Low vitamin D status in Europe: moving from evidence to sound public health policies†

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There is no doubt that interest in vitamin D has burgeoned over the past few decades. Between 1995 and 2015, annual peer-reviewed, vitamin D–related publications have quadrupled (1). Over this same period, media coverage of vitamin D–related topics has also increased exponentially. Enthusiasm in the research, clinical, and lay communities about this unique prohormone is likely related to its touted pleiotropic effects (based largely on observational research) and the seductive simplicity with which “better” vitamin D status is theoretically achievable. However, controversy exists over the most appropriate threshold for defining optimal vitamin D status (2, 3), as well as the most effective strategies to improve vitamin D status in the general population.

In this issue of the Journal, Cashman et al. (4) report serum 25-hydroxyvitamin D [25(OH)D] concentrations from >55,000 adults and children in more than a dozen different studies from many countries within the European Union (EU). The investigators found that 13% of individuals had 25(OH)D concentrations <30 nmol/L and 40% had concentrations <50 nmol/L. All measurements were performed by using liquid chromatography–mass spectrometry and in accordance with Vitamin D Standardization Program (VDSP) protocols (5). Interestingly, 11 of the cohorts included in the present study had previously measured 25(OH)D levels, and reanalysis using VDSP protocols resulted in significant differences in the estimated prevalence of low vitamin D status. These results not only emphasize the importance of standardizing 25(OH)D testing but also highlight the potential impracticality of public health policies that encourage universal 25(OH)D testing, which may use laboratory assay methodologies of variable quality. However, converting to and maintaining VDSP standards in all clinical laboratories throughout the EU would be an expensive undertaking and may not be the most cost-effective means of addressing the pandemic of low vitamin D status or of improving general population health.

Although 1,25-dihydroxyvitamin D is the most biologically active form of vitamin D, it has a relatively short half-life and is tightly regulated in humans. Indeed, 1,25-dihydroxyvitamin D concentrations are not consistently associated with disease states that are thought to be modifiable through vitamin D supplementation. On the other hand, circulating 25(OH)D, the most abundant vitamin D metabolite, is widely accepted as the best indicator of vitamin D exposure, and numerous epidemiologic studies have shown inverse associations of 25(OH)D concentrations with various diseases (6). However, randomized controlled trials of vitamin D supplementation have yielded mixed results to date, suggesting that the association between “low” 25(OH)D concentrations and disease outcomes may not always be causal. Current evidence suggests that the bioavailable component of 25(OH)D may be a better marker of vitamin D status (7). 25(OH)D is predominantly (~88%), and tightly, bound to vitamin D binding protein (DBP); the remaining ~12% is loosely bound to albumin, and only 0.03% of 25(OH)D is found in its free form (8). Bioavailable 25(OH)D refers to the free and albumin-bound 25(OH)D and is thought to represent the mobile pool of vitamin D that is available for autocrine and paracrine activity in times of metabolic demand. Moreover, polymorphisms in the DBP gene and in the vitamin D receptor likely have a strong influence on individual need for vitamin D and on the response to supplementation (9). Taken together, emerging evidence suggests that simply measuring total 25(OH)D concentrations may not be the most informative or biologically relevant assessment of vitamin D status. However, until future research can establish the physiologic significance of bioavailable 25(OH)D and the contributions of vitamin D–related gene polymorphisms to human health, it appears reasonable to make recommendations for vitamin supplementation in the general population on the basis of achieving targeted 25(OH)D concentrations.

The optimal 25(OH)D concentration for maximizing the health benefits of vitamin D is a hotly debated topic, but there is general consensus that concentrations ≥50 nmol/L are desirable in the general population (based primarily on bone health outcomes). And although the Recommended Dietary Allowance (RDA) for...

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Abbreviations used: EU, European Union; RDA, Recommended Dietary Allowance; VDSP, Vitamin D Standardization Program; 25(OH)D, 25-hydroxyvitamin D.

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vitamin D in the United States and Canada is based on the 2011 report (2) published by the Institute of Medicine, most countries within the EU set their own nutrient recommendations and thus they vary from country to country. Several nations within the EU have recently adopted recommendations for vitamin D supplementation, but these, too, are highly variable and the use of dietary supplements throughout the EU is typically quite low. For example, it is estimated that only 2–7% of adults in Greece use dietary supplements (10). As such, fortification of basic foods such as dairy products, bread, and cereals may be an effective strategy to achieve an RDA that would result in 25(OH)D concentrations ≥50 nmol/L in most community-dwelling Europeans. However, unlike the United States and Canada, most countries within the EU do not have fortification policies (11). In the few EU nations that do have such policies, low amounts of vitamin D are typically added to low-fat milk, nondairy substitutes, margarine, or cereals, primarily for prevention of low vitamin D status in children. Even in Scandinavian countries, where the traditional diet includes oil-rich fish, adequate vitamin D consumption has been challenging to achieve and has led to the adoption of supplementation and fortification policies (11). Although fortification seems like a logical and simple solution to increasing population-based vitamin D consumption within the EU, cultural barriers (e.g., the high value placed on consumption of purely organic foods, resistance to the use of additives in staple foods such as bread, “sun-bathing” as the perceived most effective method of optimizing vitamin D status) represent substantial challenges. Of note, the Institute of Medicine’s RDA for vitamin D of 600–800 IU/d in adults assumed minimal sun exposure (2) and did not recommend strategies aimed at increasing UV light exposure (because of concerns about skin cancer).

The present study by Cashman et al. (4) highlights that low vitamin D status is highly prevalent throughout the EU and that effective, evidence-based policies are needed to address this potential public health crisis. The reflexive response to such findings is often to suggest widespread “screening,” coupled with high-dose vitamin D supplementation. However, current evidence does not suggest that these approaches improve general health in community-dwelling individuals (12). Because food fortification is deeply lacking within the EU, we suggest that future work, which may lead to realistic and actionable public health policies, should focus on determining the most effective fortification strategies to meet requirements for vitamin D among community-dwelling Europeans. Such policies may involve addressing relevant cultural barriers to fortification. The development of effective fortification practices, together with incidental sun exposure and targeted screening of patients at high risk of vitamin D deficiency (e.g., those with malabsorption, bone health disorders, or other relevant conditions), should substantially reduce the prevalence of low vitamin D status in the EU population.

REFERENCES