

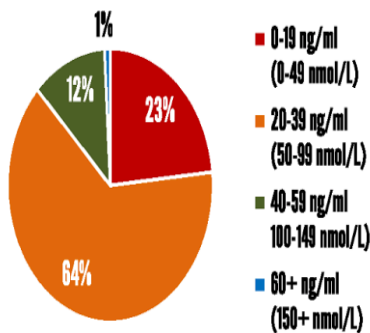
Vitamin D

There are two forms of vitamin D: D2 (ergocalciferol) and D3 (cholecalciferol). The D2 version needs to be converted into D3 and that process is not very efficient. D2 may also be more sensitive to humidity and temperature fluctuations, so it can degrade more over time. A meta-analysis by the Cochrane Database of 50 randomized controlled trials with 94,000 people showed that D3 reduced overall mortality by 6%, while D2 showed a small increase in death rate. So it is best to use D3 directly.

The D3 is often taken from animals, while D2 comes from plant sources, dietary supplements, and food fortification (e.g. breakfast cereal, orange juice, milk). So strict vegans may have some concerns over using D3.

Vitamin D can be made by exposure to UV-B sunlight. Sunlight exposure is best between about 10 AM and 3 PM, and with exposure to the face, arms, legs, or back will help with getting enough. How long you need exposure varies with latitude, season, and time of day. Being behind glass (such as while driving) blocks UV-B, so that does not count. Cloudy locations can also reduce sun exposure.

Vitamin D Levels in the General U.S. Population

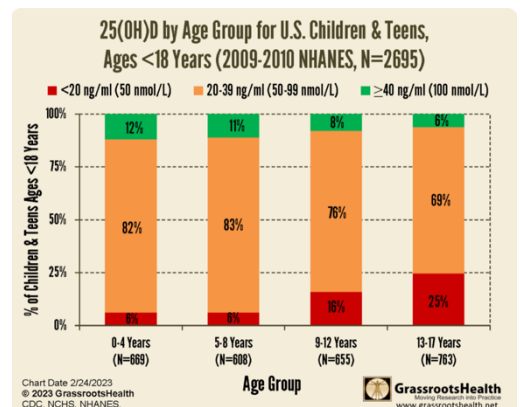


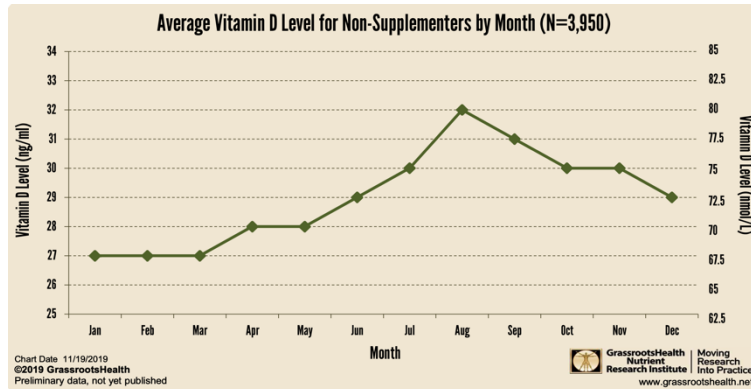
Based on NHANES, 2009-2014 data, ages 18+ years

A NHANES study (National Health & Nutrition Examination Study) ran from 2009-2014. It found that 23% of the US adult population had low vitamin D levels (below 20 ng/ml). However, almost 90% of adults in this study were below the recommended level of 40-60 ng/ml which is considered best for preventing diseases. And 93% of kids and teens in the NHANES had a level below 40 ng/ml, with 16% more below 20.

One warning is that various labs used for determining blood levels of vitamin D can offer vastly different results (e.g. one study had blood levels ranging between 36 and 66 ng/ml for the same blood used). Periodic testing of blood levels of vitamin D is also advised if supplements are used to insure it remains within a healthy and safe level.

What's worse than 23% of adults having low ADHD? 25% of teens age 13-17 being below 20 ng/ml, according to a NHANES study, which is about 4 times more than little kids under the age of 4.





This graph shows one study of almost 4,000 people who do not take vitamin D as a nutritional supplement. They never reach a level of 40 ng/ml during the year from just diet and sun exposure alone.

What it does

Vitamin D helps with the absorption of calcium and phosphorous and in the process with bone health. Magnesium is needed for vitamin D to be activated and without enough your body cannot properly utilize the vitamin D you take. Of the 30 leading causes of death in the U.S. as of 2010, 19 have been linked to vitamin D levels being too low (e.g. cardiovascular, diabetes, Alzheimer's, cancers, falls and fractures among the elderly, etc.). If vitamin D levels were boosted up to 40 ng/ml it has been estimated that as many as 336,000 deaths in the U.S. per year could be prevented, with a reduction of cost upwards of \$130 billion/year. (Journal of the American College of Nutrition, "Sunlight and Vitamin D: necessary for public health" Carole Baggerly et al, June 2015).

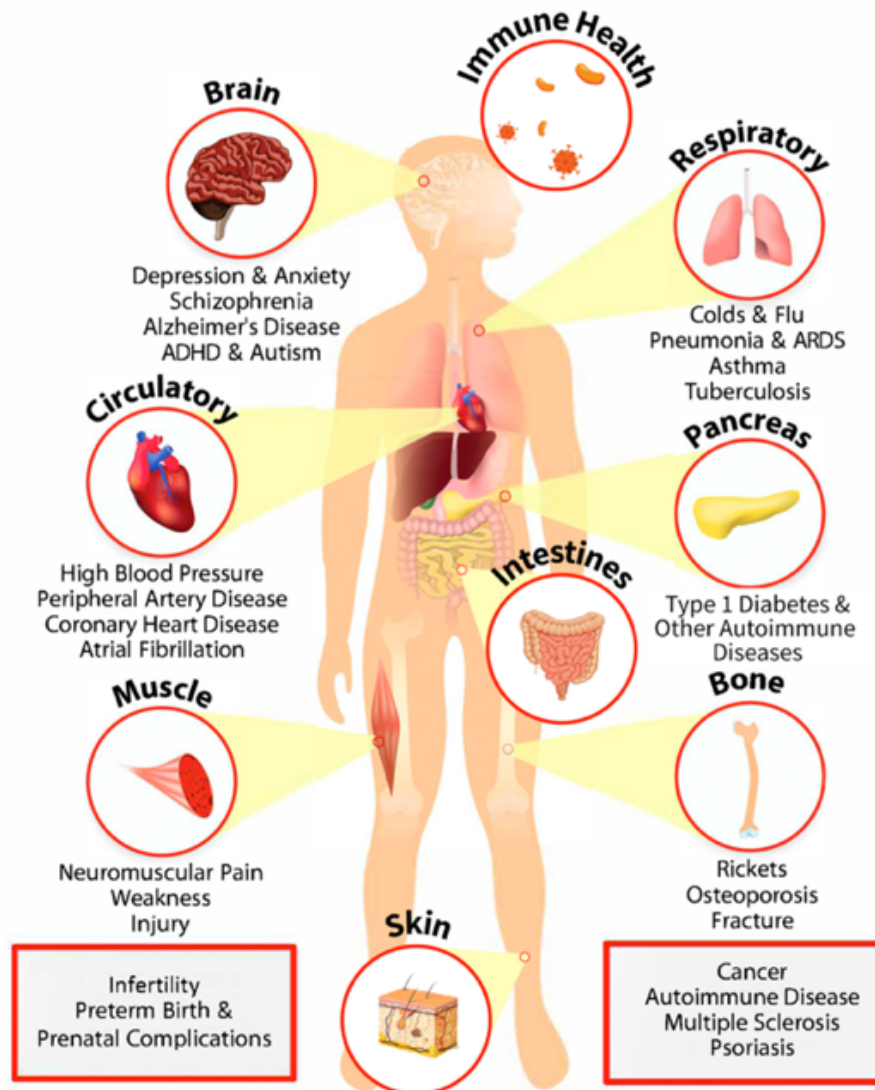
Vitamin D also is important for muscle health and cognitive function, and the immune system. One study (Alzheimer's and Dementia, "Brain vitamin D forms, cognitive decline, and neuropathology in community-dwelling older adults" M. Kyla Shea et al, 12/7/22) looked at 290 people who had participated in the Rush Memory & Aging Project (as to risk factors for Alzheimer's) and had died. Their findings were that higher levels of vitamin D3 in the brain were related to better cognitive function scores, a slower rate of cognitive decline and better semantic and working memory before death. Higher concentrations were also associated with a 25-33% decreased risk of dying of dementia or mild cognitive impairment.

Vitamin D deficiency may raise blood pressure and damage the heart. One study involving 18,000 men who were followed for 10 years found that those deficient in vitamin D were twice as likely to have a heart attack compared to those with adequate levels, although other research has not found vitamin D supplementation reducing cardiovascular risk. There is also a relationship between magnesium levels and vitamin D as to blood pressure. One study (Frontiers in Nutrition, "Dietary magnesium intake modifies the association between vitamin D and systolic b/p: results from NHANES 2007-2014" Weichao Huang et a., Feb. 2022, with 8,799 adults age 20 and up) looked at magnesium levels at or above 299 mg/day, or below that level. The relationship between systolic b/p and vitamin D levels was stronger for those getting higher levels of magnesium compared to the low magnesium group, with the effect greater than the sum of the parts. This study found that there was a 51% lower rate of high blood pressure for vitamin D levels ≥ 50 ng/ml vs. below 40 ng/ml. There was also a relationship found between vitamin D and afib and post-operative afib. For those with deficiency (<20 ng/ml), insufficiency (21-29 ng/ml)

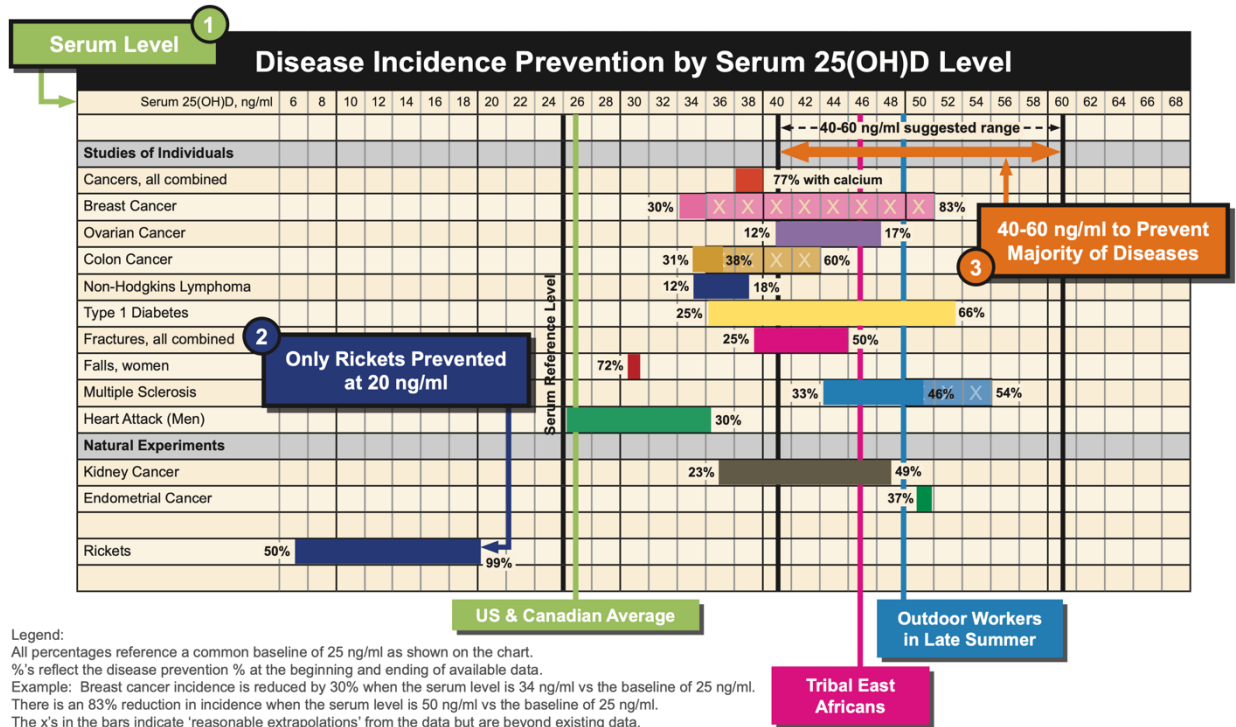
there was increased risk of afib. And for each 10 ng/ml increase in vitamin level there was a risk reduction of 12%. Greater effects were found for people age 65 and older.

Vitamin D also strengthens the immune system. For instance, there was research done on 8,695 people and it found that in comparing those with vitamin D levels below 20 ng/ml vs. 40 or more ng/ml there was a 15% reduction in colds, and a 41% reduction in flu cases.

VITAMIN D DEFICIENCY Affects Every Part of the Body



Below is a summation of some research showing that blood levels between roughly 40-60 ng/ml have significant benefit in reducing the risk of various diseases compared to a level of 25 ng/ml.

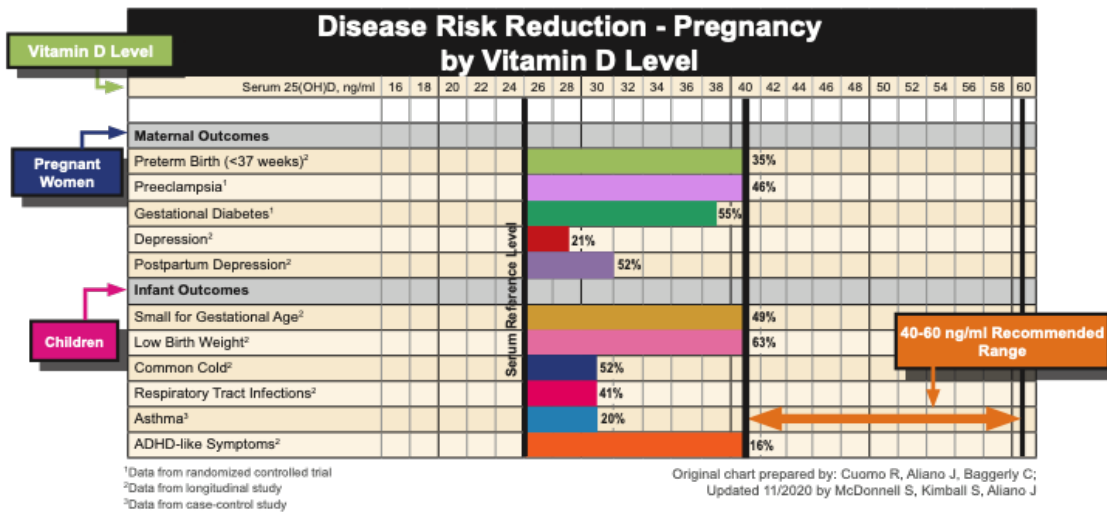


Legend:

All percentages reference a common baseline of 25 ng/ml as shown on the chart.
 %'s reflect the disease prevention % at the beginning and ending of available data.
 Example: Breast cancer incidence is reduced by 30% when the serum level is 34 ng/ml vs the baseline of 25 ng/ml.
 There is an 83% reduction in incidence when the serum level is 50 ng/ml vs the baseline of 25 ng/ml.
 The x's in the bars indicate 'reasonable extrapolations' from the data but are beyond existing data.

References:

All Cancers: Lappe JM, et al. Am J Clin Nutr. 2007;85:1586-91. Breast: Garland CF, Gorham ED, Mohr SB, Grant WB, Garland FC. Breast cancer risk according to serum 25-Hydroxyvitamin D: Meta-analysis of Dose-Response (abstract). American Association for Cancer Research Annual Meeting, 2008. Reference serum 25(OH)D was 5 ng/ml. Garland, CF, et al. Amer Assoc Cancer Research Annual Mtg, April 2008. Colon: Gorham ED, et al. Am J Prev Med. 2007;32:210-6. Diabetes: Hyppönen E, et al. Lancet 2001;358:1500-3. Endometrium: Mohr SB, et al. Prev Med. 2007;45:323-4. Falls: Broe KE, et al. J Am Geriatr Soc. 2007;55:234-9. Fractures: Bischoff-Ferrari HA, et al. JAMA. 2005;293:2257-64. Heart Attack: Giovannucci et al. Arch Intern Med/Vol 168 (No 11) June 9, 2008. Multiple Sclerosis: Munger KL, et al. JAMA. 2006;296:2832-9. Non-Hodgkin's Lymphoma: Purdue MP, et al. Cancer Causes Control. 2007;18:989-99. Ovary: Tworoger SS, et al. Cancer Epidemiol Biomarkers Prev. 2007;16:783-8. Renal: Mohr SB, et al. Int J Cancer. 2006;119:2705-9. Rickets: Arnaud SB, et al. Pediatrics. 1976 Feb;57(2):221-5. Canadians: Janz T, Pearson C. Vitamin D blood levels of Canadians. Statistics Canada. 2013 January, ISSN 1925-6493. US: Al-khalidi et al., Standardized serum 25-hydroxyvitamin D concentrations are inversely associated with cardiometabolic disease in U.S. adults: a cross-sectional analysis of NHANES, 2001-2010. Nutrition Journal. 2017, 16:16. Tribal Africans: Luxwolda M.F, et al. Traditionally living populations in East Africa have a mean serum 25-hydroxyvitamin D concentration of 115 nmol/L. Br J Nutr. 2012 November; 108(9):1557-61. Outdoor Workers: Barger-Lux M.J, Heaney R.P. Effects of Above Average Summer Sun Exposure on Serum 25-Hydroxyvitamin D and Calcium Absorption. J Clin Endocrinol Metab. 2002 November. 87(11):4952-6



Legend:
 Percents reflect the risk reduction found in the selected studies compared to a common reference level of 25 ng/ml.
 Example: Preterm birth risk is reduced by 35% when the serum level is 40 ng/ml compared to the reference level of 25 ng/ml.
 Note: Risk reduction for levels above 40 ng/ml were not reported on a majority of the studies selected.

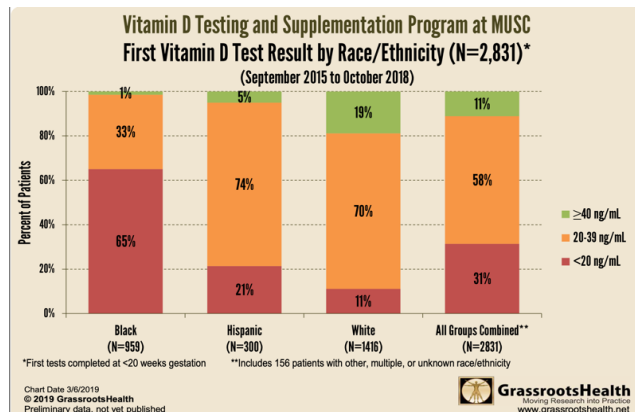
References:
 Preterm Birth: McDonnell et al., PLoS One, 2017. Preeclampsia: Mirzakhani et al., J Clin Invest., 2016. Gestational Diabetes: Mojibian et al., Iran J Reprod Med., 2015. Depression: Robinson et al., Arch Womens Ment Health, 2014. Postpartum Depression: Gur et al., Eur J Obstet Gynecol Reprod Biol., 2014. Small for Gestational Age, Low Birth Weight: Barebring et al., BMC Pregnancy Childbirth., 2018. Common Cold, Respiratory Tract Infections: Shin et al., COCOA Study, Korean J Pediatr., 2013. Asthma: Magnus et al., Paediatr Perinat Epidemiol., 2013. ADHD-like Symptoms: Morales et al., Epidemiology, 2015.

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The above graph also shows benefit to mothers and infants for blood levels above 25 ng/ml for various health problems.

Blood levels above 40 ng/ml were even better for such issues. e.g. With mothers having a vitamin D level of 40 or more the

- ❖ risk of preterm birth was reduced by 62% compared to those with levels below 20 ng/ml.
- ❖ preterm birth prior to the 37th week was reduced by 59%.



One study done at the Medical University of SC (MUSC) and which is representative of levels across the U.S. looked at vitamin D levels during pregnancy. In their first prenatal visit 89% were below 40 ng/ml, and 31% were below 20 ng/ml. Black women especially were low, with 99% under 40 ng/ml, and 65% were <20 ng/ml. (PLOS 1, "Maternal 25(OH)D concentrations ≥40 ng/ml associated with 60% lower preterm birth risk among general obstetrical patients at an urban medical center" Sharon McDonnell, et al 7/24/17)

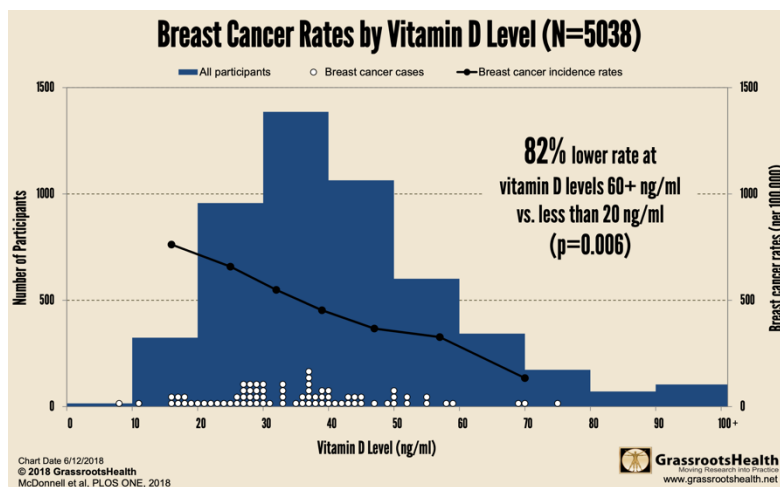
For women with vitamin D blood levels below 20 ng/ml vs 30 or higher, risk of miscarriage was increased by 94% for those with a deficiency of

the vitamin. The risk of having two more successive miscarriages (usually prior to 20 weeks) is four times more likely with low D levels. There was also a three times greater likelihood of becoming pregnant when the male partner had a vitamin D level of at least 30 ng/ml compared to men with a level below that.

Vitamin D has an important role in the production of progesterone, estradiol and estrone, FSH and follicular maturation. During fertilization, vitamin D levels of the woman facilitates sperm selection and influences the selection of the 'best sperm.' For IVF patients, vitamin D levels are strongly correlated with success rate independently of age, BMI, ethnicity, and the number of embryo transfers.

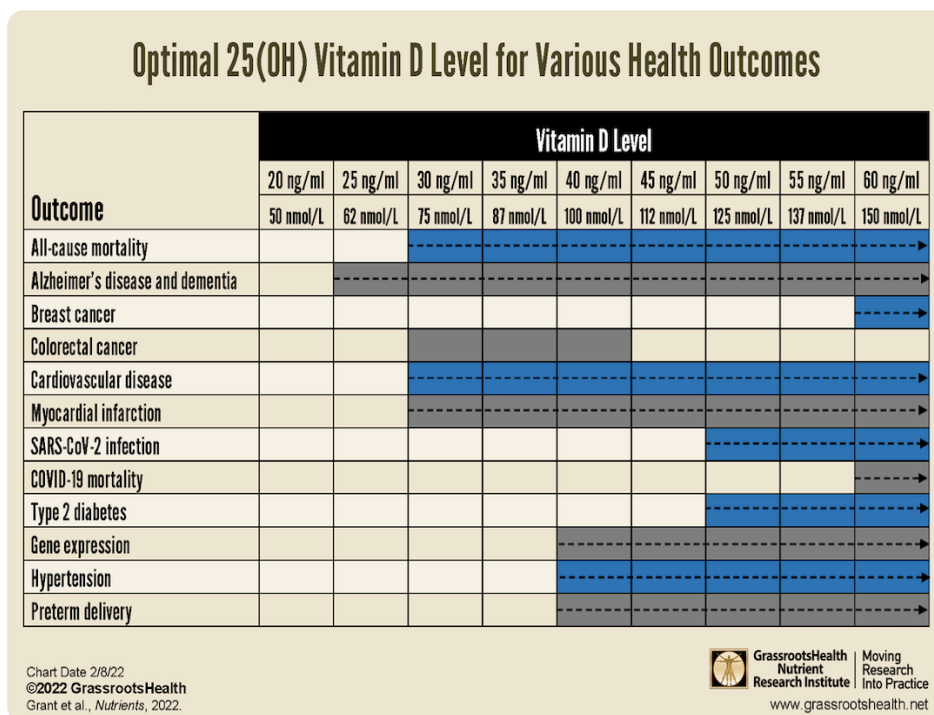
Vitamin D deficiency occurs in 67-85% of women with PCOS. For women with PCOS live births were 44% lower for those with vitamin D levels below 30 ng/ml, and 4 fold higher for those with levels of above 45 ng/ml. Ratio of live births increased by 2% for every one ng/ml increase in D levels. PCOS women also have a higher chance of implantation and occurrence of clinical pregnancy when vitamin D levels were higher.

Vitamin D is correlated with improved sperm count, motility, and increased fertility overall. There was a 3 times higher chance of pregnancy in men with vitamin D levels of at least 30 ng/ml vs. below that level. There is also a positive association between vitamin D and testosterone levels in older men, but it is not seen in younger adolescent males.



Breast cancer risk was reduced by 78% for those with D levels at or greater than 60 ng/ml vs. less than 20 ng/ml. One meta-analysis done in 2019 found a 6% lower risk of developing breast cancer for every 2 ng/ml increase of vitamin D in blood levels.

Vitamin D deficiency is said to be a major factor in at least seventeen types of cancer developing including prostate, along with stroke, heart attack, and chronic pain. One study on prostate cancer (Journal of Steroid Biochemistry and Molecular Biology, "Vitamin D3 supplementation, low-risk prostate cancer, and health disparities" Bruce Hollis et al, July 2013) took 52 men who had been diagnosed with stage 1 prostate cancer and gave all of them 4,000 IU of vitamin D for a year while they were on a 'wait and see' approach with the cancer. Almost 60% had a reduction in tumors, and 29% went from stage 1 or 2 cancer down to no cancer cells being detected. (Vitamin D blood levels at the end of the year averaged 60 ng/ml, but ranged between 38-95 ng/ml so getting yourself tested to see where yours is at is advised.)



The above graph came from a study ([Nutrients](#), “A narrative review of the evidence for variations in serum 25-hydroxyvitamin D concentration thresholds for optimal health” William Grant et al, 2/2/22, with the table coming from [GrassrootsHealth.net](#)). What it shows is that various diseases have optimal levels that are different, and almost all are at or above 30 ng/ml with several being at 40 or more ng/ml. As an example, between blood levels <20 ng/ml and >30 ng/ml for risk of heart attack, there was a 73% reduction with the higher amounts. Among over 5000 women the risk of breast cancer developing was reduced by 82% for those with vitamin D concentrations >60 ng/ml vs. <20 ng/ml.

Higher vitamin D levels are associated with lower mortality from diabetes, with supplementation of 4000 IU/day or higher improving the manifestation of diabetic complications. The authors of this study note that people can produce 10,000-25,000 IU of vitamin D through whole-body exposure to simulated sunlight, such as a mid-day sun, without burning. Their thinking is that such a dose should be inherently safe. There is also research that with vitamin D supplementation insulin resistance is reduced by 15% and the risk of type 2 diabetes by 40-60% when blood levels are 40-60 ng/ml. For those who are prediabetic and keep vitamin D levels at least at 50 ng/ml the reduction of developing type 2 diabetes is 76% compared to those with a vitamin D level in the 20-29 ng/ml range.

Other research has found that having sufficient levels of magnesium vs. insufficient (defined as at or above, or below 267 mg/day) coupled with sufficient or insufficient levels of vitamin D make a difference. With high magnesium and sufficient D the risk of type 2 diabetes declined by 35%. With low magnesium intake the two different levels of vitamin D led to comparable rates of (insignificant differences) of diabetes ([Frontiers in Nutrition](#), “Dietary magnesium intake affects

the association between serum vitamin D and type 2 diabetes: a cross-sectional study” Weichao Huang et al, 11/25/21).

A meta-analysis was done on exposure to UV radiation (i.e. sunlight and hence vitamin D, that came out in Medicine, “Exposure to solar ultraviolet radiation and breast cancer risk,” Yilun Li et al, 11/6/2020) and breast cancer risk. It found that there is a negative correlation between UV exposure and such cancer in women over age 40. They note in their conclusions that vitamin D can help protect against liver cancer by inhibiting tumor necrosis factor. As to breast cancer specifically, “We found an association between not tanning and breast cancer risk. We also found a correlation between limb coverage and breast cancer risk, perhaps via reduction of the area exposed to sunlight, thereby inhibiting the synthesis of vitamin D and melanin. No significant association was found for sunscreen use.”

A Chinese study (Journal of the Chinese Medical Association, “Vitamin D in gynecological diseases” Ta-Wei Chu et al, Nov. 2021) looked at 7,699 women ages 20 on up. Those with vitamin D levels of 30 ng/ml or higher compared to those with levels below 20 ng/ml, there was a

- ❖ 27% decreased risk of HPV infection of the cervix
- ❖ 17% decreased risk of dysmenorrhea
- ❖ 14% decreased risk of abnormal breast ultrasounds, 33% of the uterus, and 54% of the endometrium

There was also research done by the World Health Organization’s International Agency for Research on Cancer (WHO IARC) in 2012 that found that “continuous regular sun exposure was not associated with melanoma, but rather, sunburn doubled the risk of developing melanoma and intermittent high intensity sun exposure proposed a 61% increased risk for melanoma.”

A study (in Alzheimer’s & Dementia, Fearst et al, 2017) looked at almost 1,000 French people age 65 on up, and their cognitive decline was tracked for a dozen years. The mean vitamin D level of this group was just 14 ng/ml. Risk of dementia for those with deficiency or insufficiency of vitamin D was doubled, and the risk almost tripled for Alzheimer’s when compared to sufficient concentrations of vitamin D (which for this study was defined as just 20 ng/ml). A more recent study (BMC Neurology, “Vit. D deficiency as a risk factor for dementia and Alzheimer’s disease: an updated meta-analysis”, Bingyan Chai et al, 11/13/2019) looked across studies from Denmark, Finland, France, Sweden, Germany, the Netherlands, and the US and involving almost 22,000 people. It too found strong associations between severe deficiency (<10 ng/ml) and dementia and Alzheimer’s compared to more moderate deficiency (10-20 ng/ml).

Another study looked at ADHD, vitamin D and magnesium supplementation (International Journal of Preventative Medicine, “Effect of vit. D and magnesium supplementation on behavior problems in children with ADHD” Mostafa Hemamy et al, 1/24/2020). It was a double-blind, randomized controlled trial on 66 kids in Iran. Kids were given 50K IU of vitamin D/week and 6 mg/kg/day of magnesium, or a placebo. The treated group had a significant effect on conduct

problems (a decrease of 20% vs. 1% increase for the placebo group), social problems (22% lower vs. 2% higher for the placebo), and anxiety/shy scores (17% lower vs. no change for placebo).

Other research has found that vitamin D insufficiency is associated with changes in the gut microbiome that promoted inflammation. UVB light conversely has a beneficial impact on the diversity and abundance of the gut microbiome. Supplementing with vit. D has a positive impact on the gut bacteria composition such as in quality of life for patients with IBS. Other research found it helpful in healthy individuals (e.g. [Scientific Reports](#), “The potential role of vitamin D supplementation as a gut microbiota modifier in healthy individuals” Parul Singh, et al, 12/10/2020). Conclusions included “Vitamin D supplementation significantly increased gut microbial diversity. Specifically, the Bacteroidetes to firmicutes ratio increased along with the abundance of the health-promoting probiotic taxa Akkermansia and Bifidobacterium.” A higher ratio of Firmicutes to Bacteroidetes is correlated with obesity and other diseases, while a relative decrease in Firmicutes resulted in improvements to gut permeability and inflammation.

Then there are dermatological diseases associated with low vitamin D levels, such as psoriasis, skin cancer, skin infections, and Raynaud’s. One study found that there was a 96% lower risk of melanoma for people with vitamin D levels at ≥ 30 ng/ml (after adjusting for age, sex, and BMI) compared to those with levels ≤ 20 ng/ml. The study had 137 melanoma patients and 99 healthy controls. Melanoma patients had average vitamin D levels 10 ng/ml lower than controls, and the majority of the cancer patients were < 20 ng/ml compared to just 15% of the healthy controls. There was a meta-analysis of 25 studies ([Journal of the European Academy of Dermatology and Venerology](#), “The association between serum vitamin D level and risk and prognosis of melanoma: a systematic review and meta-analysis” T.Y. Tsai et al, Jan. 2020) looking at over 11,000 melanoma patients. Not only did such patients have a more frequent vitamin D deficiency compared to controls, but if they had lower D levels there was also a higher mortality rate.

Musculoskeletal Benefits of Vitamin D – Different Concentrations Required					
25(OH)D3 level	10 (ng/mL)	20 (ng/mL)	30 (ng/mL)	40 (ng/mL)	50 (ng/mL)
Rickets	↔				
Falls		↔	↔		
Stress fracture and fractures				↔	
Athletic performance enhancement ¹⁴					↔

[Sports Health](#), “Sports health benefits of vitamin D” Franklin Shuler et al, 11/4/2012.

Then there is the musculoskeletal system. The researchers for the [Sports Health](#) cited study offer that “vitamin D deficiency affects all age groups and demographics. Fifty to seventy percent of children and adolescents are vitamin D deficient. Over 75% of whites and 90% of African Americans and Latinos are vitamin D deficient, with increasing age increasing the likelihood of

deficiency. In addition, deficiency rates have doubled from 1994-2004 with multiple factors responsible, including sun avoidance, sunblock use, and increasing obesity rates causing sequestration of this fat-soluble vitamin. ...Peak neuromuscular performance [i.e. for athletes] is associated with a level of 50 ng/ml. In athletics, the only demographic group that normally achieve levels in this range is lifeguards, following a full summer of sun exposure. The incidence of vitamin D deficiency in elite indoor athletes is up to 94% of basketball players and 83% of gymnasts. Recent reports including testing of NY Giants (football players) during spring practice showed that 81% were vitamin D deficient. In this NFL study, white players averaged 30 ng/ml and African Americans averaged 20 ng/ml.”

There was also a study done on what is called chronic, non-specific musculoskeletal pain which is in the bones, muscles, joints, or connective tissue of more than one region of the body and that has been occurring for at least three months. The cause of such pain is typically not known, and it has impact on both physical and mental health. The study took 50 people ages 30-60 and they were given 60,000 IU of vitamin D weekly for a month and then 60,000 IU/month for the next two months. Plus, they were given 1000 mg calcium daily for all three months. They looked at vitamin D and calcium levels, pain, physical activity, fatigue, mood and sleep pre- and post-study. Pain was measured on a 0-10 scale (none to worst), with 2 categorized as low, 4-6 as moderate, and 8-10 as severe pain. Average pain level was 6.22 at the beginning and 3.52 at the end. Vitamin D deficiency was found in 90% of the participants, and blood levels rose from an average of 17 ng/ml to 39 between pre- and post-. Calcium levels and physical activity increased. Pain, weight, BMI and waist-to-hip ratio all decreased significantly. Sleep problems decreased from 74% to 20% comparing pre- and post- results. Mood problems (e.g. anger, irritability, stress, low confidence, poor concentration, memory loss, or crying) was reported by 72% initially. After the supplementation 48/50 reported an improvement in mood. Their conclusions included “supplementation with vitamin D and calcium decreases chronic non-specific musculoskeletal pain.” (Journal of Family Medicine & Primary Care, “Effect of supplementation of vitamin D and calcium on patients suffering from chronic non-specific musculoskeletal pain: a pre-post study” 5/31/2021, Vrinda Goyal et al.)

One Swiss study (Medicine, “Effect of vitamin D3 on self-perceived fatigue” Albina Nowak et al, Dec. 2016) using a double-blinded and random control trial approach took 128 otherwise healthy people ages 20-50 who reported fatigue (with main causes of it being excluded such as mental or physical illnesses) and had a vitamin D level below 20 mcg/l. They were given a single dose of 100,000 IU of vitamin D or a placebo. The vitamin D led to a significant improvement in fatigue compared to the placebo group

There was another study looking at the combination of omega-3 and vitamin D, using 42 women in each of four groups (placebo only, omega-3 + placebo vitamin D, vitamin D plus omega-3 placebo, genuine omega-3 + vitamin D). They were also pre-diabetic and had low D levels. It was done over eight weeks. All 3 groups with genuine supplements benefitted, but the completely placebo group did not. The biggest benefit was in the fourth group, with both vitamin D and omega-3 being genuine as to reducing anxiety, depression, and stress, while improving sleep quality. (Brain & Behavior, “Effect of omega-3 and vitamin D co-supplementation on

psychological distress in reproductive-aged women with pre-diabetes and hypovitaminosis D: a randomized controlled trial” M. Rajaba-Naeeni, et al, 9/2/2021).

A national study (NHANES, involving 7,970 people ages 15-39) found that with vitamin D levels <20 ng/ml there was a significantly greater risk of depression vs those with vitamin D levels \geq 30 ng/ml.

There is also research on vitamin D levels among military vets and suicide attempts done over 2010-2018. Supplementing with vitamin D2 or D3 (with approximately 170K and 491K vets, respectively, matched to controls) led to a 45-48% reduction in suicide attempts or self-harm with a 44% reduction between the treated vs. control groups. There was a 60% reduction of attempts among Black vets on a supplement. For vets with a vitamin D level below 20 ng/ml the reduction in suicide attempts was 64%. Higher doses of supplementation led to greater risk reduction. (PLoS 1, “The association between vitamin D serum levels, supplementation, and suicide attempts and intentional self-harm” Jill Lavigne et al, 2/1/2023.) More than 30% of vets and service members are said to have vitamin D levels below 20 ng/ml according to some DoD research.

Various meta-analyses have also found the benefit of vitamin D for reducing depression. e.g. One study involving 18 placebo-controlled randomized controlled trial found that those with more severe depression responded even better than those with less severe depression, with more than 2,800 IU/day being done for 8 weeks or longer. Another meta-analysis found those with low vitamin D have a higher risk of developing depression than those with a sufficient level. And supplementation especially with higher doses of vitamin D reduced depression more than a placebo did. (Nutrition, “Efficacy and acceptability of vitamin D supplements for depressed patients: a systematic review and meta-analysis of randomized controlled trials” Maytinee Srifuengfung, et al, April 2023). Their conclusions included noting “We found no moderating effect of concurrent antidepressant use.”

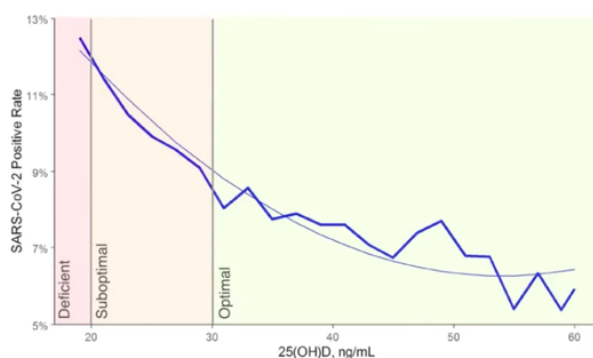
Co-factors of vitamin D such as magnesium and vitamin K2 are important to keep in mind. Half of all adults in the U.S. are said to have inadequate magnesium, and up to 97% of older adults suffer from an insufficiency or deficiency of vitamin K2 according to research. (Integrative Medicine, “Vitamin D (like every nutrient) is a team player” Lara Pizzorno et al, Sept. 2022). Supplementing with vitamin K2 for women with PCOS has been helpful for significantly alleviating depression.

There is also research on vitamin D and thyroid function. One study on 11,017 people (Endocrine, “Physiological serum 25-hydroxyvitamin D concentrations are associated with improved thyroid function - observations from a community based program” Nagmeh Mirhoseeini et al, 10/24/2017) found that hypothyroid individuals were three times more likely to be low in vitamin D (levels of <20 ng/ml), and people who had subclinical hypothyroidism were twice as likely to

be deficient. Supplementing with an average of 6000 IU/daily of vitamin D led to a 30% reduction of hypothyroidism for those who achieved blood levels of vitamin D ≥ 50 ng/ml by the end of the study. There was also a significantly lower risk of brain fog, low mood, sleep that was not refreshing, weight gain, or low energy - all of which are symptoms of low thyroid function, by the end of the study. There is also some research that higher levels of vitamin D may help with hyperthyroidism such as Graves' disease. Research results are mixed as to whether a higher vitamin D level increase, decrease or have no effect on developing thyroid cancer.

There is some circumstantial evidence to suggest that vitamin D deficiency might be related to autism. One factor is that the vitamin is involved with anti-inflammatory processes. It also enables glutathione, 'the master antioxidant' to clear our system of free radicals as well as bind toxic heavy metals like mercury. Kids with autism have difficulty clearing their systems of it. Autistics are most often born in March, the end of winter, when vitamin D levels would be at the lowest. Blacks in the U.S., and Europeans who are darker skinned immigrants have higher rates of autism, and also have a higher rate of vitamin D deficiency. There is also evidence that gestational and early childhood deficiency of the vitamin (levels below 40 ng/ml) might cause some autism. Two studies found that high doses of vitamin D improved core symptoms of autism in about 75% of autistic kids ([Review of Endocrine Metabolic Disorders](#), "Vitamin D and autism, what's new?" John Cannell, June 2017). Another study found that kids in rainy counties of Oregon, Washington and California were two times more likely to be diagnosed with autism than their counterparts in drier parts of the state. One psychiatrist, John Cannell, said that about a quarter of autistic kids respond dramatically to high doses of vitamin D, half respond significantly, and a quarter do not respond at all. It has been said that it is advisable for using vitamin K2 and magnesium with D, as to preventing vitamin D toxicity.

Lower 25-hydroxyvitamin D levels are strongly associated with higher SARS-CoV-2 test positivity rates, despite race/ethnicity, age, sex, and latitude.

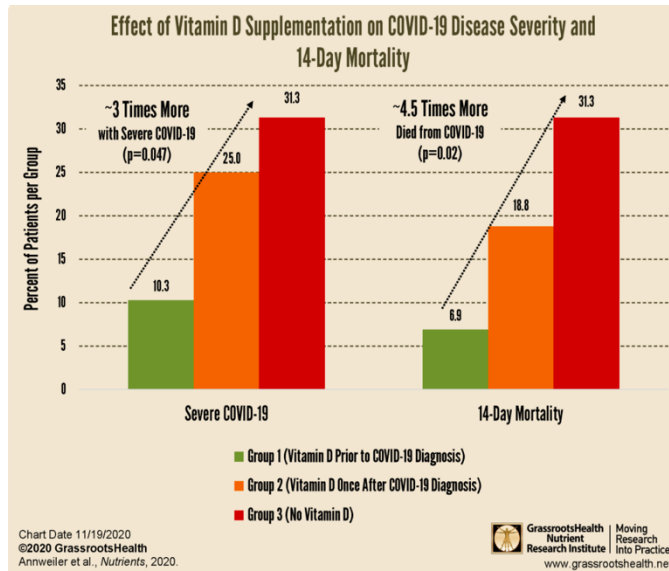


“ SARS-CoV-2 [...] test positivity is strongly and inversely associated with circulating 25(OH)D levels, a relationship that persists across latitudes, races/ethnicities, sexes, and age ranges.

This is research on over 190K people looking at the association between vitamin D and covid rate, showing the steepest drop in contracting it between <20-30 ng/ml.

SARS-CoV-2 nucleic acid amplification test positivity rates and circulating 25(OH)D levels in the total population. Smooth line represents the weighted second order polynomial regression fit to the data associating circulating 25(OH)D levels (x) and SARS-CoV-2 positivity rates (y).

Kaufman, Harvey W., et al. "SARS-CoV-2 positivity rates associated with circulating 25-hydroxyvitamin D levels." *PLoS One* 15.9 (2020): e0239252.



This was a study done on 77 people ages 78-100 who were hospitalized for COVID-19. The first group had regularly supplemented with vitamin D over the past year getting either 50K IU monthly, or 80K-100K every 2-3 months). Group 2 was given 80K IU of vitamin with a few hours after being diagnosed with COVID-19. Group 3 did not have any vitamin D before or after the diagnosis. Survival rate after 14 days as well as the severity of it was measured. At the end of 2 weeks 17 people had severe COVID, and 15 died. The graph shows the stark difference between the groups.

A meta-analysis of eight studies found that there is an inverse correlation between COVID-19 mortality and vitamin D levels. Zero deaths were found among people who have vitamin D at least at around 50 ng/ml (*Nutrients*, COVID-19 mortality risk correlates inversely with vitamin D3 status, and a mortality rate close to zero could theoretically be achieved at 50 ng/ml 25(OH)D3: results of a systematic review and meta-analysis” Lorenz Borsche et al, 10/14/21). They conclude that “low D3 is a predictor rather than just a side effect of the infection. Despite ongoing vaccinations, we recommend raising serum 25(OH)D levels to above 50 ng/ml to prevent or mitigate new outbreaks.”

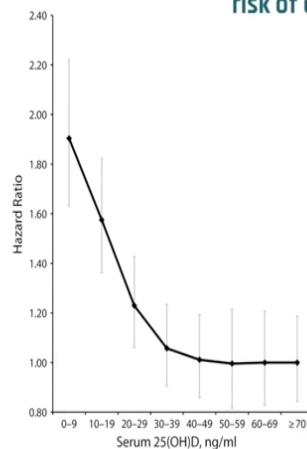
One research study found that 98% of patients with sleep apnea had vitamin D deficiency. And the more severe the apnea the more severe the deficiency of the vitamin WAS.

Researchers out of Cairo found that most patients with lupus (SLE) have a level of vitamin D from below 10 ng/ml to up to 30 ng/ml. There is also research that has shown vitamin D supplementation (4,000 IU/day) combined with resistance training helps to decrease the waist-to-hip ratio - a measurement that is far better at determining risk of type 2 diabetes and heart disease than the BMI index.

One study gave people with epilepsy a single megadose of vitamin D3, ranging from 40K-200K IU, followed by a daily dose of 2,000 - 2,600 IU/day for three months to bring each person up to at least a 30 ng/ml level. Ten of thirteen patients had a decrease in the number of seizures, with five of those experiencing more than a 50% reduction. Overall, the group had a 40% reduction in the number of seizures.

This shows all-cause mortality and vitamin D rates. However, not all agree with information provided here. The Institute of Medicine (IOM, but now called the National Academy of Medicine) offers a very different perspective. They say that blood levels at or above 50 ng/ml (and daily intakes above 4,000 IU) may put people at risk for adverse effects. This is based on several studies including:

A meta-analysis of 32 studies, spanning nearly 50 years, suggests that 25-hydroxyvitamin D levels below 30 ng/mL are associated with a higher risk of death from all causes.



“ This study confirmed an inverse association between serum 25-hydroxyvitamin D concentrations and age-adjusted all-cause mortality rates. Overall, individuals whose 25-hydroxyvitamin D concentrations were in the lowest quantile (0 - 9 ng/mL) had nearly twice the age-adjusted death rate as those in the highest quantile (> 35 ng/mL).

Overall age-adjusted hazard ratios for mortality, in 32 studies of serum 25-hydroxyvitamin D in association with all-cause mortality combined: 1966-2013

Garland, Cedric F., et al. "Meta-analysis of all-cause mortality according to serum 25-hydroxyvitamin D." *American Journal of Public Health* 104.8 (2014): e43-e50.

- ❖ A Danish study done over 3 years found that vitamin D levels between 20-24 ng/ml were associated with the lowest risk of dying, and a level of 56 ng/ml was associated with a 42% higher risk of dying than people who had levels of 20 ng/ml.
- ❖ An American study involving over 14,000 people age 17 and over found mortality rates fell until blood levels reached 39 ng/ml. Lowest mortality rates were between 30-39 ng/ml.
- ❖ An Israeli study done over 4 ½ years on nearly 500K people age 45 and older found that levels between 20-36 ng/ml had the lowest risk of heart attack or death. Below 10 ng/ml there was a 91% higher rate, 26% higher among those with levels of 10-26, and 13% higher above 36 ng/ml.
- ❖ research using another NHANES study (1999-2000, 2009-2010) found that there was a 35% increase in cancer-related death and 111% increase in all-cause death who had blood levels ≥ 20 ng/ml and were supplementing with more than 400 IU/day. Their conclusions included “We found that dietary supplement use was not associated with mortality benefits. There were some suggestions that adequate nutrient intake from foods were associated with reduced mortality and excess nutrient intake from supplements could potentially be harmful.” (*Annals of Internal Medicine*, “Association between dietary supplement use, nutrient intake, and mortality among US adults: a cohort study”, Fan Chen et al, May 7, 2019).

How to reconcile these very different opinions as to optimal blood levels being below 40, or 40-60 ng/ml? The IOM made their recommendations based on calculations that 600 IU/day would be enough for 97.5% of the population to achieve a level of at least 20 ng/ml. As it turns out their calculations were wrong, and 600 IU/day would only get 50% of the population to that level. Another researcher (published in *Nutrients*, “A statistical error in the estimation of the RDA for vitamin D” Paul Veugelers et al, Oct. 2014) offered that using the correct analysis the RDA should

be closer to 8,895 IU/day. The Endocrine Society said in 2011 that up to 10K IU/day was safe for adults.

Something else to consider is that if given the chance by being exposed to the sun sufficiently, the human body will reach levels of 40-60 ng/ml. Mother nature and human evolution are such that what occurs naturally is generally healthy.

One more issue concerning vitamin D and cancer is that there is some research that found taking a supplement on a daily basis is better than use of a large, infrequent dose. Some research found that there was a 42% reduction in total cancer among normal weight people getting a daily dose (e.g. 400-4000 IU), but not for people overweight or obese. Large, infrequent doses (e.g. 20K IU per week, or 500K IU per year) may be rapidly cleared from circulation.

Another study looked at 5,670 men and women in nine countries who were at increased risk for cardiovascular disease. Oral supplements of 60K IU per month for up to 5 years led to a 29% increased risk of all-cause death compared to a placebo. Plus, such supplementation did not cut the risk of cardiovascular disease, fractures, falls, or cancer (Nutrition, Metabolism & Cardiovascular Disease, "Vitamin D supplementation and adverse skeletal outcomes in individuals at increased cardiovascular risk: results from the International Polycap Study (TIPS)-3 randomized controlled trial" P. Joseph, et al, 11/15/22).

Symptoms of deficiency:

- ❖ loss of bone density
- ❖ broken/fractured bones
- ❖ osteoporosis
- ❖ muscle weakness
- ❖ rickets (a softening and distortion of the bones)

Then there are some health problems that are associated with vitamin D deficiency, which does not necessarily mean you can cure them just by taking D, but which may be more prevalent with low levels of it. These include

- ❖ inexplicable aches and pains (vitamin D receptors are present in the nerve cells that sense pain)
- ❖ depressed mood especially in older adults
- ❖ excessively sweaty especially on the forehead
- ❖ increased risk of flu
- ❖ getting sick more often (vitamin D works with the immune cells that help ward off pathogens)
- ❖ increased risk of developing metabolic syndrome

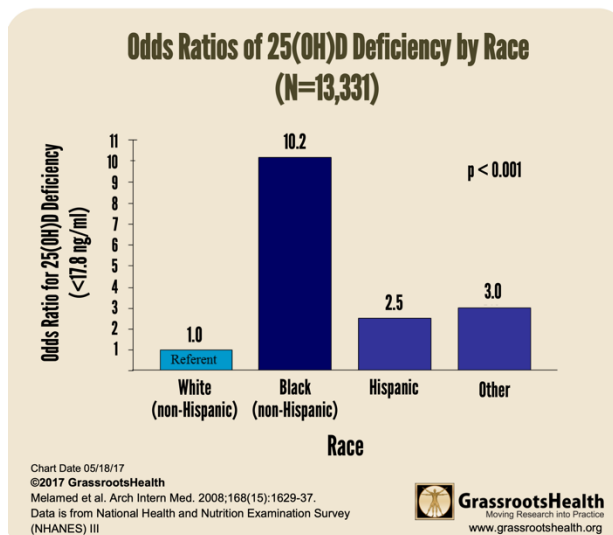
- ❖ heart disease (vit. D helps reduce the buildup of cholesterol and atherosclerosis. Research published in Scientific Reports, “Association of changes in lipid levels with changes in vitamin D levels in a real-world setting” Yonghong Li et al, 11/2/2021 looked at roughly 19,000 people over the course of 2017-2020. For those with a vitamin D level that increased by 10 ng/ml or more had a significant decrease in total cholesterol (~10-12 mg/dl), LDL (~7-8 mg/dl) and triglyceride levels (~21-28 mg/dl). Conversely, those who had a drop of 10 ng/ml or more there was a significant increase in those factors.)
- ❖ osteoporosis & bone fractures (calcium is important to get for strong bones, but it also needs vitamins D & K along with magnesium to ensure bone health)
- ❖ cancer (some research has found that those with the highest level of vitamin D compared to the lowest had a 50% reduction in colorectal cancer. A 4 year study looking at women taking calcium and D3 supplementation found that they had a significantly lower risk for all types of cancer. Again, not all research has supported this finding.)
- ❖ decreased adrenal hormone production
- ❖ atopic dermatitis
- ❖ decreased strength
- ❖ increased body fat
- ❖ low birthweight of newborn babies
- ❖ multiple sclerosis (deficiency of it may be linked to the development of the disease, and those with higher levels appear to have reduced disease activity). Those with higher vitamin D levels tends to experience less disabling symptoms. One researcher has found that some MS patients reach remission after taking massive doses of it such as 150 IU/kg body weight and going as high as 1K IU/kg of body weight, along with other supplements. Patients are routinely tested for parathyroid hormone, calcium, and other micronutrients to make sure they are in balance. (Nutrients, “Safety data in patients with autoimmune diseases during treatment with high doses of vitamin D3 according to the ‘Coimbra Protocol’ Ulrich Amon et al, April 2022). Other autoimmune diseases like lupus, IBD, Crohn’s, psoriasis, and rheumatoid arthritis, have been treated with vitamin D and Coimbra says most have reported significant improvements.
- ❖ psoriasis
- ❖ rheumatoid arthritis
- ❖ schizophrenia

Who is at risk:

Research suggests that vitamin D levels are inversely related to diabetes, glucose concentration, and insulin resistance and that a deficiency in vitamin D may be a risk factor for the metabolic syndrome. Fat basically absorbs vitamin D and reduces blood levels. Those who are overweight are at greater risk for metabolic syndrome and diabetes, and therefore the inverse relationship with vitamin D levels is thought to be due to being too heavy.

Breast-feeding infants may not be getting enough vitamin D through breastmilk because the mother is low herself in the vitamin.

People with celiac disease, cystic fibrosis, Crohn’s, IBS, gallbladder problems, or any other disease that impairs nutrient absorption from fat may have impaired vitamin D levels. Those who have had bariatric weight-loss surgery are also in this category. Hyperparathyroidism (meaning too much of a hormone that controls the calcium levels in the body) can be a risk factor. People who do not go outdoors much to get exposure to the sun can have lower levels of vitamin D.

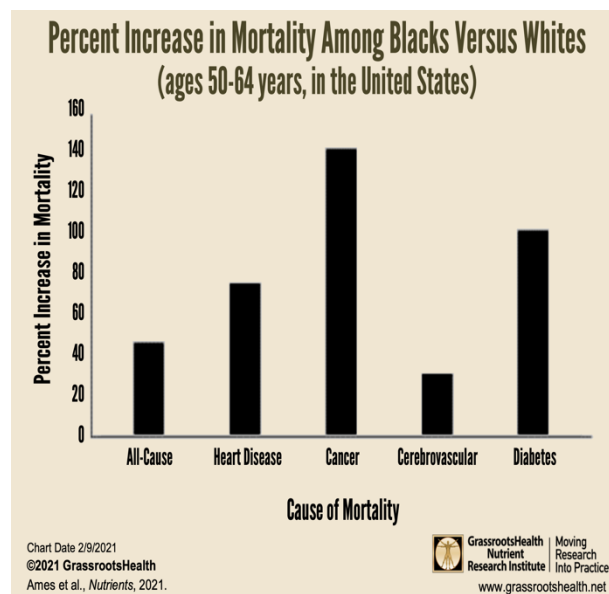


Others at risk for lower vitamin D include people with darker skin. The graph to the left, based on national research, shows that Blacks have the highest risk for a vitamin D deficiency.

Others at risk include those who follow a vegan or other plant-based diet and do not consume vitamin D fortified foods or take supplements, or who are over the age of 50 (getting it from the sun decreases with age).

Among Blacks there is an increased risk of mortality to various vitamin-D related diseases, due to their frequently having low blood levels. However, if Blacks have comparable to Caucasians vitamin D levels such as up at 30-40 ng/ml, rates of mortality are comparable.

However, Black women have a 15-20 times higher prevalence of vitamin D deficiency, putting them at a much higher risk for giving birth preterm. Two-thirds of Black females have vitamin D levels below 20 ng/ml, and as a result are expected to have a 20% preterm birth rate. Again, if D levels are increased the problem virtually disappears.



Granulomatous disorders including sarcoidosis, TB, and lymphomas can lead to a hypersensitivity of vitamin D meaning that sunlight or small intake of it can cause problems and make a person develop toxic levels of the vitamin along with too much calcium in their system. However, sun therapy can help heal TB, and higher vitamin D levels have been associated with an increased

survival rate of lymphoma patients. So, talk to your healthcare provider if you have these types of diseases.

Certain medications can adversely affect vitamin D levels including:

Acid blockers:

- ❖ Cimetidine/Tagamet
- ❖ Esomeprazole/Nexium
- ❖ Famotidine/Pepcid
- ❖ Lansoprazole/Prevacid
- ❖ Nizatidine/Axid
- ❖ Omeprazole/Prilosec
- ❖ Pantoprazole/Protonix
- ❖ Rabeprazole/Aciphex
- ❖ Ranitidine/Zantac

Antacids

- ❖ Aluminum & magnesium hydroxide/Maalox, Mylanta
- ❖ Aluminum carbonate gel/Basaljel
- ❖ Aluminum hydroxide/Amphojel, AlternaGEL
- ❖ Calcium carbonate/Rolaids, Titalac, Tums
- ❖ Magnesium hydroxide/Milk of Magnesia
- ❖ Sodium bicarbonate/Alka-Seltzer, baking soda

Antibiotics

- ❖ Amoxicillin/Amoxil
- ❖ Azithromycin/Z-pak
- ❖ Cefaclor/Ceclor
- ❖ Cefdinir/Omnicef
- ❖ Ciprofloxacin/Cipro
- ❖ Clarithromycin/Biaxin
- ❖ Doxycycline/Doryx
- ❖ Erythromycin
- ❖ Levofloxacin/Levaquin
- ❖ Minocycline/Minocin
- ❖ Sulfamethoxazole and trimethoprim/Bactrim, Septra
- ❖ Tetracycline/Sumycin

Anticonvulsants

- ❖ Carbamazepine/Tegretol, Carbatrol
- ❖ Ethosuximide/Zarontin
- ❖ Gabapentin/Neurontin
- ❖ Phenobarbital Phenytoin/Dilantin
- ❖ Primidone/Mysoline

- ❖ Valproic acid/Depakene, Depakote

Antifungals

- ❖ Ketoconazole/Feoris, Nizoral

Anti-TB agents

- ❖ Ethambutol/Myambutol
- ❖ Isoniazid/INH
- ❖ Rifampin/Rifadin

Barbiturates

- ❖ Butalbital-containing drugs/Fiorinal, Fioricet, Zebutal

Blood pressure

Calcium channel blockers:

- ❖ Diltiazem/Cardizem
- ❖ Felodipine/Plendil
- ❖ Isoptin amlodipine/Norvasc
- ❖ Verapamil/Calan

Diuretics that may increase vitamin D levels:

- ❖ Triamterene/Maxzide, Dyazide, Dyrenium

Cholesterol:

- ❖ Cholestyramine/Questran
- ❖ Colestipol/Colestid

Fibrates (which are thought to be likely to deplete vitamin D)

- ❖ Clofibrate/Atromid
- ❖ Fenofibrate/Tricor
- ❖ Gemfibrozil/Lopid

Statins (some studies suggest they can induce a deficiency in vitamin D leading to muscle cramps and pain. Monitoring your level twice a year is advised by some.)

- ❖ Fluvastatin/Lescol
- ❖ Lovastatin/Altacor, Altoprev, Mevacor
- ❖ Pravastatin/Lipostat, Pravachol, Selektine
- ❖ Rosuvastatin/Crestor
- ❖ Simvastatin/Lipex, Zocor
- ❖ Simvastatin and ezetimibe/Vytorin
- ❖ Simvastatin and niacin/Simcor

Corticosteroids:

- ❖ Dexamethasone/Decadron
- ❖ Hydrocortisone/Cortef
- ❖ Methylprednisolone/Medrol

- ❖ Prednisone/Deltasone, Sterapred, Liquid pred

Inhaled corticosteroids:

- ❖ Budesonide/Rhinocort
- ❖ Flunisolide/Nasarel, Nasalide
- ❖ Fluticasone/Flonase

Laxatives that contain magnesium:

- ❖ e.g. Milk of Magnesium, stimulant laxatives

Nonsteroidal aromatase inhibitors for breast cancer:

- ❖ Anastrozole/Arimidex

Selective Estrogen Receptor Modulators – used for breast cancer:

- ❖ Raloxifene/Evista
- ❖ Tamoxifen/Nolvadex
- ❖ Toremifene/Fareston

Miscellaneous:

- ❖ Alcohol
- ❖ antidepressants (SSRIs)
- ❖ antiepileptic drugs
- ❖ benzodiazepines
- ❖ bile acid sequestrants
- ❖ chemotherapy
- ❖ proton pump inhibitors
- ❖ statins (some research shows higher vitamin D levels, some show lower levels)
- ❖ Lack of sunlight
- ❖ Olestra (often used in 'lite' potato chips)
- ❖ OTC diet aids and fat blockers (e.g. kidney bean extract, starch neutralizer)
- ❖ Liver or kidney damage

Sources:

Sunlight is the easiest and free way to get vitamin D. However, sunscreen blocks much of the process.

Other sources include:

- ❖ oily fish (e.g. salmon, sardines, herring, mackerel, trout, tuna)
- ❖ red meat
- ❖ cheese
- ❖ egg yolks
- ❖ fortified food (e.g. breakfast cereals)
- ❖ mushrooms that have been exposed to UV light

RDA

The average person's level of vitamin D is 16-25 ng/ml. However, it should be appreciated that

'more is not always better.' e.g. Some research for people ages 55-70 (with 3 groups taking 400 IU, 4000 IU, or 10K IU/day) found that those taking the highest dose of vitamin D had the biggest dip in bone strength when measured over three years. The researchers consequently recommended staying between 400-2K IU/day for most people. Research also has found that those with the highest levels of D have more bone fractures, fall more often, do not sleep as well, and die sooner. A 2006 review looking at vitamin D intake and health outcomes such as risk of falls, fractures, colorectal cancer, and bone mineral density found the most advantageous level of vitamin D to be between 36-40 ng/ml.

Suggestions as to what amount to take varies.

	NIH	National Osteoporosis Foundation	American Geriatric Society
Up to age 50		400-800 IU	
Age 50+		800-1000 IU	
Up to 12 months	400 IU		
1-70 years	600 IU		
71+	800 IU		
Pregnant and lactating	600 IU		
Geriatrics at high risk for falling			4000 IU

The vitamin D Council recommendations are

- ❖ 1000 IU for every 25 pounds of body weight for kids
- ❖ 5000 IU for adults including pregnant and lactating women.
- ❖ the upper limit that is recommended is 10K IU for those living in the north (with less sun exposure).

The council's recommendations for blood levels of vitamin D are:

Risk Category	ng/ml
Deficient	<40
Sufficient	40-80
High normal	80-100
Undesirable	100-150
Toxic	>150

Then there is upper intake levels recommended by the National Academy of Sciences for vitamin D and calcium.

Age	Vitamin D3 IU	Calcium mg
1-3 years	2,500	2,500
4-8 years	3,000	2,500
9-18 years	4,000	3,000
19-50 years	4,000	2,500
>50 years	4,000	2,000

One study involving over 7000 people (age 18+) found that different levels of vitamin D intake had different probabilities of reaching a certain blood level. More specifically:

Dosage per day per lb. of body weight	>40 ng/ml	>60 ng/ml	>100 ng/ml
20 IU	66%	24%	<1%
35 IU	84%	43%	<1%
40 IU	88%	50%	1%
60 IU	95%	72%	5%

A simple approach for getting an idea of how much vitamin D you need to boost your level can be found in this chart. However, it is based on weighing 150 lbs. Different weights, and people with different amounts of fat even for that weight will likely have different results than what is shown here. Moreover, how light or dark one’s skin color also impacts how much sunlight is absorbed. Lack of co-nutrients like magnesium, calcium, boron, zinc, and vitamin K-2 can impact vitamin D levels. Too much vitamin A can also cause a reduction in vitamin D levels. Digestive problems such as Crohn’s, leaky gut, celiac disease, people having had bariatric surgery, or IBD may limit the absorption of the vitamin. Liver diseases (e.g. fatty liver) or of the pancreas, or who have had their gallbladder removed may result in lower vitamin D levels. Genetics may lead to decreased conversion of vitamin D within the body. And then there are meds (see below) that may decrease absorption of the vitamin. Even the time of the day you do a blood test for the vitamin can make a difference. According to one study, mid-day levels were about 20% higher than in the morning, and 13% higher than in the evening. So testing, and later re-testing, preferably around the same hour each time, is needed to know how you are responding. But it gives you a general idea of the ballpark figure you are looking at for obtaining D from food, sun, and supplements.

Vitamin D intake observed to produce noted 25(OH)D serum levels in 90% of adults (age 18 years and older), weighing 150 lbs. (N=7324)

RECOMMENDED RANGE: 40-60 ng/ml

WHAT TO DO

- 1 Test
- 2 Establish recommended intake level
- 3 Test again in 3-6 months

(For supplements, vitamin D3, cholecalciferol may be used.)

Individuals should consult with a health care practitioner to develop a custom plan.


Chart Date 12/09/15
© 2015 GrassrootsHealth

Change in Serum Level Based on Intake (IU/day) for 90% of Adults* (N=7324)

Expected Level (ng/ml)	20	30	40	50	60
10	2000	4000	6000	10,000	10,000
15	1000	3000	6000	9000	10,000
20		2000	5000	8000	10,000
25		1000	4000	7000	10,000
30			3000	6000	10,000
35			1000	5000	9000
40				3000	8000
45				2000	6000
50					4000

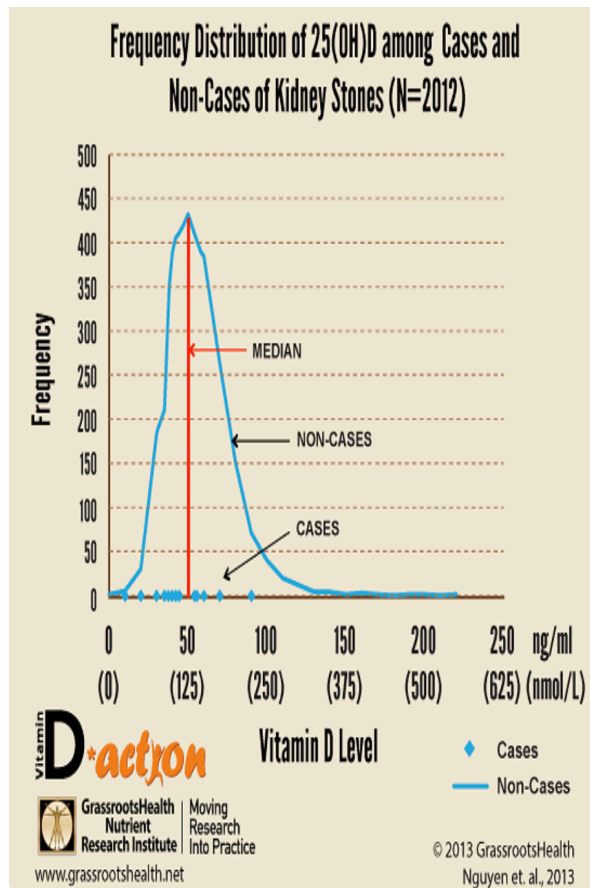
* values rounded to the nearest 1000 IU; highest recommended intake is 10,000 IU/day

Example: With a starting serum level of 20 ng/ml, an additional intake of approximately 5000 IU/day would be sufficient for 90% of adults (age 18 years and older, weighing 150 lbs) to achieve a serum level of at least 40 ng/ml.



A different way of calculating how much to take is that for every 1 ng/ml that you want to increase your blood level you need to take 100 IU/day. So to go from 20 ng/ml to 30 would require 1000 IU/day. It can take six weeks to hit the peak, and then keeping taking the vitamin to stay there. Taking D with a meal containing fat is advised because this can increase absorption by as much as 50%. Obese people may need perhaps twice that amount. Statin users may also need a higher

than expected dose, although some drugs in this class may actually increase levels of vitamin D. Other research has found that for every 1000 IU/day there is roughly a 7-10 ng/ml increase in blood levels – but this is true more for lower blood levels. The dose response curve starts to plateau as it goes up.



NIH recommends no more than 4000 IU/day, and 60K IU/day is considered toxic. Taking too much can cause kidney stones, bone pain, muscle weakness, nausea and vomiting. It can also lead to calcium deposits in the lungs or heart, cause constipation or weight loss, or poor appetite. It is not possible to overdose on vitamin D from food or sun exposure.

Then again, there is research showing the exact opposite. The graph to the left reflects there being zero association between blood levels of vitamin D and kidney stones. The largest study to look at this issue came out of Harvard Medical school involving 45,616 people done over 14 years, and they found no increased risk of kidney stones from vitamin D. (Journal of the American Society of Nephrology, “Dietary risk factors and the risk of incident kidney stones in men. New insights after 14 years of follow-up” Eric Taylor et al, Dec. 2004). Other studies have actually found that low levels of vitamin D make a person twice as likely to develop kidney stones.

Then there are some paradoxical research results about taking mega doses of vitamin D that can lead to insufficiency and negative health effects. What has been found is that taking large amounts of vitamin D without regular maintenance doses such as daily or weekly can lead to changes in enzymes that handle the vitamin. They over-adapt when too much vitamin D is received to prevent toxicity, and so an insufficiency can result. If large doses are followed by regular maintenance doses this insufficiency does not result.

You can do an informal vitamin D test on yourself for free. It will not give you a specific blood level, and only will reflect if you might have a deficiency. However, it is best at capturing very low blood levels, such as <10 ng/ml such as is found with osteomalacia (a softening of the bones). What you do is take your thumb and give a firm push to the tibia (shin bone) which is below the knee. Also push on your sternum (breastbone) in a similar manner. You can do the ulna too (the bone between the elbow and wrist and pain felt there is reflective of a vitamin D deficiency. If there is pain over a longer period of time with the tibia, the risk of D levels <10 ng/ml is 20 times

more likely. If you feel pain in both the breastbone and tibia the likelihood of a D deficiency is 93% according to some.

It should be appreciated that taking a vitamin D supplement is different than getting it from sunlight. Sunshine is made up of different colors. The red light as an example promotes wound healing and tissue repair, and builds collagen which has a variety of benefits such as reducing wrinkles and strengthening blood vessels. Blue and UV light helps to regulate the circadian rhythm and sleep. Sunlight also produces serotonin and beta-endorphins which promote mood enhancement, relaxation, relieves pain, and boosts immunity. There is a feedback loop so that when vitamin D levels are low the 'reward' of enhancing mood and feeling good is increased. As vitamin D levels rise the 'feel good' quality such as from endorphins being released is reduced since there is less need for the vitamin. UV-A light leads to the release of nitric oxide which dilates blood vessels which can lower blood pressure, and helps with immunity and cellular function.

Vitamin D should not be taken with thiazide diuretics because it could lead to excess calcium in the body. Use of calcium-channel blockers should be avoided with vitamin D except under a doctor's supervision because it may interfere with the drug.

Those with low parathyroid function may be at higher risk of high blood calcium levels while taking vitamin D.

Some of the drugs that D3 can interact with (**red indicates serious**, **blue moderate**, black milder interactions) include:

- ❖ **amobarbital**: it may decrease the vitamin. A dose adjustment or special test may be needed.
- ❖ **bendroflumethiazide**: it can increase calcium levels too high. Contact your doctor if there are symptoms such as dizziness, drowsiness, weakness, lethargy, headache, nausea, vomiting, or seizures. A dose adjustment or special test may be needed.
- ❖ **benzthiazide**: it can increase calcium levels too high. Contact your doctor if there are symptoms such as dizziness, drowsiness, weakness, lethargy, headache, nausea, vomiting, or seizures. A dose adjustment or special test may be needed.
- ❖ **butabarbital**: it may decrease the vitamin. A dose adjustment or special test may be needed.
- ❖ **butalbital**: it may decrease the vitamin. A dose adjustment or special test may be needed.
- ❖ **calcifediol**: these should generally be avoided being used together, in that they are both forms of vitamin D which could lead to toxic effects of excessive calcium. Symptoms of toxicity could include irregular pulse, seizures, kidney stones, calcification of blood vessels or cornea or soft tissues of the body. Close monitoring of calcium and phosphorous levels is needed to use these together. A sudden increase in dietary calcium intake should be avoided. Seek medical attention if symptoms of excessive vitamin D result such as weakness, fatigue, headache, being drowsy, vertigo, ringing in the ears, loss of appetite,

nausea, vomiting, constipation, dry mouth, metallic taste, muscle or bone pain, muscle incoordination, or low muscle tone. Late occurring symptoms may include frequent urination, excessive thirst, weight loss, 'pink eye,' light sensitivity, runny nose, itching, increased body temperature, and irregular pulse.

- ❖ **calcipotriene topical:** it may cause blood calcium levels to become too high. A dose adjustment or more frequent monitoring by a doctor may be needed. Contact your doctor if there are symptoms of high blood calcium such as dizziness, weakness, lethargy, muscle pain, headache, loss of appetite, nausea, vomiting, or seizure.
- ❖ **calcitriol:** these should generally be avoided being used together, in that they are both forms of vitamin D which could lead to toxic effects of excessive calcium. Symptoms of toxicity could include irregular pulse, seizures, kidney stones, calcification of blood vessels or cornea or soft tissues of the body. Close monitoring of calcium and phosphorous levels is needed to use these together. A sudden increase in dietary calcium intake should be avoided. Seek medical attention if symptoms of excessive vitamin D result such as weakness, fatigue, headache, being drowsy, vertigo, ringing in the ears, loss of appetite, nausea, vomiting, constipation, dry mouth, metallic taste, muscle or bone pain, muscle incoordination, or low muscle tone. Late occurring symptoms may include frequent urination, excessive thirst, weight loss, 'pink eye,' light sensitivity, runny nose, itching, increased body temperature, and irregular pulse.
- ❖ **calcitriol topical:** it may cause blood calcium levels to become too high. A dose adjustment or more frequent monitoring by a doctor may be needed. Contact your doctor if there are symptoms of high blood calcium such as dizziness, weakness, lethargy, muscle pain, headache, loss of appetite, nausea, vomiting, or seizure.
- ❖ **carbamazepine:** it may decrease the effects of the vitamin. A dose adjustment or special test may be needed.
- ❖ **chlorothiazide:** it may cause blood calcium levels to become too high. A dose adjustment or more frequent monitoring by a doctor may be needed. Contact your doctor if there are symptoms of high blood calcium such as dizziness, weakness, lethargy, muscle pain, headache, loss of appetite, nausea, vomiting, or seizure.
- ❖ **chlorothalidone:** it may cause blood calcium levels to become too high. A dose adjustment or more frequent monitoring by a doctor may be needed. Contact your doctor if there are symptoms of high blood calcium such as dizziness, weakness, lethargy, muscle pain, headache, loss of appetite, nausea, vomiting, or seizure.
- ❖ **cholestyramine:** it may interfere with the absorption of the vitamin. The vitamin should be taken at least 1 hour before or 4-6 hours after the drug.
- ❖ **cimetidine:** it may interfere with metabolism of the vitamin but is likely to be little clinical importance for most people.
- ❖ **colesevelam:** it may decrease the effects of the vitamin. The vitamin should be taken at least 4 hours before the drug. A dose adjustment or special test may be needed.
- ❖ **colestipol:** it may interfere with absorption of the vitamin. The vitamin should be taken at least 1 hour before or 4-6 hours after the drug.

- ❖ **digitoxin**: it can increase calcium levels in the body leading to irregular heartbeat. A dose adjustment or more frequent monitoring may be needed. Large intakes of dietary calcium should be avoided. Contact your doctor if there are symptoms of high blood calcium such as weakness, fatigue, headache, being drowsy, dizziness, ringing in the ears, loss of appetite, nausea, vomiting, constipation, dry mouth, a metallic taste in the mouth, bone or muscle pain, incoordination, frequent urination or weight loss. If symptoms arise such as nausea, vomiting, blurred vision, slow pulse or irregular pulse medical attention should be sought.
- ❖ **digoxin**: it can increase calcium levels in the body leading to irregular heartbeat. A dose adjustment or more frequent monitoring may be needed. Large intakes of dietary calcium should be avoided. Contact your doctor if there are symptoms of high blood calcium such as weakness, fatigue, headache, being drowsy, dizziness, ringing in the ears, loss of appetite, nausea, vomiting, constipation, dry mouth, a metallic taste in the mouth, bone or muscle pain, incoordination, frequent urination or weight loss. If symptoms arise such as nausea, vomiting, blurred vision, slow pulse or irregular pulse medical attention should be sought.
- ❖ **dihydroxyvitamin D₃**: these should generally be avoided being used together, in that they are both forms of vitamin D which could lead to toxic effects of excessive calcium. Symptoms of toxicity could include irregular pulse, seizures, kidney stones, calcification of blood vessels or cornea or soft tissues of the body. Close monitoring of calcium and phosphorous levels is needed to use these together. A sudden increase in dietary calcium intake should be avoided. Seek medical attention if symptoms of excessive vitamin D result such as weakness, fatigue, headache, being drowsy, vertigo, ringing in the ears, loss of appetite, nausea, vomiting, constipation, dry mouth, metallic taste, muscle or bone pain, muscle incoordination, or low muscle tone. Late occurring symptoms may include frequent urination, excessive thirst, weight loss, 'pink eye,' light sensitivity, runny nose, itching, increased body temperature, and irregular pulse.
- ❖ **doxercalciferol**: these should generally be avoided being used together, in that they are both forms of vitamin D which could lead to toxic effects of excessive calcium. Symptoms of toxicity could include irregular pulse, seizures, kidney stones, calcification of blood vessels or cornea or soft tissues of the body. Close monitoring of calcium and phosphorous levels is needed to use these together. A sudden increase in dietary calcium intake should be avoided. Seek medical attention if symptoms of excessive vitamin D result such as weakness, fatigue, headache, being drowsy, vertigo, ringing in the ears, loss of appetite, nausea, vomiting, constipation, dry mouth, metallic taste, muscle or bone pain, muscle incoordination, or low muscle tone. Late occurring symptoms may include frequent urination, excessive thirst, weight loss, 'pink eye,' light sensitivity, runny nose, itching, increased body temperature, and irregular pulse.
- ❖ **erdafitinib**: this can lead to changes in the phosphate level in the blood. Your doctor should check phosphate levels 14-21 days after starting treatment with the drug and monthly afterward, and adjust the dose as needed. If high phosphate symptoms develop such as muscle cramps, convulsions, tingling or numbness around the mouth, or bone pain contact your doctor soon.

- ❖ **ergocalciferol**: these should generally be avoided being used together, in that they are both forms of vitamin D which could lead to toxic effects of excessive calcium. Symptoms of toxicity could include irregular pulse, seizures, kidney stones, calcification of blood vessels or cornea or soft tissues of the body. Close monitoring of calcium and phosphorous levels is needed to use these together. A sudden increase in dietary calcium intake should be avoided. Seek medical attention if symptoms of excessive vitamin D result such as weakness, fatigue, headache, being drowsy, vertigo, ringing in the ears, loss of appetite, nausea, vomiting, constipation, dry mouth, metallic taste, muscle or bone pain, muscle incoordination, or low muscle tone. Late occurring symptoms may include frequent urination, excessive thirst, weight loss, 'pink eye,' light sensitivity, runny nose, itching, increased body temperature, and irregular pulse.
- ❖ **felbamate**: it may decrease the effects of the vitamin. A dose adjustment or special test may be needed.
- ❖ **fosphenytoin**: it may decrease the effects of the vitamin. A dose adjustment or special test may be needed.
- ❖ **hydrochlorothiazide**: it may cause blood calcium levels to become too high. Call your doctor if you experience symptoms such as dizziness, drowsiness, weakness, lethargy, headache, nausea, vomiting or seizures. A dose adjustment or special test may be needed.
- ❖ **hydroflumethiazide**: it may cause blood calcium levels to become too high. Call your doctor if you experience symptoms such as dizziness, drowsiness, weakness, lethargy, headache, nausea, vomiting or seizures. A dose adjustment or special test may be needed.
- ❖ **indapamide**: it may cause blood calcium levels to become too high. Call your doctor if you experience symptoms such as dizziness, drowsiness, weakness, lethargy, headache, nausea, vomiting or seizures. A dose adjustment or special test may be needed.
- ❖ **isoniazid**: it may decrease the effects of the vitamin. A dose adjustment or special test may be needed.
- ❖ **magnesium amino acids chelate/aspartate/carbonate/chloride/citrate/gluconate/glycinate/hydroxide/lactate/oxide/salicylate/sulfate**: elevated magnesium levels may result especially in those with kidney problems. Symptoms of high magnesium include nausea, vomiting, flushing, drowsiness, dizziness, confusion, muscle weakness, reduced reflexes, low blood pressure, slower pulse, impaired breathing, and medical attention should be sought if these are experienced. High levels of magnesium can lead to bone problems. People on dialysis should generally avoid taking magnesium without first talking to a doctor.
- ❖ **mephobarbital**: it may decrease the effects of the vitamin. A dose adjustment or special test may be needed.
- ❖ **methylclothiazide**: it may cause blood calcium levels to become too high. Call your doctor if you experience symptoms such as dizziness, drowsiness, weakness, lethargy, headache, nausea, vomiting or seizures. A dose adjustment or special test may be needed.

- ❖ **metolazone**: it may cause blood calcium levels to become too high. Call your doctor if you experience symptoms such as dizziness, drowsiness, weakness, lethargy, headache, nausea, vomiting or seizures. A dose adjustment or special test may be needed.
- ❖ **mineral oil**: it may decrease the effects of the vitamin. The vitamin should be taken at least 3 hours before or after the oil. A dose adjustment or special test may be needed.
- ❖ **orlistat**: it can decrease absorption of the vitamin. Taking the vitamin at least 2 hours before or after the drug is advised.
- ❖ **oxcarbazepine**: it may decrease the effects of the vitamin. A dose adjustment or special test may be needed.
- ❖ **paricalcitol**: these should generally be avoided being used together, in that they are both forms of vitamin D which could lead to toxic effects of excessive calcium. Symptoms of toxicity could include irregular pulse, seizures, kidney stones, calcification of blood vessels or cornea or soft tissues of the body. Close monitoring of calcium and phosphorous levels is needed to use these together. A sudden increase in dietary calcium intake should be avoided. Seek medical attention if symptoms of excessive vitamin D result such as weakness, fatigue, headache, being drowsy, vertigo, ringing in the ears, loss of appetite, nausea, vomiting, constipation, dry mouth, metallic taste, muscle or bone pain, muscle incoordination, or low muscle tone. Late occurring symptoms may include frequent urination, excessive thirst, weight loss, 'pink eye,' light sensitivity, runny nose, itching, increased body temperature, and irregular pulse.
- ❖ **pentobarbital**: it may decrease the effects of the vitamin. A dose adjustment or special test may be needed.
- ❖ **phenobarbital**: it may decrease the effects of the vitamin. A dose adjustment or special test may be needed.
- ❖ **phenytoin**: it may decrease the effects of the vitamin. A dose adjustment or special test may be needed.
- ❖ **polythiazide**: it may cause blood calcium levels to become too high. Call your doctor if you experience symptoms such as dizziness, drowsiness, weakness, lethargy, headache, nausea, vomiting or seizures. A dose adjustment or special test may be needed.
- ❖ **primidone**: it may decrease the effects of the vitamin. A dose adjustment or special test may be needed.
- ❖ **rifabutin**: it may decrease the effects of the vitamin. A dose adjustment or special test may be needed.
- ❖ **rifampin**: it may decrease the effects of the vitamin. A dose adjustment or special test may be needed.
- ❖ **rifapentine**: it may decrease the effects of the vitamin. A dose adjustment or special test may be needed.
- ❖ **rufinamide**: it may decrease the effects of the vitamin. A dose adjustment or special test may be needed.

- ❖ **secobarbital**: it may decrease the effects of the vitamin. A dose adjustment or special test may be needed.
- ❖ **sevelamer**: it may decrease the effects of the vitamin. Taking the vitamin at least 4 hours before the drug is advised. A dose adjustment or special test may be needed.
- ❖ **sucroferric oxyhydroxide**: it may interfere with absorption of the vitamin. Your doctor may prescribe something else that does not have such an interaction.
- ❖ **trichloromethiazide**: it may cause blood calcium levels to become too high. Call your doctor if you experience symptoms such as dizziness, drowsiness, weakness, lethargy, headache, nausea, vomiting or seizures. A dose adjustment or special test may be needed.

Arrhythmia: vitamin D can worsen arrhythmias especially in people using glycosides. Monitoring of cardiac function and electrolytes is advised.

Electrolyte imbalance: electrolyte concentrations should be corrected before vitamin D therapy is started, and monitored during it.

High calcium levels: vitamin D should not be given to anyone who has high calcium levels, malabsorption syndrome, or high levels of vitamin D already.

Kidney dysfunction: people with such problems also need to be careful of vitamin D, and other forms of it (e.g. calcitriol) might be considered.

Liver/biliary dysfunction: people with such problems also need to be careful of vitamin D, and other forms of it (e.g. calcifediol, calcitriol) might be considered.