We thank Dr. Grant (1) for his comments on the Vitamin D Pooling Project of Rarer Cancers (VDPP), a collaborative, multicenter project pooling data from 10 prospective cohorts (2). Specifically, Dr. Grant raises concerns about the differences in the findings of the VDPP, a prospective cohort study of the associations between circulating concentrations of 25-hydroxyvitamin D (25(OH)D) and development of rarer cancers, and findings from ecologic studies using ultraviolet B exposure as a proxy measure for vitamin D. Ecologic studies, which examine correlations between group characteristics and cancer rates, are subject to ecologic fallacy—the problem of assuming that the average applies to the individual. Thus, in the hierarchical evaluation of evidence, ecologic studies provide one of the weakest levels of evidence and should be viewed as hypothesis generating (3). Prospective cohort studies, such as the VDPP, provide a more rigorous test of the hypothesis of the association between vitamin D and development of rarer cancers. In the case of the cancer sites examined in the VDPP, the hypothesis that high circulating 25(OH)D offers protection against non-Hodgkin lymphoma or cancers of the ovary, endometrium, kidney, pancreas, stomach, or esophagus was not supported.

Dr. Grant also raises concerns about the discrepancy between our results and those of studies using predicted (not measured) vitamin D status. The VDPP had the advantage of measuring serum concentrations of vitamin D and thus provides a more accurate assessment of actual vitamin D status than studies using statistical algorithms to predict vitamin D status.

Dr. Grant raises concern about the time frame covered in the VDPP and the possible failure to capture relevant vitamin D history in a single measure. The VDPP cohorts included data from studies initiated as far back as 1974, with follow-up to the present time. The conclusion by Jorde et al., cited by Dr. Grant, was that “[t]racking of serum 25(OH)D appears similar to that for blood pressure and serum lipids, and it provides some support for the use of a single 25(OH)D measurement to predict future health outcomes” (4, p. 903). Additional support for the use of a single measure in prospective studies comes from the analysis of 5 years of vitamin D data from participants in the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial (5) and data presented in our papers (6).

Contrary to the statement by Dr. Grant that individuals with skin cancer have a lower risk of other cancers, cohort studies have observed an increased risk of solid tumors following diagnosis of nonmelanoma skin cancer (7).

While well-conducted randomized clinical trials are viewed as the best test of the hypothesis that vitamin D can prevent cancer, it is highly unlikely that trials will be large enough to have adequate power to examine the impact of vitamin D supplementation on the rarer cancer sites examined in the VDPP. The trial referred to by Dr. Grant is inadequately powered to address rare cancer sites.

Our studies do not support the hypothesis generated from ecologic studies of a protective association between vitamin D concentrations and the development of cancer at the rarer sites we examined.

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**REFERENCES**


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