

# Abstract

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## Vitamin D Deficiency and Risk of Cardiovascular Disease

Wang TJ, Pencina MJ, Booth SL, Jacques PF, Ingelsson E, Lanier K, Benjamin EJ, D'Agostino RB, Wolf M, Vasan RS.

Framingham Heart Study, Framingham, Mass.

**BACKGROUND:** Vitamin D receptors have a broad tissue distribution that includes vascular smooth muscle, endothelium, and cardiomyocytes. A growing body of evidence suggests that vitamin D deficiency may adversely affect the cardiovascular system, but data from longitudinal studies are lacking.

**METHODS:** We studied 1739 Framingham Offspring Study participants (mean age 59 years; 55% women; all white) without prior cardiovascular disease. Vitamin D status was assessed by measuring 25-dihydroxyvitamin D (25-OH D) levels. Prespecified thresholds were used to characterize varying degrees of 25-OH D deficiency (<15 ng/mL, <10 ng/mL). Multivariable Cox regression models were adjusted for conventional risk factors.

**RESULTS:** Overall, 28% of individuals had levels <15 ng/mL, and 9% had levels <10 ng/mL. During a mean follow-up of 5.4 years, 120 individuals developed a first cardiovascular event. Individuals with 25-OH D <15 ng/mL had a multivariable-adjusted hazard ratio of 1.62 (95% confidence interval 1.11 to 2.36, P=0.01) for incident cardiovascular events compared with those with 25-OH D  $\geq$ 15 ng/mL. This effect was evident in participants with hypertension (hazard ratio 2.13, 95% confidence interval 1.30 to 3.48) but not in those without hypertension (hazard ratio 1.04, 95% confidence interval 0.55 to 1.96). There was a graded increase in cardiovascular risk across categories of 25-OH D, with multivariable-adjusted hazard ratios of 1.53 (95% confidence interval 1.00 to 2.36) for levels 10 to <15 ng/mL and 1.80 (95% confidence interval 1.05 to 3.08) for levels <10 ng/mL (P for linear trend=0.01). Further adjustment for C-reactive protein, physical activity, or vitamin use did not affect the findings.

**CONCLUSIONS:** Vitamin D deficiency is associated with incident cardiovascular disease. Further clinical and experimental studies may be warranted to determine whether correction of vitamin D deficiency could contribute to the prevention of cardiovascular disease.

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