



## Serum 1,25-Dihydroxyvitamin D Level Is Inappropriate for Use in Prospective Studies of Cancer Incidence

### To the Editor:

In a recent paper, Umehara and colleagues reported that baseline serum 1,25-dihydroxyvitamin D [ $1,25(\text{OH})_2\text{D}$ ] levels in a 10-year follow-up study in Japan were significantly inversely correlated with all-cause, cardiovascular, and respiratory infection mortality rates but not significantly correlated with the all-cancer mortality rate.<sup>1</sup> However, it has been found from ecological studies that cancer mortality rates are inversely correlated with solar UVB doses in Japan<sup>2</sup> and other mid-latitude countries.<sup>3</sup> Solar UVB exposure is the most important source of vitamin D for most people. In addition, serum 25-hydroxyvitamin D [ $25(\text{OH})\text{D}$ ] levels are inversely correlated with cancer incidence, especially for short follow-up times,<sup>4</sup> and with survival after cancer diagnosis.<sup>5</sup> The preponderance of the evidence supports the UVB-vitamin D-cancer hypothesis.<sup>6</sup>

Most observational studies do not investigate the relationship between serum  $1,25(\text{OH})_2\text{D}$  levels and cancer risk. There are at least a couple of reasons for not doing so. One reason is that serum  $25(\text{OH})\text{D}$  levels are considered the most important index of vitamin D status, so are routinely measured. The second reason, important for cancer, is that most organs can readily convert serum  $25(\text{OH})\text{D}$  to  $1,25(\text{OH})_2\text{D}$  as needed via  $1-\alpha$  hydroxylase.<sup>7</sup>

A search of pubmed.gov found 1 paper that investigated mortality rates with respect to both serum  $25(\text{OH})\text{D}$  and  $1,25(\text{OH})_2\text{D}$  levels. Although it found significantly increased risk of all-cancer mortality rates for  $25(\text{OH})\text{D}$  level

<20 ng/mL, it found limited significant correlations with  $1,25(\text{OH})_2\text{D}$  level after adjustment for various cancer risk-modifying factors.<sup>8</sup>

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