Symposium: Vitamin D Insufficiency: A Significant Risk Factor in Chronic Diseases and Potential Disease-Specific Biomarkers of Vitamin D Sufficiency

Vitamin D Intake: A Global Perspective of Current Status[1]

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ABSTRACT Global high prevalence of vitamin D insufficiency and re-emergence of rickets and the growing scientific evidence linking low circulating 25-hydroxyvitmain D to increased risk of osteoporosis, diabetes, cancer, and autoimmune disorders have stimulated recommendations to increase sunlight (UVB) exposure as a source of vitamin D. However, concern over increased risk of melanoma with unprotected UVB exposure has led to the alternative recommendation that sufficient vitamin D should be supplied through dietary sources alone. Here, we examine the adequacy of vitamin D intake worldwide and evaluate the ability of current fortification policies and supplement use practices among various countries to meet this recommendation. It is evident from our review that vitamin D intake is often too low to sustain healthy circulating levels of 25-hydroxyvitmain D in countries without mandatory staple food fortification, such as with milk and margarine. Even in countries that do fortify, vitamin D intakes are low in some groups due to their unique dietary patterns, such as low milk consumption, vegetarian diet, limited use of dietary supplements, or loss of traditional high fish intakes. Our global review indicates that dietary supplement use may contribute 6–47% of the average vitamin D intake in some countries. Recent studies demonstrate safety and efficacy of community-based vitamin D supplementation trials and food staple fortification introduced in countries without fortification policies. Reliance on the world food supply as an alternative to UVB exposure will necessitate greater availability of fortified food staples, dietary supplement use, and/or change in dietary patterns to consume more fish. J. Nutr. 135: 310–316, 2005.

KEY WORDS: • *vitamin D intake* • *25-hydroxyvitamin D* • *food fortification* • *dietary supplements* • *vitamin D dietary requirements*

Controversy over the source of vitamin D

Adequate circulating 25-hydroxyvitamin D [25(OH)D][3] concentrations are critical to maintaining the health and the function of the immune, reproductive, muscular, skeletal, and integumentary system of men and women of all ages and races (1). In most individuals, the majority of the circulating 25(OH)D originates from cholecalciferol or vitamin D-3, which is synthesized in the skin upon exposure to sufficient UV blue light (UVB) to cleave the B steroid ring of 7-dehydrocholesterol (2). Vitamin D-3 must undergo 2 separate hydroxylation steps to become functional in its primary biological role in calcium and phosphorus homeostasis. After synthesis in the skin, it is transported to the liver, where it is metabolized to 25(OH)D and may be stored or released to circulation. This intermediary metabolite is the major circulating and storage form that is delivered to tissue for further activation. When physiological demands for calcium and phosphorus arise, circulating 25(OH)D is metabolized to its biologically active hormonal form, 1,25-dihydroxyvitamin D [1,25(OH)$_2$D] primarily in the renal tubular cells (1,2). The best characterized target organs for 1,25(OH)$_2$D are the intestine, the kidney, and the bone, but nuclear receptors for this secosteroid hormone have been identified for >30 tissues (2); thus it has other important functions in addition to calcium homeostasis.

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[3] Abbreviations used: 1,25(OH)$_2$D, 1,25-dihydroxyvitamin D; 25(OH)D, 25-hydroxyvitamin D; UVB, UV blue light.

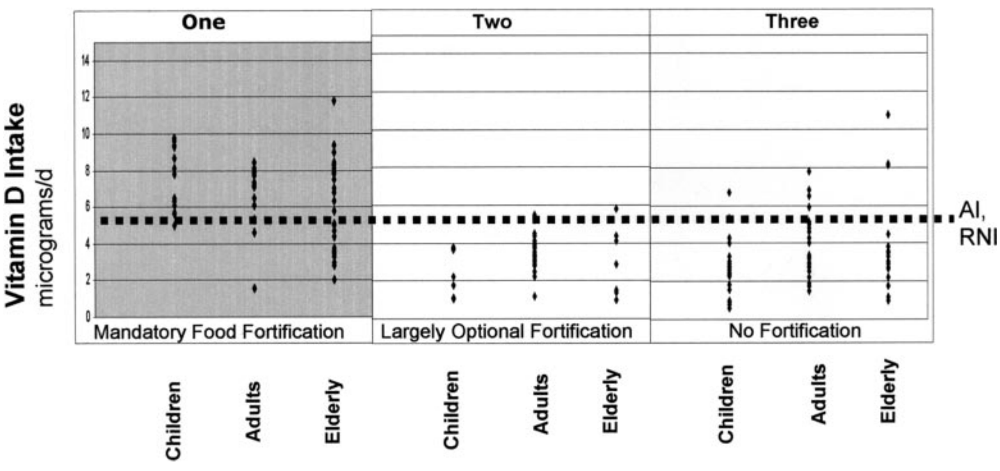

FIGURE 1 Vitamin D intake of children, adults, and elderly subjects from studies conducted in countries classified into Categories One, Two, and Three according to the national food fortification policy (data taken from references 19–101). AI, adequate intake (Canada and United States); RNI, recommended nutrient intake (United Kingdom).

Adequacy of vitamin D nutritional status is measured by the circulating levels of 25(OH)D, which is the combined product of cutaneous synthesis from solar exposure and dietary sources. In free-living children and adults, the majority of circulating 25(OH)D originates from UVB exposure. Several recent studies have identified a high prevalence of vitamin D deficiency and insufficiency in otherwise healthy adults and children living in North America (3,4), Europe (5,6), and even sun-drenched countries (7,8). The importance of vitamin D deficiency to health relates to its role as a significant risk factor for osteoporosis, diabetes, cancer, ischemic heart disease, and autoimmune and infectious diseases (9). The widespread prevalence of vitamin D deficiency and its function in these chronic diseases has called attention to the critical need for adequate exposure to the sun. However, many dermatologists who are concerned about the anticipated 55,000 annual cases of melanoma, the most deadly form of skin cancer, have dismissed the importance of this call for prudent exposure to sunlight. Despite the high prevalence of vitamin D insufficiency, these experts consider the health risks to be small compared with the danger of melanoma. They caution that no level of unprotected sun exposure is prudent or warranted. One skin cancer expert recently emphasized that "people can get all the vitamin D they need from eating fish or drinking more milk" (10). Regrettably, little consideration has been given to the accuracy of this statement. Do we consume enough vitamin D in our diets in the United States, Canada, or the rest of the world, even in sun-drenched countries where exposure is difficult to avoid and there should be little dependency on dietary sources to maintain adequate circulating levels of 25(OH)D? Are there adequate levels of vitamin D in the food supply to meet physiological needs even in populations that are at greatest risk, such as the elderly and individuals with dark skin who live at the highest latitudes? These are the questions that we seek to address in this paper, as well as review the adequacy of current intake levels in maintaining healthy circulating levels of 25(OH)D.

Vitamin D intake and the importance of food fortification and dietary supplement use

The evidence continues to grow that demonstrates the strong association between vitamin D status and the reduced risk of chronic disease that now can be undeniably linked to vitamin D intake, as well as reduced sun exposure. The importance of vitamin D intake in the prevention of chronic disease is further strengthened by several recent cross-sectional or longitudinal studies that demonstrate a significant association between estimates of vitamin D intake and reduction in risk of osteoporosis (11–12), diabetes (13,14), cancer (15–17), multiple sclerosis (18), and rheumatoid arthritis (19).

When environmental, social, or physiological circumstances prevent adequate exposure to sunlight, dietary compensation must occur to maintain serum 25(OH)D levels. For those countries in which high levels of fatty fish are not consumed, the richest natural source of vitamin D, the only alternative to increasing their exposure to natural or artificial UVB light is to fortify their food or to use vitamin supplements. The effect of food fortification and dietary supplement use in different countries on estimates of vitamin D intake among different age groups in their populations are presented (**Fig. 1**). We compared intake estimates from studies conducted over the last 25 y (19–101) that reported quantified vitamin D intakes estimated from FFQs, 24-h recall, or multiple-day food records to illustrate the impact of food fortification, dietary supplement use, or dietary patterns featuring high fish consumption without extensive food fortification. Dependent on their country of origin, studies were assigned to 1 of 3 categories that reflect their countries' overall national policy of food fortification with vitamin D. Category One reflects countries with some mandatory fortification of staple foods, such as milk and margarine, and allows optional fortification of other classes of food that includes the United States and Canada (19–42). Category Two includes the United Kingdom, Ireland, Scotland, Australia, and similar countries (43–63) with no required fortification of foods; however, these countries allow optional fortification of a number of foods, including staples such as margarine and breakfast cereals. Countries where no mandatory fortification of foods with vitamin D occurs and where there is limited or restricted use of optional food fortification were assigned to Category Three; this category includes Europe and the majority of other countries in the world (64–96). The third category also contains vitamin D intake estimates from countries like Japan and Norway that have little or no fortification of foods but that consume relatively high vitamin D intakes due to their high fish consumption (97–101).

Because so few studies take on the difficult task of assessing vitamin D intake, we considered data from nationally representative surveys as well as small focused clinical studies. A number of confounders contribute to the variability that occurs in Figure 1. Primarily, there is a lack of consistency in the methods used to collect the dietary intake information and

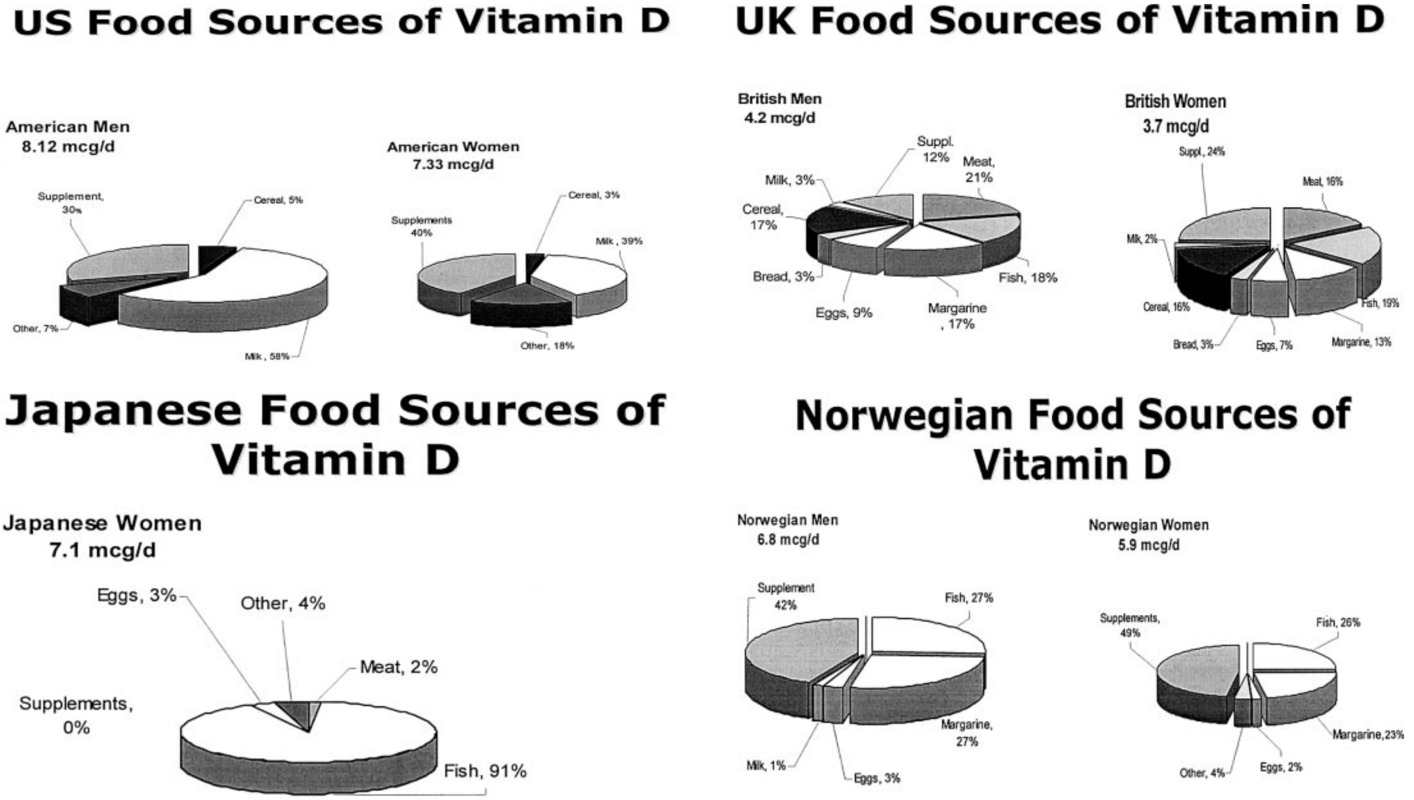

FIGURE 2 Percentage of contribution of various food groups to mean daily vitamin D intake in the United States (*upper left panel*), United Kingdom (*upper right panel*), Japan (*lower left panel*), and Norway (*lower right panel*), demonstrating the influence of different food fortification practices and contributions from dietary supplement use [data taken from references (57,68,101,103)].

large variability in nutrient composition databases used to quantitate vitamin D intake. Vitamin D intake estimates from Category One countries with the highest level of food fortification practices show 2–3 μg higher intakes than the other 2 categories (42,54). We believe this albeit crude approach reveals the significance of food fortification and nutritional supplement use to vitamin D intake. Overall comparisons of calcium and vitamin D intakes of the general population of North America (United States and Canada; Category One) relative to that of many European countries (Category Three) show both moderately low calcium and vitamin D intake in North America, whereas in Europe, calcium intake is much higher but vitamin D intake is quite lower (2–4 μg/d), reflecting the lack of milk fortification.

The percentage contributions of various food groups to mean daily vitamin D intake in 4 different countries with distinct food fortification practices is presented (**Fig. 2**). Among these countries, young adult Caucasian American men and women have the highest average daily vitamin D intake (8.12 and 7.33 μg/d) with ~5.1 and 3.1 μg/d contributed by fortified foods (42). British men and women consume much lower levels of vitamin D (4.2 and 3.7 μg/d, respectively), with a modest estimated 1.4 and 1.1 μg contributed by fortified foods based on the fact that some breakfast cereals are fortified with vitamin D, and vitamin D is required by law to be added to margarine and is also added to most reduced and low-fat spreads (57). Unlike Americans, the British report ~41 and 44% contributions for men and women, respectively, from meat, fish, eggs, and milk (not fortified), which probably reflects the application of new analytical methods by the British who report measurable amounts of vitamin D in meat and eggs (57). Most European food composition databanks do not contain information on vitamin D and are not standardized with regard to analytical methods; therefore, many studies do not calculate vitamin D intake. The United States and Canada are also in need of updating and reanalyzing foods for vitamin D content. No vitamin D fortification is practiced in Japan (101), and there is limited fortification of foods in Norway (68); however, there are higher mean vitamin D intakes for Norwegian men (6.8 μg/d) and women (5.9 μg/d), and for Japanese women (7.1 μg/d) than their British counterparts, who allow some foods to be fortified (Fig. 2). Their higher intake is attributed to high fish consumption, contrib-

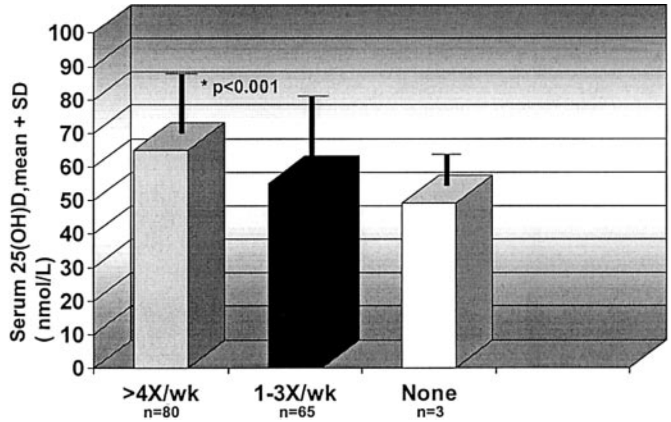

FIGURE 3 Serum concentrations of 25-hydroxyvitamin D in elderly Japanese women plotted by frequency of fish consumption [data taken from reference (101)].

TABLE 1

Vitamin D intake varies with gender, age, and national fortification and supplementation practices

Country	Vitamin D Intake,[1] *µg/d*					
	Women	Men	Women	Men	Women	Men
	12–19 y		*20–49 y*		*50 y+*	
United States. *Calvo et al. (42)*	6.47 ± 0.28[2]	8.43 ± 0.43	7.33 ± 0.26	8.12 ± 0.35	8.37 ± 0.32	8.11 ± 0.21
	19–24 y		*35–49 y*		*50–64 y*	
United Kingdom. *Henderson et al. (57)*	2.9 ± 2.47	3.0 ± 1.59	3.5 ± 2.89	4.2 ± 3.08	5.1 ± 4.11	4.9 ± 3.25
	18–35 y		*36–50 y*		*50+ y*	
Ireland. *Hill et al. (62)*	3.26 ± 0.87	3.67 ± 1.14	3.96 ± 1.23	4.71 ± 1.47	5.09 ± 0.9	5.05 ± 1.48
	6–18 y		*35–45 y*		*65–75 y*	
Spain, Catalonia	2.5	3.3	3.3	4.8	3.0	4.3
Canary Islands. *Serra-Majem (86)*	2.34	3.06	1.76	2.77	1.51	1.87

[1] Values are means ± SD.
[2] Means ± SD for Caucasians only.

uting an average 1.8 and 1.5 µg/d to Norwegian daily intakes and 6.4 µg to daily Japanese vitamin D intake (68,101). Fish consumption appears to be a significant factor in maintaining adequate concentrations of serum 25(OH)D, especially during the winter in Japan. Nakamura and colleagues (101) found that fish consumption was positively associated with serum 25(OH)D concentrations in elderly Japanese women. They observed that subjects who ate fish frequently (≥4 times/wk) had significantly higher 25(OH)D concentrations by an average of 10 nmol/L than women who ate fish 1–3 times/wk (**Fig. 3**). Japanese women consume very low levels of calcium but experience 33–50% lower incidence of osteoporosis compared with elderly women in the United States and northern Europe (101). The authors suggest that frequent fish consumption helps maintain adequate concentrations of serum 25(OH)D in elderly Japanese women and may explain this lower incidence of osteoporosis, despite low calcium intakes. Other studies have demonstrated that diet is a significant independent predictor of plasma 25(OH)D levels. This is evident when indigenous inhabitants, often in extreme northern or southern latitudes, change from traditional foods naturally rich in vitamin D, such as fish and blubber, to Westernized diets (102).

The growing importance of the use of dietary supplements to mean daily vitamin D intakes is presented (Fig. 2). In adult Caucasian men and women in the United States, nutritional supplements contributed 30 and 40%, respectively, to total vitamin D intake (42,103) to 42 and 49% of vitamin D intake of Norwegian men and women, respectively (68), and to 12 and 24% of the average daily intake of British men and women, respectively (57), whereas nutritional supplements do not contribute to average daily intake in Japanese women (98–101). On average, nutritional supplement use in the United States is associated with increases in daily vitamin D intakes of ~2 to 3 µg/d (42). We observed a tendency for increased contributions from nutritional supplement use with age and greater use by women (42,57). In younger British men and women, supplements providing vitamin D increased mean intakes from food sources alone by 14% for men (from 3.7 to 4.2 µg/d) and by 32% for women (from 2.8 to 3.7 µg/d), whereas supplement use by British men and women, 50–64 y old, increased mean intakes of vitamin D by 46% from 3.5 µg/d from food alone to 5.1 µg/d (57).

Overall patterns of dietary vitamin D intake (food and supplements) vary with gender, age, and national fortification and supplementation practices. There clearly is a significant trend ($P \leq 0.0001$) for higher intakes in men than in women, except in those countries with increased nutritional supplement use by elderly women (United States, United Kingdom, and Ireland) (**Table 1**). Among the Caucasian or white populations that are shown in Table 1, there is a trend for increased vitamin D intake with increasing age. Significant racial and ethnic differences in vitamin D intake and nutritional status can occur within a population. This point is illustrated, showing racial differences in vitamin D status, intakes, food sources, and nutritional supplement use in white and black adults in the United States (**Table 2**) (103). Black men and women in the United States have significantly lower serum 25(OH)D concentrations than their white counterparts ($P \leq 0.0001$), but this is not entirely attributable to impaired skin synthesis, due to the high melanin content of skin blocking UVB. In the United States, black men and women consume significantly lower ($P \leq 0.0001$) vitamin D from milk and ready-to-eat cereals, and consume significantly lower ($P \leq 0.0001$) vitamin D from dietary supplement use (Table 2) (103). We observed similar lower serum 25(OH)D levels and lower vitamin D intakes in Mexican-Americans (data not

TABLE 2

Racial differences in vitamin D status, intakes, food sources, and supplement use in white and black adults in the United States: results from the third National Health and Nutrition Examination Survey, 1988–1994[1]

Parameter	White adults	Black adults
Sample size[2,3]	6456	4316
Serum 25(OH)D,[4] *nmol/L*	79.0 ± 0.95	48.2 ± 1.05*
Vitamin D intake:		
Total: food + supplements, *µg/d*	7.92 ± 0.15	6.20 ± 0.13*
Supplements alone, *µg/d*	2.84 ± 0.14	2.00 ± 0.11*
Fluid milk and milk based beverages, *µg/d*	1.99 ± 0.06	1.01 ± 0.04*
Plain fluid milk, *µg/d*	1.86 ± 0.06	0.92 ± 0.04*
Ready-to-eat breakfast cereals, *µg/d*	0.39 ± 0.02	0.23 ± 0.02*

[1] From reference 103. * Significantly lower in black compared with white adults; $P < 0.0001$.
[2] Weighted mean ± SEM.
[3] Includes only persons who had complete and reliable dietary intake data; excludes pregnant and breast-feeding women or women who did not report this status.
[4] Includes samples taken at all latitudes during summer and winter, i.e., not controlled for differences in UV intensity.

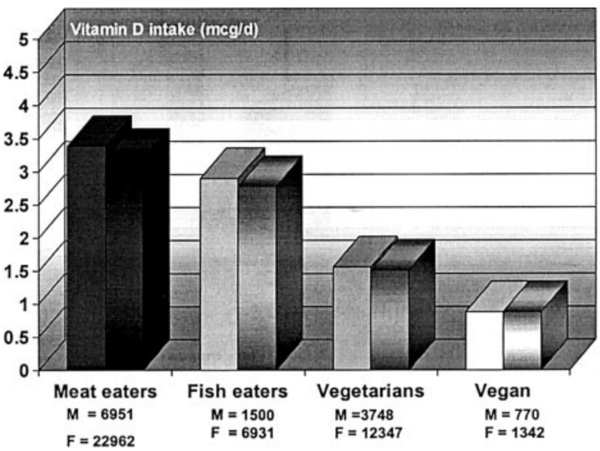

FIGURE 4 Mean daily vitamin D intakes in men and women with dietary patterns characterized as meat-eaters, fish-eaters, vegetarians, and vegans [data taken from reference (56)].

shown) (42,104). Asians residing in Canada, the United Kingdom, and Europe are also at risk of vitamin D deficiency; however, lack of sunlight is not the only contributing factor, because low dietary intake and altered physiology also appear to play a role in vitamin D deficiency in Indo-Asians (105,106). Indo-Asians residing in southern United States have been shown to have increased 24-hydroxylase activity, which alters vitamin D metabolism and may help to account for their observed low serum 25(OH)D concentration even in the sun-drenched southern states (107). A vegetarian diet followed by many Indo-Asians is another well-recognized risk factor for vitamin D deficiency due to low D content (105) and observed increased loss of vitamin D [reduced circulating half-life of 25(OH)D] through the enterohepatic circulation observed with high phytate and vegetable fiber diets (108). Strict vegetarians in all race/ethnic groups are at risk of vitamin D deficiency because of low dietary vitamin D intake (**Fig. 4**) (56,109).

Evidence of successful fortification strategies of food staples

What is the best strategy to increase vitamin D intake and to improve 25(OH)D status in vulnerable populations? Promotion of supplementation targeted to the risk groups is a primary consideration, and there are numerous studies that demonstrate that higher levels of vitamin D administered as dietary supplements are safe and effective in reducing bone loss and fracture rate (12,110). Food fortification is another consideration, but this strategy has a tendency to only benefit the general population and to not improve the intake of specific groups at risk (54,86). The effect of fortification of food with vitamin D in reducing the risk of fracture or other chronic disease risk has not been appropriately evaluated in any country (111). It is critical to identify an appropriate food vehicle, usually a food staple that would preferentially increase the intake of the target group. More recently, several small studies have examined the safety and the efficacy of fortifying margarine and milk (94–96,112) in countries where the food supply is not fortified with vitamin D. To date, none of these studies are nationally representative of the entire population (all gender and age groups) and few measure end points beyond changes in circulating concentrations of 25(OH)D. Several recently published intervention studies have successfully demonstrated the safety and the efficacy of milk as a fortification vehicle for vitamin D in Chinese women living in Malaysia (112) and in adolescent Chinese schoolgirls in Beijing. The milk vehicle consumed by Chinese women was fortified to a higher level of vitamin D than in North America (10 μg of vitamin D/d) (112). Consuming the fortified milk over 24 mo significantly raised serum 25(OH)D levels and effectively reduced bone loss at the lumbar spine and hip relative to the control group (112). The school milk intervention study conducted by Du and colleagues (95) was also 24 mo in duration. The milk fortified with vitamin D significantly improved vitamin D status compared with those who drank milk with calcium or with the control group. In this study, the vitamin fortification was lower than current recommendations, nevertheless those receiving the vitamin D fortified milk had a significantly greater percentage increase in size adjusted total bone mineral content and bone mineral density.

Conclusion

From this global review of current estimates of vitamin D intakes, it is clear that the current food supply, supplementation practices, and dietary patterns of most countries cannot adequately compensate for the existing cautionary guidelines to limit solar exposure to prevent skin cancer. It is incumbent on nutritional scientists worldwide to educate the public and regulatory agencies to the importance of developing dietary strategies to maintain adequate vitamin D nutritional status in the general population. Progress toward this goal is evident in the recent promulgation of a qualified health claim on foods in Canada concerning the need for both calcium and vitamin D (113), and the U.S. Food and Drug Administration's recent approval of the addition of vitamin D to calcium-fortified fruit juices (42). Further study is needed to demonstrate efficacy and safety of new strategies in food fortification or nutritional supplementation targeted at groups at risk of dietary vitamin D inadequacy, particularly in the elderly and with racial and ethnic groups, to help ensure adequate vitamin D intake critical to overall health and prevention of chronic disease.

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