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Vitamin D and risk of cognitive decline in elderly persons.

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BACKGROUND: To our knowledge, no prospective study has examined the association between vitamin D and cognitive decline or dementia. **METHODS:** We determined whether low levels of serum 25-hydroxyvitamin D (25[OH]D) were associated with an increased risk of substantial cognitive decline in the InCHIANTI population-based study conducted in Italy between 1998 and 2006 with follow-up assessments every 3 years. A total of 858 adults 65 years or older completed interviews, cognitive assessments, and medical examinations and provided blood samples. Cognitive decline was assessed using the Mini-Mental State Examination (MMSE), and substantial decline was defined as 3 or more points. The Trail-Making Tests A and B were also used, and substantial decline was defined as the worst 10% of the distribution of decline or as discontinued testing. **RESULTS:** The multivariate adjusted relative risk (95% confidence interval [CI]) of substantial cognitive decline on the MMSE in participants who were severely serum 25(OH)D deficient (levels <25 nmol/L) in comparison with those with sufficient levels of 25(OH)D (≥ 75 nmol/L) was 1.60 (95% CI, 1.19-2.00). Multivariate adjusted random-effects models demonstrated that the scores of participants who were severely 25(OH)D deficient declined by an additional 0.3 MMSE points per year more than those with sufficient levels of 25(OH)D. The relative risk for substantial decline on Trail-Making Test B was 1.31 (95% CI, 1.03-1.51) among those who were severely 25(OH)D deficient compared with those with sufficient levels of 25(OH)D. No significant association was observed for Trail-Making Test A. **CONCLUSION:** Low levels of vitamin D were associated with substantial cognitive decline in the elderly population studied over a 6-year period, which raises important new possibilities for treatment and prevention.

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Vitamin D and health status in elderly.

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ABSTRACT: Recently, vitamin D has aroused considerable interest for several reasons. Many epidemiological studies have shown a widespread deficiency of vitamin D at all ages, and the recent finding that many organs and tissues have vitamin D receptors has fostered the clinical and biological relevance of vitamin D. Elderly people are at high risk for vitamin D deficiency if their life style entails few outdoor activities, their skin is thick and they exhibit impairment of renal function. In the elderly, vitamin D deficiency is very important because it can affect the function of many organs such as the muscle-skeletal, cardiovascular systems and kidney, and may be involved in various diseases and pathological conditions including type II diabetes, cancer and cognitive decline. In the present review, the most relevant features of vitamin D are described as well as the clinical consequences of hypovitaminosis D in the elderly. Finally, the role of an adequate oral supplementation in the geriatric population is stressed.

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Am J Med. 2009 Sep;122(9):793-802.

Vitamin D: bone and beyond, rationale and recommendations for supplementation.

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ABSTRACT: Adequate vitamin D status is necessary and beneficial for health, although deficiency plagues much of the world's population. In addition to reducing the risk for bone disease, vitamin D plays a role in reduction of falls, as well as decreases in pain, autoimmune diseases, cancer, heart disease, mortality, and cognitive function. On the basis of this emerging understanding, improving patients' vitamin D status has become an essential aspect of primary care. Although some have suggested increased sun exposure to increase serum vitamin D levels, this has the potential to induce photoaging and skin cancer, especially in patients at risk for these conditions. Vitamin D deficiency and insufficiency can be both corrected and prevented safely through supplementation.

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Vitamin D deficiency is associated with sudden cardiac death, combined cardiovascular events, and mortality in haemodialysis patients.

Drechsler C, Pilz S, Obermayer-Pietsch B, Verduijn M, Tomaschitz A, Krane V, Espe K, Dekker F, Brandenburg V, März W, Ritz E, Wanner C. Department of Internal Medicine 1, Division of Nephrology, University of Würzburg, Oberdürrbacher Str. 6, D-97080 Würzburg, Germany.

ABSTRACT: Aims Dialysis patients experience an excess mortality, predominantly of sudden cardiac death (SCD). Accumulating evidence suggests a role of vitamin D for myocardial and overall health. This study investigated the impact of vitamin D status on cardiovascular outcomes and fatal infections in haemodialysis patients. **Methods and results** 25-hydroxyvitamin D [25(OH)D] was measured in 1108 diabetic haemodialysis patients who participated in the German Diabetes and Dialysis Study and were followed up for a median of 4 years. By Cox regression analyses, we determined hazard ratios (HR) for pre-specified, adjudicated endpoints according to baseline 25(OH)D levels: SCD (n = 146), myocardial infarction (MI, n = 174), stroke (n = 89), cardiovascular events (CVE, n = 414), death due to heart failure (n = 37), fatal infection (n = 111), and all-cause mortality (n = 545). Patients had a mean age of 66 +/- 8 years (54% male) and median 25(OH)D of 39 nmol/L (interquartile range: 28-55). Patients with severe vitamin D deficiency [25(OH)D of <= 25 nmol/L] had a 3-fold higher risk of SCD compared with those with sufficient 25(OH)D levels >75 nmol/L [HR: 2.99, 95% confidence interval (CI): 1.39-6.40]. Furthermore, CVE and all-cause mortality were strongly increased (HR: 1.78, 95% CI: 1.18-2.69, and HR: 1.74, 95% CI: 1.22-2.47, respectively), all persisting in multivariate models. There were borderline non-significant associations with stroke and fatal infection while MI and deaths due to heart failure were not meaningfully affected. **Conclusion** Severe vitamin D deficiency was strongly associated with SCD, CVE, and mortality, and there were borderline associations with stroke and fatal infection. Whether vitamin D supplementation decreases adverse outcomes requires further evaluation. PMID: 20688781

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Vitamin D supplementation and regulatory T cells in apparently healthy subjects: vitamin D treatment for autoimmune diseases?

Prieti B, Pilz S, Wolf M, Tomaschitz A, Obermayer-Pietsch B, Graninger W, Pieber TR. Division of Endocrinology and Nuclear Medicine, Medical University of Graz, Austria.

BACKGROUND: Epidemiological data show significant associations of vitamin D deficiency and autoimmune diseases. Vitamin D may prevent autoimmunity by stimulating naturally occurring regulatory T cells. **OBJECTIVES:** To elucidate whether vitamin D supplementation increases Tregs frequency (%Tregs) within circulating CD4+ T cells. **METHODS:** We performed an uncontrolled vitamin D supplementation trial among 50 apparently healthy subjects including supplementation of 140,000 IU at baseline and after 4 weeks (visit 1). The final follow-up visit was performed 8 weeks after the baseline examination (visit 2). Blood was drawn at each study visit to determine 25-hydroxyvitamin D levels and %Tregs. Tregs were characterized as CD4+CD25++ T cells with expression of the transcription factor forkhead box P3 and low or absent expression of CD127. **RESULTS:** Forty-six study participants (65% females, mean age +/- SD 31 +/- 8 years) completed the trial. 25(OH)D levels increased from 23.9 +/- 12.9 ng/ml at baseline to 45.9 +/- 14.0 ng/ml at visit 1 and 58.0 +/- 15.1 ng/ml at visit 2. %Tregs at baseline were 4.8 +/- 1.4. Compared to baseline levels we noticed a significant increase of %Tregs at study visit 1 (5.9 +/- 1.7, P < 0.001) and 2 (5.6 +/- 1.6, P < 0.001). **CONCLUSIONS:** Vitamin D supplementation was associated with significantly increased %Tregs in apparently healthy individuals. This immunomodulatory effect of vitamin D might underlie the associations of vitamin D deficiency and autoimmune diseases. Hence, our finding provides a rationale for further studies to investigate vitamin D effects on autoimmunological processes. PMID: 20684175

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Are commonly recommended dosages for vitamin D supplementation too low? Vitamin D status and effects of supplementation on serum 25-hydroxyvitamin D levels-an observational study during clinical practice conditions.

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ABSTRACT: Vitamin D deficiency is associated with increased fracture risk. The observational study aimed to investigate vitamin D status and supplementation in ambulatory patients. Only 20% of patients had optimal serum 25-hydroxyvitamin D [25(OH)D] levels. Commonly recommended dosages were insufficient to achieve clinically relevant increase of 25(OH)D levels. Higher dosages were safe and effective under clinical practice conditions. **INTRODUCTION:** Vitamin D deficiency is associated with adverse health outcome. The study aimed to investigate vitamin D status and supplementation in ambulatory patients. **METHODS:** Nine hundred seventy-five women and 188 men were evaluated for bone status from January 2008 to August 2008 within an observational study; 104 patients (n = 70 osteoporosis) received follow-up after 3 months. Dosage of vitamin D supplementation was documented and serum 25(OH)D and parathyroid hormone (PTH) determined. **RESULTS:** In all patients (age, 60.4 +/- 14.1 years), distribution of 25(OH)D was 56.3 +/- 22.3 nmol/L (normal range, 52-182 nmol/L) and PTH 53.8 +/- 67.5 ng/L (normal range, 11-43 ng/L). The proportion of patients with 25(OH)D < 25, 25 to <50, 50 to <75, >=75 nmol/L was 7.5%, 33.3%, 38.9% and 20.2% in the total group and 20.1%, 38.5%, 30.8%, 10.6% at baseline in the follow-up group, respectively. After 3 months, 3.9% had still 25(OH)D < 25 nmol/L; only 12.5% achieved 25(OH)D >= 75 nmol/L. In osteoporosis patients, 25(OH)D increased more in those taking >=1,500 (median, 3,000) IU vitamin D per day (33.1 +/- 14.7 nmol/L) compared with <=1,000 (median, 800) IU/day (10.6 +/- 20.0 nmol/L) (p < 0.0008). PTH decreased more in patients taking >=1,500 IU/day (-13.2 +/- 15.2 ng/L) compared with <=1,000 IU/day (-7.6 +/- 19.2 ng/L; p = 0.29). 25(OH)D was negatively correlated to PTH (r = -0.49, p < 0.0001). An increase of 25(OH)D >= 75 nmol/L resulted in normalised PTH. **CONCLUSION:** Supplementation with higher vitamin D dosages (2,000-3,000 IU/day) is required to achieve a relevant increase of 25(OH)D and normalisation of PTH.

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Vitamin D and musculoskeletal health, cardiovascular disease, autoimmunity and cancer: Recommendations for clinical practice.

Souberbielle JC, Body JJ, Lappe JM, Plebani M, Shoenfeld Y, Wang TJ, Bischoff-Ferrari HA, Cavalier E, Ebeling PR, Fardellone P, Gandini S, Gruson D, Guérin AP, Heickendorff L, Hollis BW, Ish-Shalom S, Jean G, von Landenberg P, Largura A, Olsson T, Pierrot-Deseilligny C, Pilz S, Tincani A, Valcour A, Zittermann A. Laboratoire de Physiologie, CHU Necker, Paris, France.

BACKGROUND: There is increasing evidence that, in addition to the well-known effects on musculoskeletal health, vitamin D status may be related to a number of non-skeletal diseases. An international expert panel formulated recommendations on vitamin D for clinical practice, taking into consideration the best evidence available based on published literature today. In addition, where data were limited to smaller clinical trials or epidemiologic studies, the panel made expert-opinion based recommendations. **METHODS:** Twenty-five experts from various disciplines (classical clinical applications, cardiology, autoimmunity, and cancer) established draft recommendations during a 2-day meeting. Thereafter, representatives of all disciplines refined the recommendations and related texts, subsequently reviewed by all panelists. For all recommendations, panelists expressed the extent of agreement using a 5-point scale. **RESULTS AND CONCLUSION:** Recommendations were restricted to clinical practice and concern adult patients with or at risk for fractures, falls, cardiovascular or autoimmune diseases, and cancer. The panel reached substantial agreement about the need for vitamin D supplementation in specific groups of patients in these clinical areas and the need for assessing their 25-hydroxyvitamin D (25(OH)D) serum levels for optimal clinical care. A target range of at least 30 to 40ng/mL was recommended. As response to treatment varies by environmental factors and starting levels of 25(OH)D, testing may be warranted after at least 3months of supplementation. An assay measuring both 25(OH)D(2) and 25(OH)D(3) is recommended. Dark-skinned or veiled individuals not exposed much to the sun, elderly and institutionalized individuals may be supplemented (800IU/day) without baseline testing.

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Vitamin D and calcium insufficiency-related chronic diseases: molecular and cellular pathophysiology.

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Abstract: A compromised vitamin D status, characterized by low 25-hydroxyvitamin D (25-(OH)D) serum levels, and a nutritional calcium deficit are widely encountered in European and North American countries, independent of age or gender. Both conditions are linked to the pathogenesis of many degenerative, malignant, inflammatory and metabolic diseases. Studies on tissue-specific expression and activity of vitamin D metabolizing enzymes, 25-(OH)D-1 alpha-hydroxylase and 25-(OH)D-24-hydroxylase, and of the extracellular calcium-sensing receptor (CaR) have led to the understanding of how, in non-renal tissues and cellular systems, locally produced 1,25-dihydroxyvitamin D(3) (1,25-(OH)(2)D(3)) and extracellular Ca(2+) act jointly as key regulators of cellular proliferation, differentiation and function. Impairment of cooperative signalling from the 1,25-(OH)(2)D(3)-activated vitamin D receptor (VDR) and from the CaR in vitamin D and calcium insufficiency causes cellular dysfunction in many organs and biological systems, and, therefore, increases the risk of diseases, particularly of osteoporosis, colorectal and breast cancer, inflammatory bowel disease, insulin-dependent diabetes mellitus type I, metabolic syndrome, diabetes mellitus type II, hypertension and cardiovascular disease. Understanding the underlying molecular and cellular processes provides a rationale for advocating adequate intake of vitamin D and calcium in all populations, thereby preventing many chronic diseases worldwide.

PMID: 19724293

Diabetes Care. 2005 Dec;28(12):2926-32.

Dietary calcium, vitamin D, and the prevalence of metabolic syndrome in middle-aged and older U.S. women.

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OBJECTIVE: To examine whether and to what extent intakes of calcium and vitamin D are related to the metabolic syndrome in middle-aged or older women. RESEARCH DESIGN AND METHODS: We analyzed data from 10,066 women aged > or =45 years participating in the Women's Health Study who were free of cardiovascular disease, cancer, or diabetes and who never used postmenopausal hormones. We used multiple logistic regression models to estimate multivariable odds ratios (ORs) and 95% CIs comparing different dietary intake levels of calcium and vitamin D. RESULTS: In age- and calorie-adjusted analyses, higher intakes of total, dietary, and supplemental calcium were significantly and inversely associated with the prevalence of metabolic syndrome. After further adjusting for smoking status, exercise, alcohol intake, multivitamin use, and parental history of myocardial infarction before age 60 years, the ORs of having the metabolic syndrome for increasing quintiles of total calcium intake were 1.00 (reference), 0.82 (95% CI 0.70-0.97), 0.84 (0.71-0.99), 0.70 (0.59-0.83), and 0.64 (0.54-0.77) (P for trend <0.0001). This association was not appreciably altered by additional adjustment for other dietary factors or total vitamin D intake. In contrast, neither total (P for trend = 0.13) nor supplemental (P for trend = 0.45) vitamin D was significantly associated with metabolic syndrome. Dietary vitamin D was inversely associated with prevalence of metabolic syndrome but was not independent of total calcium intake. Similar strong relations between intakes of dairy products and metabolic syndrome were also observed. After adjustment for lifestyle and dietary factors, the multivariable ORs comparing highest with lowest intake categories were 0.66 (0.55-0.80) (P for trend <0.0001) for total dairy products and 0.85 (0.71-1.02) (P for trend = 0.05) for total milk intake. CONCLUSIONS: Our results indicate that intakes of calcium and dairy products may be associated with lower prevalence of the metabolic syndrome in middle-aged and older women.

PMID: 16306556

J Bone Miner Res. 2007 Dec;22 Suppl 2:V28-33.

Vitamin D and skin physiology: a D-lightful story.

Holick MF, Chen TC, Lu Z, Sauter E. Department of Medicine, Section of Endocrinology, Nutrition, and Diabetes, Vitamin D, Skin, and Bone Research Laboratory, Boston University Medical Center, Boston, Massachusetts, USA.

Abstract: Throughout evolution, exposure to sunlight and the photosynthesis of vitamin D(3) in the skin has been critically important for the evolution of land vertebrates. During exposure to sunlight, the solar UVB photons with energies 290-315 nm are absorbed by 7-dehydrocholesterol in the skin and converted to previtamin D(3). Previtamin D(3) undergoes a rapid transformation within the plasma membrane to vitamin D(3). Excessive exposure to sunlight will not result in vitamin D intoxication because both previtamin D(3) and vitamin D(3) are photolyzed to several noncalcemic photoproducts. During the winter at latitudes above approximately 35 degrees, there is minimal, if any, previtamin D(3) production in the skin. Altitude also has a significant effect on vitamin D(3) production. At 27 degrees N in November, very little (approximately 0.5%) previtamin D(3) synthesis was detected in Agra (169 m) and Katmandu (1400 m). There was an approximately 2- and 4-fold increase in previtamin D(3) production at approximately 3400 m and at Everest base camp (5300 m), respectively. Increased skin pigmentation, application of a sunscreen, aging, and clothing have a dramatic effect on previtamin D(3) production in the skin. It is estimated that exposure in a bathing suit to 1 minimal erythemal dose (MED) is equivalent to ingesting between 10,000 and 25,000 IU of vitamin D(2). The importance of sunlight for providing most humans with their vitamin D requirement is well documented by the seasonal variation in circulating levels of 25-hydroxyvitamin D [25(OH)D]. Vitamin D deficiency [i.e., 25(OH)D < 20 ng/ml] is common in both children and adults worldwide. Exposure to lamps that produce UVB radiation is an excellent source for producing vitamin D(3) in the skin and is especially efficacious in patients with fat malabsorption syndromes. The major cause of vitamin D deficiency globally is an underappreciation of sunlight's role in providing humans with their vitamin D(3) requirement. Very few foods naturally contain vitamin D, and those that do have a very variable vitamin D content. Recently it was observed that wild caught salmon had between 75% and 90% more vitamin D(3) compared with farmed salmon. The associations regarding increased risk of common deadly cancers, autoimmune diseases, infectious diseases, and cardiovascular disease with living at higher latitudes and being prone to vitamin D deficiency should alert all health care professionals about the importance of vitamin D for overall health and well being. PMID: 18290718

J Cell Biochem. 2003 Feb 1;88(2):296-307.

Vitamin D: A millenium perspective.

Holick MF. Vitamin D Laboratory, Section of Endocrinology, Department of Medicine, Boston University Medical Center, Boston, MA 02118.

Abstract: Vitamin D is one of the oldest hormones that have been made in the earliest life forms for over 750 million years. Phytoplankton, zooplankton, and most plants and animals that are exposed to sunlight have the capacity to make vitamin D. Vitamin D is critically important for the development, growth, and maintenance of a healthy skeleton from birth until death. The major function of vitamin D is to maintain calcium homeostasis. It accomplishes this by increasing the efficiency of the intestine to absorb dietary calcium. When there is inadequate calcium in the diet to satisfy the body's calcium requirement, vitamin D communicates to the osteoblasts that signal osteoclast precursors to mature and dissolve the calcium stored in the bone. Vitamin D is metabolized in the liver and then in the kidney to 1,25-dihydroxyvitamin D [1,25(OH)(2)D]. 1,25(OH)(2)D receptors (VDR) are present not only in the intestine and bone, but in a wide variety of other tissues, including the brain, heart, stomach, pancreas, activated T and B lymphocytes, skin, gonads, etc. 1,25(OH)(2)D is one of the most potent substances to inhibit proliferation of both normal and hyperproliferative cells and induce them to mature. It is also recognized that a wide variety of tissues, including colon, prostate, breast, and skin have the enzymatic machinery to produce 1,25(OH)(2)D. 1,25(OH)(2)D and its analogs have been developed for treating the hyperproliferative disease psoriasis. Vitamin D deficiency is a major unrecognized health problem. Not only does it cause rickets in children, osteomalacia and osteoporosis in adults, but may have long lasting effects. Chronic vitamin D deficiency may have serious adverse consequences, including increased risk of hypertension, multiple sclerosis, cancers of the colon, prostate, breast, and ovary, and type 1 diabetes. There needs to be a better appreciation of the importance of vitamin D for overall health and well being. PMID: 12520530

J Nutr. 2006 Apr;136(4):1117-22.

Critique of the considerations for establishing the tolerable upper intake level for vitamin D: critical need for revision upwards.

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Abstract: The tolerable upper intake level (UL) for vitamin D is 50 mcg/d (2000 iu/d) in North America and in Europe. In the United Kingdom a guidance level exists for vitamin D, 25 mcg/d (1000 iu/d), defined as the dose "of vitamins and minerals that potentially susceptible individuals could take daily on a life-long basis, without medical supervision in reasonable safety." Exposure of skin to sunshine can safely provide an adult with vitamin D in an amount equivalent to an oral dose of 250 mcg/d. The incremental consumption of 1 mcg/d of vitamin D₃ raises serum 25-hydroxyvitamin D [25(OH)D] by approximately 1 nmol/L (0.4 microg/L). Published reports suggest toxicity may occur with 25(OH)D concentrations beyond 500 nmol/L (200 microg/L). Older adults are advised to maintain serum 25(OH)D concentrations >75 nmol/L. The preceding numbers indicate that vitamin D₃ intake at the UL raises 25(OH)D by approximately 50 nmol/L and that this may be more desirable than harmful. The past decade has produced separate North American, European, and U.K. reports that address UL or guidance-level values for vitamin D. Despite similar well-defined models for risk assessment, each report has failed to adapt its message to new evidence of no adverse effects at higher doses. Inappropriately low UL values, or guidance values, for vitamin D have hindered objective clinical research on vitamin D nutrition, they have hindered our understanding of its role in disease prevention, and restricted the amount of vitamin D in multivitamins and foods to doses too low to benefit public health.

PMID: 16549491

J Steroid Biochem Mol Biol. 2004 May;89-90(1-5):575-9.

Why the optimal requirement for Vitamin D₃ is probably much higher than what is officially recommended for adults.

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Abstract: The physiologic range for circulating 25-hydroxyvitamin D₃ [25(OH)D; the measure of Vitamin D nutrient status] concentration in humans and other primates extends to beyond 200 nmol/L (>80 ng/mL). This biologic "normal" value is greater than current population norms for 25(OH)D. Concentrations of 25(OH)D that correlate with desirable effects extend to at least 70 nmol/L, with no obvious threshold. Randomized clinical trials using 20 mcg (800 IU) per day of Vitamin D show that this suppresses parathyroid hormone, preserves bone mineral density, prevents fractures, lowers blood pressure and improves balance. Calcium absorption from diet correlates with 25(OH)D in the normal range. Health effects of Vitamin D beyond osteoporosis are mostly supported by the circumstantial evidence of epidemiologic studies and laboratory research. These include prevention of cancer and the autoimmune diseases, insulin-dependent diabetes and multiple sclerosis. One mcg per day of Vitamin D(3) (cholecalciferol) increases circulating 25(OH)D by about 1 nmol/L (0.4 ng/mL). A recommended dietary allowance (RDA) is the long-term daily intake level that meets the total requirements for the nutrient by nearly all healthy individuals (it would presume no sunshine). If 70 nmol/L is regarded as a minimum desirable target 25(OH)D concentration, then current recommendations of 15 mcg per day do not meet the criterion of an RDA.

PMID: 15225842

There is extensive research on the role of Vitamin D on overall health and wellness, biochemical function of the body, and disease / illness. The Vitamin D Council has created a comprehensive list of research abstracts sorted by function and disease.

Vitamin D Council Website: www.vitamindcouncil.org.