최근 각광받는 비타민 D 총정리

김 도 훈

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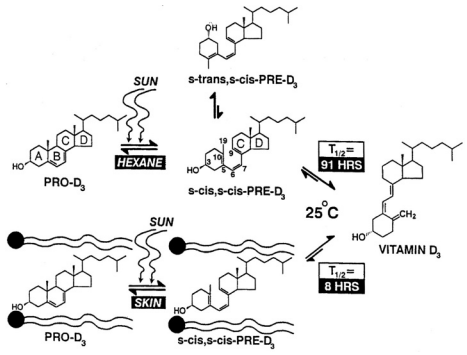
FIGURE 1. Photolysis of provitamin D3 (pro-D3) to previtamin D3 (pre-D3) and thermal isomerization of vitamin D3 in hexane and in lizard skin



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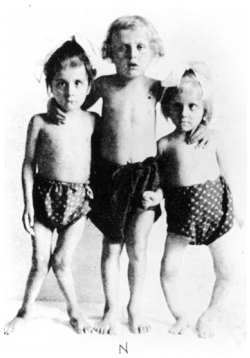
Holick, M. F Am J Clin Nutr 2004;80:1678S-1688S

FIGURE 2. Typical presentation of 2 children with rickets



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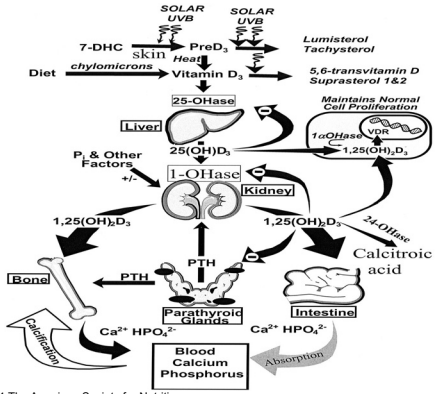
Holick, M. F Am J Clin Nutr 2004;80:1678S-1688S

FIGURE 3. Schematic diagram of cutaneous production of vitamin D and its metabolism and regulation for calcium homeostasis and cellular growth



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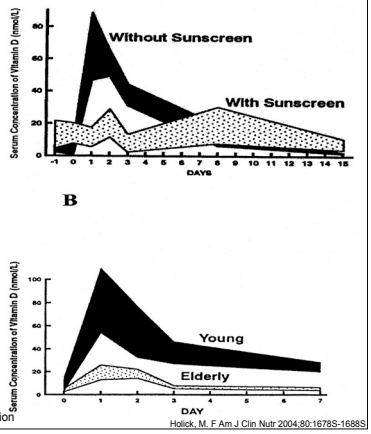
Holick, M. F Am J Clin Nutr 2004;80:1678S-1688S

FIGURE 4. A: Circulating concentrations of vitamin D3 after a single exposure to 1 MED (minimal erythemal dose) of simulated sunlight, with a sunscreen (SPF 8) or a topical placebo cream



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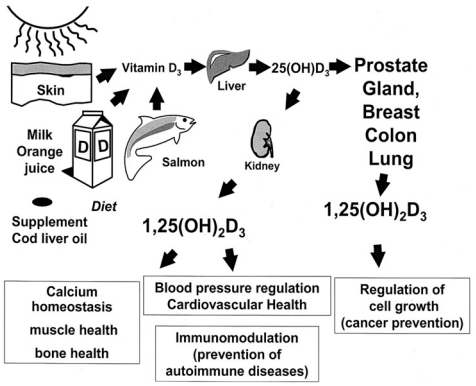
Holick, M. F Am J Clin Nutr 2004;80:1678S-1688S

FIGURE 10. Metabolism of 25(OH)D3 to 1,25(OH)$_2$D3 in the kidney and other organs and the biological consequences



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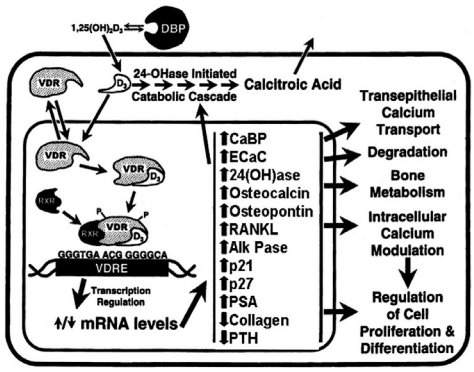
Holick, M. F Am J Clin Nutr 2004;80:1678S-1688S

FIGURE 9. Schematic representation of the mechanism of action of 1,25(OH)$_2$D in various target cells, resulting in a variety of biological responses



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Overview

- **Effect of Vitamin D on Skeletal health**
  - *Vitamin D & Osteoporosis*
  - Vitamin D & Fall
- **Effect of Vitamin D on Extraskeletal health**
  - Vitamin D & Immune function
  - Vitamin D & Cancer prevention
  - Vitamin D & Hypertension prevention
  - Vitamin D & Hyperlipidemia

Part 1.
Vitamin D & Fall

Effect of Vitamin D on falls: a meta-analysis

- Based on 5 RCTs involving 1237 participants, vitamin D reduced the corrected odds ratio (OR) of falling by 22% (corrected OR, 0.78; 95% confidence interval [CI], 0.64-0.92) compared with patients receiving calcium or placebo.
- The number needed to treat (NNT) was **15** (95% CI, 8-53)
- The inclusion of 5 additional studies, involving 10001 participants, in a sensitivity analysis resulted in a smaller but still significant effect size (corrected RR, 0.87; 95% CI, 0.80-0.96).

*Adapted from **JAMA. 2004**;291:1999-2006.*

Effects of Ergocalciferol Added to Calcium on the Risk of Falls in Elderly High-Risk Women

Background :

- **Ergocalciferol (vitamin D2)** supplementation **plays a role in fall prevention**, but the effect in patients living in the community in sunny climates remains uncertain.
- We evaluated the effect of **ergocalciferol and calcium citrate supplementation** compared with **calcium alone** on the risk of falls in older women at high risk of falling.

Adapted from Arch Intern Med. 2008 Jan 14;168(1):103-8.

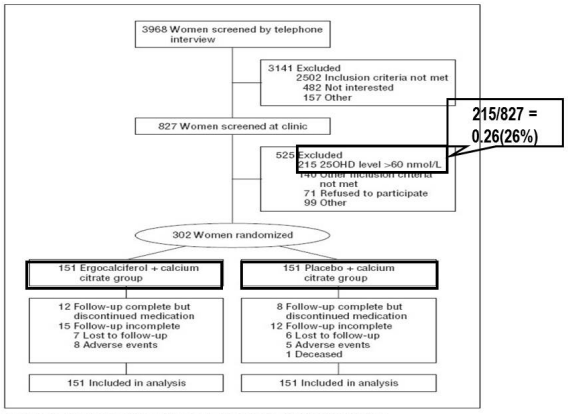


Figure 1. Participant flow through the study. 25OHD indicates 25-hydroxyvitamin D. To convert serum 25OHD to nanograms per milliliter, divide by 2.496.

Adapted from Arch Intern Med. 2008 Jan 14;168(1):103-8.

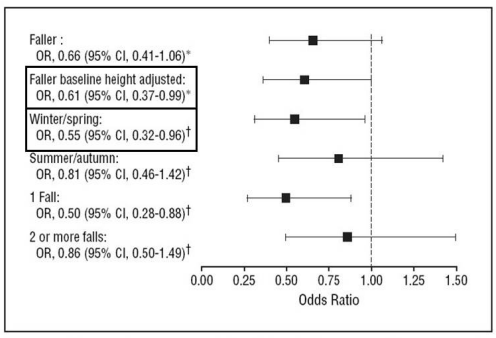


Figure 2. Effects of treatment on falls. "Faller" refers to participant who had at least 1 fall during the study period; CI indicates confidence interval; OR, odds ratio; asterisk, logistic regression analysis; dagger, multinomial logistic regression analysis; error bars, 95% CIs.

Adapted from Arch Intern Med. 2008 Jan 14;168(1):103-8.

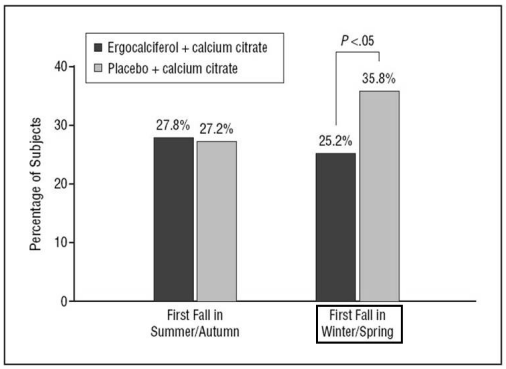


Figure 3. Percentages of subjects who had at least 1 fall, by season of first fall. Percentages of fallers were compared using χ^2 testing.

Adapted from Arch Intern Med. 2008 Jan 14;168(1):103-8.

Conclusion

▶Patients with a history of falling and vitamin D insufficiency living in sunny climates *benefit from ergocalciferol supplementation in addition to calcium*, which is associated with *a 19% reduction* in the relative risk of falling, *mostly in winter.*

Adapted from Arch Intern Med. 2008 Jan 14;168(1):103-8.

A Higher Dose of Vitamin D Reduces the Risk of Falls in Nursing Home Residents: A Randomized, Multiple-Dose Study

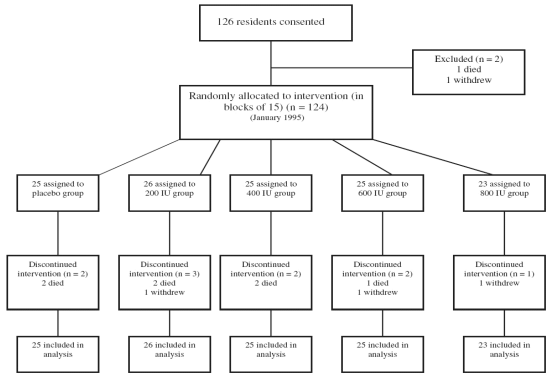


Figure 1. Consort diagram of nursing home participants in the vitamin D supplement trial.

*Adapted from J Am Geriatr Soc 55:234–239, **2007**.*

A Higher Dose of Vitamin D Reduces the Risk of Falls in Nursing Home Residents: A Randomized, Multiple-Dose Study

Table 2. Vitamin D Supplement Intake and Fall Outcomes During 5-Month Clinical Trial by Supplement Group for 124 Nursing Home Residents

Outcome	Placebo (n = 25)	200 IU (n = 26)	400 IU (n = 25)	600 IU (n = 25)	800 IU (n = 23)
Total vitamin D supplement intake, IU, mean (range)*	272.00 (0–400)	446.15 (200–600)	672.00 (400–800)	840.00 (600–1,000)	1,026.09 (800–1,200)
Serum 25-hydoxyvitamin D, ng/mL, mean ± SD†	24.12 ± 13.04	24.50 ± 8.29	21.89 ± 9.22	24.47 ± 8.78	29.92 ± 6.26
Faller, n (%)	11 (44)	15 (58)	15 (60)	15 (60)	5 (20)
Total falls, n	31	37	33	41	9
Hazard ratio (95% CI) of time to first fall‡	1.00	1.79 (0.78–3.71)	1.70 (0.77–3.73)	1.68 (0.76–3.71)	0.44 (0.15–1.28)
Incidence rate ratio (95% CI) of falls during the study‡	1.00	1.10 (0.49–2.50)	1.05 (0.48–2.28)	1.21 (0.55–2.61)	0.28 (0.10–0.75)

*Total vitamin D supplement intake = Vitamin D from the study pill + Hebrew Rehabilitation Center for Aged multivitamin (400 IU).
†Valid follow-up serum concentrations available for some participants: placebo (n = 20), 200 IU (n = 22), 400 IU (n = 22), 600 IU (n = 19), 800 IU (n = 17).
‡Adjusted for age and multivitamin use.
CI = confidence interval.

*Adapted from J Am Geriatr Soc 55:234–239, **2007**.*

A Higher Dose of Vitamin D Reduces the Risk of Falls in Nursing Home Residents: A Randomized, Multiple-Dose Study

- Nursing home residents in *the highest vitamin D group (800 IU)* had *a lower number of fallers and a lower incidence rate of falls* over 5 months than those taking lower doses.
- *Adequate vitamin D supplementation in elderly nursing home residents could reduce the number of falls* experienced by this high falls risk group

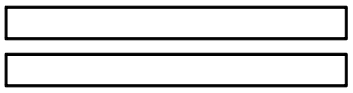
Effect of Cholecalciferol Plus Calcium on Falling in Ambulatory Older Men and Women

- little is known about

whether supplemental cholecalciferol plus calcium citrate malate will lower the long-term risk of falling in men, active older individuals, and older individuals with higher 25-hydroxyvitamin D levels.

Adapted from Arch Intern Med. 2006;166:424-430.

Effect of Cholecalciferol-Calcium on the Number of Persons Who Fell During the 3-Year Follow-up



Bischoff-Ferrari, H. A. et al. Arch Intern Med 2006;166:424-430.

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Cumulative percentage of falls by treatment group and sex

women **men**

Bischoff-Ferrari, H. A. et al. Arch Intern Med 2006;166:424-430.

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Vitamin D supplementation improves neuromuscular function in older people who fall

139 persons with a history of falls and 25-hydroxyvitamin D (25OHD) =12 /l

a single intramuscular injection of 600,000 i.u. ergocalciferol or placebo

Adapted from Age and Ageing 2004; **33:** 589–595

Vitamin D supplementation improves neuromuscular function in older people who fall

P value < 0.01

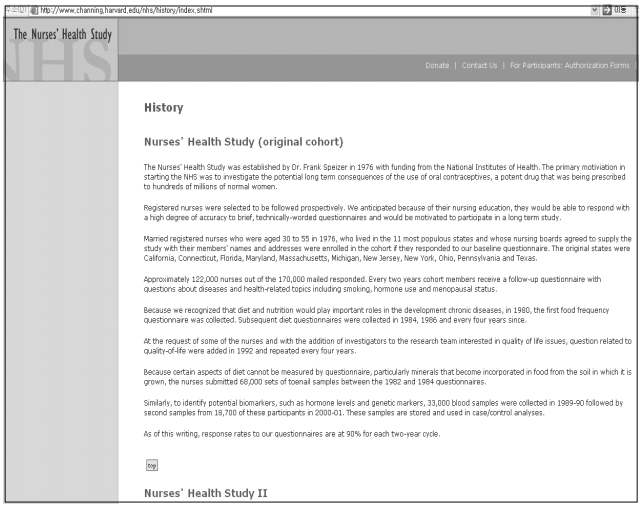
P value = 0.01

P value = 0.02

Not significant different

AFPT ? Aggregate Functional Performance Time, Functional Performance 확인
CRT ? Choice reaction time, Psychomotor function 확인
MVC ? Maximum voluntary contraction, Quadriceps contraction을 확인

Adapted from Age and Ageing 2004; **33:** 589–595


http://www.channing.harvard.edu/nhs/history/index.shtml

The Nurses' Health Study

NHS

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History

Nurses' Health Study (original cohort)

The Nurses' Health Study was established by Dr. Frank Speizer in 1976 with funding from the National Institutes of Health. The primary motiviation in starting the NHS was to investigate the potential long term consequences of the use of oral contraceptives, a potent drug that was being prescribed to hundreds of millions of normal women.

Registered nurses were selected to be followed prospectively. We anticipated because of their nursing education, they would be able to respond with a high degree of accuracy to brief, technically-worded questionnaires and would be motivated to participate in a long term study.

Married registered nurses who were aged 30 to 55 in 1976, who lived in the 11 most populous states and whose nursing boards agreed to supply the study with their members' names and addresses were enrolled in the cohort if they responded to our baseline questionnaire. The original states were California, Connecticut, Florida, Maryland, Massachusetts, Michigan, New Jersey, New York, Ohio, Pennsylvania and Texas.

Approximately 122,000 nurses out of the 170,000 mailed responded. Every two years cohort members receive a follow-up questionnaire with questions about diseases and health-related topics including smoking, hormone use and menopausal status.

Because we recognized that diet and nutrition would play important roles in the development chronic diseases, in 1980, the first food frequency questionnaire was collected. Subsequent diet questionnaires were collected in 1984, 1986 and every four years since.

At the request of some of the nurses and with the addition of investigators to the research team interested in quality of life issues, question related to quality-of-life were added in 1992 and repeated every four years.

Because certain aspects of diet cannot be measured by questionnaire, particularly minerals that become incorporated in food from the soil in which it is grown, the nurses submitted 68,000 sets of toenail samples between the 1982 and 1984 questionnaires.

Similarly, to identify potential biomarkers, such as hormone levels and genetic markers, 33,000 blood samples were collected in 1989-90 followed by second samples from 18,700 of these participants in 2000-01. These samples are stored and used in case/control analyses.

As of this writing, response rates to our questionnaires are at 90% for each two-year cycle.

top

Nurses' Health Study II

Prospective Study of Predictors of Vitamin D Status and Cancer Incidence and Mortality in Men

- Consider multiple determinants of vitamin D exposure (dietary and supplementary vitamin D, skin pigmentation, adiposity, geographic residence, and leisure-time physical activity—to estimate sunlight exposure) in relation to cancer risk in the Health Professionals Follow-Up Study
- Among 1095 men of this cohort, we quantified the relation of these six determinants to plasma 25-hydroxy-vitamin D level by use of a multiple linear regression model.

Adapted from J Natl Cancer Inst 2006;98:451 – 9

Prospective Study of Predictors of Vitamin D Status and Cancer Incidence and Mortality in Men

- We used results from the model to compute a predicted 25(OH)D level for each of 47800 men in the cohort based on these characteristics.
- We then prospectively examined this predicted 25(OH)D level in relation to cancer risk with multivariable Cox proportional hazards models
- From 1986 through January 31, 2000

Adapted from J Natl Cancer Inst 2006;98:451 – 9

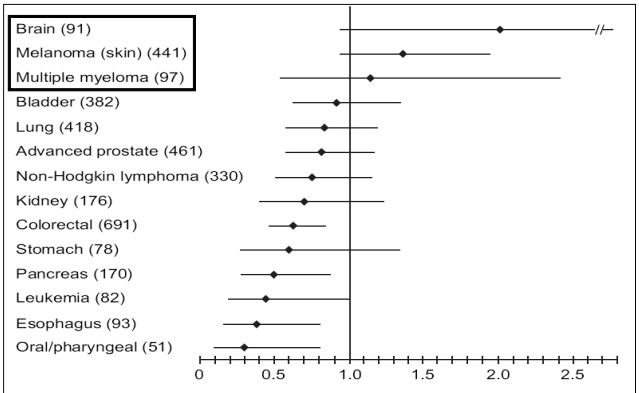

Fig. 1. Multivariable relative risks and 95% confidence intervals for an increment of 25 nmol/L in predicted plasma 25-hydroxy-vitamin D level for individual cancers in the Health Professionals Follow-up Study (1986–2000). Number in parentheses = number of cases. Covariables included in the Cox proportional hazards model: age, height, smoking history, and intakes of total calories, alcohol, red meat, calcium, retinol, and total fruits and vegetables.

Table 3. Relative risks (RRs) and 95% confidence intervals (CIs) for an increment of 25 nmol/L in predicted plasma 25-hydroxy-vitamin D [25(OH)D] level for total cancer incidence and mortality in the Health Professionals Follow-Up Study (1986–2000)

Endpoint	RR (95% CI)
Total cancer incidence (N = 4286)	
Age-adjusted	0.78 (0.70 to 0.86)
Multivariable-adjusted*	0.83 (0.74 to 0.92)
Multivariable + BMI†	0.83 (0.73 to 0.94)
Multivariable + physical activity	0.84 (0.72 to 0.98)
Total cancer mortality (N = 2025)	
Age-adjusted	0.65 (0.56 to 0.76)
Multivariable-adjusted*	0.71 (0.60 to 0.83)
Multivariable + BMI†	0.71 (0.59 to 0.84)
Multivariable + physical activity	0.69 (0.55 to 0.86)

*The following covariables were included in the Cox proportional hazards model: age, height, smoking history, and intakes of total calories, alcohol, red meat, calcium, retinol, and total fruits and vegetables.

†BMI = body mass index.

Table 4. Relative risks (RRs) and 95% confidence intervals (CIs) for an increment of 25 nmol/L in predicted plasma 25-hydroxy-vitamin D [25(OH)D] level for digestive system cancer incidence and mortality in the Health Professionals Follow-Up Study (1986–2000)

Endpoint	RR (95% CI)
Digestive cancer incidence (n = 1123)	
Age-adjusted	0.54 (0.44 to 0.66)
Multivariable-adjusted*	0.57 (0.46 to 0.71)
Multivariable + BMI†	0.59 (0.47 to 0.75)
Multivariable + physical activity	0.52 (0.38 to 0.71)
Digestive cancer mortality (n = 594)	
Age-adjusted	0.51 (0.39 to 0.67)
Multivariable-adjusted*	0.55 (0.41 to 0.74)
Multivariable + BMI†	0.54 (0.39 to 0.75)
Multivariable + physical activity	0.45 (0.30 to 0.68)

*The following covariables were included in the Cox proportional hazards model: age, height, smoking history, and intakes of total calories, alcohol, red meat, calcium, retinol, and total fruits and vegetables.

†BMI = body mass index.

Prospective Study of Serum Vitamin D and Cancer mortality in the United States

- ▶ A total of 16 818 participants in the 3rd NHNES who were 17 years or older at enrollment were followed from 1988 – 1994 through 2000.
- ▶ Levels of serum 25(OH)D were measured at baseline by radioimmunoassay.
- ▶ Our results do not support an association between 25(OH)D and total cancer mortality, although there was an inverse relationship between 25(OH)D levels and colorectal cancer mortality

Adapted from J Natl Cancer Inst 2007;99: 1594 – 602

Table 4. Relative risks (RRs) and 95% confidence intervals (CIs) for site-specific cancer mortality according to baseline serum 25-hydroxyvitamin D [25(OH)D] levels (nmol/L) in the Third National Health and Nutrition Examination Survey (NHANES III Study), 1988–2000*

	25(OH)D (nmol/L)				
Cancer site	<50	50 to <80	80 to <100	≥100	P_{trend}
Lung cancer					
No. of deaths	57	51	23	22	
RR	1.0	0.78	0.65	1.14	
95% CI		0.50 to 1.22	0.36 to 1.18	0.60 to 2.18	.41
	<62.5	≥62.5			
Digestive cancers other than colorectal cancer†					
No. of deaths	34	37			
RR	1.0	1.42			
95% CI		0.73 to 1.76			.18
Breast cancer					
No. of deaths	20	8			
RR	1.0	0.28			
95% CI		0.08 to 0.93			.76
Prostate cancer					
No. of deaths	22	25			
RR	1.00	0.91			
95% CI		0.39 to 2.14			.95
Non-Hodgkin lymphoma/leukemia					
No. of deaths	16	24			
RR	1.0	1.34			
95% CI		0.62 to 2.91			.96
	<50	50 to <80	≥80		
Colorectal cancer‡					
No. of deaths	28	24	14		
RR	1.0	0.44	0.28		
95% CI		0.20 to 0.95	0.11 to 0.68		.02
Other cancer sites§					
No. of deaths	38	60	32		
RR	1.0	1.83	1.86		
95% CI		0.93 to 3.61	0.75 to 4.63		.84

Part 3. Vitamin D & Cardiovascular risk

Vitamin D & Cardiovascular risk

- Results of several epidemiologic and clinical studies have suggested that there is an excess risk of hypertension and diabetes mellitus in persons with suboptimal intake of vitamin D
- The association between serum levels of 25-hydroxyvitamin D and cardiovascular disease risk factors in US adults.

Adapted from Arch Intern Med. 2007;167:1159-1165

Vitamin D & Cardiovascular risk

- 7186 male and 7902 female adults 20 years and older with available data in the Third NHNES

Adapted from Arch Intern Med. 2007;167:1159-1165

Age-, Sex-, and Race-Adjusted Prevalence and ORs of Select Cardiovascular Disease Risk Factors Between the First and Fourth Quartiles of Serum 25(OH)D Levels

Table 3. Age-, Sex-, and Race-Adjusted Prevalence and ORs of Select Cardiovascular Disease Risk Factors Between the First and Fourth Quartiles of Serum 25(OH)D Levels

	Prevalence of Cardiovascular Risk Factor			
Risk Factor	1st Quartile (<21 ng/mL)	4th Quartile (≥37 ng/mL)	OR (95% CI)	*P* Value
Blood pressure ≥140/≥90 mm Hg	20.46	15.10	1.30 (1.13-1.49)	.001
Fasting blood glucose level, mg/dL				
110-125	6.96	3.25	2.15 (1.69-2.74)	<.001
≥126	6.85	3.38	1.98 (1.57-2.51)	<.001
History of diabetes mellitus	6.96	3.28	1.73 (1.38-2.16)	<.001
Body mass index ≥30*	24.69	11.50	2.29 (1.99-2.63)	<.001
Triglyceride level ≥150 mg/dL	32.86	23.84	1.47 (1.30-1.65)	<.001
Total cholesterol level ≥240 mg/dL	19.98	15.92	0.97 (0.85-1.11)	.65
Non-HDL cholesterol level ≥150 mg/dL	48.99	41.49	1.04 (0.93-1.16)	.50
Serum albumin level <3.5 g/dL	2.77	1.57	2.90 (1.89-4.46)	<.001
eGFR <60 mL/min per 1.73 m^2	5.12	4.27	1.08 (0.87-1.35)	.47
ACR ≥200 for males/≥300 for females	1.59	0.76	2.54 (1.65-3.48)	<.001

Abbreviations: ACR, albumin-creatinine ratio; CI, confidence interval; eGFR, estimated glomerular filtration rate; HDL, high-density lipoprotein; 25(OH)D, 25-hydroxyvitamin D; OR, odds ratio.
SI conversion factors: To convert cholesterol to millimoles per liter, multiply by 0.0259; glucose to millimoles per liter, multiply by 0.0555; 25(OH)D to nanomoles per liter, multiply by 2.496; triglycerides to millimoles per liter, multiply by 0.0113.
*Calculated as weight in kilograms divided by the square of height in meters.

Martins, D. et al. Arch Intern Med 2007;167:1159-1165.

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Vitamin D & Cardiovascular risk

- Serum 25(OH)D levels are associated with important cardiovascular disease risk factors in US adults.
- Prospective studies to assess a direct benefit of cholecalciferol(vitamin D) supplementation on cardiovascular disease risk factors are warranted.

Adapted from Arch Intern Med. 2007;167:1159-1165

Vitamin D & Blood Pressure

- Recent clinical trials and animal studies have suggested that vitamin D insufficiency may be associated with elevated blood pressure
- VitaminD is one important nutrient that has been postulated as a contributing factor to the development of hypertension, possibly through inhibition of the renin angiotensin system

Adapted from Am J Clin Nutr 2008;87:136–41.

Vitamin D & Blood Pressure

▶ Li et al showed that 1, 25-hydroxyvitaminD [1,25(OH)2D], the active steroid hormone form of vitamin D, inhibits renin gene expression in vitamin D receptor knockout mice.

▶ These mice develop hypertension that can be reversed with treatment with captopril, an angiotensin-converting enzyme inhibitor as well as treatment with 1,25(OH)2D.

Adapted from J Clin Invest 2002;110:229 –38

Vitamin D & Blood Pressure

- The concentration of 25(OH)D needed for cardiovascular benefits may be even higher than that needed for skeletal benefits and may differ by race

Adapted from Am J Clin Nutr 2008;87:136–41.

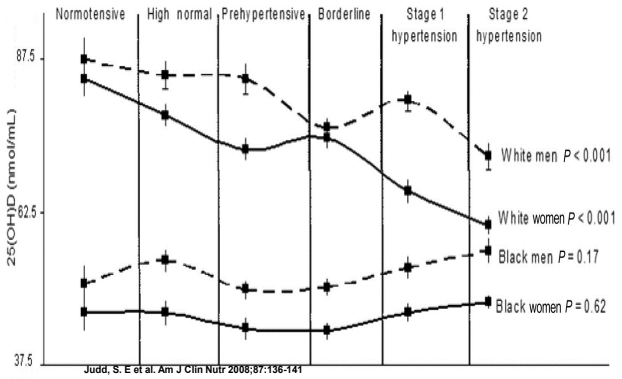
TABLE 1
Demographic characteristics of white and black adults without a diagnosis of hypertension who had a serum vitamin D measurement 25(OH)D available in the third National Health and Nutrition Examination Survey NHANES (1988–1994)[1]

	Total (n = 7699)	White (n = 4663)	Black (n = 3036)
Sex			
Men	3613 (47)	2198 (47)	1415 (47)
Women	4086 (53)	2465 (53)	1621 (53)
Age (y)[2]			
18–49	4818 (63)	2413 (52)	2405 (79)
≥50	2881 (37)	2250 (48)	631 (21)
BMI (kg/m^2)[2]			
Normal and underweight (<25)	3692 (48)	2362 (51)	1330 (44)
Overweight (25–29.9)	2514 (33)	1572 (34)	942 (31)
Obese (≥30)	1493 (19)	729 (16)	764 (25)
Season of measurement[2]			
January–March	1167 (15)	724 (16)	443 (15)
April–June	1987 (26)	1386 (30)	601 (20)
July–September	2485 (32)	1535 (33)	950 (31)
October–December	2060 (27)	1018 (22)	1042 (34)
Systolic blood pressure (mm Hg)[2]			
<110 (normotensive)	1957 (25)	1123 (24)	834 (27)
110–119 (high normal)	2133 (28)	1218 (26)	915 (30)
120–129 (prehypertensive)	1654 (21)	983 (21)	671 (22)
130–139 (borderline)	919 (12)	595 (13)	324 (11)
140–159 (stage 1 hypertension)	793 (10)	568 (12)	225 (7)
≥160 (stage 2 hypertension)	243 (3)	176 (4)	67 (2)

[1] All values are n; weighted percentage in parentheses.
[2] P value comparing number of whites and blacks in each category was <0.01 (Mantel-Haenszel chi-square test).

Adapted from Am J Clin Nutr 2008;87:136–41.

FIGURE 1. Concentrations of 25-hydroxyvitamin D [25(OH)D] by systolic blood pressure with the use of the Joint National Committee 7 (JNC 7) hypertension classifications among adults in the third National Health and Nutrition Examination Survey (NHANES III; 1988-1994)



Judd, S. E et al. Am J Clin Nutr 2008;87:136-141

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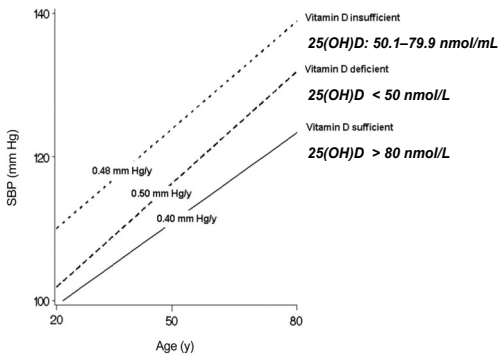
FIGURE 2. Age-related increase in systolic blood pressure (SBP) is shown in white participants not currently using medication to lower blood pressure, stratified by 3 concentrations of 25-hydroxyvitamin D [25(OH)D]



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Part 4. Vitamin D & Immune system

D-Hormone and the Immune System

- ▶ important immune system regulator that has been shown to inhibit development of autoimmune diseases including experimental inflammatory bowel disease (IBD), rheumatoid arthritis (RA), multiple sclerosis (MS), and type 1 diabetes.
- ▶ Paradoxically, other immune mediated diseases (experimental asthma) and immunity to infectious organisms were not found to be affected by D-hormone treatment.

Adapted from J Rheumatol 2005;32 Suppl 76:11-20

D-Hormone and the Immune System

- The effectiveness of D-hormone treatment of autoimmune diseases is due to inhibition of the development and function of Th1 cells and the induction of other Th cells including Th2 cells.
- The Results of microarray analysis of colons from D-hormone treated mice with experimental IBD.

Adapted from J Rheumatol 2005;32 Suppl 76:11-20

D-Hormone and the Immune System

Table 4. D-hormone targets 3 TNF-α related genes in the colon of mice with experimental IBD.

Gene	Experiment 1		Experiment 2	
	Intensity*	Ratio**	Intensity	Ratio
TNF-α	414	–2.1	309	–2.7
LPS-induced TNF-α factor#	4267	–1.7	4516	–1.9
TNF receptor	3494	–1.7	163	–3.1
VDR	745	2.6	422	1.9
Calmodulin	4663	1.7	11878	3.6
Calcium Binding Protein A6	97601	2.3	39160	4.7

* Combined median red and green intensities.
** The ratio is either the ratio of green fluorescence over red fluorescence (positive values) or the inverse (negative values). Positive ratios represent genes that are activated in the presence of D-hormone and negative ratios represent genes that are repressed in the presence of D-hormone
# LPS-induced TNF-α factor was reanalyzed using quantitative real-time PCR. The expression of this gene was 4 to 461 times lower in colons of D-hormone treated IL-10 KO mice (n=4) compared to the D–control (n=4) colons. The microarray underestimated the efficacy of D-hormone to inhibit LPS-induced TNF-α.

Adapted from J Rheumatol 2005;32 Suppl 76:11-20

D-Hormone and the Immune System

- ▶ The most evident effects of the D-hormone on the immune system seem to be in the control (down-regulation) of Th1-driven autoimmunity
- ▶ Latitude-related ecological features (i.e. different sun exposure), support a gradient of increasing prevalence of RA (Finland nearly 0.8% and 0.3% in Italy) with higher latitude, such as for other autoimmune diseases (i.e. multiple sclerosis)
- ▶ 25(OH)D3 plasma levels have been found inversely correlated with the RA disease activity showing a circannual rhythm (more severe in winter)

Adapted from Autoimmunity Reviews 2007;7:59–64

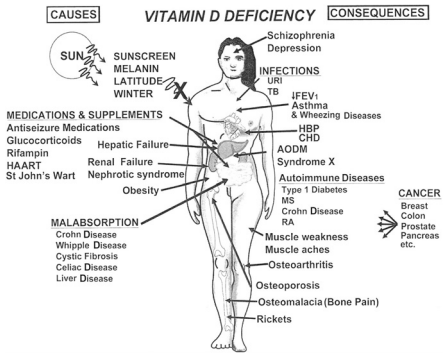
D-Hormone and the Immune System

- Recently, greater intake of vitamin D was associated with a lower risk of RA
- Recent reviews suggest that the optimal plasma 25(OH)D3 concentration lies between 50-80 nmoles/L, other experts suggesting between 75–125 nmol/L

Adapted from Autoimmunity Reviews 2007;7:59–64

Part 5.
Vitamin D daily requirement

FIGURE 3. A schematic representation of the major causes of vitamin D deficiency and potential health consequences



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Holick, M. F et al. Am J Clin Nutr 2008;87:1080S-1086S

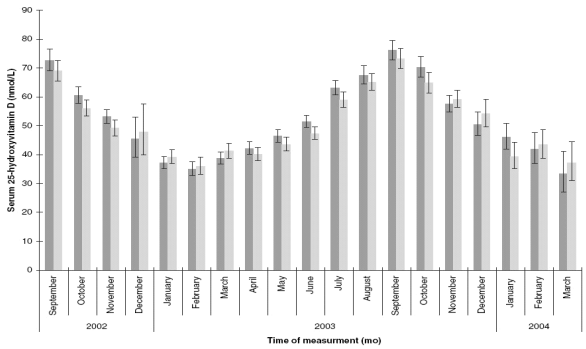


FIGURE 1. Geometric mean (95% CI) monthly variation in serum 25-hydroxyvitamin D [25(OH)D] concentrations in men (■; $n = 3725$) and women (□; $n = 3712$) in the 1958 British birth cohort at age 45 y. The interaction between sex and month was significant [$P = 0.02$, linear regression analyses on log 25(OH)D]. n per sex and month ranged from 17 to 340: 98 in December 2003 for women and <100 for both sexes in December 2002 ($n = 40$ M, 37 F), January 2004 ($n = 95$ M, 75 F), February 2004 ($n = 58$ M, 70 F), and March 2004 ($n = 22$ M, 17 F).

Adapted from Am J Clin Nutr. 2007 Mar;85(3):860-8

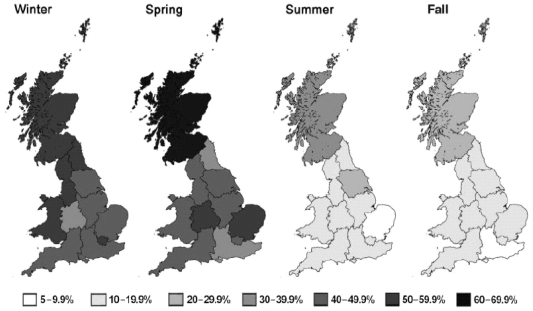


FIGURE 3. Seasonal and geographical variation in the prevalence of hypovitaminosis D (25-hydroxyvitamin D <40 nmol/L) in Great Britain.

Adapted from Am J Clin Nutr. 2007 Mar;85(3):860-8

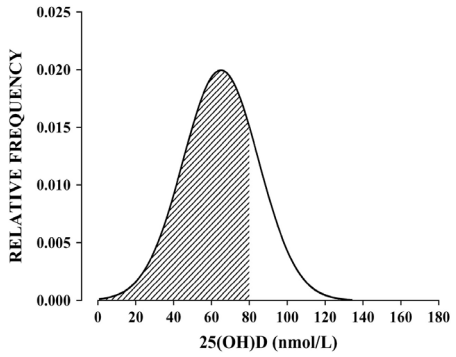
Table 1
The daily requirements of 1,25(OH)2D3 change during the life and physiological conditions

Age	Children (μg/day)	Men (μg/day)	Women (μg/day)	Pregnancy (μg/day)	Lactation (μg/day)
Birth to 13 years	5 (=200 IU)				
14 to 18 years		5 (=200 IU)	5 (=200 IU)	5 (=200 IU)	5 (=200 IU)
19 to 50 years		5 (=200 IU)	5 (=200 IU)	5 (=200 IU)	5 (=200 IU)
51 to 70 years		10 (=400 IU)	10 (=400 IU)		
71+ years		15 (=600 IU)	15 (=600 IU)		

Dietary or exogenous 1,25(OH)2D3 integrations (in IU) might be required in order to keep the optimal 25(OH)D3 plasma concentrations between 50–125 nmol/L.

Adapted from Intern Med J 2007;37:377–82.

FIGURE-1. Approximation of the NHANES distribution of serum 25(OH)D values in women aged 60-79 y



Heaney, R. P. J. Nutr. 2006;136:1123-1125

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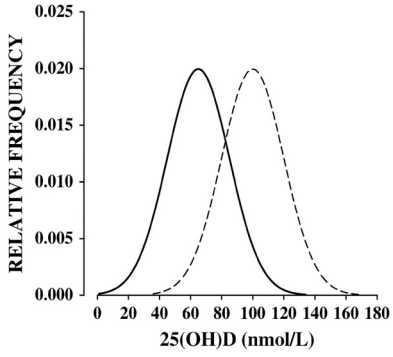
FIGURE-2. Data from Figure 1 plus a second distribution augmented by *35 nmol/L* (the approximate difference predicted to be produced by *an extra 2000 IU of cholecalciferol per day*)



Heaney, R. P. J. Nutr. 2006;136:1123-1125

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Table 1.
Oral Vitamin D Formulations

Ergocalciferol
  Vitamin D_2
Cholecalciferol
  Vitamin D_3
Calcitriol (Rocaltrol)
  Activated vitamin D_3
  $1,25(OH)_2$ vitamin D_3
Doxercalciferol (Hectorol)
  Activated vitamin D_2 analog
Paricalcitol (Zemplar)
  Activated vitamin D_2 analog

Table 2.
Oral Vitamin D_3 (Cholecalciferol) Dosing Guide

Indication	Dosage Regimen	Maximum Daily Dose or Equivalent
RDA up to age 50	200 IU daily	2000 IU daily
RDA 50–70 years of age	400 IU daily	2000 IU daily
RDA >70 years of age	600 IU daily	2000 IU daily

Part 6.
Vitamin D & Statin

- Vitamin D levels and statin effectiveness
- Vitamin D deficiency and statin myopathy
- Vitamin D as an inducer of CYP enzymes
  - Vitamin D is known to activate CYP3A4.
  - The fully active dihydroxylated vitamin D3 induces the expression of not only CYP3A4, but also CYP2B6 and CYP2C9 in primary human hepatocytes.
  - Hydroxylated vitamin D derivatives also possess 3-hydroxy-3-methyl-glutaryl-Coenzme A (HMG-CoA) reductase activity.

Q J Med 2012; 105:487–491 doi:10.1093/qjmed/hcs001