

Vitamin D is Potentially Important for Cardiovascular Health: Special Implications for African Americans

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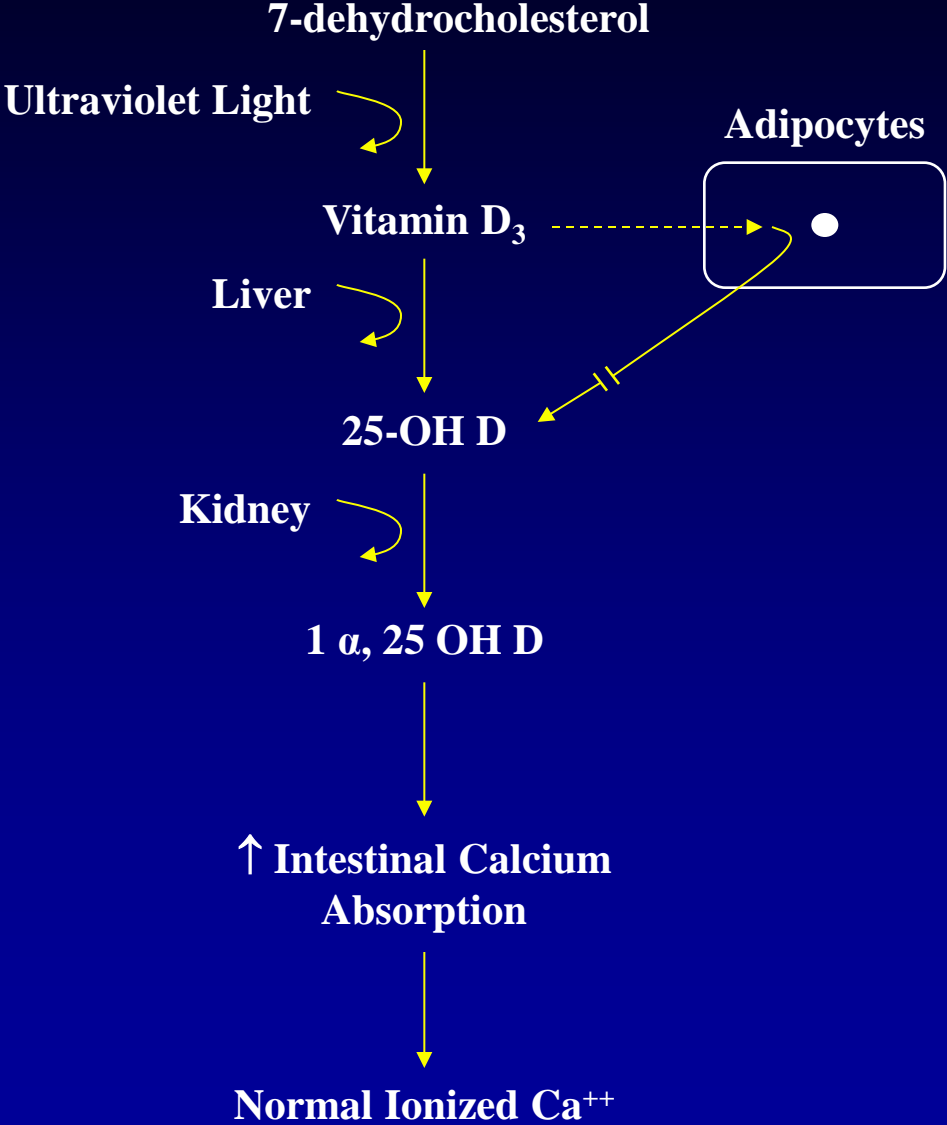
Vitamin D Facts

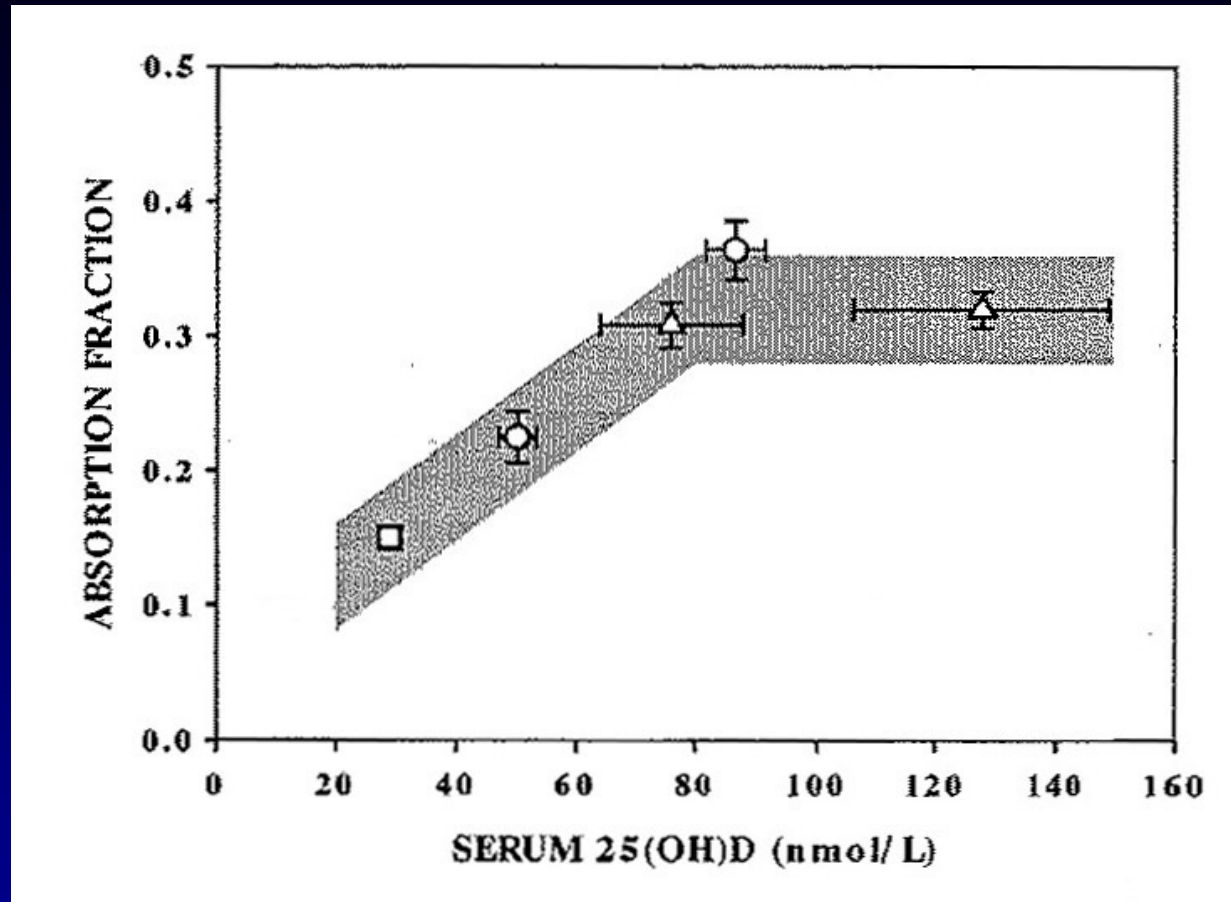
- Most persons obtain their vitamin D from sunlight exposure
- Though some foods are fortified with vitamin D, most foods contain very little vitamin D
- There are many undesirable associations with low vitamin D levels (e.g., hypertension, obesity); however, the only proven benefit of vitamin D supplementation is for bone health
- Supplementation studies with vitamin D will be necessary to prove the benefit of raising vitamin D levels

Institute of Medicine (IOM) Recommendations for Dietary Intakes of Vitamin D and Calcium

	Vitamin D (IU per day)	Calcium (mg per day)
Estimated Average Requirement	400	800
Recommended Dietary Allowance	600	1,000
Upper level intake	4,000	2,000

Highly Simplified Schema of Normal Calcium and Vitamin D Metabolism



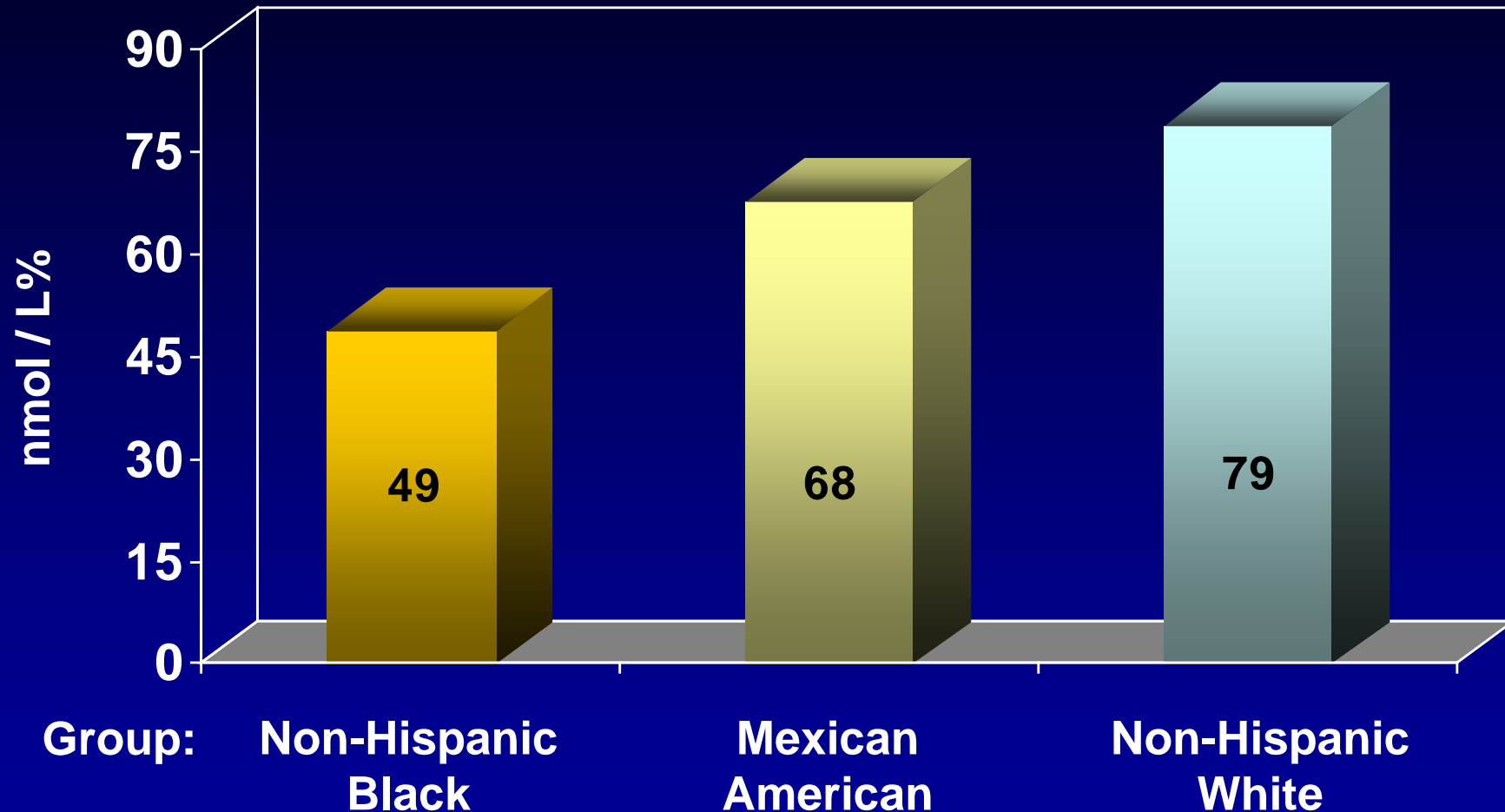


Calcium absorption fraction plotted as a function of serum 250HD concentration in three studies. The paired O symbols represent the data of one study [11]; the paired Δ symbols, a second 1121, and the \square symbol is the estimated absorption for the subjects not treated with Vitamin D in the study of Bischoff et al. [13,31].

R Heaney, *J Steroid Biochemistry & Molecular Biology* 97 (2005) 13-19

Vitamin D Levels by Race/Ethnicity¹

NHANES III (1988-94)



¹ Analyses restricted to 12,644 adults 20 years and older not taking antihypertensive medication.

Scragg R et al. *Am J Hypertens* 2007;20(7):713-9

Serum 25-Hydroxyvitamin D [25(OH)D] Concentrations and Health*

nmol/L**	ng/mL	Health status
<30	<12	Associated with vitamin D deficiency, leading to rickets in infants and children and osteomalacia in adults
30-50	12-20	Generally considered inadequate for bone and overall health in healthy individuals
≥50	≥20	Generally considered adequate for bone and overall health in healthy individuals
>125	>50	Emerging evidence links potential adverse effects to such high levels, particularly >150 nmol/L (>60 ng/mL)

* Serum concentrations of 25(OH)D are reported in both nanomoles per liter (nmol/L) and nanograms per milliliter (ng/mL)

**1 nmol/L = 0.4 ng/mL

Institute of Medicine, Food and Nutrition Board. Dietary Reference Intakes for Calcium and Vitamin D. Washington, DC: *National Academy Press*, 2010.

Prevalence of Hypovitaminosis D in Women by Race: NHANES III 1998-1994

25 - OH (D) < 37.5 nmol/L Prevalence %	
African Americans	42.4 ¹
Whites	4.2

Amongst African Americans, hypovitaminosis D was independently associated with consumption of milk < 3 times/wk, no use of vitamin D supplements, season, urban residence, low BMI (<18.5 Kg/m²), and no use of oral contraceptives

Nesby-O'Dell S et al, *Am J Clin Nutr* 2002;76(1):3-4

¹Amongst African Americans taking vitamin D supplements (200 IU/D), prevalence of hypovitaminosis D was 28.2%

BMI=body mass index; NHANES=National Health and Nutrition Examination Survey

Dietary Sources of Vitamin D

Selected Food Sources of Vitamin D

Food	IUs per serving*	Percent DV**
Cod liver oil, 1 tablespoon	1,360	340
Salmon (sockeye), cooked, 3 ounces	447	112
Mackerel, cooked, 3 ounces	388	97
Tuna fish, canned in water, drained, 3 ounces	154	39
Milk, nonfat, reduced fat, and whole, vitamin D-fortified, 1 cup	115-124	29-31
Orange juice fortified with vitamin D, 1 cup (check product labels, as amount of added vitamin D varies)	100	25
Yogurt, fortified with 20% of the DV for vitamin D, 6 ounces (more heavily fortified yogurts provide more of the DV)	80	20

* IUs = International Units.

** DV = Daily Value. DVs were developed by the U.S. Food and Drug Administration to help consumers compare the nutrient contents among products within the context of a total daily diet. The DV for vitamin D is currently set at 400 IU for adults and children age 4 and older. Food labels, however, are not required to list vitamin D content unless a food has been fortified with this nutrient. Foods providing 20% or more of the DV are considered to be high sources of a nutrient, but foods providing lower percentages of the DV also contribute to a healthful diet.

U.S. Department of Agriculture, Agricultural Research Service. *USDA Nutrient Database for Standard Reference*, Release 23, 2011.

Selected Food Sources of Vitamin D (continued)

Food	IUs per serving*	Percent DV**
Margarine, fortified, 1 tablespoon	60	15
Liver, beef, cooked, 3.5 ounces	49	12
Sardines, canned in oil, drained, 2 sardines	46	12
Egg, 1 large (vitamin D is found in yolk)	41	10
Ready-to-eat cereal, fortified with 10% of the DV for vitamin D, 0.75-1 cup (more heavily fortified cereals might provide more of the DV)	40	10
Cheese, Swiss, 1 ounce	6	2

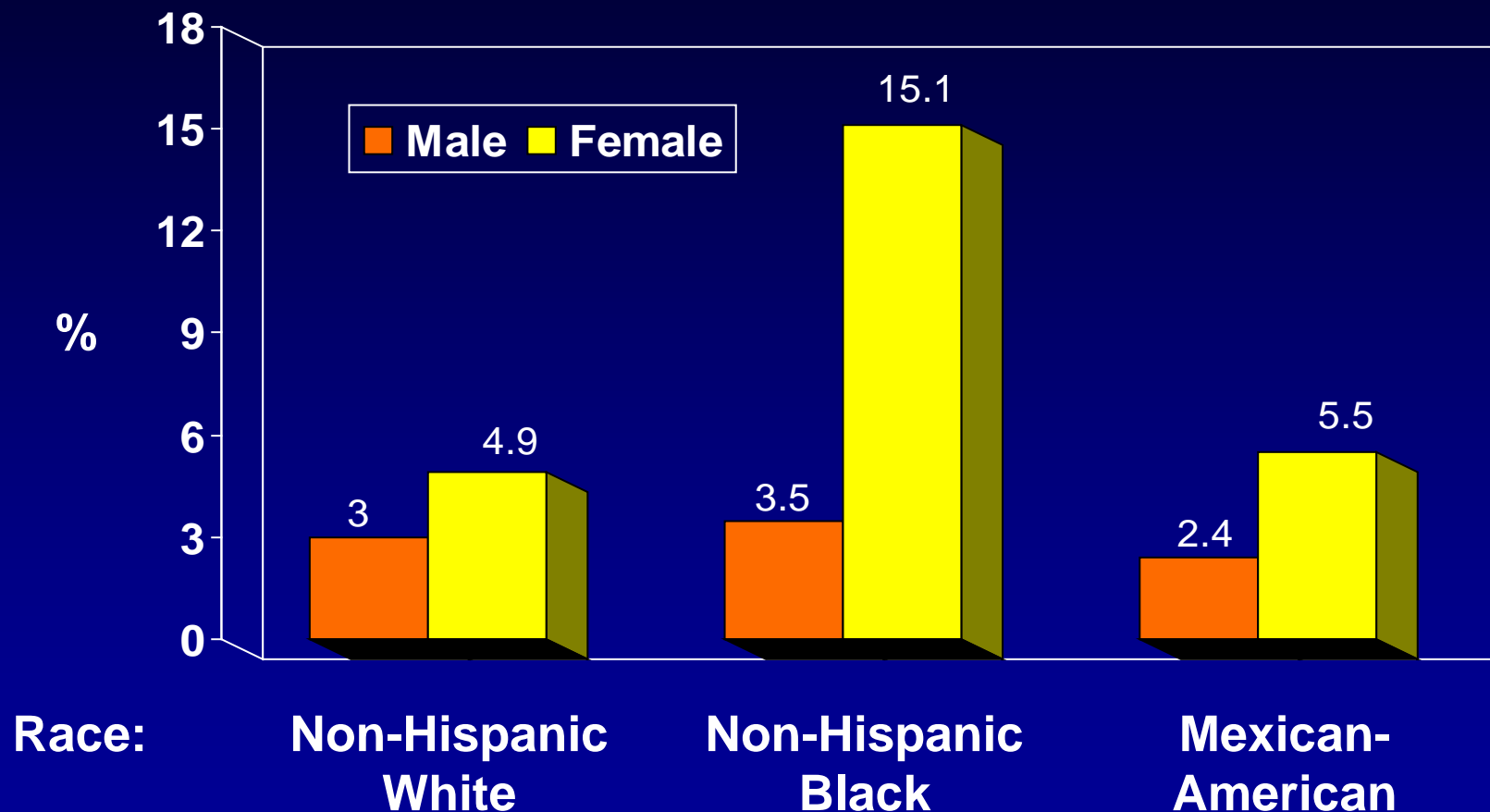
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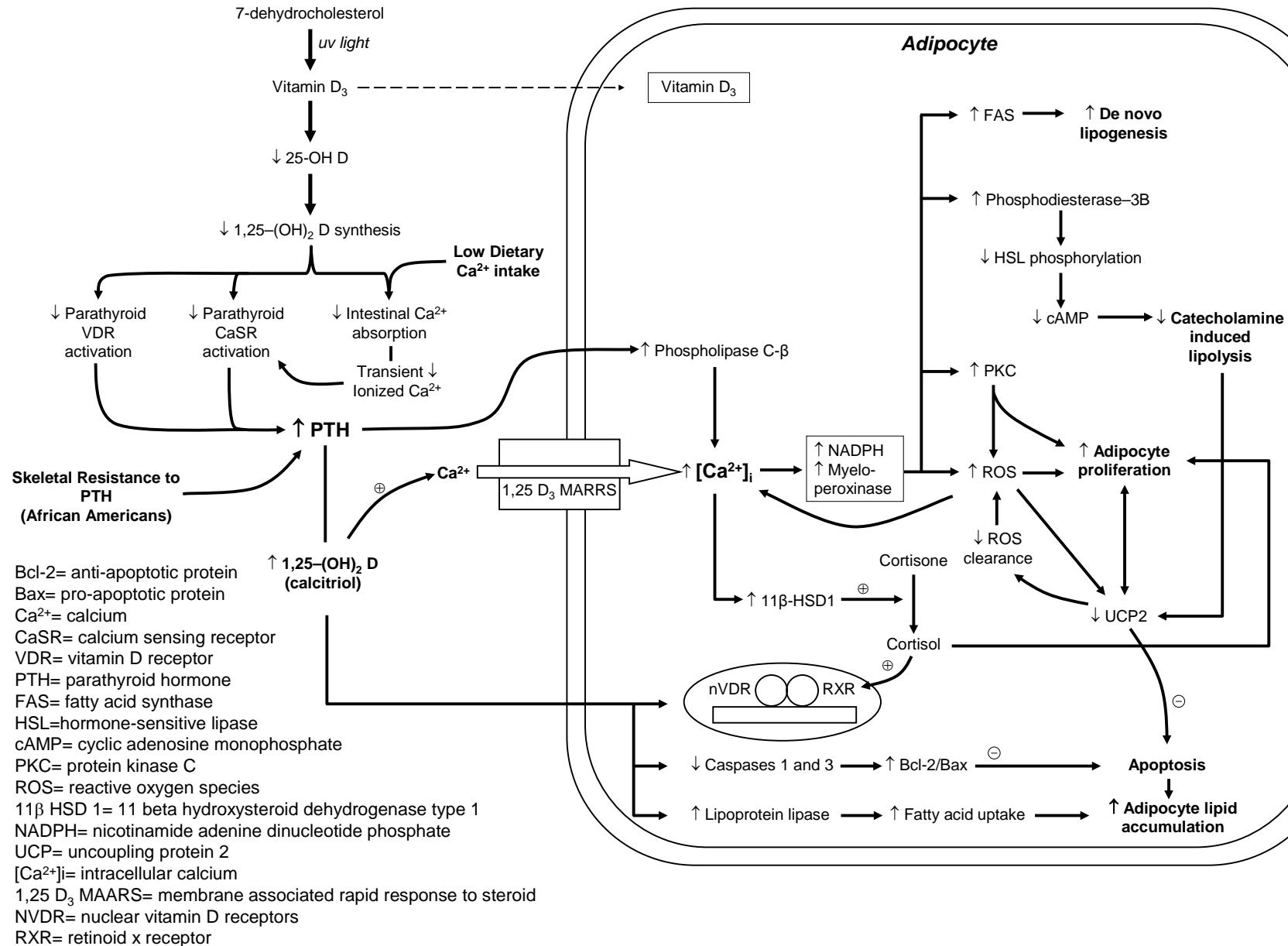
U.S. Department of Agriculture, Agricultural Research Service. *USDA Nutrient Database for Standard Reference*, Release 23, 2011.

Obesity and Vitamin D

Prevalence of Extreme Obesity (BMI ≥ 40 kg/m²) in US Population (NHANES III, 1999-2000) by Sex and Race in Persons ≥ 20 Years



Integrated Overview of Pathways Linking Vitamin D, PTH, and Calcium to Adiposity and Reactive Oxygen Species (Oxidative Stress)



Vitamin D / PTH Categories

	N (%)	Vitamin D nmol / L	PTH pg / ml
Reference (Normal)	17 (23.3)	>50	< 45
Vitamin D ↓, PTH Normal	30 (41.1)	<50	< 45
Vitamin D ↓, PTH ↑	26 (35.6)	<50	> 45

Relationship Between Vitamin D and PTH to Weight and Body Composition in Healthy African Americans: CUAAH Center

Group	Weight (Kg)	BMI Kg/m ²	Body Mass		
			Lean	Fat	% Fat
0 (↔ PTH, ↔ Vit D)	84.6	29.3	53,043	29,079	35.7
1 (↔ PTH, ↓ Vit D)	88.9	32.6	54,247	32,878	38.0
2 (↑ PTH, ↓ Vit D)	91.5	33.2	54,093	34,998	39.6
P	0.17	0.0007	0.84	0.03	

↔ Vit D (normal vitamin D)= more than 50 nmol/L

↔ PTH (normal PTH)= less than 50 nmol/L

Means adjusted for age and sex (PROC GLM)

Lean and Fat Body Mass¹ (Kg) by Category of Vitamin D / PTH: ONOSS Project (N=65)

Vitamin D / PTH Category	Lean Mass	Fat Mass	% Fat
Normal	53.0	29.0	35.4
Vitamin D ↓, PTH Normal	54.2	32.6	37.6
Vitamin D ↓, PTH ↑	54.4	34.7	38.9
P-Value	0.80	0.05	

$\Delta=2.6\%$ (Lean Mass, Normal vs Vitamin D ↓, PTH Normal)
 $\Delta=19.7\%$ (Fat Mass, Normal vs Vitamin D ↓, PTH Normal)
 $\Delta=9.9\%$ (% Fat, Normal vs Vitamin D ↓, PTH Normal)

¹Data are adjusted for age, sex, and season

Relationship of Vitamin D / PTH Category with Weight, BMI, Waist Circumference and Waist-to-Hip Ratio

Vitamin D / PTH Category	Weight (Kg)	BMI (Kg/m ²)	Waist Circum (cm)	Waist : Hip Ratio
Normal	84.3	29.3	43.4	0.84
Vitamin D ↓, PTH Normal	88.9	32.5	44.8	0.88
Vitamin D ↓, PTH ↑	91.6	33.0	45.5	0.87
P-Value	0.17	0.003	0.10	0.18

$\Delta=12.6\%$

Data are adjusted for age, sex, and season

Extremity and Trunk Fat¹ (Kg) by Category of Vitamin D / PTH: ONOSS Project

Vitamin D / PTH Category	Fat Mass		
	Trunk	Extremity	T:E Ratio
Normal	13.1	14.9	0.879
Vitamin D ↓, PTH Normal	15.6	16.0	0.975
Vitamin D ↓, PTH ↑	16.5	17.2	0.959
P-Value	0.03	0.18	

$\Delta=26.0\%$ (Trunk: Normal to Vit D ↓, PTH Normal)
 $\Delta=15.4\%$ (Extremity: Normal to Vit D ↓, PTH Normal)
 $\Delta=9.1\%$ (T:E Ratio: Normal to Vit D ↓, PTH Normal)

¹Data are adjusted for age, sex, and season

Vitamin D and Hypertension

Vitamin D and Blood Pressure/Hypertension NHANES (1988-1994)

- ❑ 25-OH D levels > 80 nmol/L attenuated the age-related rise in SBP by 20% (versus those with levels < 50 nmol/L)¹
- ❑ Only 8% of blacks had 25-OHD levels > 80 nmol/L¹
- ❑ There was an inverse relationship between 25-OH D levels and SBP that remained significant ($p < 0.05$), though weakened, after adjustment for BMI
- ❑ The inverse association of 25-OH D and SBP was stronger in those 50 years and older versus younger persons ($p = 0.021$)
- ❑ Racial differences in 25-OH D explained ~50% of the racial differences in hypertension prevalence

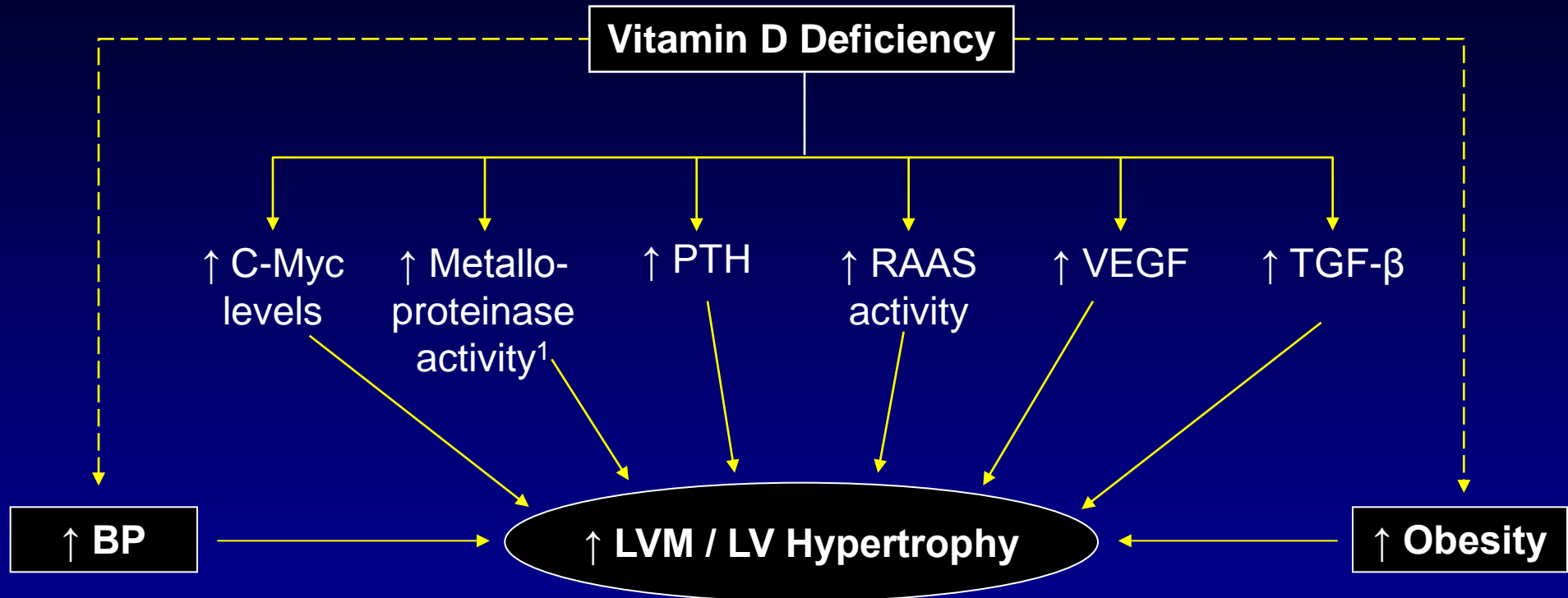
¹ Judd SE et al. *Am J Clin Nutr* 2008;87(1):136-41

² Scragg R et al. *Am J Hypertens* 2007;20(7):713-9

Age- and Sex-Adjusted Regression of Ambulatory Blood Pressure on Vitamin D and PTH Levels

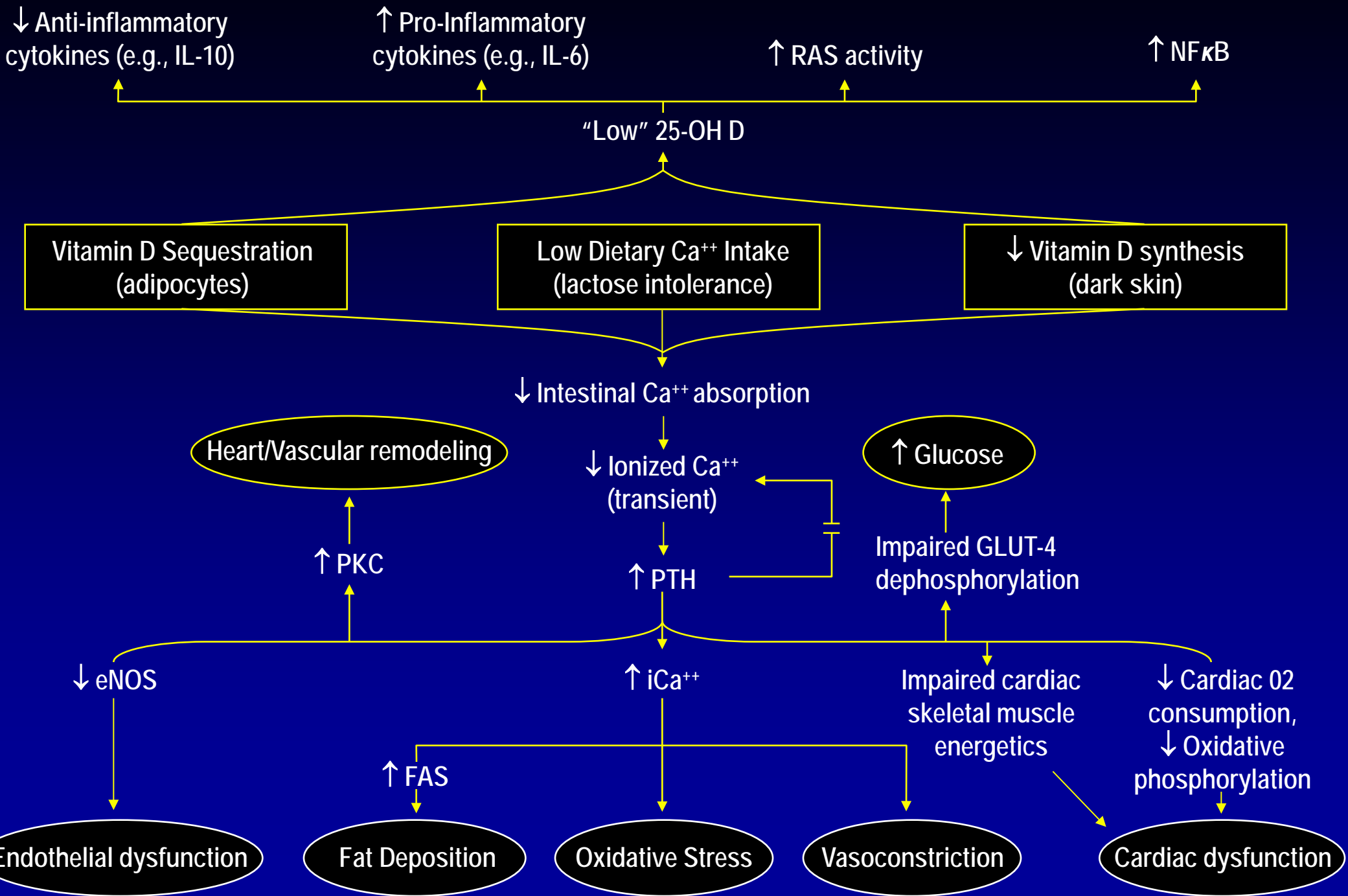
Dependent Variables (units) (sample size)	Independent Variables Coefficients (p-value)			
	Log vitamin D	Log PTH residual	Log PTH	Log vitamin D residual
ABPM daytime SBP (mmHg) (70)	-4.3 (0.11)	0.6 (0.82)	1.9 (0.39)	-4.0 (0.18)
ABPM nighttime SBP (mmHg) (57)	-3.6 (0.40)	-1.9 (0.63)	-0.4 (0.90)	-4.4 (0.35)
ABPM daytime DBP (mmHg) (57)	-4.7 (0.07)	-2.8 (0.26)	-0.8 (0.72)	-5.9 (0.04)
ABPM nighttime DBP (mmHg) (57)	-5.2 (0.15)	-4.3 (0.20)	-2.0 (0.51)	-7.1 (0.08)

Figure A. Conceptual Model Linking Vitamin D Deficiency to Left Ventricular Hypertrophy



Vitamin D= 25-OHD, C-myc=, PTH= parathyroid hormone, RAAS= renin angiotensin aldosterone system, VEGF= vascular endothelial growth factor, TGF-β= transforming growth factor beta,

¹Endogenous inhibitors of metalloproteinases increase during vitamin deficiency



Summary

- Most persons obtain their vitamin D from sunlight exposure and, in Michigan, there is inadequate sunlight to make vitamin D for much of the year
- Low vitamin D levels are associated with higher levels of blood pressure and greater body fat , two of the major contributors to heart enlargement and ultimately heart failure
- Understanding whether supplementation with vitamin D will lower blood pressure, reduce body fat, reduce heart size, etc. will require careful prospective studies
- With a higher level of proof of health benefits for vitamin D supplementation, more aggressive recommendations can be made for supplementation