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## Vitamin D and Risk for Type 2 Diabetes in People With Prediabetes

A Systematic Review and Meta-analysis of Individual Participant Data From 3 Randomized Clinical Trials

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Author, Article, and Disclosure Information

<https://doi.org/10.7326/M22-3018>

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### Abstract

#### Background:

The role of vitamin D in people who are at risk for type 2 diabetes remains unclear.

#### Purpose:

To evaluate whether administration of vitamin D decreases risk for diabetes among people with prediabetes.

#### Data Sources:

PubMed, Embase, and ClinicalTrials.gov from database inception through 9 December 2022.

### **Study Selection:**

Eligible trials that were specifically designed and conducted to test the effects of oral vitamin D versus placebo on new-onset diabetes in adults with prediabetes.

### **Data Extraction:**

The primary outcome was time to event for new-onset diabetes. Secondary outcomes were regression to normal glucose regulation and adverse events. Prespecified analyses (both unadjusted and adjusted for key baseline variables) were conducted according to the intention-to-treat principle.

### **Data Synthesis:**

Three randomized trials were included, which tested cholecalciferol, 20 000 IU (500 mcg) weekly; cholecalciferol, 4000 IU (100 mcg) daily; or eldecalcitol, 0.75 mcg daily, versus matching placebos. Trials were at low risk of bias. Vitamin D reduced risk for diabetes by 15% (hazard ratio, 0.85 [95% CI, 0.75 to 0.96]) in adjusted analyses, with a 3-year absolute risk reduction of 3.3% (CI, 0.6% to 6.0%). The effect of vitamin D did not differ in prespecified subgroups. Among participants assigned to the vitamin D group who maintained an intratrial mean serum 25-hydroxyvitamin D level of at least 125 nmol/L ( $\geq 50$  ng/mL) compared with 50 to 74 nmol/L (20 to 29 ng/mL) during follow-up, cholecalciferol reduced risk for diabetes by 76% (hazard ratio, 0.24 [CI, 0.16 to 0.36]), with a 3-year absolute risk reduction of 18.1%

(CI, 11.7% to 24.6%). Vitamin D increased the likelihood of regression to normal glucose regulation by 30% (rate ratio, 1.30 [CI, 1.16 to 1.46]). There was no evidence of difference in the rate ratios for adverse events (kidney stones: 1.17 [CI, 0.69 to 1.99]; hypercalcemia: 2.34 [CI, 0.83 to 6.66]; hypercalciuria: 1.65 [CI, 0.83 to 3.28]; death: 0.85 [CI, 0.31 to 2.36]).

### **Limitations:**

Studies of people with prediabetes do not apply to the general population. Trials may not have been powered for safety outcomes.

### **Conclusion:**

In adults with prediabetes, vitamin D was effective in decreasing risk for diabetes.

### **Primary Funding Source:**

None. (PROSPERO: CRD42020163522)

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