

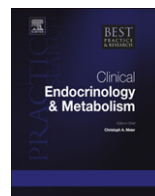


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Why the minimum desirable serum 25-hydroxyvitamin D level should be 75 nmol/L (30 ng/ml)

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The Institutes of Medicine (IOM) recently revised the recommended dietary allowances (RDA) for vitamin D, to maintain serum 25-hydroxyvitamin D (25(OH)D) at or above 50 nmol/L, to sustain bone density, calcium absorption, and to minimize risk of osteomalacia and rickets. However there are compelling reasons why 25(OH)D should preferably exceed 75 nmol/L: (A) Scrutiny of actual data specified by the IOM relating 25(OH)D to bone density and osteomalacia shows the desirable minimum 25(OH)D to be 75 nmol/L (30 ng/mL). (B) Humans are primates, optimized through evolution to inhabit tropical latitudes, with serum 25(OH)D over 100 nmol/L. (C) Epidemiologic relationships show health benefits if 25(OH)D levels exceed 70 nmol/L; these include fewer falls, better tooth attachment, less colorectal cancer, improved depression and wellbeing. Some studies of populations at high-latitude relate higher 25(OH)D to risk of prostate cancer, pancreatic cancer or mortality. Those relationships are attributable to the dynamic fluctuations in 25(OH)D specific to high latitudes, and which can be corrected by maintaining 25(OH)D at steady, high levels throughout the year, the way they are in the tropics. (D) There are now many clinical trials that show benefits and/or no adversity with doses of vitamin D that raise serum 25(OH)D to levels beyond 75 nmol/L. Together, the evidence makes it very unlikely that further research will change the conclusion that risk of disease with serum 25(OH)D higher than 75 nmol/L is lower than the risk of disease if the serum 25(OH)D is approximately 53 nmol/L.

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Introduction

The National Academy of Sciences (NAS) is an arm's-length scientific advisory body to the United States government. The Institute of Medicine (IOM) is a division of the NAS. Recently, the Canadian and United States governments supported the IOM to conduct a thorough review of all available evidence, and if necessary, to revise dietary guidelines for vitamin D and for calcium.¹ For calcium, the recommendations underwent minimal change. However, for vitamin D, the recommendations went from what had previously been referred to as an “adequate intake” – essentially a preliminary approximation – into what is now a recommended dietary allowance (RDA), which is considered more scientifically credible. The basis for the RDA was the opinion of a carefully selected panel of experts, that a serum 25(OH)D concentration as low as 50 nmol/L is enough to maintain healthy bones for most of the population.^{1,2} From this, the RDA for vitamin D was determined as the daily amount of oral vitamin D intake that assures 97.5% the population will sustain a serum 25(OH)D concentration higher than 50 nmol/L. Compared to the advice the IOM published in 1997,³ the dietary recommended intakes for vitamin D tripled for most of the population: from 200 IU up to 600 IU daily. Furthermore, the intake that can be safely consumed by adults doubled, from 2000 IU daily up to 4000 IU daily. Despite these substantial increases in dietary recommendations, should we feel comfortable with a serum 25(OH)D level of 53 nmol/L as Rosen contends?²

Vitamin D does not fit the conventional paradigms attributed to a nutrient, and it needs to be approached with a different way of thinking. Except for communities in the far north, where fish consumption is traditionally a major component of the diet, most humans rely upon sun exposure as their major source of vitamin D. The consumption of fish as well as casual sunshine exposure can provide adults with the equivalent of 3000 IU of vitamin D daily.^{4,5} In the context of the amounts of vitamin D acquired naturally, even the new RDA values are quite modest.

Only once the IOM committee was convinced by what it described as “compelling” evidence about the efficacy of vitamin D for bone health, mainly based on placebo control clinical trials (RCT's), did it consider it appropriate to select a minimum level of serum 25(OH)D against which to calibrate its intake recommendations for the nutrient.¹ For the rest of this paper I will discuss the issue of whether the 50 nmol/L minimum level selected by the IOM committee was appropriate, and address the minimum serum 25(OH)D concentration that a knowledgeable person would be comfortable with, in order to maintain health and to prevent disease?

Bone health

Let us accept for the time being, the position of the IOM panel, that bone health is the only criterion for which the evidence is compelling enough to justify a dietary recommendation.¹ To justify its recommendation for serum 25(OH)D, the IOM report presents what is reprinted here as Fig. 1. The Figure leads to the unambiguous conclusion that a serum 25(OH)D level of 50 nmol/L is more than adequate for virtually all of the population, and that beyond 50 nmol/L, there is no further health benefit. Although it is a subjective decision as to where along a continuous scale of 25(OH)D levels, the point of adequacy should be placed, it is appropriate to examine the rationale of the committee more carefully.

As “conceptualized” in Fig. 1, the relationship between serum 25(OH)D levels and bone mineral density (BMD) reaches its maximum well before 50 nmol/L. The actual data that would have led to these conceptualized graphs are not specified in the IOM report. It is safe to say that for BMD, Table 8 in Appendix C of the IOM report is the only place that contains data pertinent to the BMD representation in Fig. 1.¹ What is not mentioned in the IOM report, are the published data that are, to my knowledge, most similar to the IOM's conceptualized curve. Bischoff-Ferrari et al. presented cross-sectional data for 13,432 adults of all ages, sampled from the National Health and Nutritional Examination Survey (NHANES) cohort from across the USA.⁶ The preliminary “Ottawa report” that had been prepared for the IOM committee to summarize the pertinent knowledge on bone health, stated in reference to Bischoff-Ferrari, that “the association between serum 25(OH)D concentrations and BMD had a steep positive slope in the reference range, reaching a plateau at a concentration of 90–100 nmol/L in an

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