RE: “THE INFLUENCE OF HEALTH AND LIFESTYLE CHARACTERISTICS ON THE RELATION OF SERUM 25-HYDROXYVITAMIN D WITH RISK OF COLORECTAL AND BREAST CANCER IN POSTMENOPAUSAL WOMEN”

A recent paper (1) found that the serum 25-hydroxyvitamin D (25(OH)D) concentration at the time of enrollment in the Women’s Health Initiative was inversely correlated with invasive colorectal cancer for all models but only for the unadjusted models for breast cancer. Overlooked in the paper was any discussion of the role of follow-up time on the results. Another recent paper (2) showed that, for follow-up times longer than 3 years, no nested case-control study had found an inverse correlation between the prediagnostic serum 25(OH)D concentration and incidence of breast cancer. The regression fit to the data for relative risk went from 0.6 at 0 years for case-control studies to 0.95 at 7 years. However, for colorectal cancer, significant inverse correlations were found for follow-up times out to 12 years, although the regression fit went from relative risk = 0.4 at 5 years to 0.7 at 14 years. The changes in relative risk were 0.05/year for breast cancer and 0.033/year for colorectal cancer. Thus, the fact that the vitamin D effect is stronger for colorectal cancer than for breast cancer seems to be why it is easier to find a significant effect for longer follow-up periods.

There is additional evidence that long follow-up times with a single serum 25(OH)D concentration value from the time of enrollment are problematic. A study in Finland found a significant inverse correlation for non-Hodgkin’s lymphoma for follow-up times less than 7 years but an insignificant direct correlation for later diagnosis (3). A study in Norway found a regression coefficient of 0.4 for serum 25(OH)D concentrations measured 14 years apart (4), meaning that only 16% of the variance was explained. Because serum 25(OH)D concentrations vary because of many factors, it is incorrect to assume that a single value represents the value over a long period.

In the Women’s Health Initiative, the mean duration of follow-up was 7.0 (standard deviation, 1.4) years (5). Thus, on the basis of other nested case-control studies, it would be expected that an inverse correlation would be found for colorectal cancer with respect to 25(OH)D concentrations but not for breast cancer, which is what was found (1). However, using the value of 0.05/year change in breast cancer relative risk (1) should have found an odds ratio of 1.29 (95% confidence interval: 1.01, 1.66) for the fully adjusted model in Table 4. This value is statistically significant.

The reason for preferring nested case-control studies over case-control studies is the perception that the disease state may influence the serum 25(OH)D concentration. However, most people do not know they have cancer until so diagnosed. Thus, it seems unlikely that people with cancer would change 25(OH)D concentrations because of having cancer prior to cancer diagnosis.

Those conducting cohort studies of health outcomes with respect to serum 25(OH)D concentrations should consider drawing blood samples at least every 2 years during the study and then using all samples for those used as cases or controls.

ACKNOWLEDGMENTS

The author receives funding from the UV Foundation (McLean, Virginia), Bio-Tech Pharmacal (Fayetteville, Arkansas), the Vitamin D Council (San Luis Obispo, California), and the Vitamin D Society (Canada).

Conflict of interest: none declared.

REFERENCES


William B. Grant (e-mail: wbgrant@infinionline.net)

Sunlight, Nutrition, and Health Research Center,
San Francisco, CA 94164-1603

Editor’s note: In accordance with Journal policy, Neuhouser et al. were asked whether they wanted to respond to this letter, but they chose not to do so.