Q&A | VITAMIN D: WHAT YOU NEED TO KNOW

For many years, clinicians have been aware of the link between vitamin D levels and bone health; however, recent studies have shown that vitamin D may play a role in maintaining other aspects of overall health.[1-4] The following is a list of frequently asked questions (FAQ) with answers that further support the clinician's understanding of the clinical aspects of vitamin D.

Q: What's so exciting about vitamin D?

A: The World Health Organization's International Agency for Research on Cancer (IARC) has concluded that there appears to be a link between an individual's vitamin D levels and the risk of developing colorectal cancer.[2] Studies have also revealed that higher vitamin D levels are associated with a decreased incidence of other malignancies, including breast cancer.[5]

Q: What about bone health?

A: Vitamin D plays an integral role in calcium homeostasis and in the maintenance of healthy bone. Vitamin D stimulates the absorption of calcium at the level of the intestine and may also serve to increase calcium and phosphate resorption at the kidney level. Deficiency of vitamin D leads to the mobilization of calcium from bone, which can lead to osteoporosis, osteomalacia, and rickets.[1,3,4]

Q: Does vitamin D play a role in any other conditions?

A: Many tissues and cells in the body have a vitamin D receptor. It has been estimated that the expression of as much as one third of the human genome is influenced by 1,25-$(OH)_2$ vitamin D along with other factors.[3] Many studies have demonstrated an association of vitamin D deficiency with increased risk for:

- Autoimmune diseases, including both type 1 and type 2 diabetes, rheumatoid arthritis, Crohn's disease, and multiple sclerosis.[3]
- Infectious diseases[3] and asthma in developing fetuses and young children.[4]
- Cardiovascular disease and hypertension.[3]

Only a few randomized control trials have a dosing range adequate to provide strong evidence for the benefit of vitamin D in reducing the risk of these chronic diseases.[3]

Q: How can individuals increase their vitamin D levels?

A: There are two sources of vitamin D: diet and exposure to sunlight. The normal diet is very low in vitamin D. Most foods, with the exception of fatty fish oils, contain little vitamin D. Some foods (milk and cereals) are fortified with vitamin D. Vitamin D levels can be increased by spending some time in the sun. Energy from the sun converts a precursor in the skin to vitamin D.[3,4]

Q: Who is at greatest risk of vitamin D deficiency?

A: Vitamin D deficiency has been defined by the Institute of Medicine and an Endocrine Society practice guideline as a level of serum 25-hydroxy vitamin D of less than 20 ng/mL.[3,4] The Endocrine Society went on to define vitamin D insufficiency as levels between 21 ng/mL and 29 ng/mL.[3] Because the sun is an important source of vitamin D, serum levels in individuals tend to be lower in the winter than in the summer. Even at the end of summer, in one study that looked at median blood levels of vitamin D in a population of healthy men, more than half of the studied healthy population had levels below 30 ng/mL.[6] The elderly, individuals with dark complexion, people who do not get enough sun exposure, and people with illnesses (including malabsorption syndromes, liver disease, and kidney disease) appear to be at higher risk of deficiency.[3] As a result, a large percentage of these individuals will have low serum vitamin D levels.

Q: Do I have to worry about my vitamin D levels if I get a lot of sun?

A: Exposure to direct sunlight converts a precursor in the skin to vitamin D.[3,4] Vitamin D levels in the fall and winter tend to be lower because the energy from the sun is not high enough for optimal vitamin D production.[3] It should also be noted that some people have low vitamin D levels even with very high sun exposure.[7] In a recent study, Binkley and coworkers tested vitamin D levels of individuals in Hawaii in late March who were patrons of

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the A'ala Park Board Shop (a skateboard shop frequented by young adults) and volunteers from the University of Hawaii at Manoa.[7] More than half of these individuals had low vitamin D levels, despite reported sun exposure of three or more hours per day at least five days a week.[7] High levels of sun exposure do not necessarily correlate with optimal vitamin D levels.

Q: How much vitamin D do you need to take each day?

A: The Institute of Medicine has published Recommended Dietary Allowances (RDA) for daily intake of vitamin D by various populations.[8]

Age	Children	Men	Women	Pregnancy	Lactation
Birth to 1 years	400 IU				
1 to 70 years		600 IU	600 IU	600 IU	600 IU
71+ years		800 IU	800 IU		

The daily intake (RDA) of vitamin D recommended by the Institute of Medicine should be enough to prevent most people from experiencing vitamin D deficiency (defined as a serum level of 25-OH vitamin D of less than 20 ng/mL).[4,8] Higher levels of intake may be required to prevent vitamin D insufficiency (defined by the Endocrine Society as levels of 25-OH vitamin D between 21-29 ng/mL).[3]

Heaney and coworkers[9] showed that supplementing with levels as high as 10,000 IU/day did not cause toxicity in a healthy cohort, and supplementing with 1000 IU/day caused only a minimal increase in serum vitamin D levels.

The Endocrine Society Clinical Practice Guideline has indicated that raising serum vitamin D levels consistently above 30 ng/mL may require at least 1500-2000 IU/day.[3] These levels are significantly higher than the RDA.

Q: Are all vitamin D supplements the same?

A: The vitamin D produced in the skin and that found naturally in animal-based foods are both derived from the same cholecalciferol (vitamin D_3) family.[10] An alternate, plant-based form of vitamin D can also be manufactured by irradiation of ergosterol from yeast to produce ergocalciferol, or vitamin D_2. Both the D_2 and D_3 forms have similar biologic activity.[10]

Q: Does it matter what type of vitamin D a person takes?

A: Clinical studies have shown that vitamin D supplementation with D_3 may be more effective than supplementation with D_2.[11] Armas and coworkers showed giving the same dose of D_3 or D_2 produces the same immediate increase in total vitamin D levels[11]; however, the D_2 levels fall off precipitously while D_3 levels are maintained for a longer time (Figure 1). This study suggests that D_2 may be cleared faster than D_3, reducing the effectiveness of supplementation with D_2.

Vitamin D_3 (cholecalciferol on the label) and vitamin D_2 (ergocalciferol on the label) are both available in many stores without prescription. According to this study, to optimize the efficiency of vitamin D supplementation, the supplement should contain vitamin D_3 (cholecalciferol on the label) and not vitamin D_2 (ergocalciferol on the label). Vitamin D_3 supplements in the form of 1000 IU tablets are available in many stores without prescription.

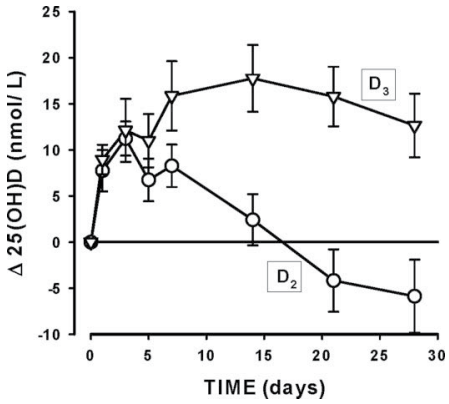

Figure 1. Time course of the rise in serum 25OHD after a single oral dose of 50,000 IU of either cholecalciferol (vitamin D_3) or ergocalciferol (vitamin D_2) in two groups of 10 normal men each.[11]

Note: A serum concentration of 30 ng/mL of vitamin D is equal to 75 nmol/L of vitamin D.

Q: What is the latest research on vitamin D and disease?

A: A few recent studies are discussed on the following pages.

Vitamin D and Bone Health

Positive association between 25-hydroxy vitamin D levels and bone mineral density: A population-based study of younger and older adults.

Bischoff-Ferrari HA, Dietrich T, Orav EJ, Dawson-Hughes B. *Am J Med.* 2004 May 1; 116(9):634-639.

In this study, the authors correlated total hip bone mineral density by dual-energy X-ray absorptiometry to measured total vitamin D levels in 13,432 subjects enrolled in the NHANES III study. Their statistical analysis took into account sex, age, estrogen use, and race/ethnicity. The figures below show the locally weighted regression (LOWESS) plots of bone density versus serum vitamin D levels. The authors observed a significant positive association between serum vitamin D levels and measured bone mineral density.

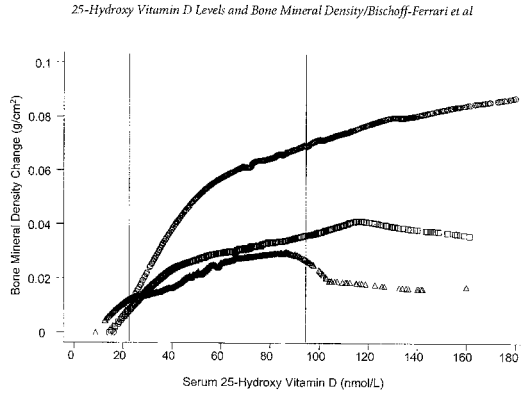

Figure 2. Regression plot of bone mineral density by 25-hydroxy vitamin D level in younger adults (20 to 49 years). Circles represent whites, squares represent Mexican Americans, and triangles represent blacks.

Reprinted from Bischoff-Ferrari HA, Dietrich T, Orav EJ, Dawson-Hughes B. *Am J Med.* 2004 May 1;116(9):634-639, with permission from Elsevier.

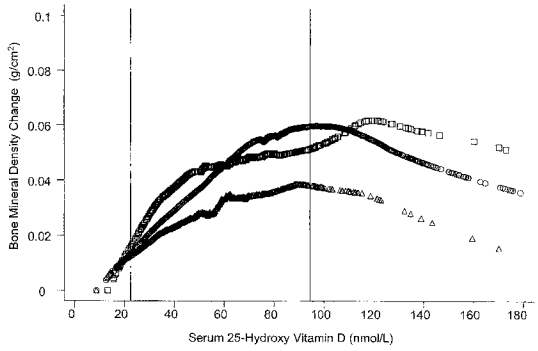

Figure 3. Regression plot of bone mineral density by 25-hydroxy vitamin D level in older adults (≥50 years). Circles represent whites, squares represent Mexican Americans, and triangles represent blacks.

Reprinted from Bischoff-Ferrari HA, Dietrich T, Orav EJ, Dawson-Hughes B. *Am J Med.* 2004 May 1;116(9):634-639, with permission from Elsevier.

Fall prevention with supplemental and active forms of vitamin D: A meta-analysis of randomised controlled trials.

Bischoff-Ferrari HA, Dawson-Hughes B, Staehelin HB et al. *BMJ.* 2009;339:b3692. doi: 10.1136/bmj.b3692.

The authors performed a systematic review of articles published between 1960 and 2008 that assessed the effectiveness of vitamin D supplementation with or without calcium in the prevention of falls among older individuals. Heterogeneity was noted among the eight randomized controlled trials (n=2426) of supplemental vitamin D dosage and achieved serum 25-OH D concentration. The authors concluded that supplementation of vitamin D of 700-1000 IU a day was associated with a 19% reduced risk of falling among older individuals. The risk of falling may not be reduced in this population if vitamin D supplementation is less than 700 IU or serum 25-OH D concentrations of less than 25 ng/mL.

Prevention of nonvertebral fractures with oral vitamin D and dose dependency: A meta-analysis of randomized controlled trials

Bischoff-Ferrari HA, Willett WC, Wong JB et al. *Arch Intern Med.* 2009;169(6):551-561.

The authors performed a systematic review of articles published between 1960 and 2008 that assessed the effectiveness of supplemental vitamin D, with or without calcium, in the prevention of nonvertebral and hip fractures among individuals 65 years of age or older. Twelve double-blind randomized controlled trials (RCTs) for nonvertebral fractures (n = 42,279) and eight RCTs for hip fractures (n = 40,886) were included. The authors noted a higher dose of vitamin D and higher achieved 25-OH D blood levels were associated with a significant increase in antifracture efficacy. The higher dose of vitamin D reduced nonvertebral fractures in individuals living in community dwellings or in institutionalized older individuals. The authors concluded that the prevention of nonvertebral fracture was dependent on the dosage of vitamin D, and with a higher dose of vitamin D, those 65 years old and older should see a reduction in fractures by at least 20%.

Serum 25-hydroxyvitamin D concentrations and risk for hip fractures.

Cauley JA, Lacroix AZ, Wu L, et al. *Ann Intern Med.* 2008 Aug 19; 149(4): 242-250.

In this study, the authors performed a nested case-control study of patients from 40 clinical centers in the United States. The goal was to determine whether low serum vitamin D concentrations are associated with hip fractures in community-dwelling postmenopausal women. Case patients and matched control patients who were not on estrogen replacement or other bone-active therapies were followed for incident hip fracture for a median of 7.1 years. Women with serum vitamin D levels of less than 19 ng/mL had a higher fracture risk than did those with vitamin D levels 28.3 ng/mL (adjusted odds ratio: 1.71 [confidence interval: 1.05 to 2.79]). The authors noted the risk increased in a statistically significantly manner across quartiles of serum vitamin D concentration (P for trend = 0.016). Findings suggest an increased risk of hip fracture for community-dwelling women with low serum vitamin D concentrations.

Serum 25-hydroxyvitamin D and hip fracture risk in older US white adults.

Looker AC, Mussolino ME. *J Bone Miner Res.* 2008; 23(1):143-150.

In this study, the authors evaluated the relationship between serum vitamin D levels and incident hip fracture risk in older non-Hispanic white adults. Data from the NHANES III cohort were mined using linked mortality and Medicare records to identify incident hip fracture cases for white men and women aged 65 or older. After correcting for age, diet, and several other confounders, the analysis showed that serum vitamin D levels greater than 24 ng/mL were associated with a significant decrease in hip fracture risk. The data revealed that higher serum vitamin D levels were associated with decreased fracture risk in this cohort.

Vitamin D and Cancer

Vitamin D and calcium supplementation reduces cancer risk: Results of a randomized trial.

Lappe JM, Travers-Gustafson D, Davies KM, Recker RR, Heaney RP. *Am J Clin Nutr.* 2007 Jun; 85(6):1586-1591.

Researchers from Creighton University evaluated the effectiveness of calcium alone and calcium in addition to vitamin D and its association in the reduction of all-cancer incidence. One thousand one hundred seventy- nine randomly selected community-dwelling women from the population of healthy postmenopausal women were randomly assigned to receive 1400 to 1500 mg of supplemental calcium per day alone (Ca-only), supplemental calcium plus 1100 IU vitamin D_3 per day (Ca+D), or placebo. The unadjusted relative risks of incident cancer in the Ca+D and Ca-only groups were 0.402 (P=0.01) and 0.532 (P=0.06), respectively. When analysis was limited to cancer diagnosed after the first 12 months, the relative risk for the Ca+D group fell to 0.232 (CI: 0.09, 0.60; P<0.005) but did not change significantly for the Ca-only group. The authors found that in multiple logistic regression models both treatment and serum vitamin D concentrations were "significant, independent predictors of cancer risk" and improvements in vitamin D nutritional status in postmenopausal women was associated with a reduced all-cancer risk.

Vitamin D and prevention of breast cancer: Pooled analysis.

Garland CF, Gorham ED, Mohr SB, et al. *J Steroid Biochem Mol Biol.* 2007 Mar; 103(3-5):708-711.

The authors performed a meta-analysis of pooled dose-response data from two studies (The Harvard Nurses Health and Saint Georges Hospital Studies). This publication reported that individuals with serum vitamin D of approximately 52 ng/mL had a 50% lower risk for breast cancer than those with levels measuring less than 13 ng/mL. This group concluded a daily intake of 2000 IU/day and an additional 10 to 15 minutes of daily sun exposure (an amount estimated to be equivalent to an oral intake of 3000 IU of vitamin D_3) would be associated with a 50% lower incidence of breast cancer.

Circulating levels of vitamin D and colon and rectal cancer: the Physicians' Health Study and a meta-analysis of prospective studies.

Lee JE, Li H, Chan AT, Hollis BW et al. *Cancer Prev Res* (Phila). 2011;4(5):735-743.

The authors performed a systematic review of articles that evaluated the association between circulating vitamin D levels and colon and rectal cancer. They conducted a meta-analysis of eight prospective studies of the relationship between circulating levels of 25-OH D and colon and rectal cancers. The combined studies included a total of 1822 colon and 868 rectal cancers. Statistical comparison of the top and bottom quantiles of circulating 25-OH D levels revealed a significant inverse association for colorectal cancer (OR = 0.66; 95% CI: 0.54-0.81. The inverse association was stronger for rectal cancer with the lowest quantile of serum vitamin D

levels experiencing double the number of rectal cancer (OR = 0.50 for top versus bottom quantiles; 95% CI: 0.28-0.88). The risk of colon cancer associated with the lower 25-OH D levels was lower than that of rectal cancer (OR = 0.77; 95% CI: 0.56-1.07). The results of this meta-analysis of multiple studies suggest that colorectal cancer and circulating 25-OH D levels show an inverse association. The results also noted a stronger inverse association between circulating 25-OH D levels for rectal cancer.

Optimal vitamin D status for colorectal cancer prevention: A quantitative meta analysis.

Gorham ED, Garland CF, Garland FC, et al. *Am J Prev Med.* 2007 Mar; 32(3):210-216.

The authors performed a meta-analysis of data from five studies and reported that raising vitamin D levels may reduce the incidence of colorectal cancer cases in the United States. They found a linear trend toward reduced risk for colorectal cancer as the levels of serum vitamin D increased. Compared with a serum vitamin D level of ≤12 ng/mL, a level of ≥33 ng/mL was associated with a 50% reduction in the incidence of colorectal cancer. The authors concluded that a vitamin D_3 intake of 1000 to 2000 IU/day would confer an appropriate balance between protection against colorectal cancer and adverse events related to excessive vitamin D intake.

Circulating 25-hydroxyvitamin D levels and survival in patients with colorectal cancer.

Ng K, Meyerhardt JA, Wu K, et al. *J Clin Onc.* 2008 Jun 20; 26:2984-2991.

The authors evaluated the association between measured vitamin D levels and mortality among 304 participants in the Nurses' Health Study (NHS) and the Health Professionals Follow-Up Study (HPFS) who were subsequently diagnosed with colorectal cancer. Higher measured vitamin D levels were associated with a significant reduction in overall mortality. Participants in the lowest and highest quartiles were compared and the highest quartile had an increased risk for overall mortality; HR=0.52 (95% CI: 0.29–0.94). Authors noted a trend in improved colorectal cancer-specific mortality; HR=0.61 (95% CI: 0.31–1.19). For overall mortality comparing extreme quartiles, the multivariate hazard ratio was 0.45 (95% CI: 0.19–1.09). The authors concluded that colorectal cancer patients with higher plasma vitamin D levels before the diagnosis were associated with a significant improvement in overall survival.

Vitamin D and Cesarean Delivery

Association between vitamin D deficiency and primary cesarean section.

Merewood A, Mehta SD, Chen TC, Bauchner H, Holick MF. *J Clin Endocrinol Metab.* 2009 Mar; 94(3):940-945.

Prior to the discovery of vitamin D and its role in healthy bone formation, many women died in childbirth. The "rachitic" pelvises of women with profound vitamin D deficiency did not allow the child to pass through, resulting in mortality. Vitamin D supplementation has essentially eliminated rickets and dramatically improved pregnancy outcomes. A number of recent studies, however, have indicated that vitamin D deficiency is on the rise and, in the US, the cesarean birth rate has been climbing. In this study, the authors analyzed the relationship between maternal serum vitamin D levels and the prevalence of primary cesarean section. Two hundred fifty-three women, 43 (17%) of whom had a primary cesarean section, were enrolled in the study. The authors found an inverse relationship between maternal vitamin D levels and the probability of having a cesarean section. Twenty-eight percent of women with vitamin D levels of less than 15 ng/mL had a cesarean section, while only 14% of women with vitamin D greater than 15 ng/mL had a cesarean section (P = 0.012). Based on the multivariable logistic regression analysis with controls that included race, age, education level, insurance status, and alcohol use, lower vitamin D levels in women was associated with four times more likely to have a cesarean than women with higher values (adjusted odds ratio 3.84; 95% confidence interval: 1.71 to 8.62). The authors concluded that lower vitamin D levels were associated with an increased likelihood of primary cesarean section.

Vitamin D and Heart Disease

Independent association of low serum 25-hydroxyvitamin D and 1,25-dihydroxyvitamin D levels with all-cause and cardiovascular mortality.

Dobnig H, Pilz S, Scharnagl H, et al. *Arch Intern Med.* 2008 Jun 23; 168(12):1340-1349.

In this study, vitamin D levels were measured in 3258 consecutive male and female patients scheduled for coronary angiography at a single tertiary center. The follow-up period consisted of 7.7 years, and during this time 737 patients (22.6%) died, 463 from cardiovascular causes. Patients with vitamin D in the lowest quartile

(median: 7.6 ng/mL) were at increased risk for all-cause mortality compared with patients in the highest 25-OH D quartile (median: 28.4 ng/mL) HR=2.08 (95% CI: 1.60–2.70). Patients with vitamin D in the second highest quartile (median: 13.3 ng/mL) were at increased risk for all-cause mortality compared with patients in the highest 25-OH D quartile, HR=1.53 (95% CI: 1.17–2.01). Hazard ratios for patients in the lower two vitamin D quartiles were also higher for cardiovascular mortality (HR=2.22 (95% CI: 1.57–3.13) and HR=1.82 (95% CI: 1.29–2.58), respectively, compared with patients in the highest 25-hydroxyvitamin D quartile. These associations were not linked to coronary artery disease, physical activity level, Charlson Comorbidity Index, variables of mineral metabolism, and New York Heart Association functional class. The authors concluded there was an independent association with low vitamin D levels (25 OH vitamin D and 1,25 dihydroxyvitamin D) and cardiovascular- and all-cause mortality.

25-Hydroxyvitamin D and risk of myocardial infarction in men: A prospective study.

Giovannucci E, Liu Y, Hollis BW, Rimm EB. *Arch Intern Med.* 2008 Jun 9;168(11):1174-1180.

The authors conducted a nested case-control study of 18,225 men enrolled in the Health Professional Follow-up Study who did not have a diagnosis of cardiovascular disease at the time of blood draw. Four hundred fifty-four men developed nonfatal myocardial infarction (MI) or fatal coronary heart disease during 10 years of follow-up. Men with low vitamin D levels (≤15 ng/mL) were at increased risk for MI compared with men who had vitamin D levels considered to be sufficient (≥30 ng/mL) (relative risk [RR], 2.42 [95% CI: 1.53–3.84; P <0.001] for trend). The relationship remained significant even with additional adjustment for family history and other risk factors (RR, 2.09 [95% CI: 1.24–3.54; P=0.02] for trend). It was noted that men who had intermediate vitamin D levels were also at elevated risk compared to those with higher vitamin D levels (22.6–29.9 ng/mL): RR, 1.60 (95% CI: 1.10–2.32); and 15.0–22.5 ng/mL: RR, 1.43 (95% CI: 0.96–2.13), respectively.

Vitamin D deficiency and risk of cardiovascular disease.

Wang TJ, Pencina MJ, Booth SL, et al. *Circ.* 2008 Jan 29; 117(4):503-511.

In this study, vitamin D levels were measured in 1739 participants of the Framingham Offspring Study who did not have prior cardiovascular disease. One hundred and twenty participants experienced a first cardiovascular event during a mean follow up of 5.4 years. Participants with vitamin D levels of less than 15 ng/mL had a multivariable-adjusted hazard ratio (HR)=1.62 (95% CI: 1.11–2.36), (P=0.01) for incident cardiovascular events relative to participants with vitamin D levels in excess of 15 ng/mL. Participants with hypertension observed an increased HR; HR=2.13 (95% CI: 1.30–3.48) but not in those without hypertension; HR=1.04 (95% CI: 0.55–1.96). The data showed a graded increase in cardiovascular risk with decreased vitamin D levels, HR=1.80 (95% CI: 1.05-3.08) for levels <10 ng/mL (P for linear trend=0.01).

Low vitamin D levels predict stroke in patients referred to coronary angiography.

Pilz S, Dobnig H, Fischer JE, et al. *Stroke.* 2008 Sep; 39(9):2611-2613.

In this study, vitamin D levels of 25(OH)D were measured in 3299 participants, and levels of 1,25-dihydroxyvitamin D (1,25(OH)2D) were measured in 3315 patients who were referred for coronary angiography. During a median follow- up period of 7.75 years, 769 patients died, including 42 from strokes. Using binary logistic-regression analyses against survivor comparison, the authors noted the odds ratios for fatal stroke was 0.58 (95% CI: 0.43 to 0.78, P<0.001) per z value of 25(OH)D and 0.62 (0.47 to 0.81, P<0.001) per z value of 1,25(OH)2D. Confounders were noted and consideration given, and the odds ratio remained significant for 25(OH) D at 0.67 (0.46 to 0.97, P=0.032) and 0.72 (0.52 to 0.99, P=0.047) for 1,25(OH)2D. The authors concluded that a low level of vitamin D is predictive for fatal strokes and suggested that vitamin D supplementation has promise for the prevention of strokes.

Vitamin D and Efficacy, Safety, and Demographics

Demographic differences and trends of vitamin D insufficiency in the US population, 1988-2004.

Ginde AA, Liu MC, Camargo CA Jr. *Arch Intern Med.* 2009 Mar 23;169(6): 626-632.

The goal of this study was to analyze the trends in vitamin D levels in the US during the last two decades. The authors performed a statistical analysis comparing the serum vitamin D levels of participants of the Third National Health and Nutrition Examination Survey (NHANES III), collected from 1988 through 1994, with NHANES data collected from 2001 through 2004. The data revealed a trend for all populations studied; the

mean values and the entire distributions of vitamin D levels had shifted downward in the time between the survey collections. Serum vitamin D levels for the entire population studied was 30 ng/mL for the earlier study group and had decreased to 24 ng/mL for the later group. Authors noted the percentage of the population with vitamin D levels of 30 ng/mL or more saw a decrease from 45% for the earlier group to 23% for the later group. In non-Hispanic blacks, vitamin D serum levels of less than 10 ng/mL rose from 9% for the early group to 29% for the later group. A decrease of vitamin D levels was also noted in non-Hispanic blacks in the prevalence of levels of 30 ng/mL or more from 12% to 3%. In the most recent NHANES population studied (2001-2004) more than 60% of non-Hispanic whites had vitamin D insufficiency (defined as serum levels less than 30 ng/mL). Vitamin D insufficiency was shown in 97% of non-Hispanic blacks and 90% of Mexican Americans. The authors concluded that a marked decrease in serum vitamin D levels had occurred from the 1988-1994 to the 2001-2004 NHANES data collections. The data revealed racial/ethnic differences in vitamin D levels, which may have some role in the etiology of known health disparities between races and ethnic groups. The authors commented there is an epidemic of vitamin D insufficiency and current recommendations for vitamin D supplementation were not adequate to address the epidemic.

Vitamin D: Criteria for safety and efficacy.

Heaney RP. *Nutr Rev.* 2008; 66(10 Suppl 2):S178-181.

In this comprehensive review of numerous recent publications, Dr Heaney concluded that serum vitamin D levels greater than 80 nmol/L may be required to achieve several health endpoints involving bone, neuromuscular function, cancer, and immune function. The author provides support for the contention that a daily intake of 1000 to 2000 IU of D_3 from combined sources (food, cutaneous production, and supplements) is required to achieve this level (80 nmol/L). The review also summarized published findings that vitamin D toxicity from excessive supplemental intake has only rarely been shown to occur at serum levels less than 500 nmol/L. Finally, this review summarizes a number of published studies that have shown that vitamin D supplementation with levels as high as 10,000 IU/day has not been associated with toxicity.

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Q: What vitamin D tests does LabCorp offer?

A: LabCorp offers several vitamin D tests that may be useful in certain clinical applications.

Vitamin D, 25-Hydroxy (Total Vitamin D)

Vitamin D, 25-Hydroxy provides the simplest method for the assessment of overall vitamin D status and for the diagnoses of deficiency or toxicity. Low blood levels of 25-hydroxy vitamin D may mean an individual is not getting enough exposure to sunlight or not enough dietary vitamin D to meet the body's demand, or there may be an issue with its absorption from the intestines. High levels of 25-hydroxy vitamin D usually reflect excess supplementation from vitamin pills or other nutritional supplements. LabCorp's Vitamin D, 25-Hydroxy test employs immunochemiluminometric methodology and is performed on the DiaSorin LIAISON® instrument at LabCorp. This highly automated test measures both D_2 and D_3 together and reports a total 25-hydroxy vitamin D. Some major clinical studies, including (but not limited to) the Centers for Disease Control (CDC) National Health and Nutrition Examination Survey (NHANES) data base, the Women's Health Initiative (WHI) studies, and the Harvard-based Health Professionals Studies, have employed DiaSorin reagents.[12-15]

Test Name	Test No.
Vitamin D, 25-Hydroxy	**081950**

Visit the online Test Menu at **www.LabCorp.com** for full test information, including CPT codes and specimen collection requirements.

LabCorp also offers the following specialized vitamin D tests.

Calcitriol (1,25 di-OH Vitamin D)

Measurement of 1,25 dihydroxy vitamin D levels may be useful in the assessment of disorders of calcium metabolism and parathyroid disease. This test should not be ordered for assessment of overall vitamin D status. Levels of 1,25-D can often be normal in individuals with overall vitamin D deficiency. The 1,25 Dihydroxy Vitamin D test uses column chromatograph, radioimmunassay (RIA) methodology. For ordering information, please consult LabCorp's Directory of Services and Interpretive Guide.

Vitamin D, 25-OH, Fractionated (Total, D_2, D_3), HPLC/MS-MS

Available through our Endocrine Sciences laboratory in Calabasas, Calif, this test provides clinicians with the levels of D_2 and D_3 vitamin D as well as the total. D_2 levels can become measurable when patients are supplemented with high-dose D_2; however, many individuals tested may have no detectable vitamin D_2. Only vitamin D_3 is produced by the body. The Vitamin D, 25 OH Fractionated Total D_2 and D_3 assay uses isotope dilution tandem mass spectrometry with HPLC after extraction (HPLC-MS/MS). For ordering information, please contact your local representative.

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