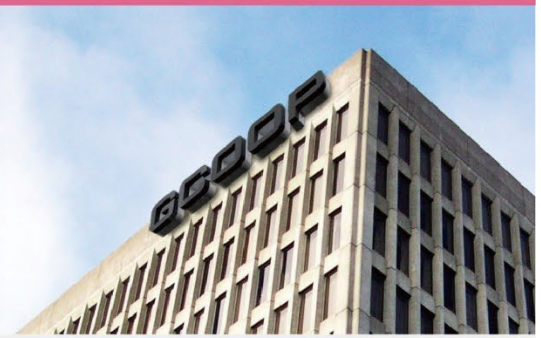
GCOOP

GENERAL BALANCE VITAMIN D

Advertising Laws Regarding Dietary Supplements

GCOOP strives to ensure that members are not mislead through unlawful or deceptive advertising methods.

We ask for your cooperation in this matter. Please refer to the guidance below to avoid unlawful or deceptive advertising methods.



1. Labels or advertisements that may be perceived as effective in the prevention or treatment of disease.
2. Labels or advertisements that may mislead consumers to recognize foods or dietary supplements as drugs.
3. Labels or advertisements that may mislead consumers to recognize products that are not dietary supplements as dietary supple-ments.
4. False or exaggerated statements and or signage/markings/logos.
5. Misleading statements and or signage/markings/logos.
6. Advertising against other companies or their products.
7. Unfairly comparing one's own products against another sales force member or their products without objective factual evidence.
8. Using unlawful or deceptive representations to encourage and solicit consumers and or using obscene language that significantly infringes pu blic morals or social ethics.
9. Advertising methods that are noncompliant to or in violation of regulations for business participants (manufacturing facilities, expiration dates, encouraging unethical methods)

[Source] MFDS Policy Info "Food Advertising Guideline"

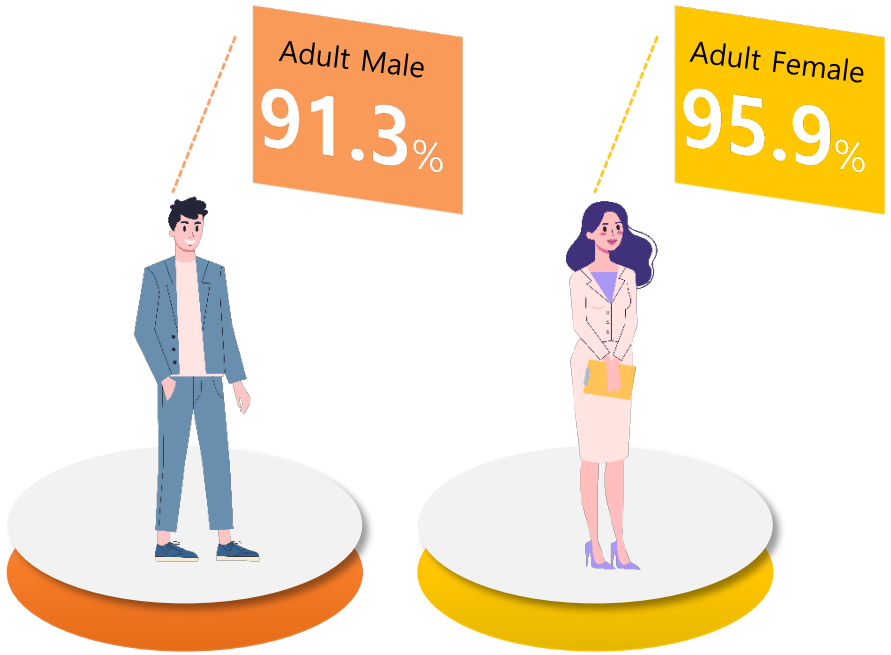
CONTENTS.

GCOOP

Vitamin D

An Introduction

90% of South Koreans are Vitamin D Deficient



Vitamin D deficiency in South Korea, Korea Center for Disease Control and Prevention 2017 National Health Statistics

Source: Korea Center for Disease Control and Prevention Agency


Health

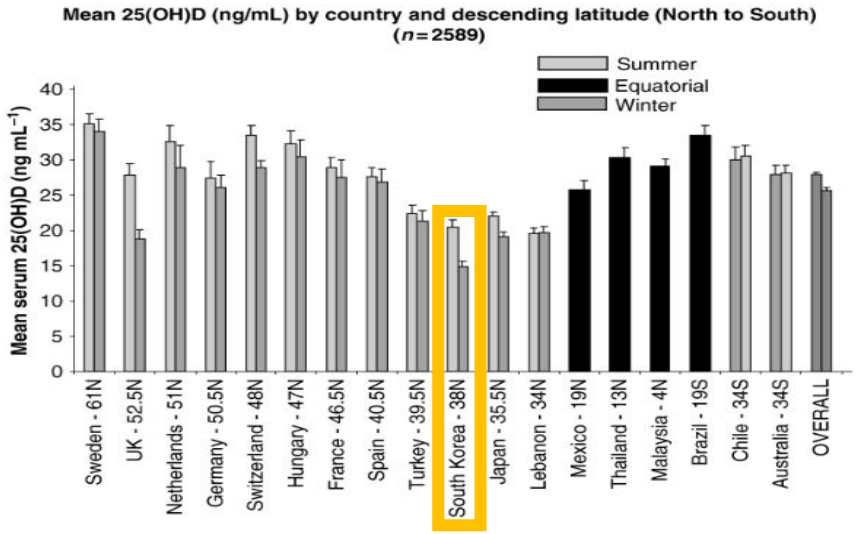
“ 8 Hours of Sunlight a Day for Optimal Vitamin D Synthesis ”

비타민D 전문가 주장 눈길

한국, 위도 높아 일조량 부족
고층건물·대기오염도 영향
“비타민D3 영양제 먹어야”

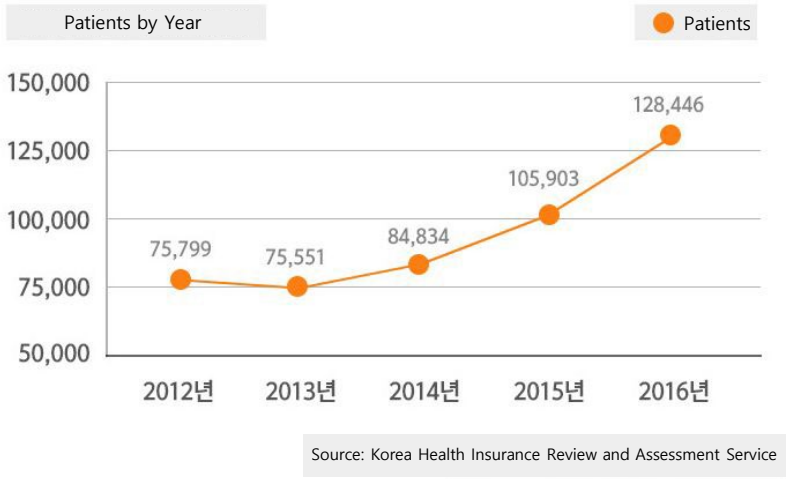
햇빛 아무리 쬐어도 비타민D 부족한 이유

Increased indoor activity and concern over UV ray exposure has left 90% of South Koreans vitamin D deficient



The Most Vitamin D Deficient Country, South Korea

Source) Atherosclerosis 215 (2011) Atherosclerosis journal



Number of Vitamin D Deficiency Patients by Year

Vitamin D Daily Value

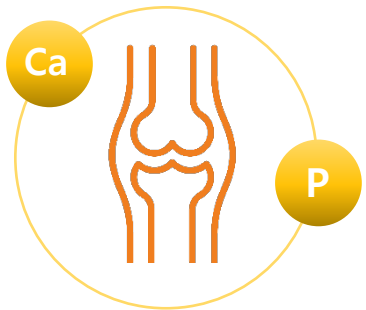
3~10 μg (120-400 IU*)

***IU**

International Unit

Internationally uniform measure
1 μg = 40 IU

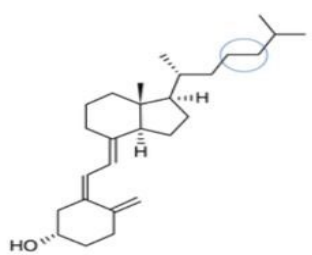
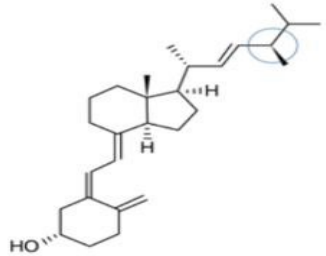
Vitamin D



Necessary for calcium and phosphorous absorption and utilization.

Necessary for bone formation and maintenance.

Helps reduce the risk of developing osteoporosis.

Vitamin D	Vitamin D used as dietary supplements are Vitamin D_2 and Vitamin D_3. They are absorbed differently by the body.	
	Vitamin D_2 (Ergocalciferol)	**Vitamin D_3** (Cholecalciferol)
	Plant-based Vitamin D_2 	**Animal-based** Vitamin D_3 
Source	**Plant-based** (Ex : Yeast, Mushroom)	**Animal-based**, Sunlight synthesized
Native Vitamin D	**Products marked "Natural Vitamin D" contain Vitamin D_2 extracted from yeast**	
Half-life	**13 days**	**21 days**
Active Vitamin D behavior	50%(Receptor affinity)	100%(Receptor affinity)

[Vitamin D_3] is highly active and bioavailable

There are five forms of vitamin D (D1-D5). D2 and D3 are the most widely studied. Vitamin D2 (ergocalciferol) is synthesized primarily in plants and invertebrates, while vitamin D3 (cholecalciferol) is synthesized in vertebrates. Both are utilized as nutritional supplements.

Of the two, vitamin D3 has the highest bioavailability and absorption rate among vitamin Ds. As a result, vitamin D3 is commonly recommended worldwide.

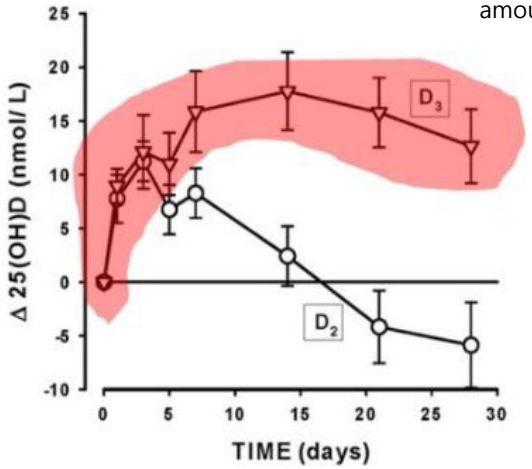
Vitamin D2 Is Much Less Effective than Vitamin D3 in Humans FREE

Laura A. G. Armas, Bruce W. Hollis, Robert P. Heaney ✉

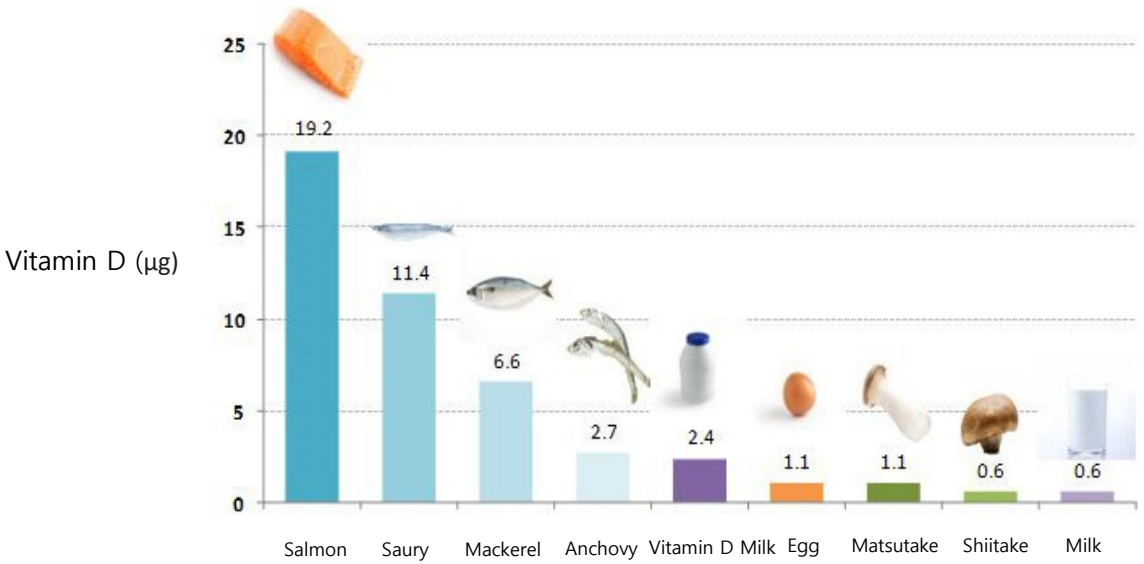
The Journal of Clinical Endocrinology & Metabolism, Volume 89, Issue 11, 1 November 2004, Pages 5387–5391, https://doi.org/10.1210/jc.2004-0360

Published: 01 November 2004 **Article history ▾**

When D2 and D3 are taken in equal amounts, D3 is absorbed 4-5 times more than D2



| Vitamin D per Serving |

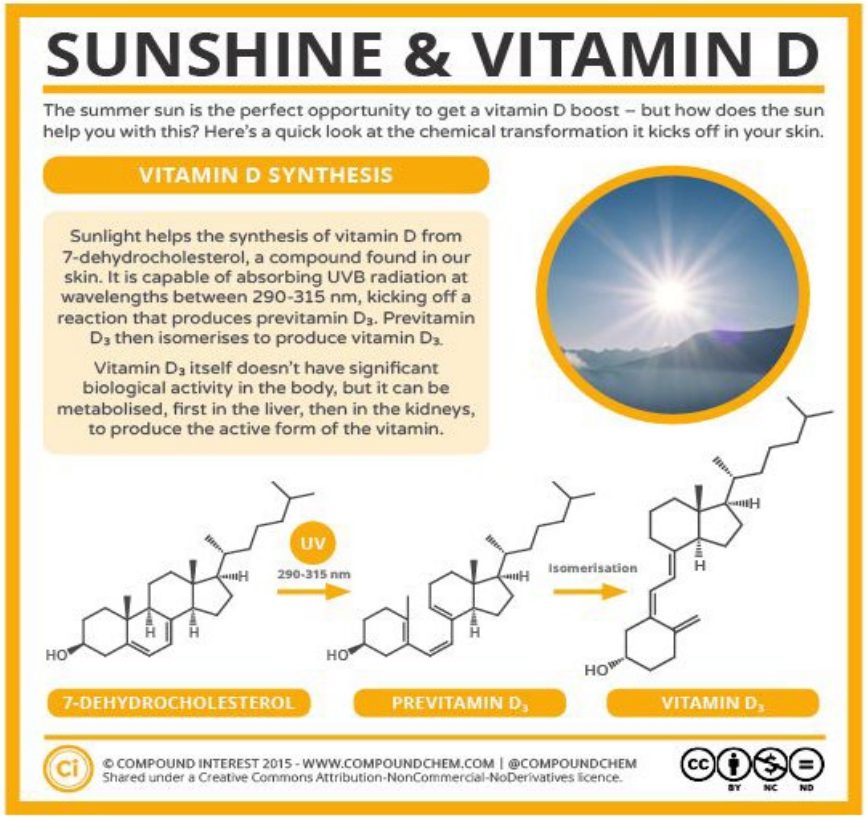


Synthesis of Vitamin D from Food

Foods rich in vitamin D include eggs, mushrooms, bluefish, and animal liver.

To get 1000 IU of vitamin D3 from food, you would need to eat 40 eggs, 10 cups (250 ml) of milk, or 3 salmon.

It is not recommended to consume the foods above in such quantities due to the amount of saturated fat and excess cholesterol.

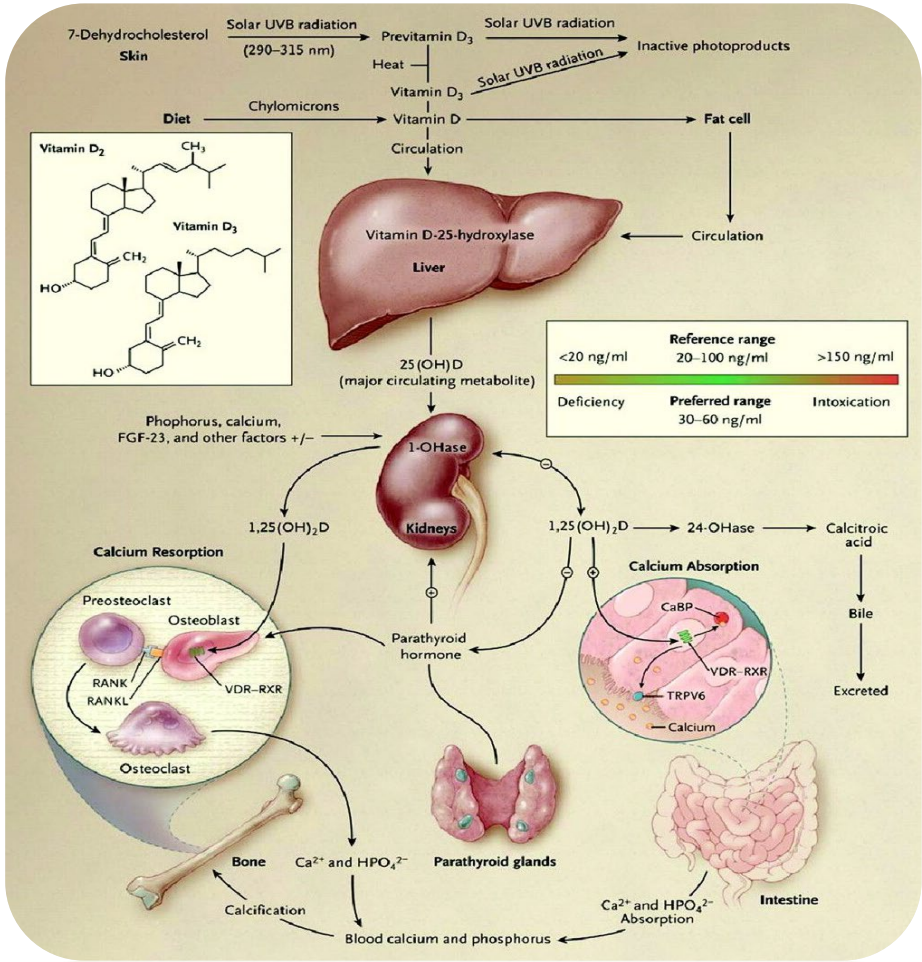


Synthesis of Vitamin D from UV light

Vitamin D is the only vitamin that is synthesized in the skin through sunlight without dietary intake.

To prevent vitamin D deficiency, it is recommended to spend at least 30 minutes outdoors without sunscreen on the arms and legs between 10 a.m. and 3 p.m., at least twice a week.

7-dihydrocholesterol, one of the metabolites of cholesterol, is present in skin cells. Pro-vitamin D3 is converted to vitamin D3 when exposed to ultraviolet radiation from sunlight. Once synthesized in the skin, vitamin D3 is metabolized in the liver to 25-hydroxyvitamin D3 (calcidiol), which is further metabolized in the kidneys to 1,25-hydroxyvitamin D3 (calcitriol).

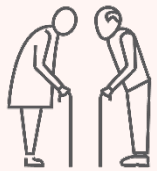


Calcium-related Benefits from Vitamin D

Active Vitamin D_3

01. Aids in the absorption of calcium and phosphorus in the small intestine.
02. Promotes calcium reabsorption in the kidneys, reducing the amount that is lost through urine.
03. Prevents calcium loss in bones.

✓ Why Vitamin D Deficiency Occurs

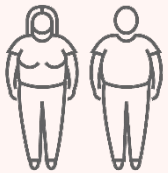


Age

Vitamin D synthesis decreases up to 75% in persons over 70 years old.

Hyperpigmentation

Increased amount of melanin pigment interferes with vitamin D synthesis



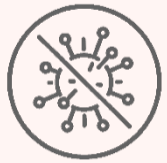
Obesity

Because Vitamin D is fat-soluble, fats cells can absorb it.

Fat-soluble vitamins are stored in adipose tissue when they enter the body. For every 1% increased in body mass index (BMI), blood vitamin D decreases by 1.15%.

Sunscreen

An SPF of 15 blocks 99% of vitamin D synthesis.

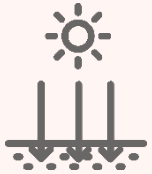


Pollution

Pollution blocks UVB rays from the air.

Time of Day

Exposure to sunlight with UVA index of 3 or higher is needed to produce Vitamin D

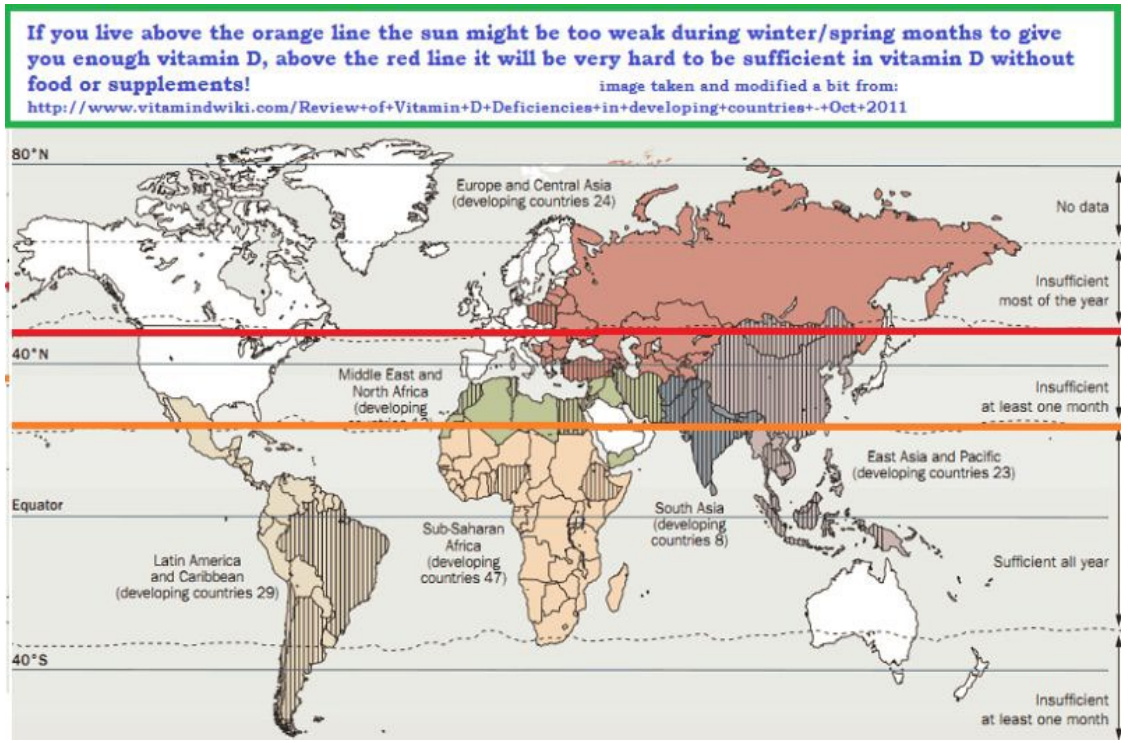


Altitude

At low-altitude locations, the atmosphere absorbs the UV rays

✔ Latitude and Seasons

South Korea is not at a latitude where optimal vitamin D synthesis can occur. Vitamin D is difficult to synthesize except in the summer.



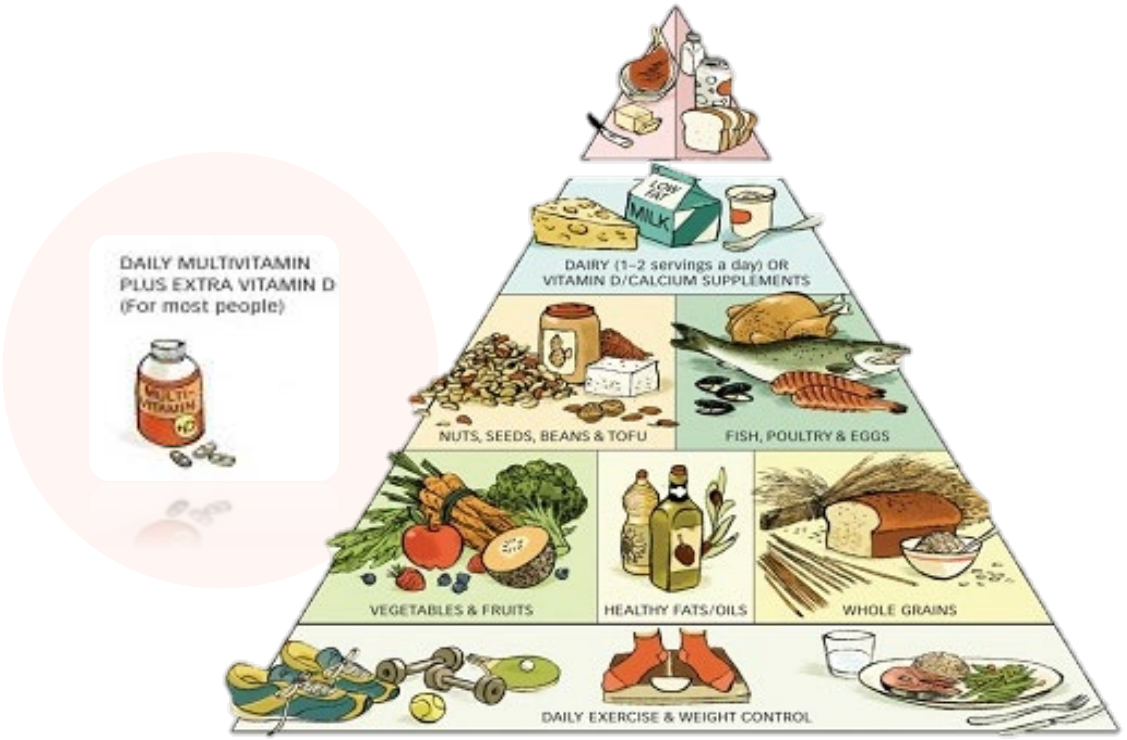
South Korea

37 degrees latitude

UV rays are less concentrated in higher latitudes. Persons living above 35 degrees north of the equator are usually able to optimally synthesize vitamin D only from late spring to early fall

➞ **A cause of vitamin D deficiency in South Korea**

The Healthy Eating Pyramid



01.

According to the 2020 Korean Nutrient Intake Guidelines published by the Ministry of Health and Welfare and the Korean Dietetic Association, the average Korean diet does not contain foods that provide optimal amounts of Vitamin D.

02.

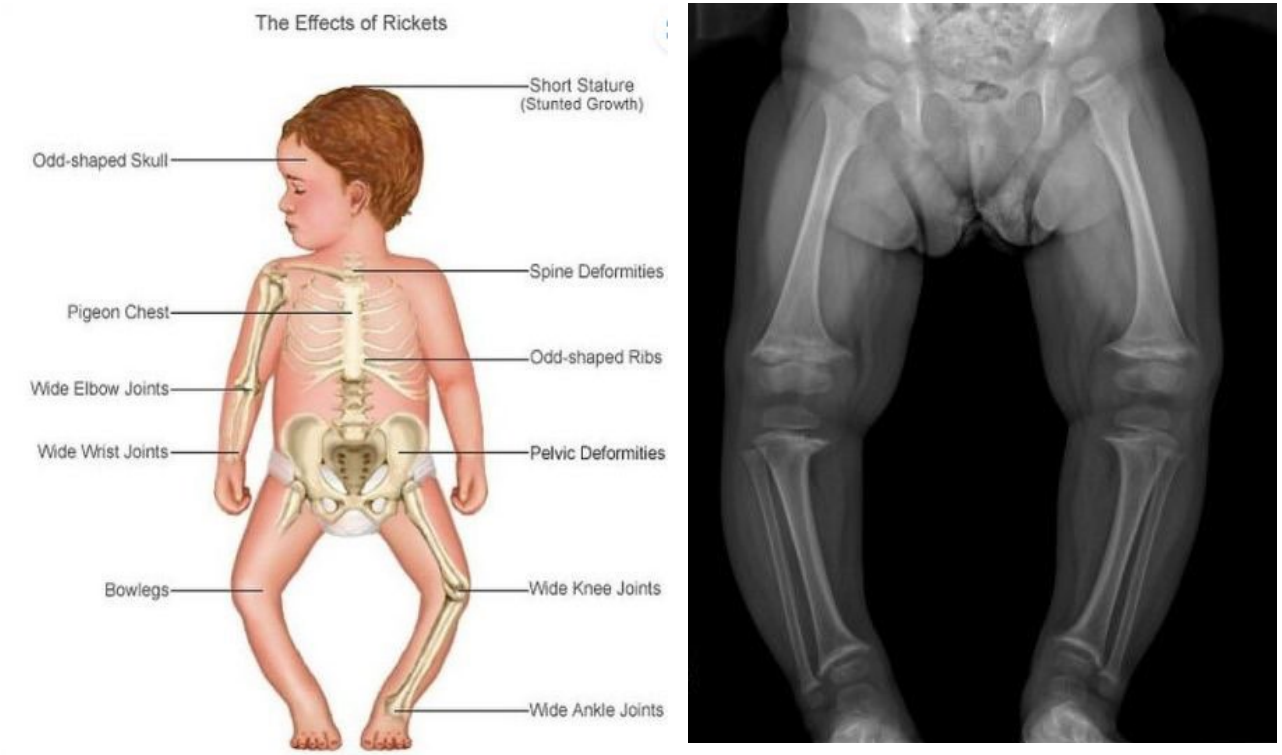
According to the food pyramid from Harvard T.H. Chan School of Public Health's Public Health Dietary Guidelines, it is difficult to get enough vitamin D from food alone. It is recommended to take vitamin D supplements when there is insufficient vitamin D from naturally occurring sources.

GCOOP

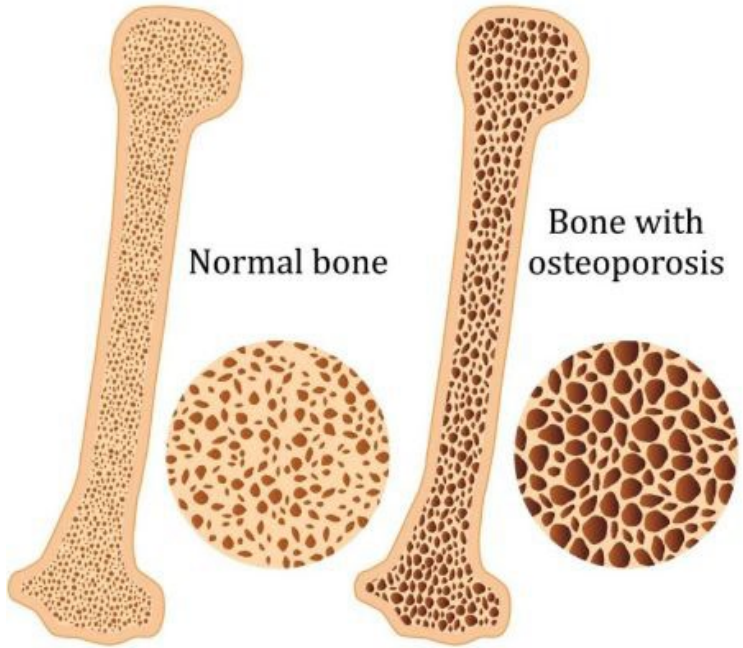
Vitamin D

The Latest Research

Conditions Caused by Vitamin D Deficiency: Rickets and Osteoporosis



Rickets



Osteoporosis

Vitamin D is not a vitamin. It is a hormone

A hormone is a chemical that is synthesized and secreted by an endocrine gland to regulate the physiology of a specific tissue or organ. Vitamin D is a steroidal hormone that is synthesized by the skin in response to sunlight.

Vitamin D was thought to be just for bone health and osteoporosis prevention.

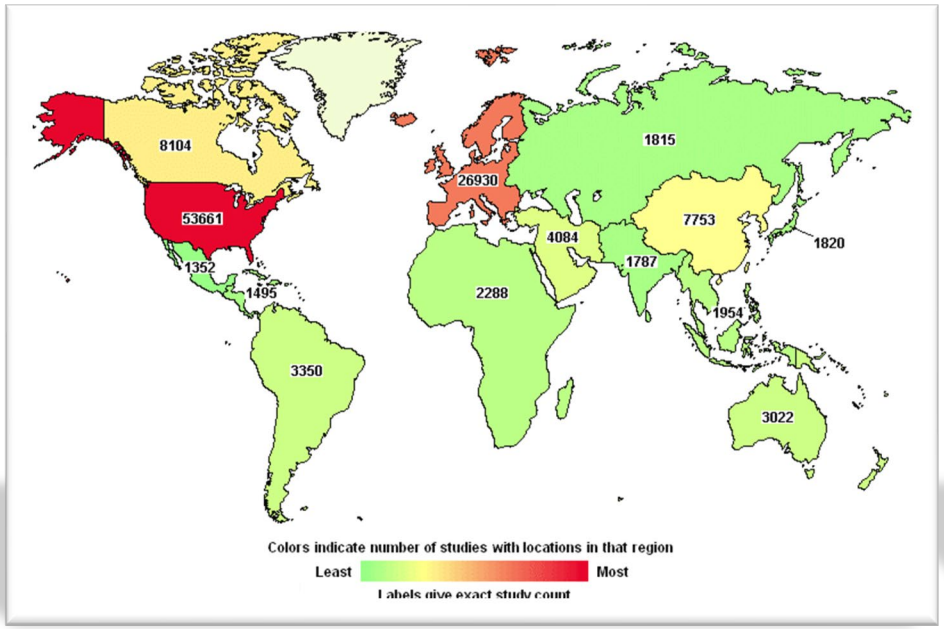
Since then, it has been gaining attention in the medical community.

Check 01. A number of shocking studies on vitamin D deficiency have been published.

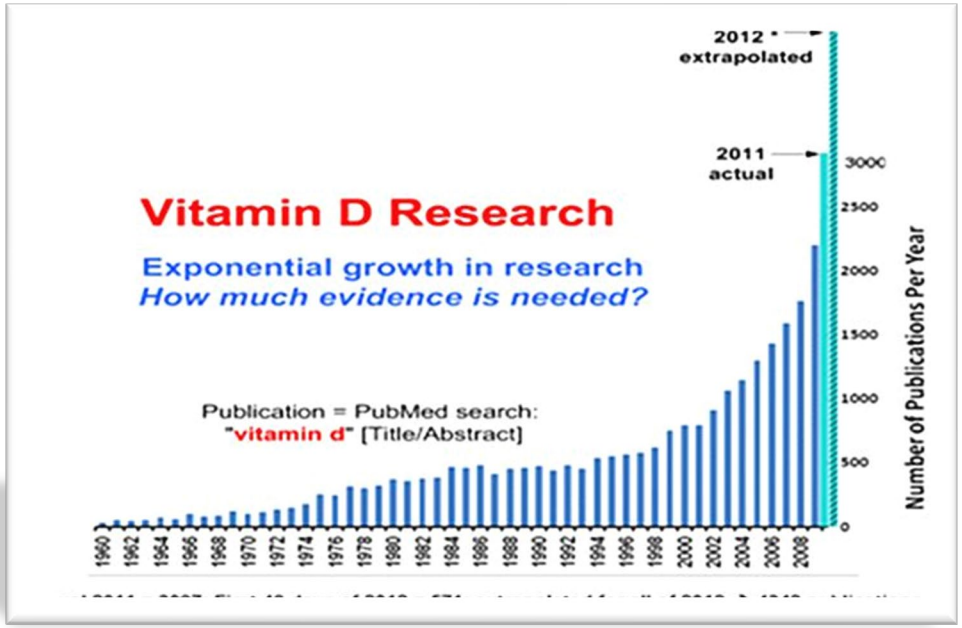
Check 02. It has been found that vitamin D not only affects the musculoskeletal system, but is also linked to numerous diseases including cancer, cardiovascular disease, and diabetes.

Check 03. Vitamin D tests have become more common

Ongoing Worldwide Research on Vitamin D

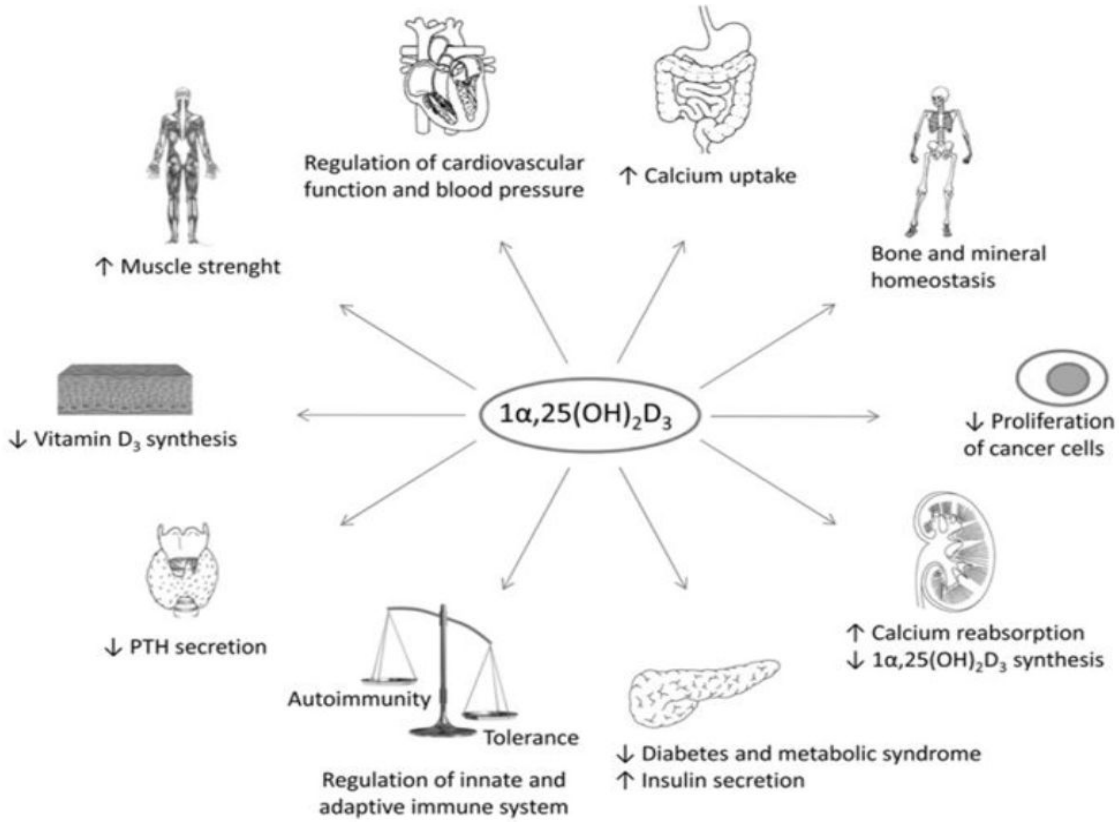


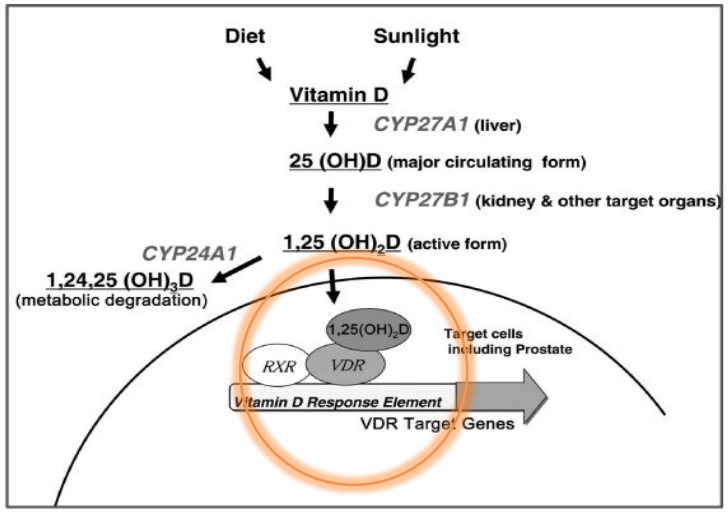
→ 106,065 clinical trials on vitamin D (2011)



Source : Endocrinol Metab Clin N Am 41 (2012) 571-594

New Research Suggests Vitamin D Affects All Diseases



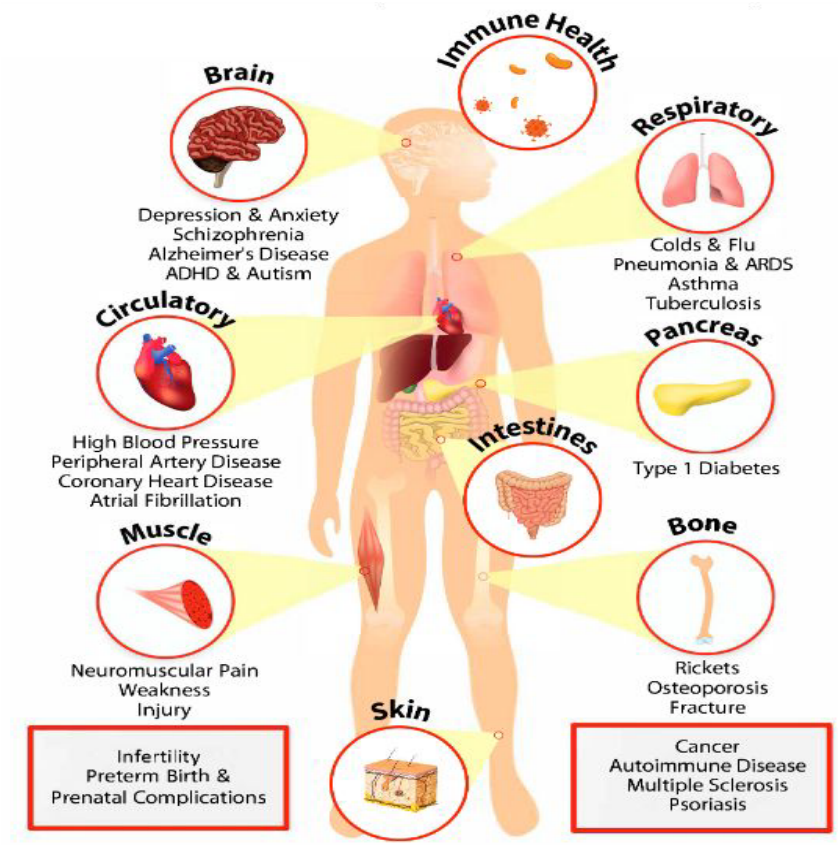


Vitamin D from food or ultraviolet light is eventually converted to the active form, 1,25(OH)2D, which is transported in blood into the cells where it is needed. It triggers specific protein genetic information in the DNA to help synthesize the proteins needed for that organ. In summary, vitamin D can affect disease prevention as it affects all cells with a VDR, not just bones cells.

Source : Endocrinol Metab Clin N Am 41 (2012) 571-594

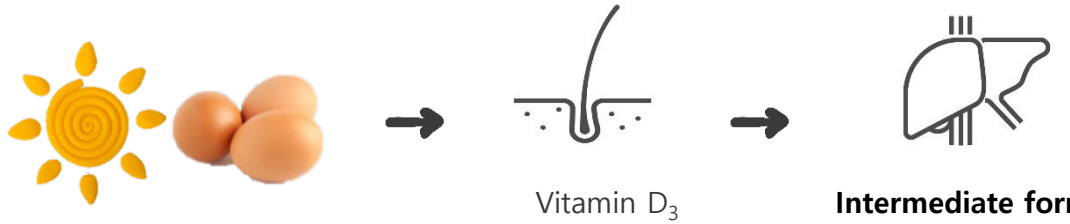
VITAMIN D DEFICIENCY

Affects Every Part of the Body



"Vitamin D is an Entire-Body Hormone"

Newly discovered processes of synthesis and metabolism



Vitamin D_3
(cholecalciferol)

Intermediate form
25-hydroxyvitamin D3

Vitamin D receptors are present in each organ. They become active and "transcribe genes" (make what they need). The medical community has been investigating the role of vitamin D receptors in the body.

thermoscientific

APPLICATION NOTE

22053

Vitamin D biomarkers in plasma

Sensitive, reproducible quantitation with SOLA HRP 30 mg SPE for clinical research

Author: Matthew Franklin
Thermo Fisher Scientific, Runcorn, UK

Keywords: 25-hydroxyvitamin D_3, 25-hydroxyvitamin D_2, SPE, solid phase extraction, LC, vitamin D, bioanalysis, triple quad, quantitation, Vanquish Horizon UHPLC system, MS/MS, Hypersil GOLD, VANQUISH, C18, SOLA, HRP, 30 mg, HRP hydrophobic retention, TSQ Quantiva, clinical research

Goal

Maximizing the sensitivity of vitamin D biomarker quantitation assay in human plasma by leveraging Thermo Scientific™ SOLA™ HRP solid phase extraction (SPE). Analysis carried out on the Thermo Scientific™ Vanquish™ Horizon UHPLC system and Thermo Scientific™ TSQ Quantiva™ mass spectrometer with the Thermo Scientific™ Hypersil GOLD™ VANQUISH™ C18 UHPLC column, 1.9 µm, 2.1 × 50 mm, for developing a fast, robust, reliable LC-MS method.

Introduction

Solid-phase extraction (SPE) is an efficient extraction technique to separate critical analytes that are dissolved or suspended in a liquid mixture according to their physical and chemical properties. The extraction detailed here from human plasma is carried out using SOLA HRP 30 mg cartridges. Its revolutionary design is specifically tailored for processing biological samples and helps reduce blocking and sample failures.

Vitamin D is widely monitored and used as an indicator for skeletal health in both children and adults. The active form of the hormone controls the concentration of calcium and phosphorous in the bloodstream, with deficiencies resulting in both rickets in children and osteoporosis in adults. Vitamin D occurs in two forms: vitamin D_2 (ergocalciferol) is found naturally in plants and is commonly used as a dietary supplement; vitamin D_3 (cholecalciferol) occurs naturally in mammals and is formed in the skin by exposure to sunlight.

Vitamin D_2 and vitamin D_3 are hydroxylated in the liver to form 25-hydroxyvitamin D_2 (OH-Vit D_2) and 25-hydroxyvitamin D_3 (OH-Vit D_3). Figure 1. These two forms of the compounds are then released into the circulation and transported via the vitamin D binding protein.

ThermoFisher SCIENTIFIC

비타민 D 작용에 대한 새로운 조명

Review

최희정*

을지대학교 의과대학 가정의학교실

New Insight into the Action of V

Hee-Jeong Choi*

Department of Family Medicine, Eulji University School

Vitamin D deficiency is now recognized as a pand
Traditionally, vitamin D has been associated prin
that adequate vitamin D status is important for o
discovery has provided new insights into the acti
association between vitamin D deficiency and th
diabetes, cancers, autoimmune diseases, and infec
Large randomized controlled trials are needed
diseases. Vitamin D deficiency and insufficiency
Recommendation of adequate vitamin D intake sh
In this article, I review its role in skeletal and ext
musculoskeletal system, cardiometabolic health, ir
and treatment of vitamin D deficiency.

Keywords: Vitamin D; Vitamin D Deficiency; Sunligh

Continuing Education Column

J Korean Med Assoc 2013 April; 56(4): 310-318
http://dx.doi.org/10.5124/jkma.2013.56.4.310
pISSN: 1975-8456 eISSN: 2093-5951
http://jkma.org

비타민 D에 대한 최신지견

박 현 아[1] · 김 수 영[2*] | [1]인제대학교 의과대학 서울백병원 가정의학과, [2]한림대학교 의과대학 강동성심병원 가정의학과

Recent advance on vitamin D

Hyun Ah Park, MD[1] · **Soo Young Kim, MD**[2*]

Department of Family Medicine, [1]Seoul Paik Hospital, Inje University College of Medicine, [2]Kangdong Sacred Heart Hospital, Hallym University College of Medicine, Seoul, Korea

***Corresponding author:** Soo Young Kim, E-mail: pclove@hallym.or.kr

Received March 11, 2013 · Accepted March 25, 2013

Vitamin D is not only a nutrient, but also a hormone that affects the musculoskeletal system. Recently, extensive attention has been drawn to the autocrine and paracrine functions of vitamin D. Consequently, its extraskeletal effect and its known effects on the skeletal system have drawn particular interest. The socioeconomic development and aging of the population of Korea have also raised interest in dietary supplements. Because vitamin D deficiency is high among Koreans, both physicians and patients are questioning whether vitamin D supplements are needed. This review assessed the skeletal and extraskeletal efficacy of vitamin D with regard to mortality, cancer, cardiovascular disease, and diabetes via an evidence-based approach. The recent interest surrounding vitamin D can be expected to motivate many more studies on its effects and adverse effects, and accordingly, the level of evidence and recommendations will be adjusted. Clinicians should familiarize themselves with updated evidence about vitamin D, and must counsel patients with that evidence in mind.

Keywords: Vitamin D; Evidence-based medicine; Accidental falls; Osteoporosis; Neoplasms; Mortality; Cardiovascular diseases

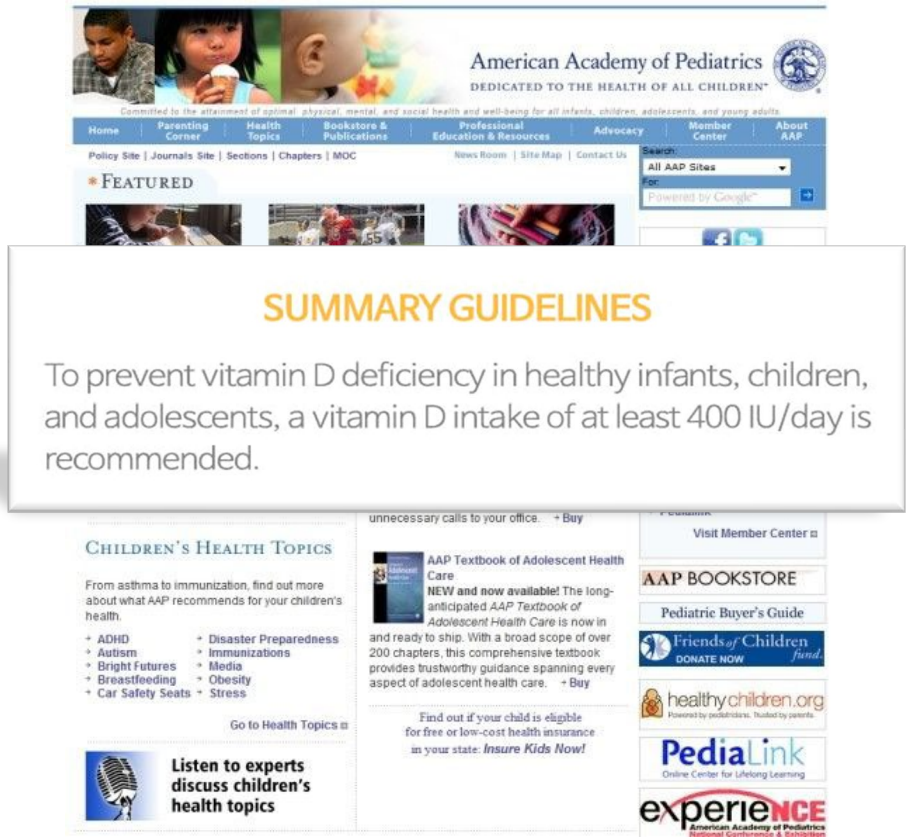
New research has proven that vitamin D is linked to a variety of diseases with the presence of vitamin D receptors (VDR) in multiple organs within the body.

American Academy of Pediatrics
DEDICATED TO THE HEALTH OF ALL CHILDREN™

The American Academy of Pediatrics recommends vitamin D supplementation [starting at birth]

In 2008, the American Academy of Pediatrics doubled the recommended daily intake for vitamin D from 200 IU to 400 IU for newborns to teenagers.
Announced at the American Academy of Pediatrics meeting in Boston on March 13. This change was since Vitamin D is not only important for maintaining healthy bones, but also in reducing the risk of many diseases, including cancer, diabetes, and heart disease.

"The new intake recommendations are targeted at babies who are exclusively breastfed or who receive a combination of breast milk and formula and children who drink little or no milk, who would need to get will need to take a vitamin D supplement to meet the 400 IU/day requirement."



SPECIAL FEATURE

Clinical Practice Guideline

Evaluation, Treatment, and Prevention of Vitamin D Deficiency: an Endocrine Society Clinical Practice Guideline

Michael F. Holick, Neil C. Binkley, Heike A. Bischoff-Ferrari, Catherine M. Gordon, David A. Hanley, Robert P. Heaney, M. Hassan Murad, and Connie M. Weaver

Boston University School of Medicine (M.F.H.), Boston, Massachusetts 02118; University of Wisconsin (N.C.B.), Madison, Wisconsin 53706; University Hospital Zurich (H.A.B.-F.), CH-8091 Zurich, Switzerland; Children's Hospital Boston (C.M.G.), Boston, Massachusetts 02115; University of Calgary Faculty of Medicine (D.A.H.), Calgary, Alberta, Canada T2N 1N4; Creighton University (R.P.H.), Omaha, Nebraska 68178; Mayo Clinic (M.H.M.), Rochester, Minnesota 55905; and Purdue University (C.M.W.), West Lafayette, Indiana 47907

Objective: The objective was to provide guidelines to clinicians for the evaluation, treatment, and prevention of vitamin D deficiency with an emphasis on the care of patients who are at risk for deficiency.

Participants: The Task Force was composed of a Chair, six additional experts, and a methodologist. The Task Force received no corporate funding or remuneration.

Consensus Process: Consensus was guided by systematic reviews of evidence and discussions during several conference calls and e-mail communications. The draft prepared by the Task Force was reviewed successively by The Endocrine Society's Clinical Guidelines Subcommittee, Clinical Affairs Core Committee, and cosponsoring associations, and it was posted on The Endocrine Society web site for member review. At each stage of review, the Task Force received written comments and incorporated needed changes.

Conclusions: Considering that vitamin D deficiency is very common in all age groups and that few foods contain vitamin D, the Task Force recommended supplementation at suggested daily intake and tolerable upper limit levels, depending on age and clinical circumstances. The Task Force also suggested the measurement of serum 25-hydroxyvitamin D level by a reliable assay as the initial diagnostic test in patients at risk for deficiency. Treatment with either vitamin D_2 or vitamin D_3 was recommended for deficient patients. At the present time, there is not sufficient evidence to recommend screening individuals who are not at risk for deficiency or to prescribe vitamin D to attain the noncalcemic benefit for cardiovascular protection. (*J Clin Endocrinol Metab* 96: 1911–1930, 2011)

TABLE 3. Vitamin D intakes recommended by the IOM and the Endocrine Practice Guidelines Committee

Life stage group	IOM recommendations				Committee recommendations for patients at risk for vitamin D deficiency	
	AI	EAR	RDA	UL	Daily requirement	UL
Infants						
0 to 6 months	400 IU (10 μg)			1,000 IU (25 μg)	400–1,000 IU	2,000 IU
6 to 12 months	400 IU (10 μg)			1,500 IU (38 μg)	400–1,000 IU	2,000 IU
Children						
1–3 yr		400 IU (10 μg)	600 IU (15 μg)	2,500 IU (63 μg)	600–1,000 IU	4,000 IU
4–8 yr		400 IU (10 μg)	600 IU (15 μg)	3,000 IU (75 μg)	600–1,000 IU	4,000 IU
Males						
9–13 yr		400 IU (10 μg)	600 IU (15 μg)	4,000 IU (100 μg)	600–1,000 IU	4,000 IU
14–18 yr		400 IU (10 μg)	600 IU (15 μg)	4,000 IU (100 μg)	600–1,000 IU	4,000 IU
19–30 yr		400 IU (10 μg)	600 IU (15 μg)	4,000 IU (100 μg)	1,500–2,000 IU	10,000 IU
31–50 yr		400 IU (10 μg)	600 IU (15 μg)	4,000 IU (100 μg)	1,500–2,000 IU	10,000 IU
51–70 yr		400 IU (10 μg)	600 IU (15 μg)	4,000 IU (100 μg)	1,500–2,000 IU	10,000 IU
>70 yr		400 IU (10 μg)	800 IU (20 μg)	4,000 IU (100 μg)	1,500–2,000 IU	10,000 IU
Females						
9–13 yr		400 IU (10 μg)	600 IU (15 μg)	4,000 IU (100 μg)	600–1,000 IU	4,000 IU
14–18 yr		400 IU (10 μg)	600 IU (15 μg)	4,000 IU (100 μg)	600–1,000 IU	4,000 IU
19–30 yr		400 IU (10 μg)	600 IU (15 μg)	4,000 IU (100 μg)	1,500–2,000 IU	10,000 IU
31–50 yr		400 IU (10 μg)	600 IU (15 μg)	4,000 IU (100 μg)	1,500–2,000 IU	10,000 IU
51–70 yr		400 IU (10 μg)	600 IU (15 μg)	4,000 IU (100 μg)	1,500–2,000 IU	10,000 IU
>70 yr		400 IU (10 μg)	800 IU (20 μg)	4,000 IU (100 μg)	1,500–2,000 IU	10,000 IU
Pregnancy						
14–18 yr		400 IU (10 μg)	600 IU (15 μg)	4,000 IU (100 μg)	600–1,000 IU	4,000 IU
19–30 yr		400 IU (10 μg)	600 IU (15 μg)	4,000 IU (100 μg)	1,500–2,000 IU	10,000 IU
31–50 yr		400 IU (10 μg)	600 IU (15 μg)	4,000 IU (100 μg)	1,500–2,000 IU	10,000 IU
Lactation[a]						
14–18 yr		400 IU (10 μg)	600 IU (15 μg)	4,000 IU (100 μg)	600–1,000 IU	4,000 IU
19–30 yr		400 IU (10 μg)	600 IU (15 μg)	4,000 IU (100 μg)	1,500–2,000 IU	10,000 IU
31–50 yr		400 IU (10 μg)	600 IU (15 μg)	4,000 IU (100 μg)	1,500–2,000 IU	10,000 IU

AI, Adequate intake; EAR, estimated average requirement; UL, tolerable upper intake level.

[a] Mother's requirement, 4,000–6,000 IU/d (mother's intake for infant's requirement if infant is not receiving 400 IU/d).

Those at risk of vitamin D deficiency

In June 2011, experts from the American College of Endocrinology issued new guidelines for the diagnosis, treatment, and prevention of vitamin D deficiency. The minimum recommended intake of vitamin D is 600 IU for people ages 19-70, 800 IU for those over 70, and 600 IU for pregnant and lactating women. The guidelines also emphasize the benefits of vitamin D in the treatment and prevention of bone conditions and osteoporosis, as well as a variety of other diseases.

| Vitamin D and Obesity |

Causal Relationship between Obesity and Vitamin D Status: Bi-Directional Mendelian Randomization Analysis of Multiple Cohorts

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Abstract

Background: Obesity is associated with vitamin D deficiency, and both are areas of active public health concern. We explored the causality and direction of the relationship between body mass index (BMI) and 25-hydroxyvitamin D [25(OH)D] using genetic markers as instrumental variables (IVs) in bi-directional Mendelian randomization (MR) analysis.

Methods and Findings: We used information from 21 adult cohorts (up to 42,024 participants) with 12 BMI-related SNPs (combined in an allelic score) to produce an instrument for BMI and four SNPs associated with 25(OH)D (combined in two allelic scores, separately for genes encoding its synthesis or metabolism) as an instrument for vitamin D. Regression estimates for the IVs (allele scores) were generated within-study and pooled by meta-analysis to generate summary effects. Associations between vitamin D scores and BMI were confirmed in the Genetic Investigation of Anthropometric Traits (GIANT) consortium ($n = 123,864$). Each 1 kg/m^2 higher BMI was associated with 1.15% lower 25(OH)D ($p = 6.52 \times 10^{-27}$). The BMI allele score was associated both with BMI ($p = 6.30 \times 10^{-62}$) and 25(OH)D (−0.06% [95% CI −0.10 to −0.02], $p = 0.004$) in the cohorts that underwent meta-analysis. The two vitamin D allele scores were strongly associated with 25(OH)D ($p \leq 8.07 \times 10^{-57}$ for both scores) but not with BMI (synthesis score, $p = 0.88$; metabolism score, $p = 0.08$) in the meta-analysis. A 10% higher genetically instrumented BMI was associated with 4.2% lower 25(OH)D concentrations (IV ratio: −4.2 [95% CI −7.1 to −1.3], $p = 0.005$). No association was seen for genetically instrumented 25(OH)D with BMI, a finding that was confirmed using data from the GIANT consortium ($p \geq 0.57$ for both vitamin D scores).

Conclusions: On the basis of a bi-directional genetic approach that limits confounding, our study suggests that a higher BMI leads to lower 25(OH)D, while any effects of lower 25(OH)D increasing BMI are likely to be small. Population level interventions to reduce BMI are expected to decrease the prevalence of vitamin D deficiency.

Please see later in the article for the Editors' Summary.

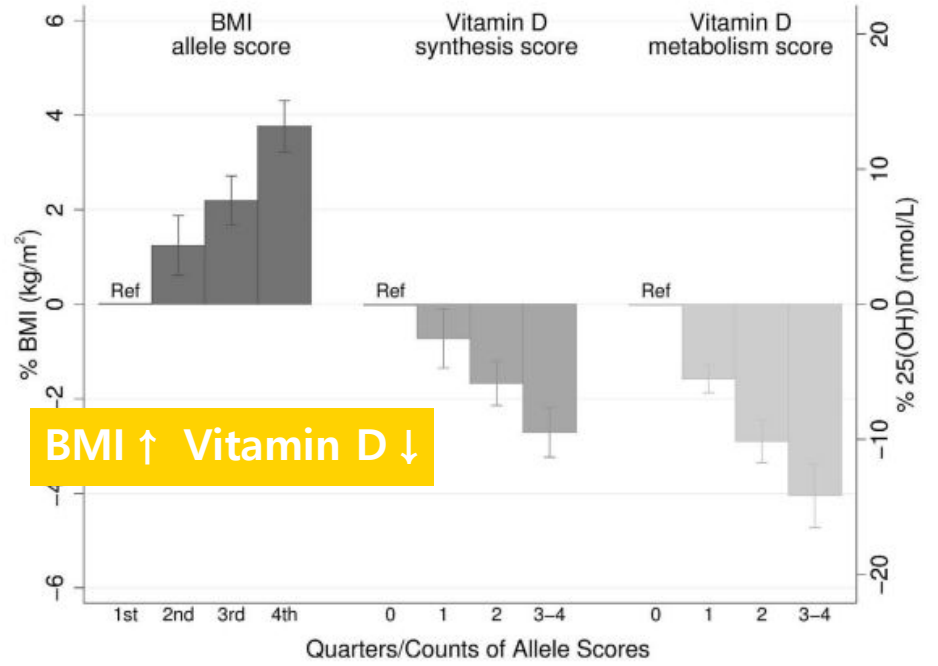

Figure 2. Meta-analysis of the BMI allele score association with BMI ($n = 32,391$), and the vitamin D synthesis ($n = 35,873$) and metabolism ($n = 38,191$) allele score association with 25(OH)D. 95% confidence intervals given by error bars.
doi:10.1371/journal.pmed.1001383.g002

For every 1-point increase in BMI, vitamin D levels decrease by 1.15%

| Vitamin D and Obesity |

Vitamin D can lower weight, blood sugar via the brain, study finds

Date: June 23, 2014

Source: Endocrine Society

Summary: Vitamin D treatment acts in the brain to improve weight and blood glucose (sugar) control in obese rats, according to a new study. "Vitamin D deficiency occurs often in obese people and in patients with Type 2 diabetes, yet no one understands if it contributes to these diseases," said the study's principal investigator. A region of the brain called the hypothalamus controls both weight and glucose, and has vitamin D receptors there.

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FULL STORY

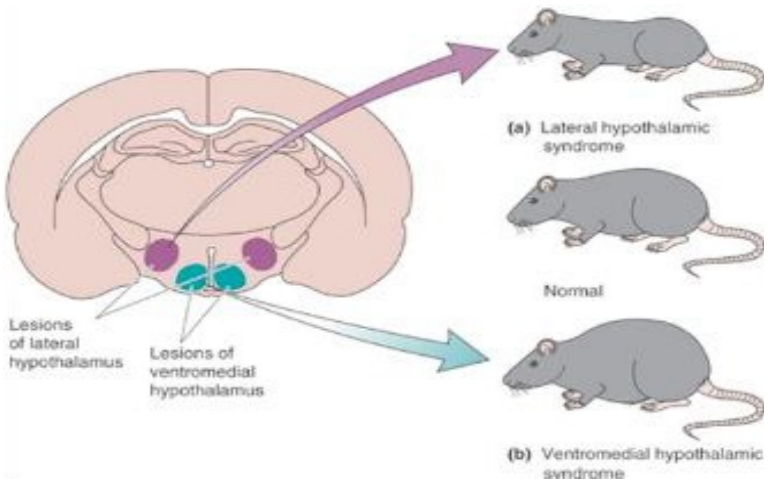
Vitamin D treatment acts in the brain to improve weight and blood glucose (sugar) control in obese rats, according to a new study being presented Saturday at the joint meeting of the International Society of Endocrinology and the Endocrine Society: ICE/ENDO 2014 in Chicago.

"Vitamin D deficiency occurs often in obese people and in patients with Type 2 diabetes, yet no one understands if it contributes to these diseases," said Stephanie Sisley, MD, the study's principal investigator and an assistant professor at Baylor College of Medicine, Houston. "Our results suggest that vitamin D may play a role in the onset of both obesity and Type 2 diabetes by its action in the brain."

"The brain is the master regulator of weight," Sisley said. A region of the brain called the hypothalamus controls both weight and glucose, and has vitamin D receptors there.

In this study funded by the National Institutes of Health, Sisley and partners at the University of Cincinnati delivered vitamin D directly

Weight & Blood Sugar Control through the Brain



Results

Vitamin D was injected into the hypothalamus of the brain of obese rats for 28 days and compared to a control group. The vitamin D group did not eat three times as much as the control group and lost 24% of their body weight in 28 days. In contrast, the control group's weights did not change at all. There are receptors in the brain's hypothalamus that vitamin D uses to regulate body weight and reduce blood sugar. Injecting vitamin D into this hypothalamus has been shown to reduce weight and lower blood sugar.

| Vitamin D and Diabetes |

National Institute of Health, Helsinki, Finland, 2007
Analysis of 4,000 people followed for 17 years

Vitamin D conc. ↑ Risk of Diabetes ↓

Serum 25-Hydroxyvitamin D Concentration and Subsequent Risk of Type 2 Diabetes

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It has been suggested that vitamin D reduces the risk of type 2 diabetes. The finding that vitamin D deficiency is associated with impaired β-cell function and insulin resistance in animals (1,2) and humans (3,4) is in line with that hypothesis. In the only cohort study published, the intake of vitamin D supplements was inversely associated with the development of type 2 diabetes (5). Since vitamin D intake covers only a part of the total vitamin D available, the purpose of this study was to evaluate the prediction of serum 25-hydroxyvitamin D (25OHD) on subsequent type 2 diabetes incidence.

RESEARCH DESIGN AND METHODS — The study population, collected from 1978 to 1980 as part of the Mini-Finland Health Survey (6), consisted of 4,423 men and women aged 40–69 years. After exclusion of 247 individuals with type 2 diabetes at baseline (i.e., fasting plasma glucose >7.0 mmol/l on two occasions or >11.0 mmol/l on a single occasion) and 79 individuals with missing values of serum 25OHD, the final sample size was 4,097. Data on education, smoking, leisure-time exercise, and hypertension medication were collected in a health examination (6). Height, weight, and blood pressure were measured, and blood samples were collected and stored at −20°C. In 2003–2004, radioimmunoassay (^{125}I RIA kit; DiaSorin, Stillwater, MN) was used to assess serum 25OHD in thawed samples. The coefficient of variation for serum 25OHD varied from 8 to 13%. During 17 years of follow-up, 187 incident type 2 diabetes cases were identified from a nationwide registry of patients receiving medication reimbursement (7), and these cases were linked to the study population by the unique social security numbers assigned to Finnish citizens.

Relative risks of type 2 diabetes between quartiles of serum 25OHD, adjusted for confounding factors, were estimated using Cox's model. The follow-up time was defined as the time from the baseline examination to the date of type 2 diabetes occurrence, death, or end of follow-up—whichever came first. Four models were defined (Table 1). The calculations were performed with SAS (version 9.1.3; SAS Institute, Cary, NC).

RESULTS — The proportion of men was 47%, the mean age 53 years, and the mean ± SD serum 25OHD concentration 43.6 ± 19.5 nmol/l. The correlation coefficients between serum 25OHD and type 2 diabetes risk factors were low, varying from −0.13 to 0.21. Participants in the highest serum 25OHD quartile had lower BMIs than those in the lowest quartile (26.0 vs. 26.4 kg/m^2; $P_{heterogeneity} < 0.001$). After adjustment for age, sex, and the month when the blood samples were collected, a statistically significant inverse association was observed between serum 25OHD concentration and incidence of type 2 diabetes. The relative risk (RR) between the highest and lowest serum 25OHD quartile was 0.60 (95% CI 0.36–0.98; $P_{trend} = 0.01$) (Table 1). This association was attenuated after further adjustments for BMI, leisure-time exercise, smoking, and education (RR 0.70 [95% CI 0.42–1.16]; $P_{trend} = 0.07$). The inclusion of blood pressure or exclusion of the first 5 years of follow-up did not notably alter the results.

CONCLUSIONS — We found a significant inverse association between serum 25OHD and risk of type 2 diabetes in the simple model. However, the association was attenuated in the multivariate analysis, adjusting for potential risk factors of type 2 diabetes. To our knowledge, this is the first cohort study investigating the association between serum 25OHD and incidence of type 2 diabetes. Our results are in line with those from the Nurses' Health Study (5), where an inverse association was observed for the intake of vitamin D supplements. We could not differentiate whether the results depended on the effect of vitamin D deficiency on β-cell function or on insulin resistance.

The strengths of this study include its longitudinal design and the use of serum 25OHD concentration as an indicator of vitamin D status, reflecting vitamin D obtained from diet, supplements, and cutaneous synthesis (8). Also, several limitations are related to the use of serum 25OHD. First, 25OHD levels in one individual fluctuate from one season to another. Blood samples were collected only once, and this took place throughout the year except for high summer, which means that the 25OHD levels for individuals might not be fully comparable. However, adjustment for time when blood samples were collected did not notably change the results. Second, the serum samples were stored at −20°C before assessing 25OHD. It cannot be excluded that the 25OHD concentrations might change during storage (9). In one study (10), the average plasma 25OHD concentration was significantly lowered during storage at −18°C, whereas another study (11) did not observe any notable changes. Our earlier study indicated good stability for selenium and α-tocopherol (12), which gives indirect evidence about the stability of 25OHD in our serum samples. Third, we observed low average serum 25OHD concentrations compared with those of other cohorts

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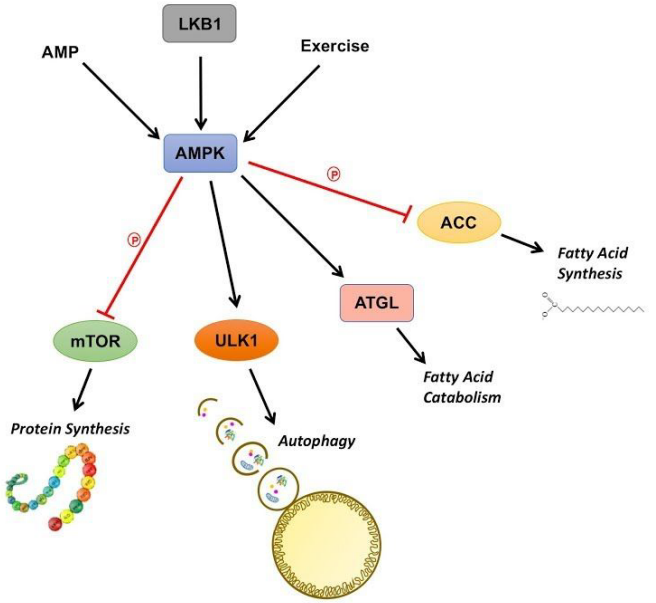
Abbreviations: 25OHD, 25-hydroxyvitamin D.
A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

2 Cade C, Norman AW: Vitamin D3 improves impaired glucose tolerance and in-
8 Standing Committee on the Scientific Evaluation of Dietary Reference Intakes FaNB. Institute of Medicine: *Dietary Ref-*
Stockell JE, Skeaff CM, Williams SM, Green TJ: Serum 25-hydroxyvitamin D concentrations of New Zealanders aged 15 years and older. *Osteoporos Int* 17:1382–1389, 2006

AMPK Signaling Pathway

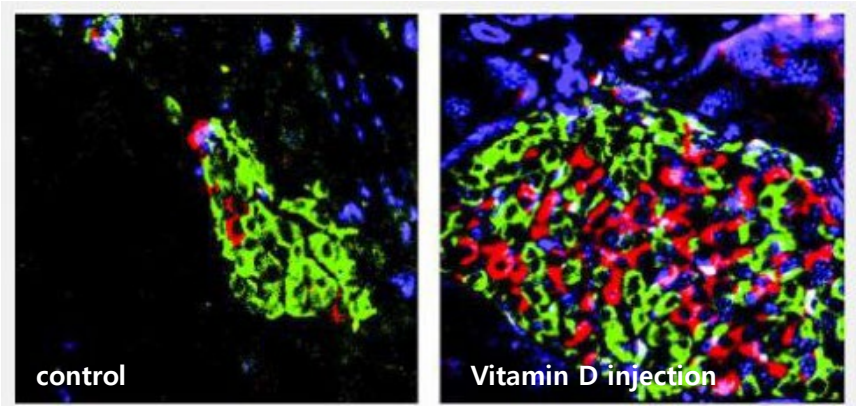


JJ MedEd

Vitamin D has been shown to be involved in the enzyme AMPK, an enzyme that reduces insulin resistance.

| Vitamin D and Diabetes |

Studies using human cells and laboratory mouse models have shown that vitamin D is useful in treating damaged beta cells.



Enhanced vitamin D activity inhibits the progression of type 2 diabetes in animal models. On the left are the damaged insulin-positive beta cells (red) in the pancreas of a rat with diabetes. On the right, the beta cells are protected by the combination of vitamin D activator and BRD9 inhibitor.

Article

Cell

Vitamin D Switches BAF Complexes to Protect β Cells

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https://doi.org/10.1016/j.cell.2018.04.013

SUMMARY

A primary cause of disease progression in type 2 diabetes (T2D) is β cell dysfunction due to inflammatory stress and insulin resistance. However, preventing β cell exhaustion under diabetic conditions is a major therapeutic challenge. Here, we identify the vitamin D receptor (VDR) as a key modulator of inflammation and β cell survival. Alternative recognition of an acetylated lysine in VDR by bromodomain proteins BRD7 and BRD9 directs association to PBAF and BAF chromatin remodeling complexes, respectively. Mechanistically, ligand promotes VDR association with PBAF to effect genome-wide changes in chromatin accessibility and enhancer landscape, resulting in an anti-inflammatory response. Importantly, pharmacological inhibition of BRD9 promotes PBAF-VDR association to restore β cell function and ameliorate hyperglycemia in murine T2D models. These studies reveal an unrecognized VDR-dependent transcriptional program underpinning β cell survival and identifies the VDR:PBAF/BAF association as a potential therapeutic target for T2D.

INTRODUCTION

Already at epidemic proportions, the incidence of type 2 diabetes (T2D) is expected to continue largely unabated over the coming decades. Initiated by insulin resistance, β cell dysfunction is characterized by defective insulin secretion, endoplasmic reticulum (ER) stress, eventual β cell loss, and disease progression (Ashcroft and Rorsman, 2012; Donath et al., 2013; Halban et al., 2014; Weyer et al., 1999). Although many therapeutic approaches are deployed to combat hyperglycemia, few (if any) treatments directly target β cell pathogenesis. Thus, long-term control of disease progression remains a persistent challenge.

Although the molecular underpinnings of obesity-induced β cell dysfunction are poorly understood, progress is being made. Increasing evidence links inflammation and specifically, the innate immune response of pancreatic islets to metabolic stress, to T2D progression (Donath and Shoelson, 2011; Fernández-Real and Pickup, 2012; Imai et al., 2013). In particular, inflammatory stress associated with increased interleukin 1β (IL1β) and other cytokines reduces insulin secretion and leads to β cell damage and loss of identity (Herder et al., 2015). Blocking IL1β signaling by antagonists has shown modest β cell functional improvement, although the long term efficacy remains to be determined (Donath et al., 2013).

While vitamin D is widely known for its role in bone homeostasis, interest in its anti-inflammatory potential continues to grow. In addition, epidemiological and human genetic studies linking vitamin D and the VDR to both type 1 and 2 diabetes (Takiishi et al., 2010), suggest a potential therapeutic role in diabetes (Baeke et al., 2010; Bouillon et al., 2008; Cantorna et al., 2004). Indeed, vitamin D supplements are claimed to reverse many diabetic phenotypes in T1D rodent models by suppressing auto-immunity (Del Pino-Montes et al., 2004; Mathieu et al., 1994). However, a therapeutic benefit in type 2 diabetic patients (or rodents) has yet to be established (Takiishi et al., 2010). Distinct from the general role in suppressing bone-derived innate and adaptive immune cells, the function of VDR in β cells remains unclear. Moreover, although VDR has been shown to be involved in anti-inflammatory responses in various contexts (Ding et al., 2013; Sherman et al., 2014), how VDR responds to signals and initiates the downstream transcriptional cascade at the chromatin level remains largely a mystery.

Bromodomain-containing proteins 7 (BRD7) and 9 (BRD9) are closely related members of a diverse nuclear and cytoplasmic family of proteins that recognize acetylated lysines (Filippakopoulos and Knapp, 2014). Interestingly, BRD9 has recently

| Vitamin D and Diabetes |

Clinical trial in Koreans, jointly published by Seoul National University and Harvard Medical School, USA, 2013

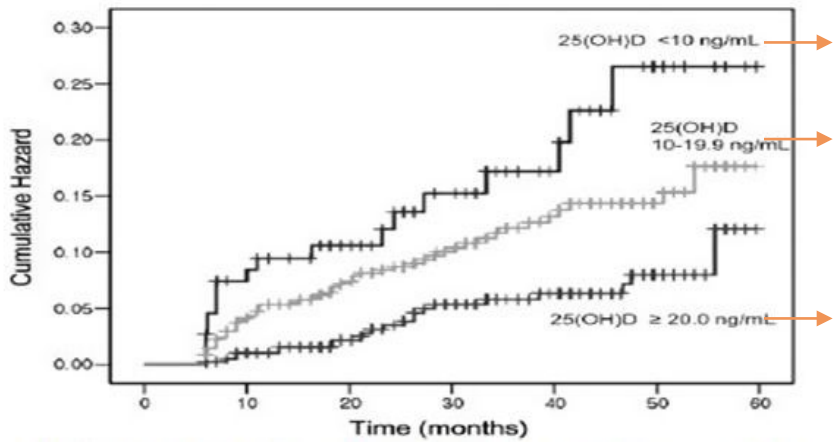


FIGURE 1. Kaplan-Meier plot for incident type 2 diabetes according to 25(OH)D status: <10, 10–19.9, and ≥20.0 ng/mL. 25(OH)D, 25-hydroxyvitamin D.

Blood level under 10ng/mL

Blood level under 10-19ng/mL

Blood level under 20ng/mL

25(OH)D ng/mL	Over 20	10~20	Under 10
Model 1	1	1.84	3.22
Model 2	1	1.8	3.25
Model 3	1	2.06	3.23

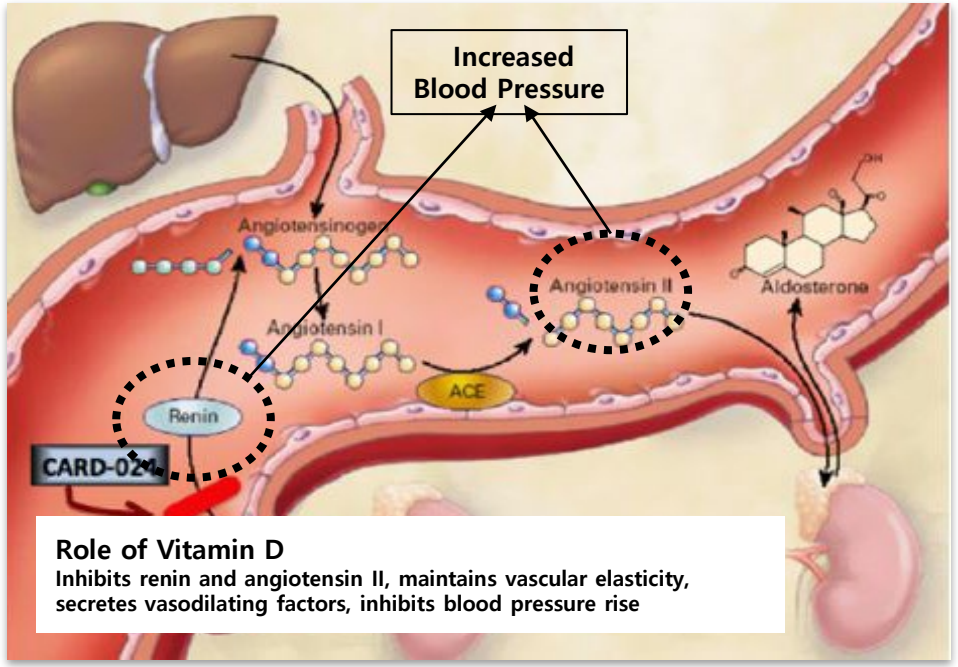
*MV : Age, gender, tobacco and alcohol use, exercise level, lifestyle/hypertension/hyperlipidemia
Model 1 : considers MV
Model 2 : considers MV and obesity
Model 3 : considers MV and obesity, insulin resistance (IR) and insulin secretion rate (IGI)

* Blood level of 20ng/mL classified as normal

Those with lower blood vitamin D levels are more likely to develop type 2 diabetes. Even without risk factors such as obesity, high blood pressure, or high cholesterol, low blood vitamin D levels have been shown to cause type 2 diabetes.

Low vitamin D levels were associated with a 3.2-fold increased risk of diabetes after 5 years.

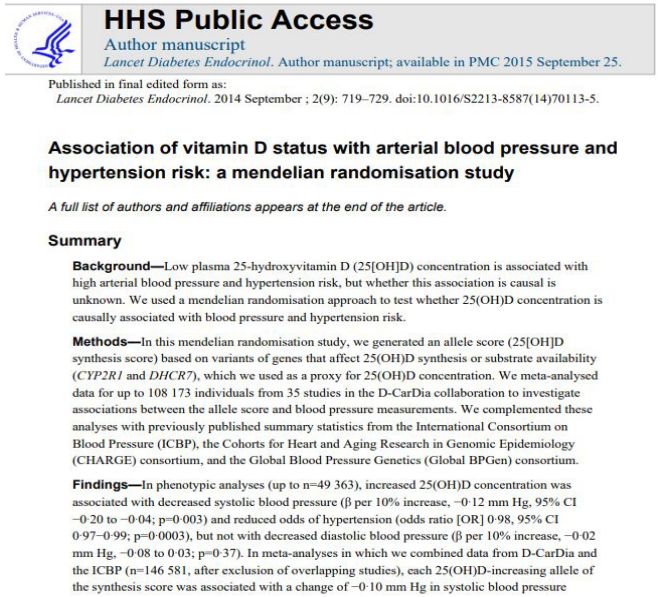
| Vitamin D and Hypertension |



Blood Vitamin D Level	Hypertension Risk Factor
Over 30 ng/mL	1.0
Over 15 ng/mL	2.67

Blood vitamin D conc. ↓ 2.67 times the risk of hypertension

| A collaborative study including Oxford University Medical School, UK |



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Association of vitamin D status with arterial blood pressure and hypertension risk: a mendelian randomisation study

A full list of authors and affiliations appears at the end of the article.

Summary

Background—Low plasma 25-hydroxyvitamin D (25[OH]D) concentration is associated with high arterial blood pressure and hypertension risk, but whether this association is causal is unknown. We used a mendelian randomisation approach to test whether 25(OH)D concentration is causally associated with blood pressure and hypertension risk.

Methods—In this mendelian randomisation study, we generated an allele score (25[OH]D synthesis score) based on variants of genes that affect 25(OH)D synthesis or substrate availability (*CYP2R1* and *DHCR7*), which we used as a proxy for 25(OH)D concentration. We meta-analysed data for up to 108 173 individuals from 35 studies in the D-CarDia collaboration to investigate associations between the allele score and blood pressure measurements. We complemented these analyses with previously published summary statistics from the International Consortium on Blood Pressure (ICBP), the Cohorts for Heart and Aging Research in Genomic Epidemiology (CHARGE) consortium, and the Global Blood Pressure Genetics (Global BPGen) consortium.

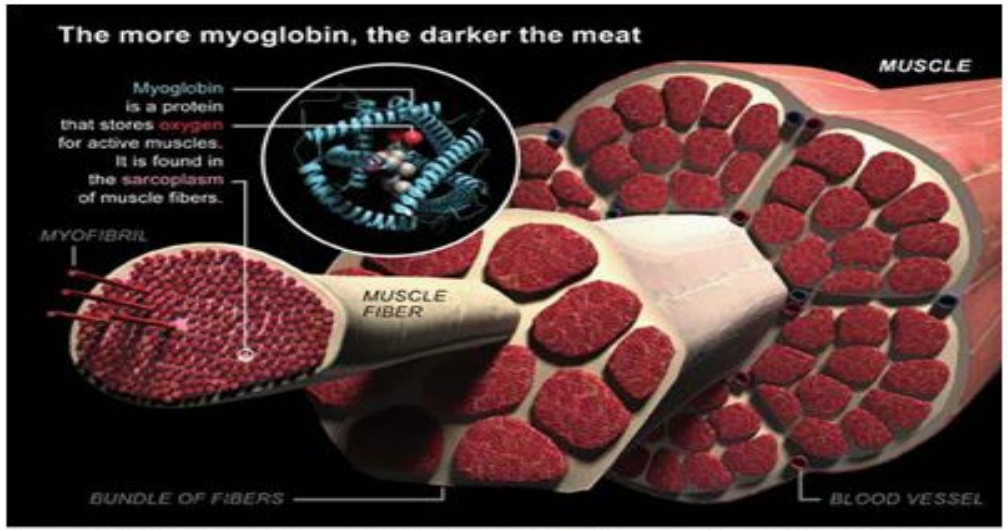
Findings—In phenotypic analyses (up to n=49 363), increased 25(OH)D concentration was associated with decreased systolic blood pressure (β per 10% increase, −0·12 mm Hg, 95% CI −0·20 to −0·04; p=0·003) and reduced odds of hypertension (odds ratio [OR] 0·98, 95% CI 0·97–0·99; p=0·0003), but not with decreased diastolic blood pressure (β per 10% increase, −0·02 mm Hg, −0·08 to 0·03; p=0·37). In meta-analyses in which we combined data from D-CarDia and the ICBP (n=146 581, after exclusion of overlapping studies), each 25(OH)D-increasing allele of the synthesis score was associated with a change of −0·10 mm Hg in systolic blood pressure

Vitamin D deficiency was associated with hypertension in 140,000 subjects tested. For every 10% increase in vitamin D levels, the risk of hypertension decreased by 8%.

| Vitamin D and Hyperlipidemia |

Common Side Effects of Hyperlipidemia Medications

Statin drugs, the most common class of drugs used to treat high blood cholesterol, can destroy muscles. It initially causes muscle pain but can also cause kidney disease (kidney failure) and death.



① Vitamin D reduces muscle pain

Risk of statin-related muscle disease	Blood Vitamin D Conc. (ng/mL)	
	Under 20	**Under 30**
	62.10%	**17.60%**

② Hyperlipidemia Medication (Statin) + Vitamin D → **Increased Effect**

* Injection of Atorvastatin (45 mg/day)

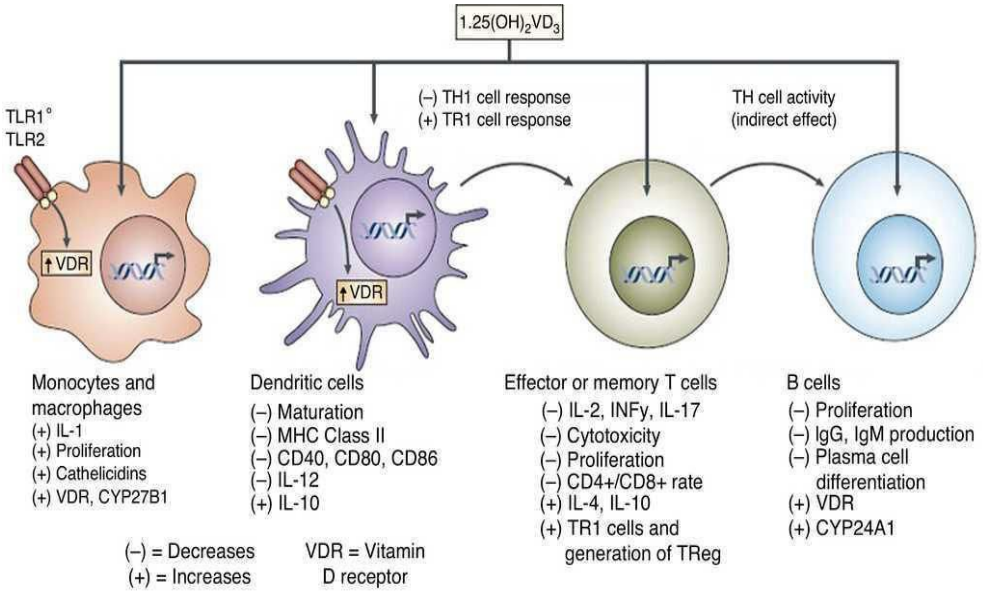
Blood vitamin D conc. (ng/mL)	No vitamin D used	**800 IU vitamin D used**
Total Cholesterol (mlg/dl)	169	**157**
LDL Cholesterol (mlg/dl)	97	**83**

③ Vitamin D deficiency is associated with higher amounts of triglycerides

	Triglyceride level based on Blood Vitamin D Level	
Active vitamin D Conc.	21.03 ng/mL	37.06 ng/mL
Triglyceride level 159 mg/dl or higher	32.80%	23.80%

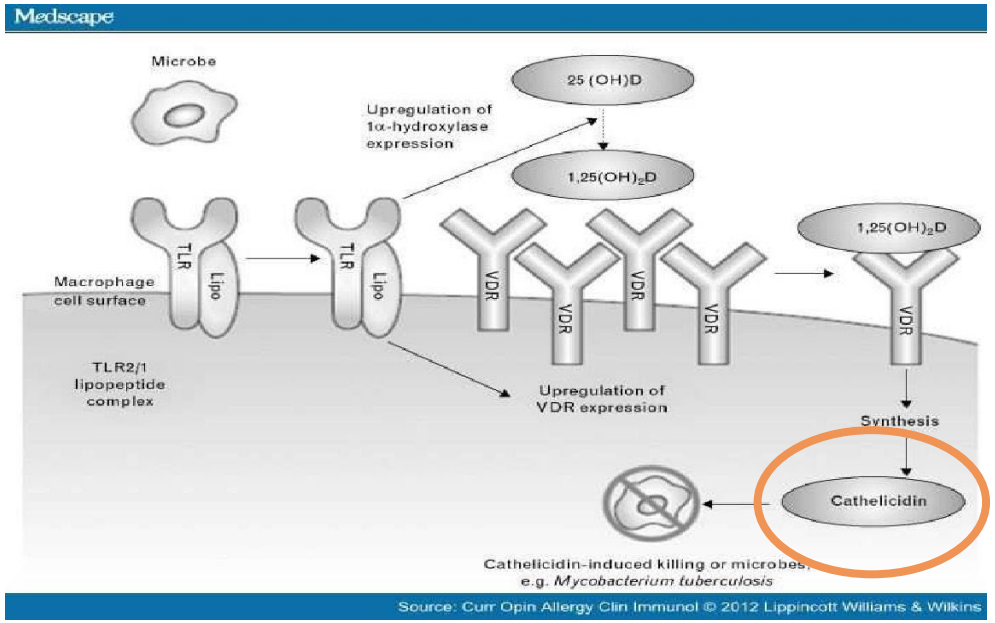
Source : Atherosclerosis 215 (2011) Atherosclerosis journal

| Vitamin D and Immune System |



Vitamin D affects immune cells, macrophages, T-cells (cellular immunity), and B-cells (humoral immunity), Dendritic cells (most important for immune cells).

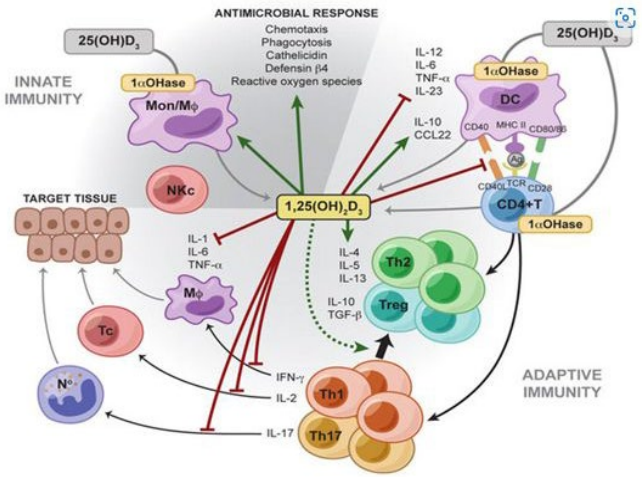
Source : Endocrinal Diabetes Nutr. 2017;64:162-73



Natural antibiotic produced by vitamin D

When a virus or bacteria invades and binds to the TRL receptor on the cell membrane, it triggers the inflammatory signature factor NfkB, which triggers vitamin D to activate genes that trigger the endogenous immune system to synthesize cathelicidine, a natural antibiotic. The antibiotic kills atopy-causing staphylococci, which can help improve atopic conditions.

| Vitamin D and Immune System |



Helps decrease Th1 (triggers asthma) and Th17(triggers inflammation). Helps regulate T-cells that suppress hypersensitivity.

Check 1. Helps Prevent Pediatric Otitis Media

	Placebo	Vitamin D3	P value
Initial blood vitamin D levels	25.8ng/mL	26.5ng/mL	< 0.001
Blood vitamin D levels after 4 months	18.7ng/mL	36.2ng/mL	< 0.001
Change in vitamin D level	7.1ng/mL	9.7ng/mL	< 0.001
Onset of non-refractory acute otitis media	50%	17.2%	< 0.001

For pediatric otitis media, supplement of 1000 IU of vitamin D for 4 months reduced the recurrence rate of otitis media from 50% to 17%.

Check 2. Helps Reduce Atopic Symptoms

Jan.- March 2010		2000 IU vitamin D/day (3 months)		
Double-blind trial		Before	After	P Value
Blood 25(OH)D ng/mL level	Range	4 - 15	5 - 24	0.001
	Avg	7.43	13.05	
SCORAD Index	Avg	26 - 78	10 - 49	0.001
	Range	45.12	19.90	

Taking 2000 IU vitamin D every day for 3 months reduced the area affected by eczema and reduced SCORAD Index (eczema index)

Check 3. Helps Reduce Asthma

Vitamin D deficiency leads to more patients with severe asthma				
25(OH) conc. (ng/mL)	30+	20-30	Under 20	P value
Patients with severe asthma	50 %	74 %	91.4 %	0.02

Criteria for severe asthma: ≥1 mg/day inhaled or oral corticosteroids

Check 4. Helps Increase Respiratory Function

Increase in vitamin D level can improve respiratory function				
25(OH)D conc. (ng/mL)	30+	20-30	Under 20	P Value
Avg age	47.4	46.1	54.1	
% with obesity ≥ 30	33.3%	41.1%	44.4%	
Function (FEV1 %)	81.6%	73.4%	68.4%	0.08

Source : The Pediatric Infectious Disease Journal 2013 May 20

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Vitamin D

Intake Guidelines

Diseases Preventable by Blood Vitamin D Level

Vitamin D Level

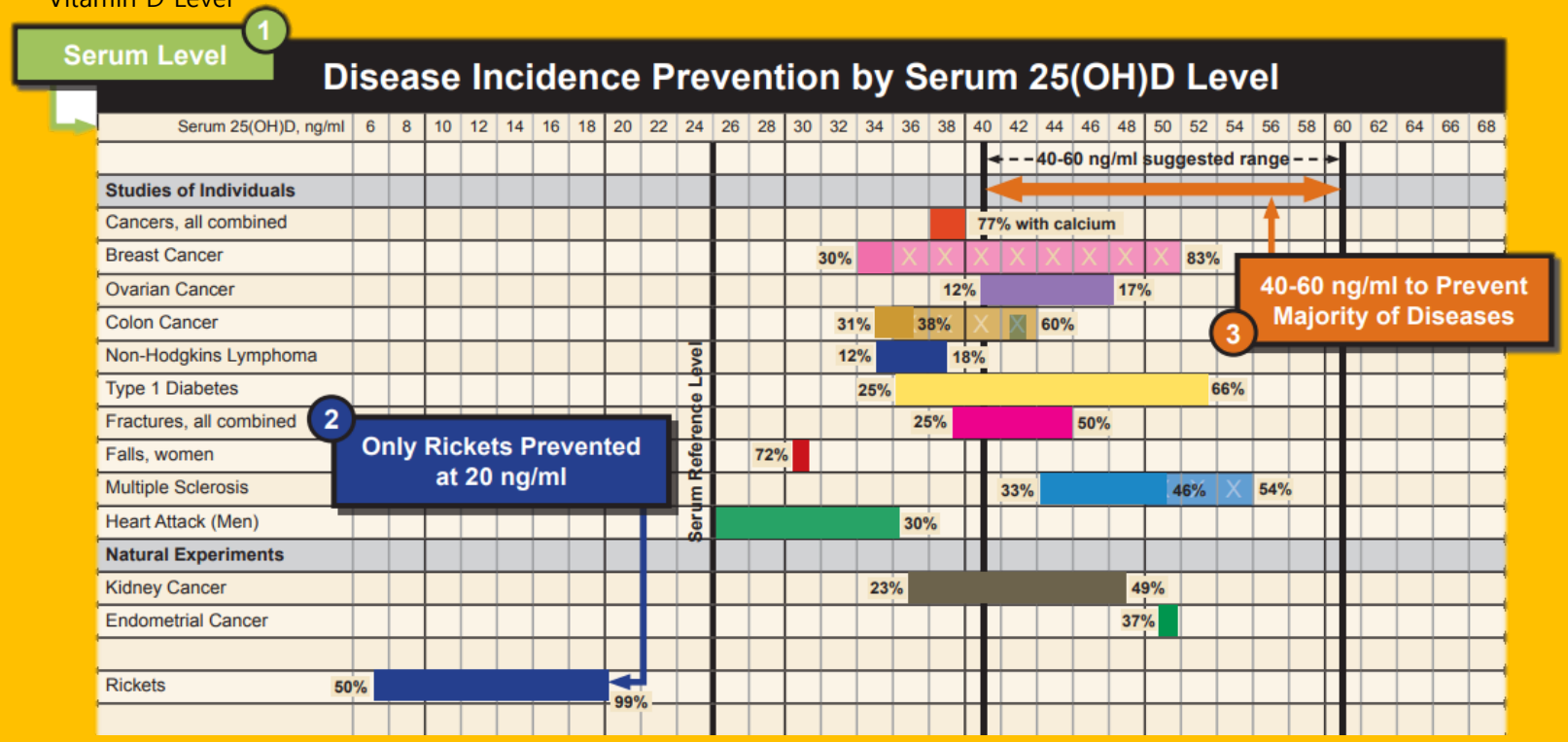
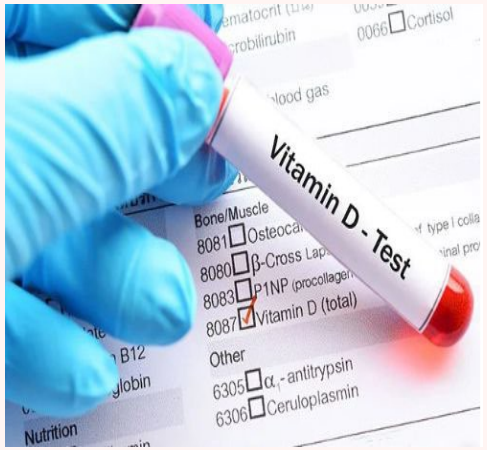


Chart prepared by : garland CF, Baggerly CA



Vitamin D Test

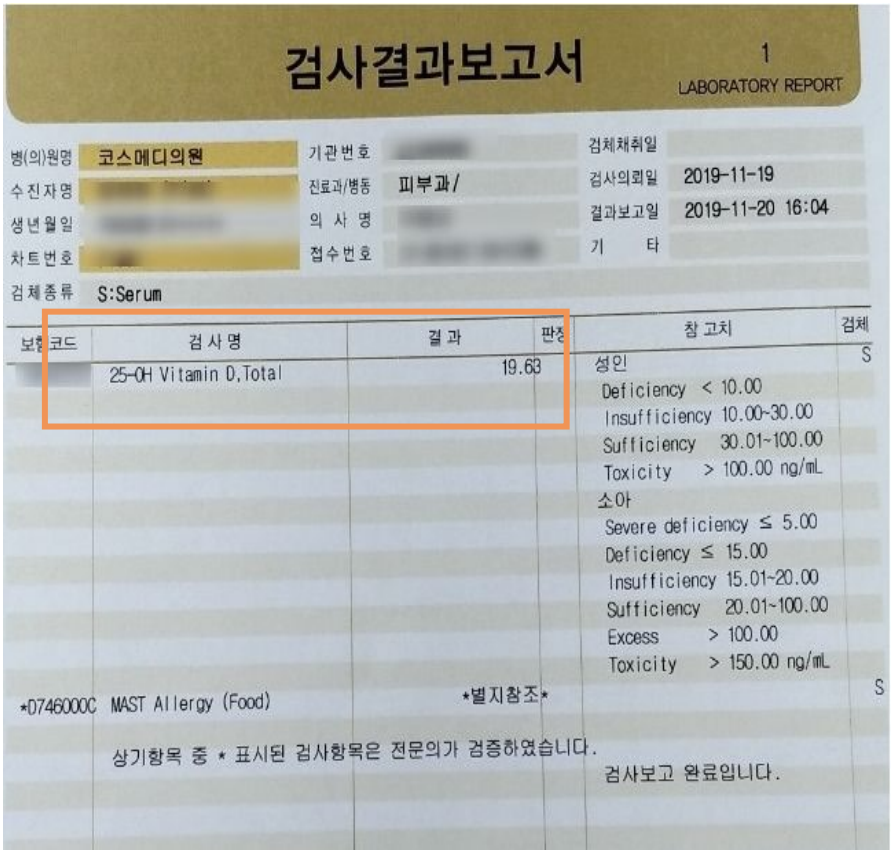
· Vitamin D test done with a blood test
· Blood vitamin D levels can be accurately monitored
· Vitamin D deficiency: blood vitamin D level < 20ng/ml

Most Koreans are vitamin D deficient (15~18ng/ml)

25-OH Vitamin D Blood Test Results

· under 10ng/ml : severely deficient
· 10-20ng/ml : deficient
· 20-30ng/ml : below average
· more than 30ng/ml : average
· 40-70ng/ml : optimal
· 150ng/ml : intoxication

비타민 D 검사결과 예시)



검사결과보고서 1 LABORATORY REPORT

병(의)원명	코스메디의원	기관번호		검체채취일	
수진자명		진료과/병동	피부과/	검사의뢰일	2019-11-19
생년월일		의 사 명		결과보고일	2019-11-20 16:04
차트번호		접수번호		기 타	
검체종류	S:Serum				

보험코드	검 사 명	결 과	판정	참 고 치	검체
	25-OH Vitamin D,Total	19.63		성인 Deficiency < 10.00 Insufficiency 10.00~30.00 Sufficiency 30.01~100.00 Toxicity > 100.00 ng/mL 소아 Severe deficiency ≤ 5.00 Deficiency ≤ 15.00 Insufficiency 15.01~20.00 Sufficiency 20.01~100.00 Excess > 100.00 Toxicity > 150.00 ng/mL	S
*0746000C	MAST Allergy (Food)	*별지참조*			S

상기항목 중 * 표시된 검사항목은 전문의가 검증하였습니다.
검사보고 완료입니다.

Daily Value of Vitamin D in South Korea

Sex	Age	Vitamin D ug/day			
		Avg intake	Rec. intake	Adequate intake	UL
Infants	0–5 (mo.)			5	25
	6–11			5	25
Children	1–2 (yr.)			5	30
	3–5			5	35
Male	6–8 (yr.)			5	40
	9–11			5	60
	12–14			10	100
	15–18			10	100
	19–29			10	100
	30–49			10	100
	50–64			10	100
	65–74			15	100
	75 +			15	100
Female	6–8 (yr.)			5	40
	9–11			5	60
	12–14			10	100
	15–18			10	100
	19–29			10	100
	30–49			10	100
	50–64			10	100
	65–74			15	100
	75 +			15	100
Pregnant				+0	100
Breastfeeding				+0	100

10mcg = 400IU / 100mcg = 4000IU

Adequate intake : amount required to maintain health

Tolerable upper intake level (UL) : maximum level of intake with no harmful effects

Recommended Daily Values

Category	Daily Value	Source
Infants, children, adolescents	400 IU	American Academy of Pediatrics (APP) (2008)
Adults & Pregnant Women	800 IU	Korea Women's Health and Osteoporosis Foundation Korean Osteoporosis Society Korean Society of Obstetrics, Gynecology and Endocrinology Join Enactment Recommendation (2011)
Adults 50+ & Menopausal Women	800–1,000 IU	Korean Society of Bone Metabolism Bone Health & Osteoporosis Foundation (NOF) (2014)
Limited Sunlight Exposure	2,000 IU	International Osteoporosis Foundation (IOF) (2010)
Vitamin D deficient 30ng/ml or less	1,500–2,000 IU	Endocrine Society (2011)

Several studies have recommended 800 to 1,000 IU of vitamin D per day for the average adult, but for those with increased indoor activity, sunscreen use, and limited sun exposure or blood vitamin D levels of 30 ng/mL or less, 2000 IU per day is recommended.

Case 1. After Vitamin D Testing

* Vitamin D levels should be measured every 6 months to determine doses based on desired vitamin D level.

Blood vitamin D level **10-20ng/mL**	
Goal	**Daily Intake**
20 ng/mL	500 IU
30 ng/mL	1,700 IU
40 ng/mL	3,200 IU
50 ng/mL	4,900 IU
60 ng/mL	7,000 IU
70 ng/mL	9,700 IU

Blood vitamin D level **20-30ng/mL**	
Goal	**Daily Intake**
30 ng/mL	600 IU
40 ng/mL	2,000 IU
50 ng/mL	3,700 IU
60 ng/mL	5,800 IU
70 ng/mL	8,600 IU

Blood vitamin D level **30-40ng/mL**	
Goal	**Daily Intake**
40 ng/mL	800 IU
50 ng/mL	2,500 IU
60 ng/mL	4,600 IU
70 ng/mL	7,300 IU

Statistically, taking 1,000 IU of vitamin D daily for 3 months will increase blood vitamin D level by 10 ng/mL

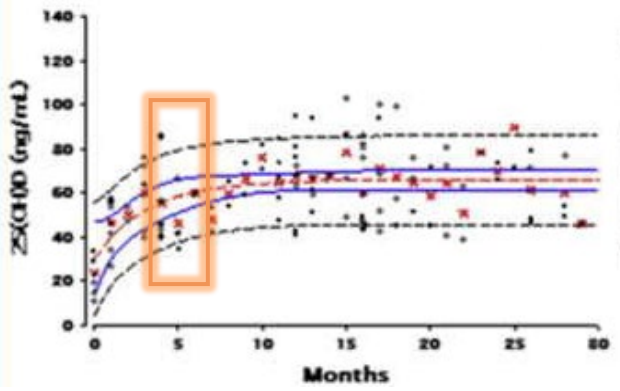
ex) If starting at 20ng/mL, take 2,000 IU for 3 months to reach 40ng/mL

Source) Bouillon, R. How to Define Optimal Vitamin D Status. In Vitamin D, Third Edition, by Feldman D, 2011

Case 2. No Vitamin D Test or Long-Term Supplement Intake

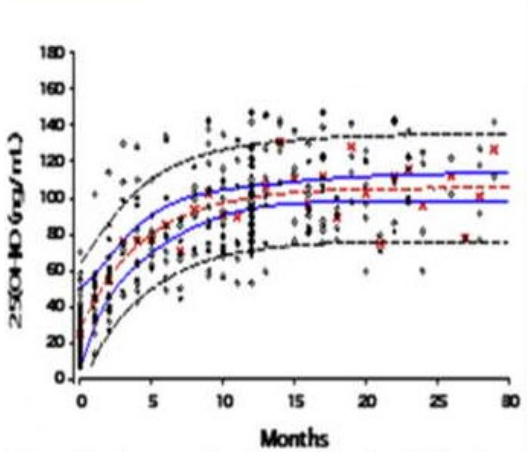
· 4,000 – 5,000 IU daily intake for 6 – 12 months
· After 6 – 12 months, 2000 IU daily is recommended for maintenance
· Blood vitamin D levels will drop again if 2000 IU daily intake is discontinued

5,000 IU Daily Intake Group

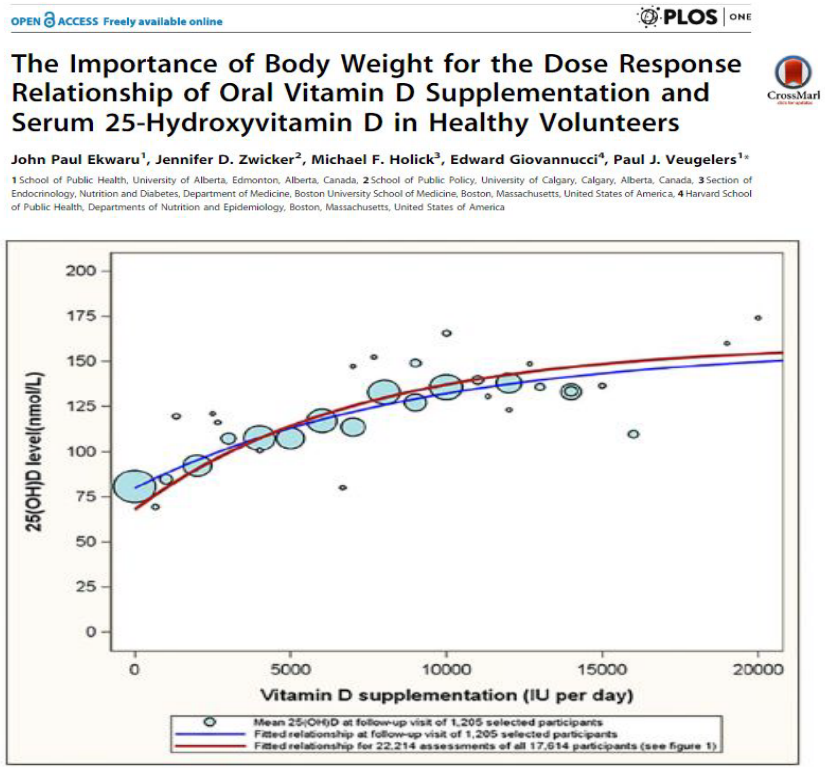


5-month intake of 5,000 IU daily increases blood vitamin D levels to the normal range of 40 ng/mL. Increases to 60 ng/mL after 10 months.

10,000 IU Daily Intake Group



5-month intake of 10,000 IU daily increases blood vitamin D levels to the normal range of 60 ng/mL. Continued supplementation pushes blood vitamin D levels to maximum.



OPEN ACCESS Freely available online PLOS ONE

The Importance of Body Weight for the Dose Response Relationship of Oral Vitamin D Supplementation and Serum 25-Hydroxyvitamin D in Healthy Volunteers

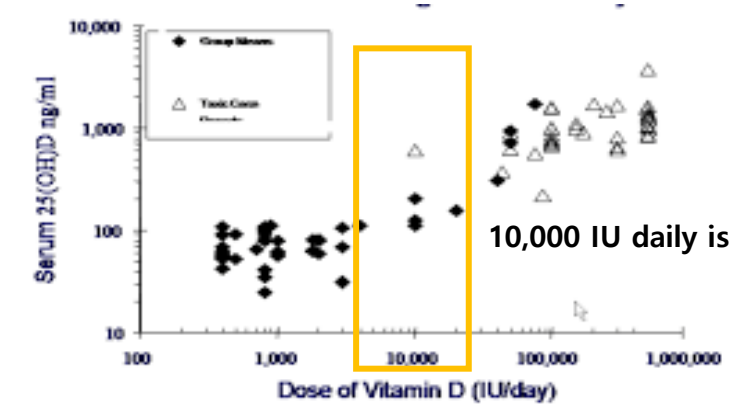
John Paul Ekwaru[1], Jennifer D. Zwicker[2], Michael F. Holick[3], Edward Giovannucci[4], Paul J. Veugelers[1]*

1 School of Public Health, University of Alberta, Edmonton, Alberta, Canada, 2 School of Public Policy, University of Calgary, Calgary, Alberta, Canada, 3 Section of Endocrinology, Nutrition and Diabetes, Department of Medicine, Boston University School of Medicine, Boston, Massachusetts, United States of America, 4 Harvard School of Public Health, Departments of Nutrition and Epidemiology, Boston, Massachusetts, United States of America

17,000 subjects followed for 5 years in Canada (2009-2013)

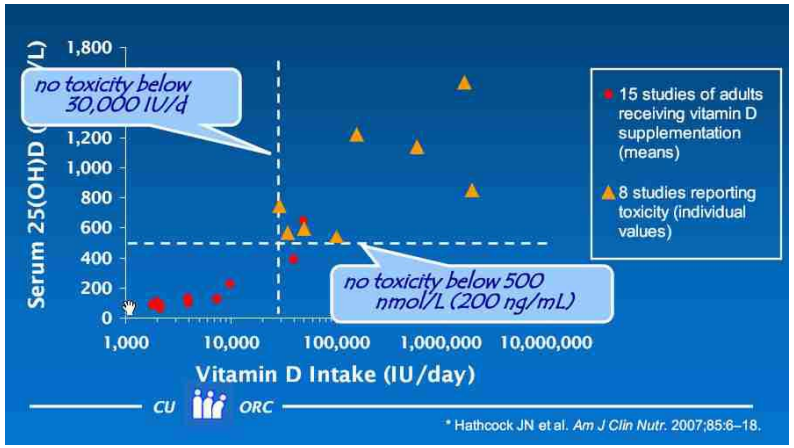
5,000 IU intake for 5 years maintained blood vitamin D levels around 40 ng/mL. Even with high intakes, blood levels remained steady rather than continuously rising.

Vitamin D Dosage and Toxicity



10,000 IU daily is still safe

Source: Vieth R. et al., *Annals Epidemiol.* (in press)



Graph shows that exceeding blood vitamin D level of 100 ng/mL is difficult
Even with high IU intake for multiple months.

| Supplements that can help with Vitamin D absorption |

Vitamin D can help calcium uptake

Calcium supplementation can lose effectiveness without sufficient vitamin D.
The active form of vitamin D, calcitriol, helps the body absorb and utilize calcium.
Korean Food and Drug Safety Administration has recognized vitamin D as
"necessary for the absorption and utilization calcium and phosphorus."

1

Combine with fats like omega3 for better absorption

Vitamin D is a fat-soluble vitamin. When looking to take vitamin D supplements,
a healthy fat supplement such as omega3 can help increase vitamin D absorption.
When cooking food with vitamin D, it is recommended to use high quality oil.

2

Q. Is Pharmaceutical Active Vitamin D or Supplemental Vitamin D more Effective?

A. 99.95% of Vitamin D in the blood exists in its intermediate active form. The remaining 0.05% becomes active form vitamin D after being converted in the liver. Most cells in the body take up the intermediate active form for use, so it is not necessary to take active form vitamin D supplements as the active form is only effective in fulfilling calcium-related functions and cannot fulfill the other recently discovered roles.

Q. Is Natural or Synthesized Vitamin D more Effective?

A. There are two major forms of vitamin D. Vitamin D3 (synthetized by the body from sunlight) is better absorbed by the body and more effective than Vitamin D2 (natural). Vitamin D2 is usually derived from yeast or mold.

Q. If I currently take calcium supplements, are vitamin D supplements still necessary?

A. The body maintains a constant blood calcium concentration (calcium homeostasis). When vitamin D levels become low and the amount of calcium absorbed into the bones decreases, bone calcium enters the blood stream, which can weaken the bones. It is recommended to take vitamin D supplements as optimal blood vitamin D levels cannot be met from food alone.

Q. Which foods and how much of it is the daily recommended allowance for disease prevention?

A. 1,000 IU of vitamin D3 is roughly 40 eggs, 10 cups of milk, 3 salmon, or 4 tablespoons of cod liver oil. It is not recommended to eat the foods above in listed quantities daily as it increases the risk of hyperlipidemia. Supplementation is recommended.

Vitamin D Supplement for

01. Those looking for a quality vitamin D3 supplement
02. Those looking to boost calcium absorption in their bodies
03. Those who are lacking adequate sunlight exposure
04. Older adults looking to improve bone health
05. Those who are vitamin D deficient and wish to raise blood vitamin D levels
06. Those with certain conditions that may disrupt vitamin D absorption in their bodies
07. Those looking to maintain an optimal blood vitamin D level.
08. Those looking forward to the newly discovered benefits of vitamin D, excluding bone health.

Product Name	General Balance Vitamin D
Product Type	Dietary Supplement
Net Wt.	400mg * 60 tablets (24g)
Suggested Use	Take 1 tablet daily with water
Ingredients	Vitamin D3 mixed formulation, Dextrin, glucose, Corn starch, Chicory root extract powder, Rapeseed oil, Corn protein extract
Storage Instructions	Store in a cool, dry place away from sunlight

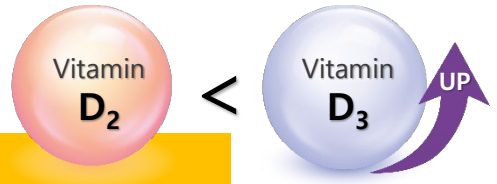
Supplement Facts

[Vitamin D] Assists with the absorption of calcium and phosphorous within the body. May improve bone health.

Daily Serving Size : 1 Tablet (400 mg)

Amount Per Serving	Content	% Daily Value*
Calories	1 kcal	
Carbohydrates	0 g	0 %
Protein	0 g	0 %
Fats	0 g	0 %
Sodium	0 mg	0 %
Vitamin D	50 ㎍	500 %

* % Daily Values are based on a 2,000 calorie diet.



Point 01. **Vitamin D3**

Vitamin D3 is more easily absorbed and utilized by the body than vitamin D2.

Point 02. **% Daily Value 500% (2000IU)**

A formula based on the latest vitamin D research.

Point 03. **Premium ingredients from DSM**

Premium Swiss ingredients from DSM, a global nutrition company.

Point 04. **Excipient Free**

No silicon dioxide, magnesium stearate, HPMC, synthetic flavors or colors.

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E.O.D