

## Vitamin D and Cancer Incidence—Response

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We thank Weir and Borek (1) for the thorough reading of our article (2). Weir and Borek mention the limitations of the use of a single vitamin D measurement despite the potential individual variations in vitamin D status. This is a valid point because a single vitamin D measurement at baseline may lose predictive power over time. However, the estimates were very similar, when we only included a 5-year follow-up period in the three studies (3). In addition, Jorde and colleagues (4), who reported significant individual changes in vitamin D status after 14 years of follow-up, found vitamin D status to be as stable a predictor as lipids and blood pressure. However, we acknowledge that the use of a single vitamin D measurement may not accurately reflect vitamin D exposure in the long term, and this misclassification likely attenuated the estimates toward no effect.

Another concern raised by Weir and Borek was whether participants from the included studies were informed of their vitamin D status. They were not, because the blood samples were stored, and vitamin

D status was measured several years after the studies took place. Consequently, we have no reason to believe that vitamin D-deficient participants were more likely to subsequently take vitamin D supplements than the vitamin D-sufficient participants.

Another interesting point raised by Weir and Borek is the mentioning of vitamin D receptor (VDR) polymorphisms. Polymorphisms are mutations with an allele frequency of 1% or more in a population, and humans carry a large number of polymorphisms that may lead to different cellular effects. VDR polymorphisms may change the effect of vitamin D through altered transcription, posttranslational activity, or tertiary structure of the VDR. Along with VDR polymorphisms, the importance of polymorphisms in the vitamin D-binding protein (VDBP) adds to the discussion of the appropriateness of using 25-hydroxyvitamin D as a marker of vitamin D status. In fact, Powe and colleagues found that lower levels of VDBP in Blacks seem to result in bioavailable 25-hydroxyvitamin D levels equivalent to Whites. Therefore, low total 25-hydroxyvitamin D levels do not necessarily indicate vitamin D deficiency—as high levels may not always indicate sufficient VDR binding. How important these polymorphisms are in determining the effect of vitamin D is not clear, and further research is needed to clarify the role of VDBP and VDR polymorphisms in the assessment of vitamin D status (5).

**Disclosure of Potential Conflicts of Interest**

No potential conflicts of interest were disclosed.

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