Vitamin D fortification in the United States and Canada: current status and data needs\textsuperscript{1–4}

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ABSTRACT
Most circulating 25-hydroxyvitamin D originates from exposure to sunlight; nevertheless, many factors can impair this process, necessitating periodic reliance on dietary sources to maintain adequate serum concentrations. The US and Canadian populations are largely dependent on fortified foods and dietary supplements to meet these needs, because foods naturally rich in vitamin D are limited. Fluid milk and breakfast cereals are the predominant vehicles for vitamin D in the United States, whereas Canada fortifies fluid milk and margarine. Reports of a high prevalence of hypovitaminosis D and its association with increased risks of chronic diseases have raised concerns regarding the adequacy of current intake levels and the safest and most effective way to increase vitamin D intake in the general population and in vulnerable groups. The usual daily intakes of vitamin D from food alone and from food and supplements combined, as estimated from the US third National Health and Nutrition Examination Survey, 1988-1994, show median values above the adequate intake of 5 \( \mu \text{g}/\text{d} \) for children 6-11 y of age; however, median intakes are generally below the adequate intake for female subjects > 12 y of age and men > 50 y. In Canada, there are no national survey data for estimation of intake. Cross-sectional studies suggest that current US/Canadian fortification practices are not effective in preventing hypovitaminosis D, particularly among vulnerable populations during the winter, whereas supplement use shows more promise. Recent prospective intervention studies with higher vitamin D concentrations provided evidence of safety and efficacy for fortification of specific foods and use of supplements. \textit{Am J Clin Nutr} 2004;80(suppl):1710S–6S.

KEY WORDS
Usual vitamin D intake, food fortification, dietary supplements, vitamin D insufficiency, dietary requirements, nutrition labeling

INTRODUCTION
Most circulating 25-hydroxyvitamin D originates from exposure to sunlight; however, seasonal changes, living at high latitudes, dark skin pigmentation, aging, and other factors can impair this process, necessitating periodic reliance on dietary sources to supply the needed precursor to 25-hydroxyvitamin D (1-4). Because so many environmental, cultural, and physiologic factors can impair sunlight-induced synthesis of vitamin D, most of us at some time in our lives are reliant on dietary sources to supply the essential precursor to 25-hydroxyvitamin D. The importance of dietary sources of vitamin D is reflected in the 1997 Dietary Guidelines for vitamin D intake established by the Institute of Medicine of the US National Academy of Science (5). This joint Canadian and American effort to establish guidelines for the adequate intake (AI) of vitamin D in the assumed absence of sunlight is discussed in depth elsewhere in these proceedings (6).

Circulating 25-hydroxyvitamin D concentrations are the best clinical indicators of overall vitamin D adequacy and represent the combined contributions of cutaneous synthesis and oral ingestion of dietary sources of vitamin D, including vitamin \( \text{D}_2 \) from plants and fungi and vitamin \( \text{D}_3 \) from animal sources, fortified foods, and supplements. In addition, the hepatic conversion of vitamin \( \text{D}_2 \) or vitamin \( \text{D}_3 \) to 25-hydroxyvitamin D is not under the tight hormonal regulation of parathyroid hormone, and circulating concentrations of 25-hydroxyvitamin D are not influenced by dietary calcium or phosphorus intake (6). Although the exact serum concentrations distinguishing vitamin D sufficiency from vitamin D insufficiency are controversial, it is clear that the prevalence of low circulating concentrations of 25-hydroxyvitamin D in the United States and Canada is increasing (7-15). Moreover, we are becoming increasingly aware of the link between these low concentrations of 25-hydroxyvitamin D and increased risks of chronic diseases, including diabetes mellitus, cancer, autoimmune disorders, and osteoporosis (1, 7, 16-26).

The US and Canadian populations are largely dependent on fortified foods and dietary supplements to meet their vitamin D needs during times of insufficient sunlight, because foods that are naturally rich in vitamin D are not frequently consumed. Natural concentrations of vitamin D in foods are variable. Fatty fish represents the richest natural source of vitamin D, with salmon being the type most commonly consumed in North America. Liver and other organ meats are also high in vitamin D but are not as popular as fish and are often avoided because of their high cholesterol content. Although mushrooms and egg yolks are listed as sources of vitamin D, the concentrations are often very low and variable, which results in poor documentation of the vitamin D content of these foods (27).

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LAWFUL ADDITION OF VITAMIN D TO FOODS IN CANADA AND THE UNITED STATES

Vitamin D is a fat-soluble vitamin with the potential for toxicity if it is chronically consumed at very high doses; therefore, in Canada and the United States, the addition of vitamin D to foods is very carefully regulated. In developing regulations concerning the lawful addition of vitamin D and calcium to foods, the 2 countries used the same dietary guidelines for ALs of vitamin D and calcium for all sex and age groups and the upper limits of safe intakes of vitamin D and calcium (5).

Canada currently has mandatory fortification of foods, through the Canadian Food and Drug Regulations (28). When a nutritional public health need is identified, the solution is to ensure that all people can benefit, and staple foods are fortified. In the case of vitamin D, the foods that require fortification with vitamin D are milk and margarine. In the case of milk, fluid milk “shall contain added vitamin D in such an amount that a reasonable daily intake of the milk contains not less than 300 IU and not more than 400 IU of vitamin D” (29). Fluid milk in Canada is labeled as providing 44% of the recommended daily intake of (400 IU) per 250-mL serving. Other milk products that require vitamin D fortification are evaporated milk, powdered milk, and goat’s milk. The proliferation of milks of plant origin (particularly soy) made it necessary to require calcium-fortified, plant-based milks to be fortified with vitamin D, as well as other nutrients (eg, vitamin B12), to yield a nutrient profile similar to that of cow’s milk (30). All margarines in Canada are fortified with vitamin D (530 IU/100 g) (31). Other foods for which vitamin D addition is permitted are meal replacements, nutritional supplements, and formulated liquid diets. The amounts of vitamin D added depend on the energy content and intended use of the product; for example, for formulated liquid diets, the amount may be no less than 300 IU and no more than 400 IU per 1000 kcal, as long as the intended total energy intake is < 2500 kcal (32). Currently, with the exception of some egg products, no other fortification with vitamin D is permitted in food. Fortified milk may be used in food manufacturing (eg, yogurt) but, in general, industrial milk that is used for baking and for making milk products such as soft and hard cheeses does not need to be fortified (33).

In the past, there has been some confusion concerning the specific regulations that govern the addition of vitamin D to foods in the United States. These regulations have been confused with the fortification or nutritional quality guidelines for foods (34) and with current good manufacturing limitations associated with some direct food substances affirmed as generally recognized as safe (GRAS) (35). Vitamin D is an affirmed GRAS ingredient [21 Code of Federal Regulations (CFR) 184.1950]. Because its addition to foods as a nutrient supplement is in accordance with 21 CFR 184.1 (b) (2), its use has strict limitations with respect to the categories of foods, functional use, and level of use (36). In accordance with 21 CFR 184.1 (b) (2), any addition of vitamin D to foods not in compliance with each of these established limitations requires a food additive regulation. Such regulatory limitations provide a control mechanism that limits overfortification with vitamin D and thus eliminates some of the concerns regarding the increasing fortification of foods with calcium that is currently underway in the United States (37, 38).

Unlike Canada, where fortification with vitamin D is mandatory for designated foods, the addition of vitamin D to eligible foods in the United States is optional in most cases, with the exception of fortified milk. Fluid milk in the United States is not required to have vitamin D added unless the label declares that it is fortified. Vitamin D, which includes crystalline vitamin D<sub>2</sub> and D<sub>3</sub> and vitamin D<sub>2</sub> and D<sub>3</sub> resin formed from the irradiation of ergocalciferol and cholecalciferol, can be added as the sole source of added vitamin D in the food categories shown in Table 1 and must not exceed the specified limitations (36). Vitamin D is also affirmed as GRAS for use in infant formula [21 CFR 184.1950 (c) (2)] and as an optional ingredient in margarine [21 CFR 184.1950 (c) (3)]. Vitamin D<sub>2</sub> is regulated as a direct food additive for use as a nutrient supplement in calcium-fortified fruit juices and fruit juice drinks (21 CFR 172.380). In addition, vitamin D may be added to olestra to compensate for any interference with absorption of fat-soluble vitamins, in accordance with 21 CFR 172.867 (14) (d).

In the United States, although many varieties of foods are eligible for controlled levels of vitamin D fortification, there is a large gap between the number of eligible foods and the number and variety of vitamin D-fortified foods observed in the United States in the local marketplace, as shown in Table 1. An unofficial limited survey of the local marketplace indicated that, for some of the food categories eligible for vitamin D fortification, few or no fortified products were found. Only 2 types of margarine, a few noodle and hot cereal products, and no macaroni, rice, or commin products were fortified with vitamin D. Milk products such as yogurt, butter, ice cream, sour cream, cream, cottage cheese, and most varieties of hard and soft cheeses were not routinely fortified with vitamin D, which calls attention to a significant public misperception that all dairy products are rich sources of vitamin D (39). Actually, fluid milk is the only dairy food that is routinely fortified with vitamin D. In the United States, milk and ready-to-eat cereals are the predominant food sources of vitamin D (5, 7).

The amounts of vitamin D found in foods are indicated in the Nutrition Facts panel on the label. An example from a ready-to-eat breakfast cereal is shown in Figure 1. The vitamin D content is expressed not in micrograms or international units but as a percentage of a general dietary guideline that the Food and Drug Administration (FDA) uses for product labels. This guideline is the reference daily intake (RDI) or the more commonly used daily value (DV), which is 10 μg or 400 IU (40). The RDI/DV figures are not recommended intake levels, because of the impracticality of stating the age- and sex-specific intake guidelines on the small label; rather, they are reference values for nutrients developed by the US FDA to help consumers use the food label nutrition information (40). The DV is equivalent to the dietary reference intake (DRI) for men and women 51 to 70 y of age (AI: 400 IU or 10 μg) and is twice the DRI set for younger men and women (AI: 200 IU or 5 μg) (40). The vitamin D content shown on the label is expressed as a percentage of the DV and is usually derived from fortification or added vitamin D. As shown here, the usual fortification level for most ready-to-eat cereals is 10-35% DV or 40-140 IU. The intake level is higher if the product is consumed with milk, as indicated. In Canada, a similar labeling system was implemented in January 2003 (41). The vitamin D content should also be expressed only as a percentage of a DV; however, the DV for vitamin D in Canada is 5 μg (200 IU). Therefore, there is potential for confusion between the 2 countries, because the same amount of vitamin D in a food would result in different percentages of DV on the label.
In the absence of nationally representative survey data for Canada, vitamin D intakes cannot be accurately estimated; however, values can be determined for the US population with data from the third National Health and Nutrition Examination Survey (NHANES III), which was conducted in 1988–1994. NHANES III is a national probability survey designed to yield nationally representative estimates of the health and nutritional status of the US population, with data collected from all latitudes in the contiguous United States (25–45° N) (42). We used the survey data to estimate vitamin D intakes for 8 specific age and sex groups in the US population. Our study cohort consisted of female and male subjects 6–11 y of age (female: \( n = 1553 \); male: \( n = 1581 \)), 12–19 y (female: \( n = 1599 \); male: \( n = 1462 \)), 20–49 y (female: \( n = 4546 \); male: \( n = 4199 \)), and \( \geq 50 \) y (female: \( n = 3554 \); male: \( n = 3271 \)). The NHANES III database contains estimates of nutrient intakes derived from a 24-h dietary recall conducted during an extensive interview with each participant. For selected individuals, a second 24-h recall was conducted for estimation of the day-to-day variations in nutrient intake, which would allow calculation of the usual dietary intake. The database also contains information on the frequency of use, number of units consumed per time, and nutrient contents per unit for each dietary supplement product the participants used during a 1-mo period. To estimate the usual dietary intake from the 24-h intake, we used the approach of the National Academy of Sciences (43). Vitamin D intake from dietary supplements was calculated through multiplication of the frequency of use of vitamin D-containing supplements during the 1-mo period by the number of units (eg, tablet, pill, or capsule) consumed each time and by the vitamin D potency per unit. We used a conversion factor of 30.4 to estimate the average daily vitamin D intake from supplements from the data on vitamin D intake per month. The usual intake of vitamin D from food plus supplements was calculated through addition of estimates of an individual’s average daily vitamin D intake from supplements and the usual vitamin D intake from food. We used SUDAAN procedures (software version 7.5.6) (44) to estimate group means and SEM values. These procedures account for the complex sample design used in NHANES III. For data describing racial and ethnic differences in vitamin D intake, we used simple \( t \) tests to compare group mean nutrient intakes according to self-identified race/ethnicity. Complex survey sample weights were used in all statistical analyses, to produce nationally representative estimates.

Nationally representative mean ± SEM and 50th percentile usual intakes for vitamin D for 8 age/sex groups are presented in Table 2 for white, African American, and Mexican American subjects. The estimated intake of vitamin D from food alone is shown in the upper part of Table 2, and the intake from both food and supplements is shown in the lower part. Both the mean and median intakes from all sources meet the AI for children 6–11 y of age but not for most adult men and women \( \geq 50 \) y. Among children 6–11 y of age, Mexican Americans have significantly higher intakes than do African Americans and whites. In general, vitamin D intakes from all sources are higher for men than for women. Among subjects 12–19 y and \( \geq 20 \) y of age, whites
consume significantly more vitamin D than do African Americans and Mexican Americans. African Americans, with the greatest physiologic need for dietary sources of vitamin D, have the lowest intake from food alone and food plus supplements.

From the NHANES III data, it is evident that the use of dietary supplements is associated with increases in daily vitamin D intakes for different countries according to the level of food fortification practiced. Countries in which milk, margarine, and other foods are fortified with vitamin D showed 2–3 times higher vitamin D intake in the healthy US population. However, this approach to nutrient intake assessment is valid only when there is an established estimated average requirement (EAR) (46). There is no established EAR for vitamin D, and the AI has inherent limitations for assessment of vitamin D intake adequacy among groups (46). According to the Standing Committee on the Scientific Evaluation of Dietary Reference Intakes (46), the AI is expected to meet or exceed the amount needed to maintain a defined nutritional state or criterion of adequacy for essentially all members of the apparently healthy population. With respect to vitamin D, a defined nutritional state refers specifically to maintenance of serum 25-hydroxyvitamin D concentrations above the concentration below which vitamin D deficiency rickets or osteomalacia occurs regardless of sun exposure (46). The AI for vitamin D was not based on observed mean intakes of population groups, and the Institute of Medicine (46) determined that the AI cannot be used to calculate the prevalence of inadequate nutrient intakes for groups; furthermore, when mean group intakes are below the AI, assumptions cannot be made regarding inadequacies of intakes. For this reason, we refrain from estimating the prevalence of dietary vitamin D inadequacy on the basis of the NHANES III intake data and simply point out that, for most older adults in the United States, mean intakes of vitamin D are well below the AI. These findings support the need for reevaluation of the DRI for vitamin D and underscore the critical need to establish an EAR for vitamin D.

Cross-sectional studies suggested that current US/Canadian fortification practices are not effective in preventing hypovitaminosis D, particularly among vulnerable populations during winter (8–13, 47). Cross-sectional studies in the United States and Canada also revealed that meeting the DRI for vitamin D intake is not sufficient to prevent vitamin D insufficiency in the winter in Canada (8) and throughout the year among younger and older African American women in the United States (13, 47). The strong association between vitamin D insufficiency and risks of chronic diseases has raised concerns regarding the efficacy of current fortification mechanisms, such as milk fortification, in the United States and Canada to prevent low circulating concentrations of vitamin D (7). Chronic disease risks were linked directly to low vitamin D intake, with significantly greater risks of type 1 diabetes mellitus (18), rheumatoid arthritis (48), multiple sclerosis (49), and hip fractures (50). Many randomized, placebo-controlled studies have demonstrated that higher concentrations of vitamin D administered as dietary supplements (∼800–1200 IU/d or 20–30 μg/d) are effective in reducing fracture rates among elderly subjects (51–53). We know much less about the efficacy of vitamin D fortification of foods in reducing the risks of osteoporosis and other chronic diseases.

Most studies that explored the safety and efficacy of fortifying milk with vitamin D either were limited to measurements of changes in circulating concentrations of 25-hydroxyvitamin D or were conducted for too short a time for accurate detection of changes in bone mineral density or other endpoints (54, 55). Only recently did intervention studies successfully demonstrate the safety and efficacy of milk as a fortification vehicle for vitamin D among Chinese women living in Malaysia (56, 57). In the most recent study, the powdered milk product was fortified to a higher vitamin D level than used in the United States or Canada (ie, 10 μg/d vitamin D and 1200 mg/d calcium) (57). Consumption of different intakes and a defined nutritional state refers specifically to maintenance of serum 25-hydroxyvitamin D concentrations above the concentration below which vitamin D deficiency rickets or osteomalacia occurs regardless of sun exposure (46). The AI for vitamin D was not based on observed mean intakes of population groups, and the Institute of Medicine (46) determined that the AI cannot be used to calculate the prevalence of inadequate nutrient intakes for groups; furthermore, when mean group intakes are below the AI, assumptions cannot be made regarding inadequacies of intakes. For this reason, we refrain from estimating the prevalence of dietary vitamin D inadequacy on the basis of the NHANES III intake data and simply point out that, for most older adults in the United States, mean intakes of vitamin D are well below the AI. These findings support the need for reevaluation of the DRI for vitamin D and underscore the critical need to establish an EAR for vitamin D.

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the fortified milk for 24 mo significantly increased serum 25-
hydroxyvitamin D concentrations and effectively reduced bone
loss at the lumbar spine and hip, compared with the control group
(57). That study presented compelling evidence that milk can be
an effective vehicle for vitamin D fortification; however, we
cannot ignore the current barriers to the use of milk as a food
vehicle for vitamin D in North America.

CURRENT BARRIERS TO ADEQUATE VITAMIN D
INTAKE

Many of the barriers that keep the current vitamin D fortifi-
cation practices from preventing hypovitaminosis D are attrib-
tutable to problems with the consumption of fluid milk. First, the
amount of vitamin D added to milk may not be adequate to
produce the desired health changes or even to increase circulating
25-hydroxyvitamin D concentrations. Furthermore, the racial/ethnicity
groups at greatest risk of vitamin D insufficiency consume less milk and ready-to-eat
cereal than do their white counterparts (7). Finally, the vitamin D
contents of food are variable, which can confound analyses be-
cause of inaccurate nutrient content information.

Focusing on improving our nutrient database of the vitamin D
contents of foods may be an exercise in futility, because the vitamin D contents of foods that are naturally rich in vitamin D
can vary according to the season and climatic conditions, the
fortification of foods in the marketplace is in constant flux, and
the added vitamin D content of fluid milk varies significantly
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