Serum Vitamin D and Risk of Bladder Cancer in PLCO–Response

Alison M. Mondul, Stephanie J. Weinstein, and Demetrius Albanes

Dr. Grant raises several points with respect to our analysis of serum 25(OH)D levels and risk of bladder cancer (1). First, he suggests that our long follow-up time prevented us from finding a true inverse association between serum vitamin D and risk of bladder cancer. As he points out, however, we had observed an inverse association in our previous analysis within the ATBC Study (2) that had a longer follow-up period than the present study that found no association.

As we have stated previously, the idea that retrospective case–control studies of serum 25(OH)D and risk of bladder cancer would provide more valid tests of the association than prospective cohort studies is not supported by widely accepted epidemiologic principles. The prospective study design is a significant strength of our study and is viewed as advantageous by most researchers for biomarker studies (for example, see recent Institute of Medicine report on vitamin D and calcium, Fig. 4–1; ref. 3). In fact, the paper by Ensrud and colleagues that Dr. Grant references in his letter acknowledges that their prospective design is a strength of their study and that their cross-sectional results may be biased (4). Retrospective biomarker studies are susceptible to reverse causation, as undiagnosed cancer (or other health outcomes, such as frailty in the cited paper) can cause metabolic and/or behavioral changes that may influence individuals’ circulating vitamin D concentrations. This well-known phenomenon is accepted by most population scientists (5). In addition, because initiation of tumors likely occurs many years before diagnosis, measurement of circulating 25(OH)D levels in serum collected several years before cancer diagnosis is likely to better reflect the relevant etiologic window for vitamin D exposure than levels measured at the time of diagnosis.

Disclosure of Potential Conflicts of Interest
No potential conflicts of interest were disclosed.

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