COMMENTS AND RESPONSES

Comment on: Davidson et al. High-Dose Vitamin D Supplementation in People With Prediabetes and Hypovitaminosis D. Diabetes Care 2013;36:260–266

In their recently published randomized, controlled trial (RCT), Davidson et al. (1) found no significant effect of high-dose vitamin D supplementation on insulin secretion, insulin sensitivity, and incident diabetes. Their RCT is of particular importance because the researchers included subjects with diabetes and vitamin D insufficiency, i.e., a cohort that according to previous observational studies should most likely benefit from vitamin D treatment (2). Although the findings of Davidson et al. clearly show no relevant effect of vitamin D supplementation, it must also be underlined that their mean dose of 88,865 IU per week, corresponding to a daily dose of 12,695 IU, was safe without causing hypercalcemia or hypercalciuria. These are crucial new data regarding vitamin D safety. In this context, there is an ongoing debate on tolerable upper intake levels for vitamin D, which are 4,000 IU according to the Institute of Medicine and 10,000 IU according to The Endocrine Society (3,4). Along with their finding that even more than 10,000 IU vitamin D per day for 1 year does not cause adverse effects, Davidson et al. also showed that maintaining a 25-hydroxyvitamin D (25[OH]D) level of nearly 70 ng/mL (175 nmol/L) is safe. It must, however, be stressed that such high 25(OH)D concentrations should not be regarded as target levels. We do not have sufficient long-term outcome data on 25(OH)D levels of 70 ng/mL (175 nmol/L). By contrast, observational studies suggest that 25(OH)D concentrations of 30–35 (or 40) ng/mL (75–87.5 [or 100] nmol/L) are optimal for multiple health outcomes including mortality, with some studies even reporting a U-shaped association (5). Therefore, and taking into account the increasing number of negative RCT results, which suggest that vitamin D is not a wonder drug for everyone, it will be important for future research to *1*) focus on vitamin D–sensitive individuals, e.g., vitamin D–deficient individuals, and *2*) use vitamin D doses to achieve optimal 25(OH)D levels. Several vitamin D hopes for outcomes with relevance for diabetic patients such as blood pressure or cardiovascular events still remain to be further evaluated in such RCTs. While waiting for these trial results, we want to note finally that, regardless of the current disappointing data on vitamin D and glycemic control, diabetic patients are prone to osteoporosis and fractures, for which vitamin D supplementation is indeed an established treatment (3,4).

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References

1. Davidson MB, Duran P, Lee ML, Friedman TC. High-dose vitamin D supplementation in people with prediabetes and hypovitaminosis D. Diabetes Care 2013;36:260–266
2. Pittas AG, Nelson J, Mitri J, et al.; Diabetes Prevention Program Research Group. Plasma 25-hydroxyvitamin D and progression to diabetes in patients at risk for diabetes: an ancillary analysis in the Diabetes Prevention Program. Diabetes Care 2012;35:565–573
3. Ross AC, Manson JE, Abrams SA, et al. The 2011 report on dietary reference intakes for calcium and vitamin D from the Institute of Medicine: what clinicians need to know. J Clin Endocrinol Metab 2011;96:53–58
4. Holick MF, Binkley NC, Bischoff-Ferrari HA, et al.; Endocrine Society. Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab 2011;96:1911–1930
5. Zittermann A, Iodice S, Pilz S, Grant WB, Bagnardi V, Gandini S. Vitamin D deficiency and mortality risk in the general population: a meta-analysis of prospective cohort studies. Am J Clin Nutr 2012;95:91–100