a potentially dangerous dose and should not be taken more than every several days. It is best to avoid such a high dose, which should only be considered when a person is known to be severely deficient in vitamin D unlikely to reliably take a daily vitamin D supplement.

Children's Products Containing Vitamin D: *Carlson Kid's Super Daily* provides 400 IU per drop and has no taste, so it can easily be added to foods and beverages. Alternatively, at somewhat lower cost, consider giving one or two drops (222 IU to 444 IU) of *Source Naturals D-3*. Another good quality drop for children is *Baby Ddrops Vitamin D3*, which we tested in 2017, but these cost about 20 per drop -- rather than 3 cents for *Carlson*.

Vitamin D and Calcium: *Bayer Citracal Petites* provide 400 mg of calcium (from calcium citrate) and 500 IU of vitamin D per 2 caplet serving for 16 cents. This is a little less than half the daily requirement for calcium, as well as enough vitamin D to boost someone who's a little low in vitamin D. Note that, despite the product name, that the caplet size is large, although narrow. If you live in Canada, *Webber Naturals Calcium Citrate Vitamin D3* is also *Top Pick* in this category, providing 300 mg of calcium (from calcium citrate) and 200 IU of vitamin D for 9 cents.

Children's Vitamin D and Calcium: Our *Top Pick*, although pricey, is *Yummi Bears Calcium + D3*, which provide 376 mg of calcium (from tricalcium phosphate) and 300 IU of vitamin D3 per 3 gummy bears for 42 cents. (Although not tested this year, a less expensive option is *L'il Critters Calcium & D3*, which was tested and approved in 2017, and provides 200 mg of calcium (from tricalcium phosphate) and 220 IU of vitamin D3 per 2 gummies for just 10 cents). We are not big fans of gummies for several reasons, including the fact that they may over-consumed as candy, resulting in overdosing. But if gummies are the only way to get a kid who otherwise won't get enough nutrients from foods or non-sweetened supplements to meet the daily requirements, they are a reasonable option.

Vitamin D and Vitamin K: Although both of the products we tested in this category (*Life Extension Vitamin D and K With Sea-Iodine* and *Zhou K2 + D3*) passed testing, *neither* is a *Top Pick* for regular use as they both provide 5,000 IU of vitamin D, a very large does that exceeds the Tolerable Upper Intake Level of 4,000 IU per day. In addition, *Life Extension* provides a very large amount of vitamin K — a total of 2,100 mcg, which is many times the daily 90 mcg to 120 mcg that is adequate for women and men, respectively. The likely basis for this are studies suggesting that very high-dose vitamin K over long periods of time may further strengthen bones, as discussed earlier. *Life Extension* also contains a very large amount of iodine -- several times the daily requirement and approaching the Tolerable Upper Intake Level for adults.

Although not tested this year, *NOW Vitamin D-3 & K-2*, a capsule that provides 1,000 IU of vitamin D and 45 mcg of vitamin K (as MK-4 K2) for 7 cents passed our tests in 2017 and would be a reasonable choice if you are just looking to boost your vitamin K intake to an adequate level while getting a bit over the daily requirement of vitamin D. (See the Vitamin K Review for more information about forms of Vitamin K).

Vitamin D, Calcium and Vitamin K: We didn't test any products in this category this year. However, if this is combination you want, *Viactiv Calcium Plus D*, which passed our tests in 2017, provides 500 mg of calcium (from calcium carbonate), 500 IU vitamin D3 and 40 mcg vitamin K1 (about half the recommended intake for women and one-third the recommended intake for men) for 10 cents per soft chew.

Children's Products Containing Vitamin D, Calcium, and Magnesium: Similar to the adult products in this category, both of the products that we tested for children primarily use calcium carbonate and magnesium oxide. Both provide the same amounts of calcium (250 mg) and vitamin D (200 IU) and similar amounts of magnesium per two chewable tablets. Our *Top Pick* is *Pioneer Children's Cal Mag & D* as it is less expensive (15 cents) than

per two chewable tablets. Our *Top Pick* is *Pioneer Children's Cal Mag & D* as it is less expensive (15 cents) than *Bluebonnet Rainforest AnimalZ* (23 cents). *Pioneer* is vanilla flavored while *Bluebonnet* is cocoa flavored.

Vitamin D, Calcium, Magnesium and Boron: *Vitalite Now! Calcium & Magnesium Plus* provides calcium (250 mg), magnesium (125 mg), and boron (1,000 mcg) in each capsule, as well as a modest amount of vitamin D (100 IU). Although the label suggests taking four capsules daily (for a relatively high daily cost of 48 cents), fewer capsules would be sufficient for most people with regard to the three minerals, although not necessarily for vitamin D. The source of calcium is a list of nearly every form of calcium, but carbonate is the first and may be the main form, so it is important to take this product with a meal, which you should anyhow to maximize vitamin D absorption.

Vitamin D, Calcium, Magnesium, and Vitamin K: Only one of two products in this category passed our tests: *New Chapter Bone Strength Take Care* However, due to its high cost, it is not a *Top Pick*. The suggested daily serving of 3 tablets provides 1,000 IU of vitamin D, 770 mg of calcium, 80 mcg of vitamin K from K1 and K2, and a modest amount of magnesium. It is best to break this into two or three servings to be taken with meal during the day, as 770 mg of calcium is too much to take at one time. This is a relatively expensive product at 96 cents per day and, considering that there is no compelling research showing superiority of algae-based calcium or magnesium, you can easily get these same ingredients for less by purchasing the ingredients separately.

Vitamin D, Calcium, Magnesium, Boron, and Vitamin K: Both of the products that we tested in this category, *GNC Calcimate and Jarrow Formulas Bone Up*, provide significant amounts of calcium, vitamin K, and boron. What sets them apart is the amount of magnesium they provide, with *Jarrow* providing several times as much as *GNC* as well as a daily dose of vitamin D (1,000 IU) that is closer to the adult requirement (600 IU to 800 IU) than *GNC*'s 2,000 IU. Although costs more (51 cents daily for 6 pills versus 25 cents daily for 4 pills), *Jarrow Formulas Bone Up* is our *Top Pick* for this category. With either product, consider cutting the suggest dose in half if you are just trying to boost your intake of these nutrients and not trying to fulfill the majority of the daily requirements from a supplement. By the way, *Jarrow Formulas Bone-Up* provides calcium as StimuCal microcrystalline hydroxyapatite — see What to Consider When Buying for more about this ingredient.

Test Results by Product:

Listed below are the test results for 26 supplements containing vitamin D. Products are grouped by main ingredients, and there are subgroupings for children's products. Within each group, products are listed alphabetically. ConsumerLab.com selected 21 of these products. Four other products (each indicated with a CL flask) were tested at the request of their manufacturers/distributors through CL's voluntary Quality Certification Program and are included for having passed testing.

Shown for each product are the claimed amount and form of the tested ingredient(s), serving size recommended on its label, pill size, price information and, for comparison purposes, the cost per 400 IU of vitamin D. Products listed as "Approved" met their label claims and ConsumerLab.com's quality criteria (see Passing Score). The full list of ingredients is available for each product in the last column.

Jump to results by ingredient:

- Children's Vitamin D and Calcium.
- Vitamins D and K

- Vitamin D, Calcium, and Magnesium
- Children's Vitamin D, Calcium, and Magnesium
- Vitamin D, Calcium, Magnesium, and Boron
- Vitamin D, Calcium, Magnesium, and Vitamin K
- Vitamin D, Calcium, Magnesium, Boron, and Vitamin K

Results of ConsumerLab.com Testing of VITAMIN D SUPPLEMENTS

(INCLUDING COMBINATIONS WITH CALCIUM, MAGNESIUM, BORON AND/OR VITAMIN K)

(Price Checks are not included in printed reviews)

Approval Status **Product Name**	**Claimed Amount of and Form of Vitamin D, Calcium, Magnesium, Boron & Vitamin K Per Serving** **Heavy Metals**	**Suggested Daily Serving on Label** **Pill Size**	**Cost for Suggested Serving** **[Price per 400 IU (10 mcg) Vitamin D]** **Price**	**Notable Features**	**Full List of Ingredients Per Serving**
Vitamin D Only: Pills/Gummies					
APPROVED Top Pick for extremely high dose vitamin D only Bronson® Vitamin D3 10,000 IU  Dist. by Bronson Laboratories	1 tablet **10,000 IU (250 mcg)** (D3) ✓ Heavy metals: Also tested for disintegration	As a dietary supplement for adults, take 1 tablet daily, preferably with a meal, or as directed by a healthcare professional. Medium circular organic	1 tablet $0.06 [<$0.01] $19.99/360 organic tablets	*USDA Organic seal. Non-GMO. Gluten-free. Soy-free. Wheat-free. Nut-free.*	1 tablet Vitamin D3 (as cholecalciferol) 250 mcg (10,000 IU). Other Ingredients: Organic corn maltodextrin, organic potato starch, organic corn syrup solids Additional Information 1 tablet Vitamin D3 (as cholecalciferol) 250 mcg (10,000 IU). Other Ingredients: Organic corn maltodextrin, organic potato starch, organic corn syrup solids, organic rice extract, organic gum acacia, organic tapioca maltodextrin, organic sunflower lecithin, organic palm oil, organic guar gum.

APPROVED Garden of Life® mykind Organics Vegan D3 2,000 IU  Dist. by Garden of Life LLC	1 tablet **2,000 IU (50 mcg)** (D3) ✓ Heavy metals: Pass	Adults chew 1 tablet daily. Children 4 years and older chew 1 tablet under adult supervision. Medium/large circular vegan chewable tablet	1 tablet $0.42 [$0.08] $12.59/30 vegan chewable tablets	Certified organic food blend 180 mg, certified organic mushroom blend 50 mg *Kosher. USDA Organic seal. Non GMO Project Verified seal. Certified Vegan Vegan.org seal. Gluten-Free.*	1 tablet Vitamin D (as D3 from Lichen) 2,000 IU, Certified Organic Food Blend [Organic Flax (seed), Organic Carrot (root), Organic Broccoli (flower & stem), Organic Cauliflower (flower & stem), Organic Spinach (leaf)] 180 mg Additional Information 1 tablet Vitamin D (as D3 from Lichen) 2,000 IU, Certified Organic Food Blend [Organic Flax (seed), Organic Carrot (root), Organic Broccoli (flower & stem), Organic Cauliflower (flower & stem), Organic Spinach (leaf)] 180 mg, Certified Organic Mushroom Blend [Organic Reishi (*Ganoderma lucidum*) mycelia, Organic Maitake (*Grifola frondosa*) mycelia, Organic Shiitake (*Lentinula edodes*) mycelia, Organic *Bionectria ochroleuca* mycelia, Organic *Schizophyllum commune* mycelia, Organic *Hericium erinaceus* mycelia, Organic *Poria cocos* mycelia, Organic *Coriolus versicolor* mycelia, Organic *Agaricus blazei* mycelia, Organic *Auricularia auricular* mycelia] 50 mg. Other Ingredients: Clean Tablet Technology™ blend (patent pending): organic tapioca dextrose, organic gum arabic, organic raspberry flavor, organic lemon Flavor, organic coating (organic tapioca maltodextrin, organic sunflower lecithin, organic palm oil, organic guar gum).
APPROVED Top Pick for high dose vitamin D only Member's Mark® [Sam's Club] Vitamin D-3  Dist. by Sam's West, Inc.	1 softgel **2,000 IU (50 mcg)** (D3) ✓ Heavy metals:	For adults, take one (1) softgel daily, preferably with a meal. Medium softgel	1 softgel $0.02 [<$0.01] $8.33/400 softgels	*No gluten. No yeast. No wheat. No milk or milk derivatives. No lactose. No sugar. No preservatives. No artificial color. No artificial flavor. No sodium (less than 5 mg per serving). Gluten free.*	1 softgel Vitamin D (as D3 Cholecalciferol) 2,000 IU. Other Ingredients: Soybean oil, gelatin, glycerin, corn oil.

APPROVED Nature Made® Vitamin D3  Dist. by Nature Made Nutritional Products	2 gummies **2,000 IU (50 mcg)** (D3) ✓ Heavy metals:	Adults, chew 2 gummies daily. Medium/large gumdrop shaped gummy	2 gummies $0.60 [$0.12] $26.98/90 gummies	*No artificial flavors - natural fruit flavors. No synthetic dyes - colors derived from natural sources. No high fructose corn syrup. No artificial sweeteners. Gluten free.*	2 gummies Calories 15, Total Carbohydrate 4 g, Total Sugars [Includes 2 g Added Sugars] 2 g, Vitamin D3 (as Cholecalciferol) 50 mcg (2,000 IU). Other Ingredients: Glucose syrup, sugar Additional Information 2 gummies Calories 15, Total Carbohydrate 4 g, Total Sugars [Includes 2 g Added Sugars] 2 g, Vitamin D3 (as Cholecalciferol) 50 mcg (2,000 IU). Other Ingredients: Glucose syrup, sugar, water, gelatin, citric acid, palm oil, natural flavors, malic acid, tartaric acid, carnauba wax, colors added.
APPROVED NOW® Vitamin D  Dist. by NOW Foods	1 capsule **1,000 IU (25 mcg)** (D2) ✓ Heavy metals:	Take 1 capsule daily with a meal. Medium/large veg capsule	1 capsule $0.04 [$0.02] $4.86/120 veg capsules	*Kosher. Non-GMO. Not manufactured with wheat, gluten, soy, milk, egg, fish, shellfish or tree nut ingredients.*	1 capsule Vitamin D2 (as Ergocalciferol) 25 mcg (1,000 IU). Other Ingredients: Rice flour, hypromellose (cellulose capsule), magnesium stearate (vegetable source) and silica.
APPROVED Top Pick for very high dose vitamin D only Vitacost Vitamin D3  Dist. by Vitacost.com	1 softgel **5,000 IU (125mcg)** (D3) ✓ Heavy metals:	As A Dietary Supplement For Adults 18 Years Of Age And Over, Take 1 Softgel Daily Or As Directed By A Healthcare Professional. Medium softgel	1 softgel $0.03 [<$0.01] $6.69/20 softgels	*Free of: milk, eggs, peanuts, tree nuts, crustacean shellfish, fish, soy, gluten, titanium dioxide.*	1 softgel Vitamin D (as cholecalciferol, D3) 5,000 IU. Other Ingredients: Safflower oil, corn oil, gelatin, glycerin and water.
Vitamin D Only: Liquid					
APPROVED Seeking Health® Vitamin D Drops  Dist. by Seeking Health, LLC	1 drop [0.033 ml] **2,000 IU (50 mcg)** (D3) ✓ Heavy metals: NA	Carefully dispense one drop and take by mouth daily, or use as directed by your healthcare professional. Liquid from bottle	1 drop $0.02 [<$0.01] $19.95/1 fl oz. [30 ml] bottle (approx. 900 servings)	*Does Not Contain: Milk, eggs, fish, shellfish, tree nuts, peanuts, wheat, soy, gluten, GMO, sweeteners, flavors, colors, or preservatives.*	1 drop Calories 0, Total Fat 0 g, Cholesterol 0 mg, Vitamin D3 (as cholecalciferol) 50 mcg (2,000 IU). Other Ingredients: Olive oil.

APPROVED Top Pick for vitamin D only Source Naturals® Vitamin D-3  Dist. by Source Naturals, Inc.	9 drops [0.17 ml] **2,000 IU (50 mcg)** (D3) ✓ Heavy metals:	9 drops once daily in a drink. Liquid from bottle	9 drops $0.02 [<$0.01] $13.29/4 fl oz. [118.28 ml] bottle (approx. 695 servings)	*Contains no yeast, dairy, egg, gluten, corn, soy or wheat. Contains no sugar, starch, salt, preservatives, or artificial color, flavor or fragrance.*	9 drops Vitamin D-3 (as cholecalciferol) 2,000 IU. Other Ingredients: Medium chain triglycerides, orange and lemon essential oils.
Children's Products Containing Vitamin D:					
APPROVED Top Pick for children's vitamin D only Carlson® Kid's Super Daily® D3  Dist. by Carlson Div. of J.R. Carlson Laboratories, Inc.	1 drop [0.028 ml] **400 IU (10 mcg)** (D3) ✓ Heavy metals:	Children two years of age or older: give one drop daily or as directed by your healthcare professional. Liquid from bottle	1 drop $0.03 [$0.03] $9.68/0.35 fl. oz. [10.3 ml] bottle (approx. 365 servings)	*Gluten-free. Soy-free. No artificial preservatives.*	1 drop Vitamin D (as cholecalciferol) (400 IU) 10 mcg. Other Ingredients: Medium chain triglyceride oil (coconut and pal source).
Vitamin D & Calcium:					
APPROVED Top Pick for vitamin D & calcium Bayer Citracal® Petites  Dist. by Bayer HealthCare LLC	2 caplets **500 IU (12.5 mcg)** (D3) ✓ 400 mg (calcium citrate) ✓ Heavy metals: Pass Also tested for disintegration	Adults: Take 1 serving (2 caplets) twice daily with or without food or as recommended by your physician, pharmacist, or health care professional. Large coated caplet	2 caplets $0.16 [$0.13] $8.24/100 coated caplets	None.	2 caplets Vitamin D (as cholecalciferol) 500 IU, Calcium (element) 400 mg. Ingredients: Calcium citrate, polyethylene glycol, croscarmellose sodium, hydroxypropyl methylcellulose, magnesium silicate Additional Information 2 caplets Vitamin D (as cholecalciferol) 500 IU, Calcium (element) 400 mg. Ingredients: Calcium citrate, polyethylene glycol, croscarmellose sodium, hydroxypropyl methylcellulose, magnesium silicate, titanium dioxide (color), propylene glycol dicaprylate/ dicaprate, oligofructose enriched inulin, magnesium stearate, vitamin D3 (cholecalciferol).

APPROVED Kirkland Signature™ [Costco] Adult Gummies Calcium  Dist. by Costco Wholesale Corporation	2 gummies **1,000 IU (25 mcg)** (D3) ✓ 500 mg (tribasic calcium phosphate) ✓ Heavy metals: Pass	As a dietary supplement for adults, chew two (2) gummies daily, preferably with a meal. Very large gumdrop shaped gummy	2 gummies $0.22 [$0.09] $12.99/120 gummies	*USP® dietary supplement verified seal. No preservatives. No artificial flavors. No yeast or gluten. No lactose.*	2 gummies Calories 20, Total Carbohydrate 5 g, Total Sugars [Includes 3 g Added Sugars] 3 g, Vitamin D 25 mcg (1,000 IU), Calcium 500 mg, Phosphorus 230 mg. Ingredients: Sugar, corn syrup, tribasic calcium phosphate, water Additional Information 2 gummies Calories 20, Total Carbohydrate 5 g, Total Sugars [Includes 3 g Added Sugars] 3 g, Vitamin D 25 mcg (1,000 IU), Calcium 500 mg, Phosphorus 230 mg. Ingredients: Sugar, corn syrup, tribasic calcium phosphate, water, modified food starch, gelatin (porcine), citric acid, natural flavors, vegetable and fruit juice (color), maltodextrin, lactic acid, cholecalciferol.
APPROVED Webber Naturals® Calcium Citrate Vitamin D3  Dist. by WN Pharmaceuticals® Ltd.	1 tablet **200 IU (5 mcg)** (D3) ✓ 300 mg (calcium citrate) ✓ Heavy metals: Pass Also tested for disintegration	2-4 tablets daily, a few hours before or after taking other medications, or as directed by a physician. Large tablet	1 tablet $0.09 [$0.17] $29.99/350 tablets	*Free of artificial colours, preservatives or sweeteners; no dairy, sugar, wheat, gluten, yeast, soy, egg, fish, shellfish, salt, tree nuts or GMOs. Suitable for vegetarians.*	1 tablet Calcium (citrate) 300 mg, Vitamin D3 (cholecalciferol) 200 IU (5 mcg). Non-medicinal Ingredients: Coating (carbohydrate gum, glycerin), croscarmellose sodium, vegetable grade magnesium stearate (lubricant).
Children's Products Containing Vitamin D & Calcium:					

APPROVED Top Pick for children vitamin D & calcium Yummi Bears® Calcium + D3  Dist. by Hero Nutritionals, Inc.	3 gummies **300 IU (7.5 mcg)** (D3) ✓ 375 mg (tricalcium phosphate) ✓ Heavy metals: Pass	As a dietary supplement, give each child three (3) bears per day. Large bear shaped gummy	3 gummies $0.42 [$0.56] $12.61/90 gummies	Phosphorus 175 mg *Vegetarian approved.* *Free of: GMOs, gluten, yeast, wheat, dairy, eggs, soy, tree nuts, peanuts, shellfish, fish, gelatin, artificial flavors, artificial colors and artificial preservatives.*	3 gummies Calories 20, Total Carbohydrate 5 g, Sugars 4 g, Vitamin D (Vitamin D3 as cholecalciferol USP) 300 IU, Calcium (as tricalcium phosphate) 375 mg, Phosphorus (as tricalcium phosphate) 175 mg. Other Ingredients: Organic tapioca syrup, natural cane sugar Additional Information 3 gummies Calories 20, Total Carbohydrate 5 g, Sugars 4 g, Vitamin D (Vitamin D3 as cholecalciferol USP) 300 IU, Calcium (as tricalcium phosphate) 375 mg, Phosphorus (as tricalcium phosphate) 175 mg. Other Ingredients: Organic tapioca syrup, natural cane sugar, pectin, citric acid, sodium citrate, natural flavors (orange, pineapple, strawberry), organic colors (carrot, pumpkin, apple, blackcurrant concentrates), fumaric acid.
Vitamin D & Vitamin K:					
APPROVED Life Extension® Vitamin D and K With Sea-Iodine™  Dist. by Quality Supplements and Vitamins, Inc.	1 capsule **5,000 IU (125 mcg)** (D3) ✓ 1,000 mcg (K1) 1,000 mcg (MK-4 K2) 100 mcg (MK-7 K2) 2,100 mcg (total vitamin K) ✓ Heavy metals:	Take one (1) capsule once daily with food, or as recommended by a healthcare practitioner. Medium/large capsule	1 capsule $0.30 [$0.02] $18.00/60 capsules	Iodine™ complex blend 1,000 mcg	1 capsule Vitamin D3 (as cholecalciferol) 5,000 IU, Vitamin K activity from: [Vitamin K1 (phytonadione) 1,000 mcg, Vitamin K2 (as menaquinone-4) 1,000 mcg, Vitamin K2 (as all-trans menaquinone-7) 100 mcg] 2,100 mcg Additional Information 1 capsule Vitamin D3 (as cholecalciferol) 5,000 IU, Vitamin K activity from: [Vitamin K1 (phytonadione) 1,000 mcg, Vitamin K2 (as menaquinone-4) 1,000 mcg, Vitamin K2 (as all-trans menaquinone-7) 100 mcg] 2,100 mcg, Iodine [from Sea-Iodine™ Complex Blend (organic kelp and bladderwrack extracts, potassium iodide)] 1,000 mcg. [Note: Product contains a large amount of iodine; several times the recommended daily intake of iodine. It exceeds the Upper Tolerable Intake Level (UL) for individuals below the age of 19 and is close to the UL for adults (1,100 mcg).] Other Ingredients: Microcrystalline cellulose, vegetable cellulose (capsule), maltodextrin, modified food starch, dicalcium phosphate, stearic acid, silica.

APPROVED Zhou® K2 + D3  Dist. by Zhou Nutrition®	1 capsule **5,000 IU (125 mcg)** (D3) ✓ 90 mcg (MK-7 K2) ✓ Heavy metals:	Take 1 vegetable capsule with food once daily or as directed by your healthcare professional. Large veggie capsule	1 capsule $0.26 [$0.02] $15.64/60 veggie capsules	*Zero gluten, soy, milk, eggs, fish, shellfish, tree nuts, peanuts & wheat. Made with non-GMO ingredients.*	1 capsule Vitamin D3 (as Cholecalciferol) 5,000 IU, Vitamin K2 (as Menaquinone) (MK-7) 90 mcg. Other Ingredients: Rice flour, cellulose (vegetable capsule).
Vitamin D, Calcium & Magnesium:					
APPROVED Caltrate® Bone Health Advanced  Dist. by Pfizer	1 tablet **800 IU (20 mcg)** (D3) ✓ 600 mg (calcium carbonate) ✓ 40 mg (magnesium oxide) ✓ Heavy metals: Pass	Take one (1) chewable tablet up to two times daily with or without food or as directed by your physician. Medium/large circular chewable tablet	1 tablet $0.10 [$0.05] $14.97/155 chewable tablets	None.	1 tablet Calories 0, Total Carbohydrates <1 g, Total Sugars [Includes 0 g Added Sugars] 0 g, Sugar Alcohol <1 g, Vitamin D3 20 mcg (800 IU), Calcium 600 mg, Magnesium 40 mg, Zinc 7.5 mg, Copper 0.25 mg, Manganese 1.8 mg Additional Information 1 tablet Calories 0, Total Carbohydrates <1 g, Total Sugars [Includes 0 g Added Sugars] 0 g, Sugar Alcohol <1 g, Vitamin D3 20 mcg (800 IU), Calcium 600 mg, Magnesium 40 mg, Zinc 7.5 mg, Copper 0.25 mg, Manganese 1.8 mg. Ingredients: Calcium carbonate, xylitol, maltodextrin, magnesium oxide, contains <2% of: blue 2 lake, cholecalciferol (vit. D3), citric acid, copper sulfate, corn syrup solids, hydrogenated palm oil, magnesium stearate, manganese sulfate, mono- and di-glycerides, natural and artificial flavors, polydextrose, red 40 lake, sucralose, sugar, tocopherols (to preserve freshness), yellow 6 lake, zinc oxide.

APPROVED Top Pick for vitamin D, calcium & magnesium Puritan's Pride® Calcium Magnesium Vitamin D3  Dist. by Puritan's Pride, Inc.	3 caplets **400 IU (10 mcg)** (D3) ✓ 1,000 mg (calcium from oyster shell) ✓ 500 mg (magnesium oxide) ✓ Heavy metals: Pass Also tested for disintegration	For adults, take three (3) caplets daily, preferably with meals. Large coated caplet	3 caplets $0.20 [$0.20] $7.99/120 coated caplets	*No artificial flavor, no artificial sweetener, no preservatives, no sugar, no milk, no lactose, no soy, no gluten, no wheat, no yeast. Sodium free.*	3 caplets Vitamin D (as D3 Cholecalciferol) 10 mcg (400 IU), Calcium (as Oyster Shell) 1,000 mg, Magnesium (as Magnesium Oxide) 500 mg. Other Ingredients: Vegetable cellulose, contains <2% of: natural palm leaf glaze, polydextrose, titanium dioxide color, triacetin Additional Information 3 caplets Vitamin D (as D3 Cholecalciferol) 10 mcg (400 IU), Calcium (as Oyster Shell) 1,000 mg, Magnesium (as Magnesium Oxide) 500 mg. Other Ingredients: Vegetable cellulose, contains <2% of: natural palm leaf glaze, polydextrose, titanium dioxide color, triacetin, vegetable magnesium stearate, vegetable stearic acid.
APPROVED Rainbow Light® Food-Based Calcium™ With Magnesium & Vitamin D3  Dist. by Rainbow Light Nutritional Systems®	1 tablet **500 IU (12.5 mcg)** (D3) ✓ 500 mg (calcium carbonate, amino acid chelate, citrate-malate) ✓ 250 mg (magnesium oxide, aspartate) ✓ Heavy metals: Pass Also tested for disintegration	For pure and potent protection, take one tablet per day, with or between meals. May take 2 per day in divided doses for advanced usage. Large tablet	1 tablet $0.10 [$0.08] $17.99/180 tablets	Betaine HCl 20 mg, stinging nettle [tops] 20 mg, horsetail [whole herb] 20 mg, organic spirulina 20 mg *Free of gluten, wheat, milk/dairy, nuts, soy, eggs, fish, shellfish, yeast, sugar, artificial additives.*	1 tablet Calcium (as Carbonate, Amino Acid Chelate, Citrate-Malate) 500 mg, Magnesium (as Oxide, Aspartate) 250 mg, Vitamin D (as D3 Cholecalciferol) 500 IU, Betaine HCl 20 mg, Stinging Nettle [tops] 20 mg, Horsetail [whole herb] 20 mg, Organic Spirulina 20 mg Additional Information 1 tablet Calcium (as Carbonate, Amino Acid Chelate, Citrate-Malate) 500 mg, Magnesium (as Oxide, Aspartate) 250 mg, Vitamin D (as D3 Cholecalciferol) 500 IU, Betaine HCl 20 mg, Stinging Nettle [tops] 20 mg, Horsetail [whole herb] 20 mg, Organic Spirulina 20 mg. Other Ingredients (natural mineral or vegetable source): cellulose, stearic acid, modified cellulose gum, silica. Coating: vegetable food glaze (hydroxypropyl cellulose, pharmaceutical glaze).
Children's Products Containing Vitamin D, Calcium & Magnesium:					

APPROVED Bluebonnet Rainforest AnimalZ® Calcium Magnesium & Vitamin D3 - Vanilla Frosting Flavor  Dist. by Bluebonnet Nutrition Corporation	2 chewables **200 IU (5 mcg)** (D3) ✓ 250 mg (calcium carbonate, citrate, malate) ✓ 50 mg (magnesium oxide, bisglycinate chelate) ✓ Heavy metals: Pass	As a dietary supplement for children three years of age or older, take two animal-shaped chewables once daily or as directed by a healthcare practitioner. Medium/large animal-shaped chewable tablet	2 chewables $0.23 [$0.46] $10.24/90 chewables	Super fruit and veggie blend 30 mg *Kosher. Gluten free. Free of milk, egg, fish, crustacean shellfish, tree nuts, peanuts, peanuts, wheat and soybeans. Also free of yeast, gluten, barley and sodium.*	2 chewables Calories 6, Total Carbohydrate 1.5 g, Sugars [Includes 1.5 g added sugars] 1.5 g, Vitamin D3 (as 200 IU cholecalciferol) 5 mcg, Calcium (as carbonate, citrate, malate) 250 mg, Magnesium (as oxide, bisglycinate chelate) 50 mg Additional Information 2 chewables Calories 6, Total Carbohydrate 1.5 g, Sugars [Includes 1.5 g added sugars] 1.5 g, Vitamin D3 (as 200 IU cholecalciferol) 5 mcg, Calcium (as carbonate, citrate, malate) 250 mg, Magnesium (as oxide, bisglycinate chelate) 50 mg, Super Fruit and Veggie Blend (from wild blueberry , cranberry, prune, cherry, strawberry, grape, raspberry, bilberry, fig and date fruits, grape seed, raspberry seed, broccoli, broccoli sprouts, brussels sprouts, carrot, kale, onion, spinach, tomatoes) 30 mg. Other Ingredients: Natural vanilla flavor, EarthSweet® [juice concentrates (wild blueberry, cranberry, prune, cherry, strawberry, grape, raspberry and bilberry fruits, grape seed and raspberry seed extract), cane crystals], vegetable magnesium stearate, stearic acid.
APPROVED Top Pick for children vitamin D, calcium & magnesium Pioneer® Children's Cal Mag & D - Cocoa  Mfd. by Healthway Corp.	2 tablets **200 IU (5 mcg)** (D3) ✓ 250 mg (calcium carbonate, citrate) ✓ 85 mg (magnesium oxide, citrate) ✓ Heavy metals: Pass	Children ages 4-8: Two chewables once daily. Children ages 9-13: Two chewables two times daily. Medium/large circular chewable tablet	2 tablets $0.15 [$0.31] $9.18/120 chewable tablets	Trace mineral complex 10 mg *Gluten free. Product contains no added artificial colors or flavors. Formulated to be free of dairy.*	2 chewables Calories 5, Total Carbohydrate 2 g, Sugar Alcohol 1 g, Vitamin D-3 (from cholecalciferol) 200 IU, Calcium (3:1 from carbonate: citrate) 250 mg, Magnesium (2:1 from oxide: citrate) 85 mg, Trace Mineral Complex (from sea vegetation: *Lithothamnion* spp.) 10 mg Additional Information 2 chewables Calories 5, Total Carbohydrate 2 g, Sugar Alcohol 1 g, Vitamin D-3 (from cholecalciferol) 200 IU, Calcium (3:1 from carbonate: citrate) 250 mg, Magnesium (2:1 from oxide: citrate) 85 mg, Trace Mineral Complex (from sea vegetation: *Lithothamnion* spp.) 10 mg. Other Ingredients: Maltitol, xylitol, cellulose, organic cocoa, natural dark chocolate flavor, magnesium stearate, maltodextrin, guar gum, stearic acid, silica and stevia leaf extract.
Vitamin D, Calcium, Magnesium & Boron:					

***NOT* APPROVED** Natural Vitality® Natural Calm Plus Calcium - Raspberry-Lemon Flavor  Dist. by Natural Vitality	1 teaspoons [2.5 g] **35 IU (2.6 mcg)** (D3) Found only 22.1 IU (0.55 mcg) vitamin D per serving (63.1% of listed amount) 70 mg (calcium gluconate) ✓ 106.7 mg (magnesium citrate) ✓ 88.3 mcg (boron citrate) Found 198.5 mcg boron per serving (224.7% of listed amount) Heavy metals: Pass	Take 1 - 1 1/2 rounded teaspoons twice per day at any time, at least 5 hours apart. Powder in container	1 teaspoon $0.52 [$1.98 based on amount *listed*] [$3.13 based on amount *found*] $15.57/8 oz [226 g] container (approx. 90 servings)	Vitamin C 88.3 mg, potassium (elemental from potassium citrate) 35 mg *Vegetarian. Gluten-Free. Non GMO Project Verified seal. Contains no yeast, dairy, egg, gluten, soy, wheat, sugar, starch, preservatives or artificial color or flavor.*	1 teaspoon Vitamin C (as ascorbic acid) 88.3 mg, Vitamin D3 (as cholecalciferol) 35 IU, Calcium (elemental from calcium gluconate) 70 mg, Magnesium (elemental from magnesium citrate) 106.7 mg, Potassium (elemental from potassium citrate) 35 mg, Boron (elemental from boron citrate) 88.3 mcg. Ingredients: Calcium gluconate Additional Information 1 teaspoon Vitamin C (as ascorbic acid) 88.3 mg, Vitamin D3 (as cholecalciferol) 35 IU, Calcium (elemental from calcium gluconate) 70 mg, Magnesium (elemental from magnesium citrate) 106.7 mg, Potassium (elemental from potassium citrate) 35 mg, Boron (elemental from boron citrate) 88.3 mcg. Ingredients: Calcium gluconate, a proprietary blend of citric acid and magnesium carbonate - which, in combination with water, creates ionic magnesium citrate - ascorbic acid, organic raspberry and lemon flavors, potassium citrate, organic stevia, vitamin D3, and boron citrate.

APPROVED Top Pick for vitamin D, calcium, magnesium & boron Vitalite Now! Calcium & Magnesium Plus  Dist. by Vitalite Now!	4 capsules **400 IU (10 mcg)** (D3) ✓ 1,000 mg (calcium carbonate, dicalcium phosphate, citrate, amino acid chelate, hydroxyapatite, gluconate, lactate, orotate, succinate and alpha ketoglutarate) ✓ 500 mg (magnesium oxide) ✓ 4,000 mcg (boron amino acid chelate) ✓ Heavy metals: Pass	4 capsules daily preferably with meals or as directed by a healthcare professional. Large capsule	4 capsules $0.47 [$0.47] $27.90/240 capsules	Phosphorus 77 mg **Precaution:** This product is manufactured and packaged in a facility which may also process milk, soy, wheat, egg, peanuts, tree nuts, fish and crustacean shellfish.	4 capsules Vitamin D-3 (cholecalciferol) 400 IU, Calcium (from carbonate, dicalcium phosphate, citrate, amino acid chelate, hydroxyapatite, gluconate, lactate, orotate, succinate and alpha ketoglutarate) 1,000 mg, Phosphorus (dicalcium phosphate) 77 mg, Magnesium (from oxide) 500 mg, Boron (from amino acid chelate) 4 mg. Other Ingredients: Gelatin (bovine), vegetable magnesium stearate and rice flour.
Vitamin D, Calcium, Magnesium & Vitamin K:					

APPROVED New Chapter® Bone Strength Take Care™  Dist. by New Chapter, Inc.	3 tablets **1,000 IU (25 mcg)** (D3) ✓ 770 mg (calcium from algae *Lithothamnion calcareum* & *corallioides*) ✓ 58 mg (magnesium from algae *Lithothamnion calcareum* & *corallioides*) ✓ 35 mcg (K1) 45 mcg (MK-7 K2) 80 mcg (total vitamin K) ✓ Heavy metals: Pass Also tested for disintegration	Three tablets daily with food. Large slim tablet	3 tablets $0.96 [$0.38] $38.37/120 slim tablets	Strontium 5 mg, silica 2 mg, vanadium 13 mcg *Kosher. Non GMO Project Verified seal. Gluten free; 100% vegetarian; no artificial flavors or colors.* **Precaution:** Contains: Fermented soy.	3 tablets Vitamin D3 (as cholecalciferol from ferment media) 1,000 IU, Vitamin K1 (as phylloquinone from ferment media) 35 mcg, Vitamin K2 (as menaquinone-7 from natto) 45 mcg, Calcium (from algae *Lithothamnion calcareum* & *corallioides*) 770 mg, Magnesium (from algae *Lithothamnion calcareum* & *corallioides*) 58 mg, Strontium (from algae *Lithothamnion calcareum* & *corallioides*) 5 mg, Silica (from algae *Lithothamnion calcareum* & *corallioides*) 2 mg, Vanadium (from algae Lithothamnion calcareum & corallioides) 13 mcg Additional Information 3 tablets Vitamin D3 (as cholecalciferol from ferment media) 1,000 IU, Vitamin K1 (as phylloquinone from ferment media) 35 mcg, Vitamin K2 (as menaquinone-7 from natto) 45 mcg, Calcium (from algae *Lithothamnion calcareum* & *corallioides*) 770 mg, Magnesium (from algae *Lithothamnion calcareum* & *corallioides*) 58 mg, Strontium (from algae *Lithothamnion calcareum* & *corallioides*) 5 mg, Silica (from algae *Lithothamnion calcareum* & *corallioides*) 2 mg, Vanadium (from algae Lithothamnion calcareum & corallioides) 13 mcg. Other Ingredients: Ferment media (organic milled soy, organic Saccharomyces cerevisiae, organic maltodextrin, organic gum acacia, organic alfalfa powder, lactic acid bacteria [*Lactobacillus acidophilus, Bifidobacterium bifidum and Lactobacillus rhamnosus*], papain [deactivated] and bromelain [deactivated]), organic barley grass, organic gum acacia, maltodextrin, hypromellose, silicon dioxide and sunflower oil.

***NOT* APPROVED** Thorne® Basic Bone Nutrients  Mfd. by Thorne Research, Inc.	1 capsule **500 IU (12.5 mcg)** (D3) Found only 348.5 IU vitamin D per serving (69.7% of listed amount) 200 mg (DimaCal® DiCalcium Malate) ✓ 50 mg (Albion® DiMagnesium Malate) ✓ 45 mcg (MK-7 K2) Found only 1 mcg vitamin K per serving (2.2% of listed amount) Heavy metals: Pass	Take 1 capsule one to four times daily or as recommended by a health-care practitioner. Large capsule	1 capsule $0.32 [$0.25 based on amount *listed*] [$0.36 based on amount *found*] $38.00/120 capsules	*Gluten Free.*	1 capsule Vitamin D (as Vitamin D3) (500 IU) 12.5 mcg, Vitamin K (as K2 (MK-7)) 45 mcg, Calcium (as DimaCal® DiCalcium Malate) 200 mg, Magnesium (as Albion® DiMagnesium Malate) 50 mg. Other Ingredients: Hypromellose (derived from cellulose) capsule, calcium laurate.
Vitamin D, Calcium, Magnesium, Boron & Vitamin K:					

APPROVED GNC Calcimate Complete™  Dist. by General Nutrition Corporation	4 caplets **2,000 IU (50 mcg)** (D3) ✓ 800 mg (calcium citrate malate) ✓ 100 mg (magnesium oxide) ✓ 1,000 mcg (boron hydrolyzed protein chelate) ✓ 50 mcg (K2) ✓ Heavy metals: Pass Also tested for disintegration	As a dietary supplement, take two caplets at breakfast and two caplets at dinner for a total of four caplets daily. Large caplet	4 caplets $0.25 [$0.05] $14.99/240 caplets	Zinc 7.5 mg, copper 1 mg, manganese 1 mg, MBP® 40 mg *No artificial colors, no artificial flavors, no wheat, gluten free, yeast free.* ***Precaution:*** *Contains: Milk and soybeans.*	4 caplets Vitamin D (as Cholecalciferol D-3) 2,000 IU, Vitamin K-2 (as Menaquinone) 50 mcg, Calcium (as Calcium Citrate Malate) 800 mg, Magnesium (as Magnesium Oxide) 100 mg, Zinc (as Zinc Oxide) 7.5 mg, Copper (as Copper Glycinate) 1 mg, Manganese (as Manganese Gluconate) 1 mg, MBP® 40 mg, Boron (as Hydrolyzed Protein Chelate) 1 mg. Other Ingredients: Cellulose, titanium dioxide (natural mineral whitener), vegetable acetoglycerides.

APPROVED Top Pick for vitamin D, calcium, magnesium, boron & vitamin K Jarrow Formulas® Bone-Up®  Dist. by Jarrow Formulas®	6 capsules **1,000 IU (25 mcg)** (D3) ✓ 1,000 mg (StimuCal™ microcrystalline hydroxyapatite) ✓ 500 mg (magnesium oxide) ✓ 3,000 mcg (boron citrate) ✓ 45 mcg (MK-7 K2) ✓ Heavy metals: Pass	Take 2 capsules 3 times per day (for a total of 6) with meals to facilitate maximum absorption, or as directed by your qualified healthcare professional. Large capsule	6 capsules $0.51 [$0.20] $20.37/240 capsules	Vitamin C 200 mg, zinc 10 mg, copper 1 mg, manganese 1 mg, potassium 99 mg *No wheat, gluten, egg, fish/shellfish, or peanuts/tree nuts.* **Precaution:** Contains: Soy (in trace amounts).	6 capsules Vitamin C (as Calcium Ascorbate) 200 mg, Vitamin D3 (Cholecalciferol) 25 mcg (1,000 IU), Vitamin K2 (as Natural MK-7 [Menaquinone-7]) 45 mcg, Calcium (Elemental) (from StimuCal™ Microcrystalline Hydroxyapatite) 1,000 mg, Magnesium (as Magnesium Oxide) 500 mg, Zinc (L-OptiZinc®) (as Zinc L-Methionine Sulfate) 10 mg, Copper (as Copper Gluconate) 1 mg Additional Information 6 capsules Vitamin C (as Calcium Ascorbate) 200 mg, Vitamin D3 (Cholecalciferol) 25 mcg (1,000 IU), Vitamin K2 (as Natural MK-7 [Menaquinone-7]) 45 mcg, Calcium (Elemental) (from StimuCal™ Microcrystalline Hydroxyapatite) 1,000 mg, Magnesium (as Magnesium Oxide) 500 mg, Zinc (L-OptiZinc®) (as Zinc L-Methionine Sulfate) 10 mg, Copper (as Copper Gluconate) 1 mg, Manganese (as Manganese Citrate) 1 mg, Potassium (as Potassium Citrate) 99 mg, Boron (as Boron Citrate) 3 mg. Other Ingredients: Maltodextrin, magnesium stearate (vegetable source) and silicon dioxide. Capsule consists of bovine gelatin.

ConsumerTips™:

What to Consider When Buying:

Before buying a vitamin D supplement, be aware that vitamin D can be obtained in sufficient amounts from exposure to sunlight, fortified milk (400 IU per quart or 100 IU per cup), and other fortified foods (e.g., many breakfast cereals and nutrition bars, some brands of orange juice, yogurt, margarine, and soy beverages).

Fatty (oily) fish are also good sources of vitamin D. For example, you can get significant amounts of vitamin D from a 3-ounce (85 gram) serving of canned sockeye salmon (17.9 mcg or 716 IU), canned pink salmon (12.3 mcg or 492 IU), light tuna (e.g., skipjack or yellowtail) (5.7 mcg or 228 IU), sardine (4.1 mcg or 164 IU). (U.S. Dietary Guidelines 2015-2020). Interestingly, canned fish tends to provide more vitamin D than traditionally cooked fish (see our Review of Canned Fish).

Small amounts of vitamin D are found in beef liver (about 0.17 to 1.2 mcg per 3-ounce serving), cheese (up to

0.85 mcg per 3-ounce serving), and egg yolks (0.7 to 1 mcg per yolk). A ½ cup of portabella mushrooms exposed to ultraviolet light can provide 7.9 mcg or 316 IU). Animal-based products can also provide small amounts of calcifediol, the 25-hydroxylated form of vitamin D. For instance, you can get small amounts of calcifediol from a

3-ounce (85 gram) serving of beef liver (0.06 to 0.65 mcg), pork liver (0.37 mcg), and chicken thigh (0.17 mcg), as well as from egg yolk (0.09 to 0.14 mcg) and butter (about 0.1 mcg per tablespoon) (Schmid, Adv Nutr 2013).

Getting vitamin D from sunlight

UVB light from the sun, the primary wavelength of light that can cause sunburn and contribute to sun cancer, is necessary for the synthesis of vitamin D in the skin. However, just ten to fifteen minutes of sun exposure at least two times per week to the face, arms, hands, or back without sunscreen is usually sufficient to provide adequate vitamin D. It has been estimated that getting the equivalent of a 1,000 IU dose of vitamin D requires exposing the face, hands and arms to full sunlight at noon for 6 to 15 minutes in Miami or 9 to 19 minutes during non-winter months in Boston, based on a darker-skinned Caucasian. Times are shorter by about 33% for people with very fair skin and double for those with dark skin. To get only 400 IU, times would be 40% as long.

A study in Turkey among 40 nursing home residents (average age 76), slightly less than half of whom had low blood levels of vitamin D (< 20 ng/mL), found that sunlight exposure (at 40° north latitude, similar to Boulder, Colorado and Philadelphia) significantly increased vitamin D blood levels — measured as 25(OH)D. Among the residents who received sun exposure without sunscreen for about 20 minutes per day, five days per week, to approximately 33% of the body (hand, face, neck, forearms and lower legs) for one month during summer, levels increased from 24 ng/mL to 32 ng/mL, in contrast to little change in residents who did not receive this sun exposure. Participants were advised to get their sun exposure between 10:30 and 11:30 am in order to avoid the hottest times of the day. It's worth noting that all of the participants had light or fair skin. As noted earlier, longer sun exposure times may be needed to raise vitamin D levels in people with darker skin (Okan, J Clin Densitom 2021).

Sun exposure cannot cause toxic levels of vitamin D because excessive exposure to sunlight degrades *pre*vitamin D3 (which is normally converted by sunlight into vitamin D3 in the skin) and degrades vitamin D3 itself (Holick, N Engl J Med 2007). In fact, a study in which Caucasian subjects with more than sufficient levels of 25-hydroxyvitamin D (the form of vitamin D commonly measured in blood tests), averaging 33 ng/mL, were exposed to full midday sun in shorts (and, for women, sports bras) on their backs for 15 minutes and stomachs for another 15 minutes, levels of vitamin D in the blood increased significantly, but there was no increase in levels of 25-hydroxyvitamin D, and subjects with particularly high starting levels of vitamin D in their blood showed no increase in these levels with sun exposure. Older people in the study produced somewhat less vitamin D than younger people but the difference was not statistically significant (Chalcraft, Nutrients 2020).

Increased awareness about skin cancer has caused people to avoid the sun or use **sunscreen**. Concern has been raised as to whether the use of sunscreen causes a potential risk of reduced vitamin D. One study suggested that use of a low SPF sunscreen may provide protection from sun damage while still allowing enough UVB exposure for the body to synthesize vitamin D, although it's important to note that the study was funded by the makers of the sunscreen used in the study (Walgreens Boots Alliance Inc.). The study showed that in fair-skinned adults (average age 35) with sufficient blood levels of vitamin D who were outside for approximately 5 ½ hours per day for one week, consistent use of one of two sunscreens each with a sun protection factor (SPF) of 15 but having either low or high UVA protection prevented sunburn and resulted in modest average increases in blood levels of vitamin D (5 ng/mL with the low UVA formula and 8 ng/mL with the high UVA formula). (Note: Higher UVA formulas allow more UVB light, which, as noted above, is needed for vitamin D synthesis) (Young, Br J Dermatol 2019).

Furthermore, an observational study among 3,418 people ages 20 and older (average age 40) found that frequent **sun protective behaviors** — including wearing long sleeves, staying in the shade, and/or using sunscreen "most

of the time or always" when going outside for more than one hour — was *not* associated with reduced total, upper body, or lower body bone mineral density or increased risk of osteoporotic bone fractures compared to rare sun protective behaviors. Blood levels of vitamin D were not assessed in this study (although dietary intake of vitamin

D appeared to be similar across the groups), and strength, type and amount of sunscreen used were not reported (Afarideh, JAMA Dermatol 2021).

However, a study among adults aged 20 to 49 years with moderately dark skin in Korea who had vitamin D levels below 20 ng/mL found that 30 minutes of daylight to the hands, arms, and legs (while protecting the face and neck) three times a week for four weeks in the summer only raised levels by an average 0.9 ng/mL. Another group instructed to block as much sunlight as possible (with sunscreen and protective clothing) had an average decrease of -0.7 ng/mL, while a third group whose members did the same but took 600 to 800 IU of vitamin D daily had an average increase of 3.5 ng/mL. The researchers concluded that the amount of sun exposure in the first group -- although similar to some standard recommendations -- was inadequate for this population (Lee, J Korean Med Sci 2020).

Who is likely to get too little vitamin D?

Inadequate vitamin D intake is common in people who live in northern climates (north of a line from Boston to the northern border of California), especially if they are dark-skinned.

Older individuals are at increased risk of vitamin D insufficiency (Omdahl, Am J Clin Nutr 1982; Holick, J Clin Endocrinol Metab 2005; van der Wielen RP, Lancet 1995), particularly the very old (Passeri, J Clin Endocrinol Metab 2003). This may be due to a variety of factors, including reduced time outdoors with reduced skin exposure to the sun. A study showed that surgical skin samples from older people was less able to convert a vitamin D precursor compound toward vitamin D than skin from younger individuals and there was less of this precursor in the top (epithelial) layer of older skin - although amounts in the lower layer were the same (MacLaughlin J, J Clin Invest 1985). However, an experiment in living people found that exposing the backs or entire bodies of old and young people to equal amounts of light produced the same amounts of vitamin D (Davie, Clin Sci 1980).

People who are obese also tend to have a low plasma concentration of 25-hydroxyvitamin D, as subcutaneous fat may sequester the vitamin.

Because vitamin D is a fat-soluble vitamin, people with reduced ability to absorb fat in the gut may also require vitamin D supplementation.

Gummies vs. tablets

To enhance its absorption, it is **advisable to take vitamin D with a meal containing fats or oils**. However, if you take it only with water, you may absorb more vitamin D from chewing a gummy supplement than from swallowing a tablet, as demonstrated in a study funded by the makers of *VitaFusion* gummies (Church & Dwight). In the study, 31 participants who were not deficient in vitamin D consumed a single, very high dose (20,000 IU) of vitamin D3 either as eleven and three-quarters *VitaFusion* D3 gummies or four and three-quarters vitamin D3 tablets from *Nature Made*) with 8 oz. of water on an empty stomach 30 minutes before a standardized breakfast. Over a 48-hour period, average blood levels of vitamin D were found to be approximately twice as high with the gummies than the tablets (Wagner, Nutrients 2019). Possible reasons for the better absorption with the gummies were that only the gummies contained oils and this, plus chewing them, better stimulated the digestive process. Had the supplements been taken with a meal containing oils, the results for each would likely have been more similar to each other.

Be aware that gummy vitamins are difficult to manufacture, their ingredients can more easily degrade, and ConsumerLab's Review of Multivitamins has found gummies more likely to fail tests than tablets or capsules for

containing more or less of ingredients than listed.

Oral Sprays

Vitamin D **oral sprays** are commercially available (although not legally, as sprays are not considered dietary supplements) and have been promoted as an alternative for people with gastrointestinal issues (such as Crohn's disease, ulcerative colitis and steatorrhea) which can reduce intestinal absorption of vitamin D. This is based on the premise that sprayed vitamin D can be absorbed directly through the lining of the mouth. However, there do not appear to be studies proving that oral absorption actually occurs. Nevertheless, sprays can certainly work as well as any other type of oral delivery, possibly because one is still swallowing the liquid. In fact, a small study in India in people having various bowel diseases and very low levels of vitamin D found that 1,000 IU of vitamin D3 given as an oral spray daily for one month significantly increased blood levels of vitamin D (by an average of 10.5 ng/mL) compared to the same dose of D3 taken as a softgel (which resulted in an average increase of 4 ng/mL) (Satia, Nutr J 2015). In the same study, vitamin D3 spray also significantly increased vitamin D blood levels of healthy people compared to supplementation with the softgel — resulting in average increases of 8 ng/mL and 4 ng/mL, respectively. However, this may not have been a fair comparison, since both the spray and capsules were taken 30 minutes *following a meal*. This is not an ideal way to take vitamin D from a pill, which should be taken *with* a meal for best absorption -- and properly taking 1,000 IU of vitamin D as a softgel daily should increase blood levels by about 10 ng/mL in a lean individual.

A study in Ireland compared 3,000 IU of vitamin D given daily to healthy adults as an oral spray (*DLux3000* from Better You, UK, which includes lecithin -- a fat) or as a capsule. After 4 weeks, the spray and capsule were found to increase vitamin D levels, respectively, by 10.6 ng/mL and 12.2 ng/mL, with the difference between the two not statistically significant. No instruction was given to take either formulation at the time of a meal, perhaps explaining the modest increases despite the large dose (Todd, Br J Nutr 2016). A 6-week, placebo-controlled trial in England also found that 3,000 IU of vitamin D per day given as a spray resulted in similar increases in blood levels of vitamin D as the same dose given as a capsule. Average blood levels increased by about 16.3 ng/mL with both the capsules and the spray. Two participants reported the formation of small blisters on the cheek and tongue, one of whom discontinued the study -- although the researchers did not specify if this occurred in those given the spray or capsules, they did note that only 86% of the spray group was fully compliant versus 96.4% of the capsule group. As in the study above, participants were not instructed to take the capsules or spray with a meal. The vitamin D spray was provided by Better You, which funded the study (Williams, Eur J Clin Nutr 2019). Sprays tend to be more expensive: about 8 to 10 cents per 1,000 IU dose. The same dose can be obtained from a vitamin D liquid drop or pill for little as 1 or 2 cents as shown in this Review.

In short, in healthy individuals, non-sprays can be as effective as sprays and are less expensive. In people with intestinal absorption problems, either may raise vitamin D levels but absorption may be greater with a spray.

Other tips when buying:
When buying vitamin D, be aware that it is measured in International Units (IU) of vitamin D activity or as micrograms (mcg) of cholecalciferol (D_3) or ergocalciferol (D_2). 10 mcg = 400 IU.

Some calcium supplements contain the trace mineral boron, typically in amounts ranging from less than 1 mg up to about 6 mg per daily serving. Some, but not all evidence suggests that boron may reduce calcium loss in the urine, especially when magnesium intake is low (Neilson, FASEB J 1987). Although some preliminary research suggests boron supplementation in doses of 3 mg to 10 mg per day may be helpful for osteoarthritis and osteoporosis, one small trial found no increase in spine or thigh bone mineral density in postmenopausal women who took 3 mg of boron daily for one year compared to placebo (Biquet, Osteoporos Int 1996). Americans typically get an average of about 1 mg to 1.25 mg of boron daily from foods such as leafy vegetables, raisins, prunes, non-citrus fruits like apples, and some grains (Rainey, J Am Diet Assoc 1999). There is no established daily requirement for boron, but there is a Tolerable Upper Intake Level of 20 mg for per day for adults. Be aware

that even at doses of 3 mg to 10 mg daily, boron may increase estrogen levels in both women and men (Neilson, FASEB J 1987; Naghii, Biol Trace Elem Res 1997). This may be of particular concern for women on hormonal therapy or those with a history of estrogen-sensitive cancer.

A small news article appeared in 2010 regarding research on the content of vitamin D supplements presented at a Multiple Sclerosis conference by a team at Johns Hopkins University. The results showed the mean actual dose in 10 supplements to be only 33.5% of the labeled dose, with a range from 0.24% to 81.7%. ConsumerLab.com contacted the research team to learn more about the findings. We spoke with Dr. Norman Haughey who oversaw the testing. It appears that the report was preliminary: The team had not yet performed extraction efficiency testing, i.e., making sure that they got all of the vitamin D out of the tested samples. Poor extraction recovery will yield low results and is a well-known problem with vitamin D in supplements where other components of the product can interfere with measurements.

What to Consider When Using:

In November 2010, recommended intake levels of vitamin D for Americans and Canadians were increased by the Institute of Medicine (IOM). For infants up to 12 months of age, the daily Adequate Intake (AI) was set at 400 IU (10 micrograms). Note that the AI is only relevant if an infant is not getting adequate exposure to sunlight. The following Recommended Dietary Allowances (RDAs) were established for other age groups: 600 IU (15 micrograms) for people aged 1 to 70 and 800 IU (20 micrograms) for those aged 71 and older.[17]Confusing matters is that the FDA uses somewhat different daily amounts to establish the "Daily Values" in the "%DV" figures appearing in Supplement Facts panels on labels. For decades, the Daily Value for vitamin D for adults and children ages 4 and older was set at 400 IU (which turned out to be too low) and, in 2016, the FDA announced that the DV is now 800 IU (which is higher than necessary for most people) but that labels are not required to reflect this change until the beginning of 2020. So, for now, if you see 100% as the "%DV," that means the product provides 400 IU per serving.

While some studies suggest that even higher intakes of vitamin D may be useful for a range of purposes, the IOM considered the data behind those suggestions preliminary. Nevertheless, based on studies that showed a decreased risk of cancer associated with increased vitamin D intake and/or blood levels, the Canadian Cancer Society recommends a daily intake of 1,000 IU for adults in the fall and winter. The Canadian recommendation reflects the fact that there is reduced sun exposure in northern latitudes. The recommendation is for 1,000 IU intake year-round for people who are older, have dark skin, don't go outside often, or wear clothing that covers most of their skin.

In infants, the IOM and American Academy of Pediatrics recommend a vitamin D target level of 20 ng/dL. Both organizations recommend 400 IU daily to achieve this level (Wagner, Pediatrics 2008). A convenient way to give this is to add a single 400 IU drop of a liquid vitamin D (such as *Baby Ddrops* — 400 IU per drop -- as listed in the Results table above) to bottled milk per day. Supplementation should occur even if children are breastfed -- particularly if breastfeeding continues for more than one year: A study in Canada found that without supplementation, the probability of breastfed children being vitamin D deficient was 16% by age 2 and 29% by age 3 (Darmawikarta, Am J Pub Health 2016).

Some groups suggest higher levels in infants of 30-60 ng/dL, however, this is controversial (Endo Soc, J C Endrocrinol Metab, 2011; Can Paed Soc Paediatr Child Health 2007). A clinical study shows that 400 IU of vitamin D3 daily was adequate to achieve the target level of 20 ng/dL in 97.5% of healthy, breastfed infants after 3 months of treatment. Higher doses were also studied (800 IU, 1200 IU, and 1600 IU daily). The 1600 IU dose caused excessively high levels in many infants. Additionally, there was no difference in bone mineral content between the lower and higher doses after a year of treatment (Gallo, JAMA 2013). These data confirm that 400 IU daily is an adequate dose for most healthy infants. Higher doses should be used cautiously. See Concerns and Cautions.

For building bone in young girls (ages 9 to 13), a study found benefit with a supplement providing, on a daily basis, 800 mg of calcium (from calcium citrate and calcium carbonate), 400 IU of vitamin D_2, and 400 mg of magnesium (from magnesium citrate) when taken regularly for six months (Greene, Osteoporosis Int 2011). The supplement (*Active Calcium Chewable*, USANA Health Sciences, Inc. - not tested in this Review) was taken as four chewable tablets, two with breakfast and two with dinner as it is best to divide doses when taking large amounts of minerals. Another study found that a weekly dose of 1,400 IU or 14,000 IU of vitamin D_3 resulted in significant increases in the mineral content of hip bones -- although the majority of the girls started the study deficient in vitamin D. Interestingly, the higher weekly dose appeared to have somewhat less effect than the lower dose (Al-Shaar, Bone 2013).

For reducing the risk of fracture of the hip and nonvertebral bone in people 65 years of age or older, maintaining a serum vitamin D level above 24 ng/mL appears to be beneficial.[39]

For reducing the risk of cardiovascular disease and stroke in men, 600 IU or more of vitamin D per day from food and supplements may be helpful. (A similar cardiovascular benefit in women has not been shown).[21]

For reducing high blood pressure in people already taking a calcium channel blocker (nifedipine), 2,000 IU of vitamin D_3 per day has been shown reduce systolic and diastolic pressures by a few points (Chen, Atherosclerosis 2014). However, a study giving 100,000 IU of vitamin D_3 quarterly showed no benefit (Witham, JAMA 2013) and a review of 46 studies concluded that vitamin D appears ineffective for lowering high blood pressure (Beveridge, JAMA Int Med 2015).

For improving cholesterol levels in people already taking a statin medication, 2,000 IU of vitamin D_3 per day has been shown to be effective, particularly among people with lower blood levels of vitamin D (Qin, Clin Nutr 2015).

For improving balance and muscle strength in older adults 800 to 1,000 IU daily of vitamin D may be beneficial.[30] (Cangussu, Osteoporos Int 2015).In older women deficient in vitamin D, 4,000 IU daily of vitamin D_3 has been shown to increase muscle fiber size, although not physical functioning (Ceglia, J Clin Endocrin Metab 2013).

For reducing symptomatic pain in fibromyalgia, 2,400 IU of vitamin D_3 for people with vitamin D levels below 24 ng/mL, and 2,400 IU for those starting with levels between 24 ng/mL and 32 ng/mL have been successfully used (although treatment was stopped as a precaution when levels exceeded 48 ng/mL, which occured with several patients) (Wepner, Pain 2013).

For reducing menstrual pain in women, a single high dose of 300,000 IU vitamin D_3 taken 5 days before the start of menstruation may be beneficial for the following two months.[29] However, there are potential concerns with such a high dose (see Concerns and Cautions).

During pregnancy, raising vitamin D blood levels to 32 ng/mL in a population with a high rate of vitamin D deficiency decreased by half the incidence of pre-term labor, pre-eclampsia, and/or gestational diabetes. Women were given vitamin D starting at week 20 and dosage depended on initial vitamin D status, ranging from one dose of 60,000 IU to monthly doses of 120,000 IU for two to four months (Sablok, Clin Endocrinol 2015).

For reducing the risk of exacerbations of COPD, 100,000 IU of vitamin D monthly or 120,000 IU every two months has been helpful among people deficient in vitamin D (Martineau, Lancet Resp Med 2014; Lehouck, Ann Intern Med 2012).

D_2 or D_3?

Vitamin D can be found in dietary supplements in the D_2 or D_3 form. A number of studies have compared the

abilities of vitamin D_2 and vitamin D_3 to raise vitamin D blood levels. Some have found them equally effective, and some have found D_3 more effective (Armas, J Clin Endocrinol Metab 2004; Trang, Am J Clin Nutr 1998; Holick, J Clin Endocrinol Metab 2008; Biancuzzo, Am J Clin Nutr 2010). As either form can be obtained inexpensively, it

seems prudent to use supplements containing the D_3 form, particularly as D_2 may cause erroneously low vitamin D blood test results. The potential advantage of D_3 was illustrated in a small, but well-controlled, study in New Zealand in which 1,000 IU of vitamin D_2 or D_3, or a placebo, was given to healthy, non-obese individuals (ages 18 to 50) from the end of summer to the end of winter (Logan, Br J Nutr 2013). On average, vitamin D levels dropped 18 ng/mL among those taking placebo and 8 ng/mL among those taking vitamin D_2, while those taking D_3 maintained their levels (at 32 ng/mL). It's worth noting that, unlike the U.S., there is little vitamin D fortification of milk or other foods in New Zealand. Also, due to the relatively high latitude of the study region (46° — similar, for example, to Portland, Oregon) sunlight was relatively limited during the period of the study. Consequently, the dose of vitamin D_3 given may have been greater than needed to maintain vitamin D levels in similar individuals in much of the U.S. A large study among women in England, which used a lower dose — 600 IU per day, also demonstrated vitamin D_3 to be superior to D_2. In this study, which occurred during winter months, 12 weeks of supplementation with D_3 raised blood levels by 73% compared to only 34% for vitamin D_2. The researchers speculated that the greater effect of D_3 may be due to 1) a possible shorter half-life in the body of D_2 than D_3, and 2) the fact that each form has been shown to reduce levels of the active 25(OH)D form of the other but, since only D_3 is naturally found in the body, D_2 may have more of a negative effect on total blood levels (Tripkovic, Am J Clin Nutr 2017).

D_3 or Calcifediol?

Vitamin D_3 may be the preferred supplement form of vitamin D for raising 25(OH)D levels compared to vitamin D_2, but calcifediol, a 25-hydroxylated form of vitamin D, may be even more effective than vitamin D_3. Most research shows that calcifediol is about three to five times more potent for increasing 25(OH)D levels than vitamin D_3 when taken by mouth. The rate of absorption of calcifediol has also been shown to be higher than that of vitamin D_3. While 25(OH)D levels increase by about 0.7 to 1 ng/mL for every 100 IU of vitamin D_3 taken *when vitamin D levels are low*, the rate of absorption decreases as 25(OH)D levels rise. On the other hand, the absorption of calcifediol is linear, meaning that the rate of absorption does not decline as blood levels of 25(OH)D increase (Cesareo, Nutrients 2019). Unlike vitamin D_3, however, calcifediol is available only as a prescription drug in the U.S. and not as a supplement. Similarly, calci*triol*, the active hormone form of vitamin D formed in the body from calcifediol, is also available only as a prescription drug in the U.S. However, animal-based foods may contain calcifediol, as it is found in animal muscle and adipose (fat) tissue (Taylor, J Nutr 2014).

How Much Do You Need and "How Much is Too Much?"

After being ingested, both vitamin D_2 and D_3 are metabolized in the liver to form 25-hydroxy vitamin D and in the kidneys to 1,25-hydroxy vitamin D. Total serum levels (sometimes referred to as "blood levels") of 25-hydroxyvitamin D (also referred to as 25-(OH)D) are commonly used clinically to evaluate vitamin D status.

Based on the latest recommendations of the Institute of Medicine (IOM), the Estimated Average Requirement (EAR) for vitamin D among individuals ages 1 to 70 for bone growth and maintenance is daily intake of 400 IU of vitamin D, assuming minimal to no sun exposure, corresponding to a blood level of vitamin D (known as serum 25-(OH)D levels) of just 16 ng/mL. Some people will need more than this "average" requirement" so the IOM calculated an amount which would satisfy the requirements of practically all (97.5%) individuals; this amount, the **Recommended Daily Allowance (RDA), is 600 IU of vitamin D, corresponding to a vitamin D blood level of 20 ng/mL**. [Another way of expressing these levels is in nanomoles per liter (the unit of measurement commonly used in Canada): 1 ng/mL = 2.5 nmol/L, so 20 ng/mL = 50 nmol/L and 30 ng/mL = 75 nmol/L]. **For individuals over age 70, the RDA is 800 IU.**

In people deficient in vitamin D, long-term effects are bone softening, known as osteomalacia in adults and rickets in children -- who can also suffer bone deformities. Other symptoms can be vague but can include bone

pain and muscle weakness, joint pain (particularly of the wrists, ankles, shoulders, and shins), chronic tension headaches, depression, insomnia and hair loss (Khan, J Oncol Pract 2010). In infants, a common early symptom of deficiency can be excessive sweating (Hossein-nezhad, Mayo Clin Proc 2013).

From reviewing national surveys of blood levels, the IOM concluded that the majority of Americans and Canadians are getting enough vitamin D (as well as calcium), although elderly individuals are more likely to fall short on both and some adolescent girls may not get quite enough calcium. The IOM has determined that just 6% of U.S. population is vitamin D deficient (≤ 12.5 ng/mL), and 13% of Americans between the ages of 1 and 70 are "at risk" for vitamin D inadequacy (Manson, N Engl J Med 2016).

The IOM has cautioned that **vitamin D blood levels ≥ 50 ng/mL (and daily intakes above 4,000 IU) can put people at risk for adverse effects.** This is based on studies showing an increase in adverse events (including overall mortality, some cancers, cardiovascular disease, and fractures and falls) associated with serum 25-(OH)D levels starting at about 30 ng/mL to 48 ng/mL and higher (75 to 120 nmol/L). Examples of such adverse events include the following:

- A population study following nearly a quarter million people in Denmark for three years found that vitamin D levels of 20 to 24 ng/mL were associated with the lowest risk of dying during the study.[35] A high serum level (56 ng/mL) was associated with a 42% *higher* risk of dying during the study than people with a level of 20 ng/mL.
- An analysis of the vitamin D levels of more than 14,000 Americans aged 17 years and older found that mortality rates fell with increasing vitamin D levels until reaching 39 ng/mL (Kramer, PLoS One 2012). The lowest mortality rate was among those in the 30 to <40 ng/mL group, however, mortality rates were similar across the range of 20 to 40 ng/mL.
- A population study following nearly half a million people aged 45 years and older for 4.5 years in Israel found that people with vitamin D levels of 20 to 36 ng/mL had the lowest risk of heart attack or death. Compared to people in this range, risk of heart attack and death was 91% higher among those with levels below 10 ng/mL, 26% higher among those with levels 10 to 20 ng/mL, and 13% higher when levels were above 36 ng/mL (Dror, J Clin Endocrinol Metab 2013).
- A study comparing low-dose to high-dose vitamin D3, found that those achieving the highest blood levels fell about twice as often as those just above sufficiency (Bischoff-Ferrari, 2016).
- A study in Canada comparing the effects of different doses of vitamin D given daily for 3 years to adults with osteoporosis found that, compared to a dose of 400 IU per day, 4,000 IU and 10,000 IU *reduced* bone mineral density (BMD) in lower leg, and 10,000 IU *also reduced* BMD in the forearm. There were no significant differences bone strength for the different doses (Burt, JAMA 2019). A follow-up analysis showed that loss of BMD was *greater in women* than in men. After 3 years of treatment with 4,000 IU or 10,000 IU of vitamin D, BMD decreased in the forearms of women by 3.8% and 5.5%, respectively, compared to a nonsignificant reduction of 1.3% and 1.9%, respectively, in men. Small losses of BMD also occurred with 400 IU of vitamin D for men and women, but the rate of bone loss in these groups was similar to what would be expected to occur with normal aging. A similar, although smaller, loss of BMD in the lower leg also occurred in women taking higher doses of vitamin D but not in men. The average blood level of 25(OH)D after 3 years of treatment with 4,000 IU and 10,000 IU of vitamin D was 53 and 58 ng/mL, respectively, which are both above the vitamin D blood levels that the IOM has warned can put people at risk for adverse effects (Burt, J Bone Miner Res 2020).
- An analysis of data from the National Health and Nutrition Examination Survey (NHANES) found a 35% increase in the risk of cancer-related death and a 111% increase in all-cause death among people who already had sufficient blood levels of vitamin D (≥20 ng/mL) but were supplementing with more than 10 mcg (400 IU) of vitamin D per day (Chen, Ann Intern Med 2019). (See more about this study in the CL

Answer about getting vitamin and mineral from foods vs. supplements).

A possible explanation for why taking high-dose vitamin D has been linked with muscle weakness and increased risk of fractures and falls, comes from a study among professional athletes in Europe which found that a dose of 70,000 IU vitamin D_3 taken weekly for three months increased the production of an enzyme (24-hydroxylase) which *breaks down vitamin D* in the blood and *inactivates* the hormonally active form of vitamin D in the body. The increase in this enzyme persisted for up to 6 weeks after supplementation was discontinued (Owens, Med Sci Sports Exerc 2017). The researchers recommended that "*lower doses of vitamin D3 ingested frequently may be most appropriate and gradual withdrawal from supplementation as opposed to rapid withdrawal may be favorable*."

Giving an *extremely high* single dose (540,000 IU) of vitamin D orally to critically ill people deficient in vitamin D (averaging about 11 ng/mL) upon admission to intensive care units was *not* shown to reduce the risk of death in a large U.S. study involving over one thousand patients. In fact, within 28 days, 17.3% of those given vitamin D had died versus 13.1% of those given placebo. At 90 days, the values were, respectively, 23.5% and 20.6%. Deaths were particularly high with vitamin D versus placebo for those admitted with infections (28.4% vs. 19.9%) or sepsis (33.7% vs. 21.3%). Falls were also more frequent (7.1% vs. 5.3%). Due to the findings, the study was stopped before enrolling its target of 3,000 patients. Among those given vitamin D, levels rose to an average 46.9 ng/mL within three days (Nat Heart Lung Blood Inst, New Eng J Med 2019).

An Australian study among 22 men and women (ages 50 to 75), about two-thirds of whom had low (< 20 ng/mL) or deficient levels of vitamin D, found that adding a one-time 50,000 IU dose at the beginning of daily 1,000 IU dosing, did not raise vitamin D levels more than daily 1,000 IU alone over six weeks. For those who started the study with sufficient levels, the 50,000 IU dose appeared to *hamper* vitamin D increases during the final three weeks of the study. Both treatments equally increased circulating osteoprogenitor cells, which are involved in the formation of bone (Feehan, Exp Gerontol 2021).

High doses of vitamin D do not appear to promote or protect against the development or progression of peripheral arterial calcification (hardening of the arteries), according to a 3-year study that compared the effects of taking 4,000 IU or 10,000 IU of vitamin D to taking just 400 IU among 302 adults in Canada who were generally vitamin D sufficient (average starting vitamin D blood level of 31.6 ng/mL) (Billington, Osteopor Int 2020).

The idea has been suggested that adverse effects of very high doses of vitamin D could be eliminated by also administering high doses of vitamins A and K (Masterjohn, Med Hypotheses 2007). This has not been proven and remains only a hypothesis.

It would seem prudent, based on the latest IOM recommendations and recent studies, to maintain blood levels of vitamin D above 20 ng/mL, but not much higher than 30 ng/mL. Misinterpretation and misapplication of the IOM reference standards can have adverse implications for patient care, including unnecessary vitamin D screening and supplementation. For healthy patients, routine screening is not recommended (Manson, N Engl J Med 2016).

With regard to the combination of vitamin D and calcium, an analysis of clinical trials involving older adults found a 9% lower risk of dying over a 3-year period among those who took vitamin D along with calcium supplementation (1,000 mg) compared to those not taking these supplements.[35] The benefit was only found with low dose (400 IU) and not higher dose (800 IU or more) vitamin D, and only with daily dosing as opposed to intermittent (e.g., annual) dosing of vitamin D. The benefit was not seen among people taking

vitamin D without calcium, although this does not suggest a protective effect of calcium. It is difficult to draw useful conclusions for individuals from this study particularly because blood levels of vitamin D were not part of the analysis, i.e., it is possible that results would vary depending one's vitamin D status.

From reviewing national surveys of blood levels, the IOM concluded that the majority of Americans and Canadians are getting enough vitamin D (as well as calcium), although elderly individuals are more likely to fall short on both and some adolescent girls may not get quite enough calcium.

It should be noted that some researchers have set higher benchmarks for vitamin D sufficiency typically 30 ng/mL or above. For example, using 30 ng/mL as the benchmark for sufficiency and less than 15 ng/mL to define deficiency, a study of vitamin D levels concluded that 61% of American children and adolescents had insufficient levels of vitamin D and an additional 9% were deficient. Deficient children tended to have higher blood pressure and lower levels of HDL ("good") cholesterol than other children. Older children were more likely to be deficient, as were those who were obese, drank milk less than once a week, or spent more than four hours a day with TV, video, or computers. Those who used vitamin D supplementation were less likely to be deficient (Kumar, Pediatrics 2009).

When laboratories report your vitamin D level, they will typically show a "standard range" or "reference range" of about 20 ng/mL to 100 ng/mL. These ranges vary with the laboratory and are based on levels the lab has found in 95% of a "healthy" population. However, **these numbers do not reflect the range which has been recommended by the Institute of Medicine**, as described above, which falls at the lower end of this range. If your level is 25 ng/mL, for example, you should not interpret the results as suggesting that your level is low. Similarly, if your level is 60 ng/mL, this does not mean your level is ideal -- current evidence, as noted in the Review, suggests that it is too high.

A rule of thumb for raising serum levels of 25-hydroxyvitamin D is that about 100 IU of vitamin D_2 or D_3 daily will raise serum levels by about 1 ng/mL in adults and adolescents. However, more vitamin D is required by obese individuals to get this same increase: A study of obese adolescents found that about 200 IU was needed to for every 1 ng/mL increase in serum levels (Belenchia, FASEB J, 2011). Keep in mind, however, that there is diminishing benefit with doses of vitamin D above 1,400 IU (Cashman, Nutrients 2017). For example, at a daily dose of 600 IU, each 100 IU was found to increase blood levels by 1 ng/mL, but, at a daily dose of 3,750 IU, each 100 IU increased levels by only 0.41 ng/mL, according to a study of overweight/obese older adults in Lebanon (Bacha, J Clin Endocrinol Metab 2021).

Be aware that **people who begin supplementation with lower blood levels of 25-hydroxyvitamin D (< 20 ng/mL) may achieve approximately 60% greater increases** in levels than those who already have sufficient levels (> 20 ng/mL) when taking the same daily dose. This was shown in a 2-year study in people with type 2 diabetes taking a daily dose of 2,000 IU vitamin D3: Levels increased by 12 ng/mL when starting with a sufficient level, but by 19 ng/mL when starting with an insufficient level (Best, J Clin Endocrinol Metab 2021).

With moderate (1,000 IU per day) supplementation, it has been shown to take about 6 weeks for serum levels to reach their peak. For example, during winter with no significant sun exposure, supplementation with 1,000 IU has been shown to increase levels of around 20 ng/mL up to about 30 ng/ml at 6 weeks. In such a scenario, sun exposure or a dosage higher than 1,000 IU would be necessary to further elevate levels above 30 ng/mL (Kumar, Pediatrics 2009).

Magnesium affects vitamin D levels — make sure you get enough

Getting an adequate intake of magnesium helps maintain optimal blood levels of the prehormone form of vitamin D, 25(OH)D -- the form typically measured in blood tests. When 25(OH)D blood levels are around 30

ng/mL, magnesium boosts the conversion of vitamin D to 25(OH)D, raising levels by an average of 3 ng/mL. When levels are higher (about 30 to 50 ng/mL), magnesium actually lowers the amount of 25(OH)D by an average of about 7 ng/mL.

A study in Spain investigated the effects of magnesium supplementation (500 mg daily for two months) in postmenopausal women, many of whom had low dietary intakes of magnesium and and/or low blood or erythrocyte levels of magnesium, and most of whom had insufficient blood levels of 25-hydroxyvitamin D (< 20 ng/mL). At the end of the study, the women who supplemented with magnesium had significantly increased vitamin D levels (average increase 3 ng/mL) compared to those who took a placebo (Vázquez-Lorente, Nutrients 2020).

(Interestingly, with vitamin D2, a form not naturally made in the body, magnesium keeps boosting levels of the prehormone form, regardless of the level.) This was demonstrated in a study of 180 adults in the U.S. (Dai, Am J Clin Nutr 2018).

To keep your vitamin D blood level in an optimal range, be sure you're getting an adequate amount of magnesium — many people don't. An additional 200 mg or so of magnesium will safely bring most people up to an adequate daily intake. You can get this from supplements or magnesium-rich foods, as discussed in our Magnesium Supplements Review.

In people who are Black, the traditional measurement of vitamin D levels using *total* serum 25-hydroxyvitamin D may not be appropriate as it may overestimate vitamin D deficiency. Due to a genetic variant, many Blacks have lower levels of binding protein for vitamin D (which binds 85 to 90% of total vitamin D), allowing more of the total vitamin D to be bioavailable, i.e., available for use. Consequently, although total vitamin D levels may seem low in Blacks, the bioavailable amount of vitamin D may be sufficient. In fact, a study in Baltimore found mean total vitamin D levels to be 15.6 ng/mL in Blacks and 25.8 ng/mL in whites, while amounts of bioavailable vitamin D were the same in both groups. Furthermore, bone mineral density and calcium levels were higher among the Blacks than whites (Powe, NEJM 2013). ***The measurement of bioavailable vitamin D may, therefore, be more accurate for assessing the vitamin D status of Black individuals.*** Unfortunately, this is more difficult than measuring total vitamin D and currently relies on an indirect method in which vitamin D-binding protein must be measured and the amount of vitamin D bound to the protein is subtracted from total vitamin D.

Vitamin D Tests — Not Always Reliable

Tests to determine vitamin D levels may not always be reliable. Thousands of vitamin D readings taken in 2007 and 2008 turned out to be too high because the test was not properly performed. Newer, faster, and less expensive immunoassay tests are now widely used. However, a preliminary study found these devices to yield inaccurate results at least 40% of the time — tending to provide low results.[38] In the study, blood samples were run with an older established method (LC/MS) and two newer devices. The established method found vitamin D deficiency (less than 20 ng/mL) in 20% of the samples, but the Abbot Architect and Siemens Centaur-2 immunoassay devices respectively found deficiency in 28% and 44% of the samples, classifying some people as deficient who were not. The inaccuracies tended to occur with samples containing vitamin D2. If your test results don't seem to jive with your vitamin D intake and level of sun exposure, consider a retest using the LC/MS method, particularly if you are getting vitamin D2 from supplements or foods.

Take Vitamin D with Food

It is not uncommon for a person being treated for vitamin D deficiency to fail to achieve adequate serum levels. A small but striking study at the Cleveland Clinic Foundation Bone Clinic suggests that one reason may be that such people are taking vitamin D supplements on an empty stomach or with a small meal,

usually breakfast or lunch.[25] In the study, 17 such people were instructed, instead, to take the same supplement with the largest meal of the day, usually supper. After 2 to 3 months, researchers found that serum vitamin D levels had increased, on average, by 56.7%. This magnitude of increase was seen across

a wide range of vitamin D dosage and forms (D_2 and D_3). As vitamin D is fat soluble, it is generally recommended that it be taken with a meal containing fats. However, based on this study, it may be best to take vitamin D with your *largest* meal of the day, which is likely to contain the most fat. A more recent study re-emphasized this point. In this 1-day study, 50,000 IU of vitamin D3 was given with a breakfast that was fat-free or which included fats. Mean peak vitamin D blood levels (12 hours after taking the supplement) were 32% greater in subjects who took the supplement with a fat-containing meal than in those who took it with the fat-free meal. The ratio of monounsaturated to polyunsaturated fats in the meal did not matter (Dawson-Hughes, J Acad Nutri and Dietetics 2014). The researchers postulate that the presence of fat favors vitamin D absorption by stimulating the secretion of bile which promotes fat absorption.

Storage

After opening a bottle of a vitamin D supplement, exposing the contents to air, vitamin D will begin to lose activity over time. How fast this happens is largely a function of the *temperature* at which the open bottle is stored, but can also be affected by exposure to light (which is why dark or opaque bottles are preferable) and the formulation of the product. At 77° F (25° C), this loss has been shown to range from just 5% to as much as 40% over a year. Refrigeration is typically not necessary unless you cannot keep the product at room temperature or you don't expect to fully use the contents by the "Best By" or expiration date. In these circumstances, consider refrigerating the product, as this may significantly slow the loss of potency (Temova, Eur J Hosp Pharm 2017).

Concerns and Cautions:

Excessive intake of vitamin D as a supplement can result in **hypercalcemia** (too much calcium in the blood) with symptoms including constipation, headache, irritability, confusion, weakness, metallic taste, loss of appetite, painful calcium deposits and kidney failure (Bohon, Clin Med Insights Womens Health 2013). Although this is unlikely to occur when daily intake is under 10,000 IU, to avoid hypercalcemia and other potential problems associated with higher blood levels of vitamin D, keep total intake of vitamin D from supplements and food under the established Tolerable Upper Intake Level (UL) above which the risk of harm increases. The ULs are 1,000 IU for infants up to 6 months, 1,500 IU for infants 6 months to 12 months, 2,500 IU for children 1 to 3 years, 3,000 for children 4 to 8 years, and 4,000 IU for all other people.[17] Note: It is not thought to be necessary to factor in the amount of vitamin D produced by sun exposure when adding up total vitamin D intake. 4,000 IU daily, given for 6 months to obese adolescents who were deficient in vitamin D, was found to be safe (no hypercalcemia) as well as effective at raising vitamin D to sufficient levels (Belenchia, FASEB J 2011).

A large study in Minnesota found that, due to increased use of vitamin D supplements, the percentage of people with vitamin D blood levels above 50 ng/mL increased 26-fold from 2002 to 2011, rising from 9 to 233 cases per 100,000 person-years; although hypercalcemia was rare among this group (0.2%), occurring only among those taking 50,000 IU weekly or more often. However, as noted in the study, levels above 50 ng/mL have not been found to be beneficial and pose potential long-term risks (Dudenkov, Mayo Clinic Proc 2015).

Isolated cases of hypercalcemia have been reported from the use of supplements. A 54-year-old man developed kidney failure due to untreated hypercalcemia caused by excessive vitamin D supplementation. For 2.5 years he been taking 8 to 12 drops daily of vitamin D that contained 1,000 IU per drop (i.e., 8,000 to 12,000 IU per day) which he mistakenly thought contained 500 IU per drop. In addition to discontinuing vitamin D, hydroxychloroquine was used reduce his calcium level, but he was left with stage 3B chronic kidney disease

(Auguste, CMAJ 2019). A 50-year-old woman in England developed hypercalcemia and acute kidney injury, with symptoms including lethargy, nausea, vomiting, headache and high blood pressure after taking 8,000 to 16,000 IU of vitamin D daily from a supplement for four months. Her blood levels of vitamin D had reached 1,800 ng/mL at

the time of her admission to the hospital. She reported that she first began feeling lethargic about two months after starting supplementation (Ferreira, Med Clin Res 2019). A famous case, reported in 2010, involved Gary Null, a nutrition promoter, who was apparently sickened by his own product, *Gary Null's Ultimate Power Meal*, due to a manufacturing error that resulted in 2,000,000 IU of vitamin D per serving instead of 2,000 IU. A 22-year-old male was sickened in Australia after three months use of a protein supplement for bodybuilding. He complained of lethargy, nausea, vomiting, and had excessive thirst and urination. His blood serum level of vitamin D blood was 145 ng/mL (several times normal) and calcium was 13.2 mg/dL (about 40% above normal). The powder claimed to provide 400 IU of vitamin D and 1,200 mg of calcium per serving — although it is not known if he used more than suggested or if the product contained higher levels than claimed. Corticosteroids were used to lower calcium levels (Van, Am J Sci 2017). A 64-year-old woman in Brazil complained of stabbing abdominal pain and vomiting after meals — symptoms she had suffered for several months along with the onset of lower limb pain, headaches, fatigue, reduced appetite, large weight loss, and frequent, foamy nighttime urination. Blood tests showed hypercalcemia and she was hospitalized. It was found that she had an extremely high vitamin D blood level of 374 ng/dL, which had caused hypercalcemia and, apparently, kidney injury. She noted that she had been taking daily vitamin complexes containing vitamin D3 (product not identified) from a relative for about 6 months. After 7 weeks of hospitalization, during which supplementation was stopped and hypercalcemia treated, she was discharged with chronic kidney disease (de Paula, BMC Geriatrics 2020 with correspondence with ConsumerLab).

Women taking a daily calcium (1,000 mg) and vitamin D (400 IU) supplement showed a 17% greater incidence of **kidney stones** compared to women who did not receive the supplement.[22] The increased risk, however, is small, as only 0.35% of the women taking the calcium and vitamin D supplement reported kidney stones, compared to 0.30% of the women in the control group. A similar (17% to 20%) increase in kidney stones has been reported in studies with calcium supplementation alone, suggesting that calcium, rather than vitamin D, is the causative factor (Wallace, Am J Clin Nutr 2011). However, there is evidence that *very high-dose* vitamin D can markedly increase levels of calcium in the urine (hypercalciuria) from calcium supplementation, which, in turn, can increase the risk of kidney stones. A study of postmenopausal women who took either 600 IU or 10,000 IU of vitamin D_3 daily along with a calcium supplement (1,200 mg of calcium carbonate per day) for one year found that those who took the higher dose of vitamin D drove their vitamin D levels to an abnormally high average of 86 ng/mL and had *3.6 times the risk* of developing hypercalciuria (Aloia, Clin Endocrinol (Oxf) 2018).

Giving high-dose vitamin D (96,000 to 120,000 IU) every two months has been shown to increase the **risk of upper respiratory infections**, compared to taking a low dose (400 IU) daily (Martineau, Thorax 2015)

High-dose vitamin D may decrease the natural production of melatonin (a mediator of sleep). A small, but well-controlled study in people with multiple sclerosis being treated with interferon found that, after 3 months, those also given high dose vitamin D3 (800 IU daily plus 75,000 IU every 3 weeks — averaging 4,370 IU per day) had a significant decrease in nighttime melatonin production, while those given a low dose (800 IU daily) did not. The study continued for full year during which vitamin D levels in the both groups fell (possibly due to shorter days of winter), and, melatonin product began to increase toward original levels (Golan, Brain, Behav, Immun 2013). Consistent with this, a study found that among overweight, postmenopausal women given 2,000 IU of vitamin D daily for 12 months, those whose vitamin D blood levels rose to over 32 ng/mL showed a modest **deterioration of sleep quality** (6.2% reduction) compared to those with blood levels that remained below 32 ng/mL (5.7% improvement). The deterioration in sleep quality -- as well an increased need for sleep medication -- was also associated with larger increases in vitamin D blood levels. Most women started study with vitamin D levels ranging from about 16 to 27 ng/mL and all participated in a weight loss/exercise program as part of the study (Mason, Preventive Medicine, 2016).

The FDA has cautioned that some liquid vitamin D supplements are sold with droppers that could allow for excessive dosing of vitamin D to **infants**. It recommends that droppers hold no more than 400 IU of vitamin D to avoid this problem.

It is particularly important to avoid excessive vitamin D during **pregnancy**, as hypercalcemia in a mother can lead to seizures, mental and/or physical retardation, and other problems in an infant.

Giving high-dose vitamin D to people who are not vitamin D deficient may slightly **increase cholesterol levels**. A placebo-controlled study in Austria among older, generally overweight adults with hypertension but with vitamin D blood levels averaging 23.5 ng/mL found that giving 2,800 IU of vitamin D daily for 8 weeks resulted in slight but statistically significant *increases* in total cholesterol (+3.6 mg/dL) and triglycerides (+13 mg/dL) levels. (The average vitamin D level among those receiving vitamin D rose to 30.6 ng/mL.) The researchers speculated that high-dose vitamin D may cause increased calcium absorption from the gut, leaving less calcium to bind to (and remove) fats passing through the gut (Schwetz, J Clin Lipidol 2018). Similarly, increased triglyceride levels (+ 11 mg/dL) occurred in another study when participants with low blood levels of vitamin D (average 15 ng/mL) took 4,000 IU of vitamin D3 daily for six months, while those who took a lower dose (400 IU) actually had a slight decrease in triglycerides (- 6.2 mg/dL). There were no significant changes in total or LDL cholesterol with either dose. After six months, blood levels of vitamin D 25(OH)D among those taking the higher and lower dose had increased to an average of 30 ng/mL and 20 ng/mL, respectively (Miao, J Am Heart Assoc 2021).

Taking **elexacaftor/tezacaftor/ivacaftor (*Trikafta*)**, a prescription medication for cystic fibrosis, along with vitamin D may modestly increase the absorption of vitamin D, necessitating downward adjustment of vitamin D dosage. An analysis of data among 67 cystic fibrosis patients with pancreatic insufficiency (which impairs absorption of fat-soluble vitamins such as vitamin D) who were supplemented with very large doses of vitamin D (about 1,570 mcg or 63,000 IU per week, which is approximately 224 mcg or 9,000 IU per day) showed that, at 12 months after being prescribed treatment with elexacaftor/tezacaftor/ivacafter (*Trikafta*), vitamin D blood levels increased by about 5 ng/mL, requiring 28% of the patients to lower their maintenance dose of vitamin. This effect was attributed to the ability of *Trikafta* to improve pancreatic function, resulting in improved absorption of vitamin D (Wright, Pediatr Pulmonol 2021).

High-dose estrogen-containing **oral contraceptives** (e.g., 30 mcg ethinyl estradiol plus 150 mcg levonorgestrel) may cause an increase in vitamin D binding protein, which regulates circulating levels of vitamin D. However, this does not seem to significantly affect total (bound and unbound) amounts of vitamin D in the blood, which is what most labs measure, and it is not clear if this effect has any clinical significance. Low-dose estrogen-containing oral contraceptives do not seem to have this effect (Stanczyk, J Steroid Biochem Mol Biol 2021).

For more information see the government report on vitamin D at http://ods.od.nih.gov/factsheets/vitamind.asp.

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