

Letter to the Editor Response

Response to Letter to the Editor from Dalan: “Vitamin D Supplementation for Prevention of Type 2 Diabetes Mellitus: To D or Not to D?”

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Abbreviations: 25(OH)D, 25-hydroxyvitamin D; D2d, Vitamin D and Type 2 Diabetes Study.

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We thank Rinkoo Dalan for the comments on our paper (1, 2). We agree that although the reduction in diabetes risk with vitamin D supplementation among people at high risk for diabetes appears to be moderate (~12% relative risk reduction compared to placebo) (3), certain individuals may derive a higher (or lower) benefit based on certain characteristics. For example, in the simplest demonstration of such heterogeneity, vitamin D supplementation reduced diabetes risk by 62% among participants in the Vitamin D and Type 2 Diabetes (D2d) study who had a baseline serum 25-hydroxyvitamin D (25[OH]D) level of less than 12 ng/mL (30 nmol/L) (2).

Consistent with the focus of the scientific community on precision nutrition, we agree that we need to better understand responsiveness to vitamin D supplementation for specific outcomes of interest. The vitamin D response index is an interesting concept that reflects activation of the vitamin D receptor, and it is determined on the basis of measuring vitamin D–triggered changes in the expression of 24 target genes in peripheral blood mononuclear cells and 12 clinical and biochemical parameters (4). There are at least 2 limitations: 1) Although such an index may reflect vitamin D–induced changes in specific response parameters, these changes may not necessarily translate to clinically meaningful outcomes, such as lowering diabetes risk. 2) Low-, mid-, and high-responders are determined with statistical means within a specific cohort but that can be calculated only retrospectively;

specific cutoffs to define degree of response need to be established for use in real time in research or in the clinical setting.

The author also suggests that daily, steady exposure to vitamin D is preferred over intermittent exposure for optimal benefit, and we agree. In a secondary analysis from the D2d study, we reported that participants who received the active intervention (100 mcg [4000 units] of vitamin D₃ daily) and maintained high 25(OH)D levels that were stable throughout the trial period had the lowest risk of diabetes, whereas participants in the placebo group who maintained similar overall 25(OH)D levels that fluctuated during follow-up did not derive significant benefit (5).

Additional Information

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