THREE AUTHORS REPLY

We thank Dr. Grant for his comments (1) on our prospective study of serum 25-hydroxyvitamin D (25(OH)D) concentration and mortality in a population in Linxian, China (2). Dr. Grant writes, “This conclusion was based on the findings at the end of the 24-year follow-up period. There is no reason why the results from previous years cannot be used as well” (1, p. 1045). We did, in fact, account for the entire 24-year follow-up period by plotting the survival curves by quartiles of serum 25(OH)D concentrations and by testing the overall difference between the curves using a log-rank test. A log-rank test examines the full time course of the follow-up and not just whether there are differences at the end of the follow-up period (3). Moreover, by using models that allowed time-dependent relative risks, we tested for and found no deviations from the proportionality assumption, providing further evidence that there were no differences in the curves across time.

Regarding these survival curves, Dr. Grant writes, “Inspection of Figure 1 reveals that survival was always lower for subjects in the 3 lowest quartiles of serum 25(OH)D concentration than for subjects in the highest quartile. There were no deaths among subjects in the highest quartile..."
for the first 1.5 years, but there were deaths among subjects in the other 3 quartiles” (1, p. 000). It appears that Dr. Grant likely misread the figure. As noted in the legend for Figure 1 (“Cutpoints for quartiles 1–4 were <19.6, 19.6–31.8, 31.9–48.3, and ≥48.4 nmol/L, respectively”) (2, p. 1045) and as listed as column headings in Table 1 (2, p. 1044), the first quartile is the lowest quartile and the fourth quartile is the highest quartile of serum 25(OH)D concentrations. In contrast to Dr. Grant's interpretation of Figure 1, we actually showed that the subjects in the lowest quartile (quartile 1, solid thin line) of 25(OH)D concentrations had nonsignificantly higher survival rates than the subjects in the highest quartile (quartile 4, solid bold line). However, because no significant differences between these curves existed, the best interpretation is that subjects in each of the quartiles of 25(OH)D concentrations had the same survival experience.

We appreciate Dr. Grant's thoughts on the study's limitation in having only 1 measurement of serum 25(OH)D concentration, which may change over time. This single measurement may not adequately rank exposure status over the 24 years of follow-up, and future studies should collect appropriate biospecimens for repeated measurements. Similar to Dr. Grant's suggested method to examine risk estimates at shorter follow-up times (4), in our study we described further analyses stratified at the midpoint of follow-up (12 years) that found no difference between these risk estimates and the risk estimates accounting for the full 24-year follow-up.

Lastly, Dr. Grant writes, “The authors overlooked another ecological study of cancer with respect to solar ultraviolet B doses in China (3) [here, reference 5]. This study found a significantly increased all-cancer mortality rate in the early 1990s for low versus high solar ultraviolet B doses.” (1, p. 000). Indeed, we did not cite the noted study (5) because it is very dissimilar to our study. Our analytical prospective epidemiologic study used individually measured 25(OH)D concentrations as the exposure, adjusted for individual-level confounders, and focused on total mortality as the primary endpoint. By contrast, the ecological study cited by Dr. Grant used estimated ambient solar ultraviolet B irradiance, did not and could not adjust for individual-level confounders, and does not report on total mortality but rather on cancer mortality and incidence. Therefore, we did not prioritize citing this particular publication.

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REFERENCES

Shih-Wen Lin1, You-Lin Qiao2, and Christian C. Abnet1
(e-mail: lins4@mail.nih.gov)
1 Division of Cancer Epidemiology and Genetics, National Cancer Institute, Bethesda, MD 20892
2 Cancer Institute, Chinese Academy of Medical Sciences, Beijing 100021, People’s Republic of China