VITAMIN D:

The Current State in Canada

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## Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Meaning</th>
</tr>
</thead>
<tbody>
<tr>
<td>1,25(OH)₂D</td>
<td>1,25-dihydroxyvitamin D, or calcitriol (active state)</td>
</tr>
<tr>
<td>25(OH)D</td>
<td>25-hydroxyvitamin D, 25-hydroxycalciferol, or calcidiol</td>
</tr>
<tr>
<td>AI</td>
<td>Adequate Intake</td>
</tr>
<tr>
<td>BMD</td>
<td>Bone mineral density</td>
</tr>
<tr>
<td>BMI</td>
<td>Body mass index (kg/m²)</td>
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<tr>
<td>CCHS</td>
<td>Canadian Community Health Survey</td>
</tr>
<tr>
<td>CI</td>
<td>Confidence Interval</td>
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<tr>
<td>CNF</td>
<td>Canadian Nutrient File</td>
</tr>
<tr>
<td>CSFII</td>
<td>Continuing Survey of Food Intake by Individuals (U.S.)</td>
</tr>
<tr>
<td>DBP</td>
<td>Vitamin D binding protein</td>
</tr>
<tr>
<td>DIN</td>
<td>Drug Identification Number</td>
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<tr>
<td>DRI</td>
<td>Dietary Reference Intakes</td>
</tr>
<tr>
<td>GDM</td>
<td>Gestational diabetes mellitus</td>
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<tr>
<td>HOMA-IR</td>
<td>Homeostasis model assessment-insulin resistance</td>
</tr>
<tr>
<td>HPLC</td>
<td>High performance liquid chromatography</td>
</tr>
<tr>
<td>IOM</td>
<td>Institute of Medicine (U.S.)</td>
</tr>
<tr>
<td>IU</td>
<td>International Unit</td>
</tr>
<tr>
<td>LC-MS</td>
<td>Liquid chromatography–mass spectrometry</td>
</tr>
<tr>
<td>NHANES</td>
<td>National Health and Nutrition Examination Survey (U.S.)</td>
</tr>
<tr>
<td>NIH</td>
<td>National Institutes of Health (U.S.)</td>
</tr>
<tr>
<td>NOAEL</td>
<td>No Observed Adverse Effect Level</td>
</tr>
<tr>
<td>OR</td>
<td>Odds ratio</td>
</tr>
<tr>
<td>PE</td>
<td>Preeclampsia</td>
</tr>
<tr>
<td>PTH</td>
<td>Parathyroid hormone</td>
</tr>
<tr>
<td>RCT</td>
<td>Randomized Controlled Trials</td>
</tr>
<tr>
<td>RR</td>
<td>Relative risk</td>
</tr>
<tr>
<td>RT</td>
<td>Randomized Trials</td>
</tr>
<tr>
<td>SPF</td>
<td>Sun Protection Factor</td>
</tr>
<tr>
<td>UL</td>
<td>Tolerable Upper Intake Limit</td>
</tr>
<tr>
<td>UVB</td>
<td>Ultraviolet beta solar radiation</td>
</tr>
<tr>
<td>Vitamin D₂</td>
<td>Ergocalciferol</td>
</tr>
<tr>
<td>Vitamin D₃</td>
<td>Cholecalciferol</td>
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</table>
I. Introduction—How the Landscape has Changed

Vitamin D is considered an essential nutrient, with the main function widely accepted as being vital to maintain calcium homeostasis and bone health. Emerging roles for vitamin D point to prevention of not only osteoporosis, but also other chronic diseases including cancer, multiple sclerosis, diabetes and schizophrenia (1). Since the inaugural introduction of the USA–Canada Dietary Reference Intakes (DRI) that began in 1997 with the report on calcium and related nutrients including vitamin D (2), the volume of research related to vitamin D has increased vastly. Unfortunately, reports of vitamin D status in Canadians of all ages are not yet forthcoming, although it is clear that many Canadians are deficient in vitamin D. Deficiency has been observed across the Canadian multicultural population from south to north and is likely a function of both limited endogenous synthesis and limited dietary sources. In addition to the widespread assessment of vitamin D status, a number of societies have put forth new targets for vitamin D intake and status with the goal to optimize health outcomes. These are much different from the values presented in 1997 for the DRI recommendations. The amount of dietary vitamin D required to prevent a deficiency is much less than that thought to be required for optimal status. While vitamin D can be obtained endogenously through exposure to solar radiation, health care professionals agree upon diet as the safest source. This document provides a comprehensive summary of vitamin D nutrition across the lifespan in Canada and identifies gaps in knowledge that need to be addressed to improve vitamin D nutrition and food supply in Canada.
II. Background on Vitamin D Nutrition

1. Dietary Recommendations

The underpinning philosophy of dietary recommendations is to safely meet the needs of the majority of people. In 1997, the Institute of Medicine (IOM) published DRI values for vitamin D to be used by both USA and Canada (Table 1). The Adequate Intake (AI) for vitamin D was set at 200 IU/d for all individuals from birth to 50 years of age, 400 IU/d for those 50 to 70 years of age and 600 IU/d for those over 70 years of age (2). The IOM acknowledged that exposure to sunlight may not be the best approach to ensuring adequate vitamin D status of populations as this can be dependent on culture, skin pigmentation, and/or behaviour related to use of sun block (2, 3). Thus the AI is designed to cover the needs of most individuals for vitamin D in the absence of exposure to ultraviolet beta solar radiation (UVB). The Tolerable Upper Intake Level (UL) for vitamin D was set at 1000 IU/d for infants under 12 months of age and 2000 IU/d for all others. These values are set to have the highest likelihood of safety for the public. The No Observed Adverse Effect Level is somewhat higher and was based on the available science at that time (2). This value is not used in public policy per se, but was used to set the UL to ensure public safety.

For infants, it is assumed that physiological requirements for vitamin D are the same whether the infant is fed breast milk or formula, and that consuming one litre of formula or cows milk daily upon weaning provides 400 IU vitamin D (2). The IOM stated that 400 IU would not be excessive. For children 1 to 8 years of age, there were no data upon which to base the AI; therefore the AI value for this age group was extrapolated from data on older children. However, for ages 9 through 18 years, the IOM stated: “children who live in the far northern and southern latitudes may be unable to synthesize enough vitamin D in their skin to store for use in the winter. These children may need a vitamin D supplement.” The IOM also acknowledged that there was “little scientific information that related vitamin D intake, bone health and vitamin D status … in young adults and adult age groups”. There was no reason to believe that pregnant or lactating women had increased needs for vitamin D. For adults 51 to 70 years of age, the ability to synthesize vitamin D endogenously was acknowledged to decrease with age. For those over 70 years of age, the IOM reported that “the evidence is strong that the elderly are at high risk for vitamin D deficiency, which causes secondary hyperparathyroidism and osteomalacia and exacerbates osteoporosis, resulting in increased risk of skeletal fractures” (2).
Table 1. Dietary Reference Intakes for Vitamin D (2)

<table>
<thead>
<tr>
<th>Life Stage Group (y)</th>
<th>Adequate Intake (IU/d)</th>
<th>Tolerable Upper Intake Level (IU/d)</th>
<th>No Observed Adverse Effect Level (IU/d)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males and Females</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0 to 0.5</td>
<td>200</td>
<td>1000</td>
<td>2000</td>
</tr>
<tr>
<td>0.5 to 1</td>
<td>200</td>
<td>1000</td>
<td>2000</td>
</tr>
<tr>
<td>1 to 3</td>
<td>200</td>
<td>2000</td>
<td>2400</td>
</tr>
<tr>
<td>4 to 8</td>
<td>200</td>
<td>2000</td>
<td>2400</td>
</tr>
<tr>
<td>9 to 18</td>
<td>200</td>
<td>2000</td>
<td>2400</td>
</tr>
<tr>
<td>19 to 50</td>
<td>200</td>
<td>2000</td>
<td>2400</td>
</tr>
<tr>
<td>51 to 70</td>
<td>400</td>
<td>2000</td>
<td>2400</td>
</tr>
<tr>
<td>&gt;70</td>
<td>600</td>
<td>2000</td>
<td>2400</td>
</tr>
<tr>
<td>Pregnancy and Lactation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤18</td>
<td>200</td>
<td>2000</td>
<td>2400</td>
</tr>
<tr>
<td>19 to 50</td>
<td>200</td>
<td>2000</td>
<td>2400</td>
</tr>
</tbody>
</table>

Other Canadian recommendations exist:

- Health Canada recommends that exclusive breastfeeding be accompanied with a 400 IU supplement of vitamin D daily until 400 IU can be achieved through foods (3). This higher value compared to the AI is used within Canada based on evidence of widespread deficiency as indicated by the prevalence of rickets.

- A working group of the Canadian Paediatric Society recommends 800 IU/d for infants residing in northern Native communities during the winter months and that pregnant and lactating women take a supplement of 2000 IU/d (4).

- The Canadian Osteoporosis Society recommends 400 IU/d for women of childbearing years and both men and women under 50 years of age (5), and 800 IU/d for those over 50 years of age.1

- The Canadian Cancer Society recommends that adults living in Canada should consider taking a daily vitamin D supplement of 1000 IU during the fall and winter.2 The Society also recommends that adults at higher risk of having lower vitamin D levels should consider taking a vitamin D supplement of 1000 IU/d all year round. This includes people who are older, who have dark skin, who do not go outside often, and who wear clothing that covers most of their skin.

- The Canadian Dermatology Association recommends that people who are concerned about vitamin D levels take 1000 IU/d of vitamin D supplements.3

- Health Canada’s Eating Well with Canada’s Food Guide recommends that adults over 50 years of age take a supplement of 400 IU/d (6).

- An international panel that includes Canadian experts recommends 1000 IU/d for adults (7).

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1 The Canadian Osteoporosis Society’s recommendation is soon to be updated. Refer to www.osteoporosis.ca.

2 See www.cancer.ca/ccs/internet/mediareleaselist/0_3172_1613121606_1997621989_langId-en.html

3 www.dermatology.ca/media/position_statement/vitamin_d.html
The recommendations for vitamin D in all age groups are increasingly being scrutinized as more and more scientists, societies and institutions debate their adequacy based on a high prevalence of vitamin D deficiency in North America and throughout the world. In September 2007, the IOM held a 2-day conference on vitamin D\(^4\) to review the evidence-based science of vitamin D nutrition and bone health (8) and to begin looking forward to resolution of the discrepancy in recommendations and optimization of vitamin D status. At that meeting, the systematic review on vitamin D funded by the U.S. National Institutes of Health (NIH) was summarized (8). In addition, Health Canada is updating guidelines for nutrition in pregnancy.\(^5\)

2. Vitamin D in Canadian Foods and Supplements

In assessing vitamin D intake, the Canadian Nutrient File (CNF) is incomplete for vitamin D. Many values are assumed to be zero as no information is available. Additionally, many foods consumed by indigenous peoples are not in the file. Health Canada acknowledges this limitation and is presently working to reduce this barrier to assessment of vitamin D intake from foods.\(^6\)

There are two types of dietary sources of vitamin D: one from plants (ergocalciferol; vitamin D\(_2\)) and one from animals (cholecalciferol; vitamin D\(_3\)). Most food sources and supplements in Canada have the latter mammalian form. Vitamin D\(_3\) is estimated to be approximately 1.7 to 3 times more potent than vitamin D\(_2\) based on the rise in serum 25(OH)D in adults (9, 10). One recent study suggests that if the supplement is taken daily, both isoforms equally maintain 25(OH)D.\(^7\) Such relative potency studies have not been conducted in infants, children or pregnancy/lactation and thus the optimal intake of either isoform to support the theoretical concentration of 25(OH)D is uncertain. Nonetheless, vitamin D\(_2\) likely has a shorter half-life since it does not bind as readily to the plasma carrier protein, vitamin D binding protein (DBP) (11). Thus if vitamin D\(_2\) is not consumed on a daily basis, it might not be effective in sustaining adequate status in the longer term. This is important if dosing regimens in the form of high-dosage bolus administration (oral or intramuscular) are used as suggested by numerous research groups studying children (12), pregnant women (13, 14) and adults (8).

Since there are too few natural dietary sources of vitamin D available to realistically compensate for low endogenous synthesis, fortification of milk and margarine is mandated in Canada (15). Main food sources of vitamin D include fortified cows milk, infant formula and margarine, as well as natural sources from salmon, eggs and beef. Additional products are fortified soy beverages, rice beverages and orange juice, and yogurt made from fortified cows milk (Table 2). Sources of vitamin D typical to the exclusively breastfed infant’s diet include small amounts in the mother’s milk, vitamin D drops/syrup, and perhaps cod liver oil, although the vitamin A content of liver oils should be considered due to the risk of toxicity at sufficiently high levels. Upon weaning or through introduction of complementary foods, other sources of vitamin D include fortified cows milk or formula and possibly margarine. Consuming \(~1\) L of formula or cows milk upon weaning would provide \(~400\) IU vitamin D daily which would not be excessive (2). However, most infants do not consume this much milk and should receive a supplement

\(^4\) http://vitamindandhealth.od.nih.gov:80/default.aspx

\(^5\) The revised guidelines are expected in Summer 2008. See www.hc-sc.gc.ca/fn-an/nutrition/prenatal/index-eng.php for updates.

\(^6\) Personal communication, February 2008.

\(^7\) e-pub ahead of print http://jcem.endojournals.org/cgi/rapidpdf/jc.2007-2308v1.
until such volume is achieved. Other vitamin D containing foods such as egg yolks or salmon are not usually consumed by infants less than 9 months of age. Other products that include vitamin D, such as fortified soy and rice beverages and yogurt made from fortified cows milk, also are not typical to the infant diet. An older child or adult who drinks 2 cups of fortified milk or fortified soy beverage plus eats a 3-oz serving of salmon a week would meet the AI recommendation of 200 IU/d. Inclusion of 2 cups of fortified orange juice and regular consumption of eggs and beef would approximately double this to 400 IU/d. However, many adults do not consume fortified orange juice and do not regularly eat fish. While beef and eggs are consumed more often and represent a source of vitamin D intake, the daily intake is typically <40 IU/d. Furthermore, the AI is thought to be too low. In attempts to elevate vitamin D intakes through less commonly consumed foods, the energy and nutrient balance accompanying such high intake of juice would have to be countered against high nutrient density foods. This suggests that if the USA–Canada recommendation for vitamin D is increased to >200 IU/d, the food supply will require modification to meet the needs of vitamin D status without jeopardizing other aspects of a healthy diet. Otherwise reliance on supplements to achieve higher intakes of vitamin D must be reinforced through careful education of health care professionals and the public. It is for these reasons that the Canada’s Food Guide launched in 2007 includes a recommendation for adults over the age of 50 years to take a daily supplement containing 400 IU of vitamin D (6).

Table 2. Common Dietary Sources of Vitamin D

<table>
<thead>
<tr>
<th>Food (volume)</th>
<th>Vitamin D (IU)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cod liver oil (1 tbsp)</td>
<td>1360</td>
</tr>
<tr>
<td>Salmon (100 g cooked)</td>
<td>272(^2)</td>
</tr>
<tr>
<td>Pasteurized fortified cows milk (250 ml)</td>
<td>~88</td>
</tr>
<tr>
<td>Fortified plant beverages including soy, rice or orange juice (250 ml)</td>
<td>~80</td>
</tr>
<tr>
<td>Yogurt made with fortified cows milk (100 g)</td>
<td>~25</td>
</tr>
<tr>
<td>Egg yolk (1)</td>
<td>~25</td>
</tr>
<tr>
<td>Beef (100 g cooked)</td>
<td>~25</td>
</tr>
<tr>
<td>Margarine (1 tsp)</td>
<td>~25</td>
</tr>
<tr>
<td>Infant vitamin D syrup/drops (1 ml)</td>
<td>400</td>
</tr>
<tr>
<td>Infant formula (250 ml)</td>
<td>100</td>
</tr>
</tbody>
</table>

\(^1\) Source: Canadian Nutrient File (CNF). According to the CNF Web Site, “the CNF is the standard reference food composition database reporting the amount of nutrients in foods commonly consumed in Canada. This nutrition research tool is integral to many activities within Health Canada such as setting policies, standards and regulations, risk assessment studies and food consumption surveys.” Information available at: [www.hc-sc.gc.ca/fn-an/nutrition/fiche-nutri-data/cnf_aboutus-aproposdenous_fcen-eng.php](http://www.hc-sc.gc.ca/fn-an/nutrition/fiche-nutri-data/cnf_aboutus-aproposdenous_fcen-eng.php).

\(^2\) Nutrient content for salmon will vary according to source (farmed vs wild) and by variety (e.g. CNF #3183 Salmon, Atlantic, farmed, baked or broiled: 272 IU/100 g; #3156 Salmon, Atlantic, wild, baked or broiled 328 IU/100 g; #3053 Salmon, sockeye (red), baked or broiled, a Pacific salmon: 904 IU/100 g).

\(^8\) Source: Gray-Donald K, Johnson-Down L. Analysis of Canadian Community Health Survey Data on Food and Nutrients. Report to the Beef Information Centre, 2007.
For any individual not able to meet vitamin D requirements through food, reliance on supplementation is routine. Regarding vitamin D supplements in Canada, pediatric and adult formulations contain variable amounts of vitamin D, suggesting that the brand names of vitamins should be solicited when conducting dietary assessments and when advising individuals or health care professionals about supplementation. In addition to multivitamin sources of vitamin D, supplements containing only vitamin D at various dosages exist and can range from 200 IU to 1000 IU per tablet. For example, most multivitamins contain 400 IU/tablet while vitamin D supplements are typically 200, 400 or 1000 IU/tablet. For a quick reference of vitamin supplement contents, refer to the Health Canada Drug Product Database.9

3. Vitamin D Metabolism and Status

Vitamin D can be obtained through endogenous synthesis upon exposure to UVB (290–310 nm) or through foods. The endogenous isoform is cholecalciferol, also known as vitamin D₃, which can be obtained from animal-based food sources like fish or eggs. Another dietary isoform is ergocalciferol, also known as vitamin D₂, which can be obtained from mushrooms in natural form or in rice beverages through fortification. Very few other sources of vitamin D₂ exist with amounts that significantly contribute to intakes.

Endogenous synthesis occurs in skin exposed to UVB. During the winter months in Canada, endogenous synthesis is suppressed because all of Canada is north of the 42nd parallel and therefore UVB radiation is not strong enough to elicit endogenous synthesis (16). Typically it is assumed that endogenous synthesis can only occur from April to October (16), but this does not take into account the wide range in latitude across the Canadian north–south gradient. Regions in the far north likely do not accommodate endogenous synthesis in spring or fall, since UVB is reduced as a result of the zenith angle and the atmosphere, in addition to cold temperatures that necessitate warm clothing and thereby preclude exposure. This scenario is not unique to Canada; residents in all parts of the world above the 42nd parallel north or below the 42nd parallel south are vulnerable in the winter, and individuals who are not able to be outdoors are vulnerable year-round. Both groups will not meet the body’s requirements for vitamin D unless regularly consuming a dietary source.

Upon exposure of skin to UVB, 7-dehydrocholesterol is converted to precholecalciferol, which in turn is isomerized to vitamin D₃. The skin pigment melanin can reduce photosynthesis of vitamin D by 50-fold, placing individuals with darker skin at higher risk for vitamin D deficiency (17). Since the Canadian population is multicultural, this is a limiting factor for many people in this country. Age is also of relevance to vitamin D status of Canadians since age limits endogenous synthesis of vitamin D (18) and Canada has a rapidly aging population. It is estimated that by 2041, nearly 25% of the Canadian population will be over the age of 65 years, which represents 9.4 million individuals (19). Global trends forecast that by year 2030, 20.3% of the population in North America will be over 65 years of age (20). Sunscreen containing a sun protection factor (SPF) of 8 or greater also suppresses endogenous synthesis of vitamin D (17); this includes products designed for regular outdoor activity and for children as well as cosmetic products such as facial foundations.

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After entry into the circulation whether through endogenous synthesis or through foods, vitamin D₃ can be transported free or bound to the vitamin D binding protein (DBP). This protein is synthesized by the liver (21) and not only carries vitamin D₃ within the blood and extends its half-life, but also binds to other forms including vitamin D₂ obtained from food. Approximately 75% of vitamin D is removed from circulation by the liver upon each pass for further metabolism to 25(OH)D (22). Vitamin D from all sources is hydroxylated to 25(OH)D by the liver and released into circulation where it again binds to DBP, but with stronger affinity (21). From dose–response studies, the level of vitamin D required to elevate 25(OH)D by 0.7 to 1.2 nmol/L appears to be 40 IU (7). Because of its lipid solubility, vitamin D can also be sequestered in adipose tissue. Individuals who are obese have 20% lower vitamin D status after accounting for exposure to UVB and diet (23). It appears that obesity is a risk factor for having low vitamin D status. Since 34% of Canadian children are overweight (26% overweight and 8% obese) (25) and 15% of adult Canadians are obese (26), this reality is an important consideration in the study of vitamin D.

Vitamin D status is assessed using serum 25(OH)D (2). This is because 25(OH)D is relatively stable and has a half-life of 10–21 days (2). Serum 25(OH)D (also known as calcidiol) is a reflection of vitamin D derived from foods or endogenous synthesis and thereby reflects the cumulative vitamin D status. To assess vitamin D status, a variety of assays are available (27). Although HPLC and LC-MS methods are the most accurate (27), most institutions use radioimmunoassays and some are now using automated systems (28). Regardless of the assay, it is widely accepted that vitamin D deficiency in adults (Table 3) is diagnosed when serum 25(OH)D is <15 ng/ml or <37.5 nmol/L (2) and that insufficient concentrations are between 37.5 and 50 nmol/L. These levels are consistent with the signs and symptoms of osteomalacia, tetany and myopathy (2). For infants and children, a vitamin D deficiency is defined by a serum 25(OH)D is <11 ng/ml or <27.5 nmol/L (2). These levels are consistent with the signs and symptoms of rickets (2). While the DRI chapter does not suggest an optimal serum 25(OH)D, hypervitaminosis D is defined by the range of 400 to 1250 nmol/L.

The suggested target for optimal 25(OH)D in adults is widely accepted as at least 75 nmol/L, as recommended by an international panel of experts (7). This value is based on dose–response studies of vitamin D supplementation in men and women where a plateau in parathyroid hormone (PTH) was observed (24, 29). Whether these concentrations are appropriate for other life stage groups has not been proven. There is however a growing body of information indicating that other life stage groups can achieve a serum 25(OH)D concentration of 75 nmol/L. Similar cut-off values have been recently proposed for infants and pregnant women (Table 3) by the working group of the Canadian Paediatric Society (4).

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10 For a description of the inter-relationship between of vitamin D and PTH, see Section 4: Functions of Vitamin D.
### Table 3. Definition of Vitamin D Status Based upon Serum 25(OH)D (nmol/L)

<table>
<thead>
<tr>
<th>Category of Vitamin D Status</th>
<th>Institute of Medicine and Health Canada (2)</th>
<th>Canadian Paediatric Society (4)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Infants and Children</td>
<td>Adults</td>
</tr>
<tr>
<td>Deficient</td>
<td>&lt;27.5</td>
<td>&lt;37.5</td>
</tr>
<tr>
<td>Insufficient</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Optimal</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Pharmacological</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Potentially toxic</td>
<td>NA</td>
<td>400 to 1250</td>
</tr>
</tbody>
</table>

NA: Not applicable

There are many examples of studies in adults supporting the optimal range of 75 nmol/L. For older adults >70 years of age, PTH seems to plateau at 100 nmol/L (7). Six studies are well summarized by Dawson-Hughes et al. (7) who suggest that after correction for different assays, 75 nmol/L is the consensus concentration at which PTH plateaus in adults <70 years of age. Such consensus does not exist for children.

Caution is warranted in using these values for infants and children since dose–response studies have not been forthcoming. Particularly in infants and young children under 7 years of age there are scant data upon which to establish such criteria. In randomized controlled trials (RCT) (30) or case–control studies (31, 32) of infants where 25(OH)D was different among groups, PTH was not significantly different. However, in the only high-dosage study of vitamin D supplementation, an inverse relationship was observed between 25(OH)D and PTH (33). Unfortunately, the simple linear approach was not suitable to identify a threshold at which PTH plateaus. It is thus speculative as to whether a 25(OH)D of 75 nmol/L is optimal for infants.

Data for children under 7 years of age are lacking, but some data exist for older children. In the United States, 25(OH)D levels ≥90 nmol/L in postmenarcheal females 12 to 18 years of age were associated with plateaus in PTH (34). Similarly, in other countries such as France, a 25(OH)D level of 83 nmol/L in healthy males 13 to 17 years of age was associated with a plateau in PTH (35). For females 14 to 16 years of age in Finland, a 25(OH)D level >40 nmol/L was reported as necessary to reduce PTH, although only 3 females had a 25(OH)D level >80 nmol/L and the authors indicated that actual plateaus in PTH had not been observed (36). Even in warmer climates such as Lebanon, 25(OH)D levels >75 nmol/L in male and female children 10 to 16 years of age were associated with no abnormal PTH values (37). Thus it is unclear if a 25(OH)D of 75 nmol/L is optimal for children.

### 4. Functions of Vitamin D

The most widely understood function of vitamin D is in calcium homeostasis, but knowledge of emerging roles in other tissues is rapidly evolving. While the best serum indicator of vitamin D status is 25(OH)D, the active form required in physiology is 1,25(OH)2D. Synthesis of 1,25(OH)2D from 25(OH)D is catalyzed by the enzyme 1-alpha-25-hydroxyvitamin D in the kidney for the purpose of calcium homeostasis and in other tissues for non-calcemic functions (38).
Physiologically, when the blood calcium level falls, PTH is released to promote hydroxylation of 25(OH)D to 1,25(OH)\(_2\)D. Both PTH and 1,25(OH)\(_2\)D mobilize calcium from bone and enhance absorption of calcium from the diet and glomerular filtrate. Vitamin D and PTH follow similar circannual rhythms, with PTH fluctuating 20% above and below the annual mean in winter and summer, respectively (39). It is now accepted that PTH plateaus within the normal range when 25(OH)D concentration is over 50–80 nmol/L regardless of seasonality (7). This plateau of PTH likely is positively associated with bone accretion since a 25(OH)D concentration >75 nmol/L is associated with higher bone mass (40). Changes in 25(OH)D are followed 1 month later by changes in PTH, and changes in bone resorption follow changes in PTH by 1 to 2 months (41). Elevated PTH levels characteristically seen in individuals with inadequate vitamin D status can result in the long latency disease of osteoporosis (42), but might more readily associate with acute complications such as tetany and myopathy. In infants and children, vitamin D deficiency causes rickets and in adults it causes osteomalacia. A high PTH can also result from low dietary calcium, making the study of vitamin D status, PTH and calcium homeostasis complex.

In addition to calcium homeostasis, vitamin D in its active state (1,25(OH)\(_2\)D) has the capacity to modify cellular activity, cell differentiation and proliferation (43, 44), and is thus said to have a pleiotropic role in physiology and health. Vitamin D receptors have been reported in all organs (e.g. immune cells, brain, heart, pancreas, intestine), suggesting functionality in these tissues (45). When vitamin D receptors bind 1,25(OH)\(_2\)D, the complex heterodimerizes with the retinoid X receptor, which in turn binds to the vitamin D response element of genes. Depending on the cell type, protein transcription is regulated in response to 1,25(OH)\(_2\)D.

5. Consequences of Vitamin D Deficiency

A. Skeletal Consequences

**Rickets**

Collagen type 1 makes up greater than 90% of the organic matrix of bone (46). At about 8 weeks gestation, the appearance of primary ossification centres marks the beginning of bone mineralization (47) followed by an expected transfer of 30 g of calcium from mother to infant (48). Because of the pleiotropic actions of vitamin D (43, 44), a deficiency is associated with not only reduced fetal mineralization (31, 49), but also reduced bone growth (50) and in some cases defective bone modeling resulting in congenital rickets (51). Even if congenital rickets is not evident at birth, such deficiency is associated with a higher incidence of infant morbidity. These include symptomatic hypocalcemia that may present as seizures (52, 53), hypoplastic lungs presenting as respiratory distress syndrome (51, 54), and hypotonic musculature (54). Vitamin D status positively relates to APGAR scores (an acronym relating to the infant’s Activity, Pulse, Grimace, Appearance, and Respiration) (55), suggesting a role in critical vital signs. Thus, correction of maternal vitamin D deficiency has vast implications for fetal and neonatal health outcome.

Vitamin D deficiency in mothers (56-61) and infants (57-63) is evident throughout the world, covering a wide range of geographic regions and cultures. Vitamin D deficiency has caused congenital rickets (51, 54) and re-emergence of vitamin D dependent rickets in infants (64-68). These studies imply that maternal–fetal transfer of vitamin D is not adequate to achieve optimal health outcomes in the offspring. Lack of maternal–fetal transfer of vitamin D also manifests as
neonatal vitamin D deficiency thought to be reversible by vitamin D supplementation (3) or feeding infant formula or milks that are fortified with vitamin D upon weaning. However, the high incidence of rickets in Canada suggests that these strategies are not adequate to prevent deficiency and far from that postulated to represent optimal vitamin D status. According to the recent pediatric surveillance assessment of rickets in Canada, an estimated 2.9 cases per 100,000 occur in infants ranging from 2 weeks to 6 years of age (69). The majority of cases were characterized by darker skin pigmentation and lack of vitamin D supplementation. In the United States, 9 cases per million children were estimated to have rickets between 1990 and 1998 (70). African American children had the highest risk (75% of cases), but Caucasian (20%) and Asian (5%) children also developed rickets. The common factor among all cases was that they were breastfed term infants and supplementation practices were questionable. Even some infants fed formula will develop rickets (53) presumably since maternal–fetal transfer of vitamin D is inadequate and consumption of only 200 IU/d (0.5 L of formula) is not enough to compensate for deficiency acquired in utero.

B. Early Life Programming of Bone Mass
The fetal origins of adult disease hypothesis (71-73) is grounded in the intrauterine and early life environment. In this hypothesis, programming is defined as the “process whereby a stimulus or insult at a critical period during development, most often during gestation and infancy, has lasting or lifelong effect(s)” (71). The most common diseases associated with programming include cardiovascular diseases, diabetes, obesity and more recently osteoporosis (72). Being born small for gestational age of unknown causes is associated with lower bone mass in children (74) and elderly men (75) plus a higher incidence of hip fracture in men and women (76). In contrast, better nourishment as indicated by higher yet normal birth weights is associated with higher adult whole body, lumbar and hip bone mass even after accounting for age, sex and height plus adult behavioural factors including smoking, alcohol intake, dietary calcium and exercise (77). With respect to vitamin D and programming, maternal vitamin D status in the third trimester of pregnancy positively associated with bone mass in the offspring at 9 years of age (78). Optimal nutrition during infancy, including breastfeeding (79, 80) and vitamin D supplementation (81), is also linked to higher bone mass in children. These studies collectively suggest that bone mass is programmed through nutrition both in utero and postnatally. Providing a vitamin D supplement in infancy (median duration, 12 months) associates with higher bone mineral density (BMD) at 7 to 9 years of age (81). The BMD of the distal radius was 6% higher and the BMD of the femoral neck was 9% higher in those who received a vitamin D supplement in infancy (81). The distal radius and the femoral neck are common sites for osteoporotic fractures later in life (82, 83), further implying that optimization of vitamin D early in life may formulate an important aspect in the primary prevention of osteoporosis. Additionally, infants who are breastfed have higher osteocalcin (84), and osteocalcin also positively associates with vitamin D status (85). Higher values for osteocalcin early in life continue into childhood (86). Overall, early life nutrition, including the intrauterine environment, breast milk and vitamin D, is documented to have long-lasting affects on bone. The growing evidence that early life nutrition programs later bone health (72, 76, 87), combined with growing evidence that vitamin D status is compromised through pregnancy and childhood, places many Canadians at risk for poor bone health.

C. Children
Other age groups are also vulnerable to the effects of vitamin D deficiency on skeletal health. Strategies to optimize bone mass in children should begin early and continue throughout their
Vitamin D: The Current State in Canada  

• CCFN Report  
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In addition to the possible early life programming of bone mass in fetal and infant stages, bone mineral accretion throughout the growing years is important. Canadian data demonstrate that maximal calcium accretion is achieved at the age of 12.5 years for girls and 14.0 years for boys (88). This is important since bone mass attained early in life is considered the most important determinant of bone health later in life (89). Peak bone mass is defined as the highest bone mass achieved and in Canada this is reached by 25 years of age (90). Thus, childhood (birth to 18 years of age) accounts for most of the biological window whereby bone mass is developed.

A recent study in peri-pubertal females (ages 9 to 15 y; n=171) (91) underscores the importance of vitamin D status to support bone mineral accretion. In particular, this study points to the effects of deficient vitamin D status, versus adequate or optimal status, on bone mineral accretion. Over the 3 years of study, girls with highest vitamin D status at baseline (no intervention) had the largest positive change in lumbar spine BMD, even if adjusted for body size. Girls with 25(OH)D concentrations of 19.2 nmol/L (~7.7 ng/ml) had smaller changes in spine BMD—0.111 vs 0.140 g/cm², a difference of 0.029 g/cm² or relative elevation of 26.1% if 25(OH)D approaches adequacy. Whether higher concentrations 25(OH)D (73–83 nmol/L [29–33 ng/ml]) would elevate mineral accretion further is not known. Another study whereby adolescent girls were randomized to placebo, 200 or 400 IU/d of vitamin D for 1 year showed significant improvements in bone mass of the lumbar spine and hip with the 400 IU dosage (92). The lower dosage of 200 IU/d also improved lumbar spine bone mass, but not hip.

D. Young Adults and Aging
Clinical practice guidelines for the management of osteoporosis, a disorder occurring later in life, include weight-bearing activity, calcium, and vitamin D (5) with primary prevention being key (5). In Canada, the prevalence of low bone mass is higher than in other countries located predominantly south of 40°N (90). In theory, this observation could be linked to vitamin D status. The most well-studied age group with respect to vitamin D nutrition is adults, with emphasis on those over 65 years of age. Vitamin D supplementation trials have shown that higher intakes of vitamin D associate with higher vitamin D status, which is associated with better bone mass, tooth retention, fewer falls and some improvements in physical ability (8). This research area is well reviewed in the NIH systematic review (8) and thus not detailed herein. From that review, however, the majority of studies have used 800 IU as the upper end of the dose–response (8).

The areas requiring further study, however, are the amounts of vitamin D required to optimize peak bone mass during the consolidation years; that is, in young adults 18 through 40 years of age. It is thought that peak bone mass is achieved somewhere between 25 and 40 years of age based on stable BMD in cross-sectional studies (90).

E. Reproductive Women
Bone loss in women with vitamin D deficiency during pregnancy and lactation may also be a risk factor for osteoporosis. It is estimated that a woman can lose up to 10% of her bone mass during lactation (93-98), with greater losses evident in women who breastfeed longer (93). Notably, trabecular bone mass is lost in the femoral head and lumbar spine with lactation (99). Yet, it seems in some studies that lactation does not have long-term negative effects on the skeleton (100-102), and might in fact present an opportunity to increase bone mass or protect against osteoporotic fracture at trabecular sites (103). While vitamin D status of a woman is not expected to be compromised by pregnancy or lactation to a great extent (i.e. small amounts are transferred
to the infant), women with low vitamin D status may not recover as well from the demands of pregnancy/lactation with respect to bone mass. This is evidenced in a study of healthy Saudi women in which total duration of lactation had a negative relationship with bone mass (104). These women had very low vitamin D status, leading the authors to conclude that women with vitamin D deficiency do not fully recover bone mass after lactation (104). In many ways the hormonal milieu of pregnancy is similar to that of postmenopausal women; that is, lack of estrogen and losses of bone mass up to 7% over a short period of time (94). It is reasonable to expect that bone health of mothers will benefit from improvements in vitamin D status. This speculation is highly supported by recent work in lactating women in which high dosage vitamin D supplementation (2000 to 4000 IU/d for 3 months) had a positive affect on 25(OH)D concentrations (105) into the range associated with optimal bone mass (7). In another study, women receiving 400 IU/d vitamin D plus 1 g of calcium readily recovered mineral losses during pregnancy and lactation after an equal period of weaning (94). Thus, the benefits of lactation on bone mass might best be realized in association with optimal vitamin D status. This is an important question to address since women consolidate bone between 25 and 40 years of age (90). If bone mass lost during pregnancy and lactation is not replenished due to the high incidence of vitamin D deficiency observed in Canada (106, 107), this poses another challenge to acquisition and maintenance of peak bone mass in our population.

B. Non-Skeletal Chronic Diseases

Non-skeletal chronic diseases that might originate from vitamin D deficiency and the genomic response include cancer, multiple sclerosis, schizophrenia and diabetes (1), but the associations between vitamin D exposure and development of these chronic diseases is not yet as convincing as it is for bone. Epidemiological studies reveal that the prevalence of these diseases is greater as latitude increases, suggesting that lower exposure to UVB radiation and associated decreases in vitamin D synthesis may play a role in their pathology. Cancers associated with vitamin D deficiency include non-Hodgkin lymphoma (108), leukaemia (109), and breast cancer (110). Additionally, glioblastoma is most frequently diagnosed in a winter month (111) and incidence of brain tumours in adults is higher in those born in the winter (112). None of these studies were conducted in a Canadian population. Canada, however, is leading the path in describing the role of vitamin D in multiple sclerosis (113), while Australian research shows that during the winter months with less UVB, there is a 7–10% increase in the number of people born with schizophrenia (114). Vitamin D is also proposed as a critical neuroactive substance as it has wide-ranging effects in brain including induction of nerve growth factor (115). In recent studies, rat pups born to vitamin D deficient mothers had profound alterations in the brain at birth (116). The possible etiology of different cancers might be rooted in development and function of the immune system (1, 43, 117). These findings suggest that low maternal vitamin D has important ramifications for the developing immune system and brain. However, these studies were done at extreme vitamin D deficiencies, and the long-term effects and a clear link to learning have yet to be determined.

Epidemiological studies examining early vitamin D supplementation and the risk of type 1 diabetes (118–121) suggest vitamin D protects against development of this autoimmune disease (117). One study (120) linked subsequent type 1 diabetes status to vitamin D supplementation in infancy. The relative risk of for developing type 1 diabetes was reduced (RR=0.12, CI 0.03–0.47) with 2000 IU vitamin D supplementation. More recent intervention studies are lacking and studies showing that optimal maternal vitamin D status in pregnancy reduces the incidence of
type 1 diabetes in the child are also lacking. Vitamin D status is also associated with glucose metabolism and insulin sensitivity index in adults even after correcting for age, gender and BMI (122). This was confirmed in a secondary analysis of vitamin D supplementation originally designed to test for bone health (123). In non-pregnant adults with impaired fasting glucose, vitamin D supplementation (700 IU/d plus 500 mg/d calcium) over 3 years limited further elevation in fasting plasma glucose (123). In a short one-month RCT using 1332 IU/d vitamin D in adults with type 2 diabetes, the initial secretion of insulin following an intravenous glucose challenge was significantly elevated by 34% accompanied by non-significant reductions (24%) in insulin resistance (124). Even though 25(OH)D concentrations increased over the month (124), longer durations are required in adults to arrive at optimal concentrations of >75 nmol/L (24) that are thought to be required for glucose homeostasis (125).

Women are vulnerable to complications associated with vitamin D deficiency in pregnancy. Preeclampsia (PE) is a pregnancy disorder characterized by maternal hypertension, proteinuria, edema, and fetal growth restriction. Epidemiological studies and clinical studies demonstrate alterations in maternal calcium metabolism in PE and relationships to dietary calcium intake (126, 127). In this context, PE is characterized by lower serum calcium concentration (128), hypocalciuria (129, 130), raised PTH concentration (131) and decreased plasma 1,25(OH)2D concentration (130) in the mother and low birth weight in the offspring. All of these clinical symptoms also are associated with vitamin D deficiency, implicating vitamin D in the development of PE. This speculation is supported by a case–control study that reported an early pregnancy vitamin D <37.5 nmol/L (deficient) was associated with a five-fold elevation in the odds of developing PE (adjusted OR 5.0; 95% CI 1.7–14.1) (132). Such low values prior to 22 weeks of pregnancy were particularly associated with PE (132). Further, reduction in 25(OH)D to values lower than 50 nmol/L resulted in a two-fold risk of developing PE (OR 2.4, CI 1.1–5.4). On average this decline was between 10 and 39 weeks of pregnancy. This association was independent of race, season, BMI and education. Interestingly, 93% of the women took a prenatal supplement. However, based on the Health Canada Drug Product Database,11 this is most certainly less than 400 IU/d on average and not enough to provide for optimization of vitamin D status. Transfer of vitamin D to the fetus is also compromised in that infants of women with PE had a two-fold elevation in the prevalance of a cord 25(OH)D <37.5 nmol/L. In another small case–control study of women with normal pregnancies (n=24) and women with PE (n=24), serum 1,25(OH)2D was also lower in the women with PE (133), as is typically seen in states of vitamin D deficiency. RCT are few in the area of vitamin D and PE. In women given calcium and vitamin D supplements, the incidence of PE was reduced from 16.9% to 10.9% (134). This complements an older study from 1987 whereby women were randomly given 375 mg/d calcium and 1200 IU/d vitamin D at 20 to 24 weeks of pregnancy. At 32 and 36 weeks of pregnancy, blood pressure was lower in the intervention group, but incidence of eclampsia was not different (6 and 9%) (135). Large-scale RCT are required to establish if optimization of vitamin D throughout pregnancy is effective in reducing the incidence of pregnancy-induced hypertension and PE. The value of such a study might translate into generations of health since vitamin D status in pregnancy is now reported to be a predictor of PE later in reproductive years (136). Improvements in vitamin D function through 1,25(OH)2D treatment is also proposed to reduce spontaneous abortions (137).

As noted earlier in this report, obese women are at higher risk of vitamin D deficiency (138). Coincidentally they are also at heightened risk for developing gestational diabetes mellitus (GDM) if they do not already have type 2 diabetes. A very recent report shows that severe vitamin D deficiency (<12.5 nmol/L) is more commonly observed in women with GDM compared to the controls (22 nmol/L) and that vitamin D status strongly associates with the HOMA-IR (homeostasis model assessment-insulin resistance) index (139). Even glucose intolerance was associated with intermediate deficiency (18 nmol/L). These low values within the realm of deficiency demonstrate a dose-effect for different health outcomes, again implying that deficiency should be eradicated to promote both maternal and fetal health. The limitation with readily drawing conclusions from this study, however, is that the women with GDM also had a higher BMI than the control women. However, in a non-pregnant state, vitamin D status was strongly related to the insulin sensitivity index even after correcting for age, gender and BMI (122). Thus, the relationship between vitamin D and GDM might not necessarily be confounded by BMI and requires clarification. Pursuing such a potential intervention is important not only for prevention of GDM and the associated pregnancy complications, but also because of the possibility of reducing susceptibility to development of type 2 diabetes postpartum (140).

Primary prevention of other cancers is also linked to vitamin D. There are now many epidemiological studies suggesting that vitamin D is important in cancer prevention. Intervention studies show that for men, higher vitamin D status is associated with slower progression of prostate cancer (141). Vitamin D in a case–control study shows that higher intakes and status are associated with lower risk of breast cancer in women (142). These two studies were conducted in a Canadian population.
III. Life Stage Groups

1. Infancy

A. Dietary Vitamin D Intake of Canadian Infants
Assessment of vitamin D intake by infants in Canada is limited as a primary outcome. In primiparous mothers (n=1937) in Quebec, 58.1% of those exclusively breastfeeding gave their infant vitamin D supplements in the first six months and 62.1% of those feeding formula did not (143). However, the volume of the supplement was not reported although use of supplements was associated with having post-secondary education (143). There are no data on older infants in Canada, but in a report by Nolan et al. (144) from New York, vitamin D intake was inadequate in infants 12 to 18 months of age among low-income urban families, suggesting that transition to weaning foods might be an issue in Canada as well. The Canadian Community Health Survey (CCHS) has also examined infant diets, but data are not readily available.

B. Vitamin D Status of Canadian Infants
From the 1990s it was apparent that in Northern Canada, most infants were born with a serum 25(OH)D concentration less than 30 nmol/L (145). It was estimated that up to 80% of the non-white infants were at risk for vitamin D deficiency (145). More recently in Manitoba, 36% of infants from white or non-white parents were found to be deficient in vitamin D at birth, defined as a serum 25(OH)D <27.5 nmol/L (49). In a Northern Manitoba community, 43% of older infants 3 to 24 months of age had serum vitamin D levels below the normal range (146). While not Canadian data, but included here to reflect the Arctic, in Alaska infants between 6 and 22 months of age enrolled in the Women, Infants and Children program were studied for vitamin D status and feeding practices (147). While the study spanned 13 months that would have included summer months, 11% of infants had a vitamin D deficiency defined as a 25(OH)D <37.5 nmol/L. Infants who were breastfed had a 12-fold higher likelihood of having a deficiency and among infants who were still breastfeeding, only 34% received a supplement of vitamin D at least occasionally.

C. Evidence of Vitamin D Related Health Issues in Canadian Infants
According to the recent pediatric surveillance assessment of rickets in Canada, there are 2.9 cases per 100,000 in those ranging in age from 2 weeks to 6 years (69). The majority of cases were characterized by darker skin pigmentation and lack of vitamin D supplementation. Even some infants fed formula will develop rickets (53), presumably since maternal–fetal transfer of vitamin D is inadequate and consumption of only 200 IU/d (0.5 L of formula) is not enough to compensate for any deficiency acquired in utero. Similarly, from 1990 to 1998 in the United States, 9 cases per million of children were estimated to have rickets (70). African American children have the greatest risk (75% of cases), but Caucasian (20%) and Asian (5%) children also developed rickets. The common factor among all cases was that they were breastfed term infants for whom perinatal supplementation practices were questionable. Thus the reemergence of rickets is not unique to Canada.
D. Solutions for Improving Vitamin D Nutrition in Canadian Infants

Very few dose–response studies exist for vitamin D supplementation in infancy. The challenge is that the current recommendations have not been rigorously tested through hypothesis-driven research designs that include dosages above the suggested intake values of 400 to 800 IU/d. There are three randomized trials (RT) that were all conducted at latitudes similar to Canada, but only in infants ≤6 months of age.

One RT in breastfed infants in China (148) tested 100, 200 and 400 IU/d of vitamin D₂ but not higher amounts such as 800 IU/d. To highlight key data of the available randomized studies, an intake of 100 to 400 IU/d of vitamin D₂ in Chinese infants increased 25(OH)D on average, but some infants in the northern regions of China (40–47ºN) still had undetectable values after 6 months of supplementation even with the higher dosage (148). Compliance was not clear in this study and PTH and bone mass were not measured. Alkaline phosphatase (isoform not specified) was measured, but did not change with increasing vitamin D dosages. Likewise, no other markers of bone metabolism have been assessed in any randomized study of vitamin D intake in infants that reflect bone formation or resorption as required for modeling of bone.

In the USA, an RCT tested 400 IU/d vitamin D₂ vs placebo in breastfed infants (149). An average 25(OH)D of 92 (range 67–117) nmol/L was observed by 6 months of age, but PTH was not affected (149). In this study, bone mineral content (mg/cm) of the distal radius was measured, but no differences were observed in absolute or delta values by 6 months of age. No other measurements of bone mass were conducted, such as whole body bone mineral content which is recommended for assessing infant bone mass today (82).

The only other RT was in France (33) and tested 500 and 1000 IU/d in infants fed formula (containing vitamin D₃), but again the supplemental form was vitamin D₂. At these dosages, serum 25(OH)D concentrations approximated 70 nmol/L. Mean values were 69 nmol/L, with no value >93 nmol/L. Keeping in mind that the infants received both the supplement and supplemented formula, these data suggest that intakes >1000 IU/d might be required to optimize vitamin D status. The problem with this assumption is that the value of 25(OH)D indicative of optimal status is not clear in infants based on response of bone metabolism, including PTH, and bone mass. Additionally, those infants with low baseline 25(OH)D did not demonstrate normalization of PTH. Further, it is becoming well accepted that vitamin D₂ (plant form) is not as suitable as vitamin D₃ (mammalian form) due to differences in metabolism.

There are no RCT for vitamin D₃, as is used in Canada, at dosages beginning at 400 IU and extending to 800 IU and above as recommended by Health Canada (3) and the Canadian Paediatric Society (4). It is important to provide evidence to support an oral dosage of vitamin D for optimal bone health outcomes, including safety. Two RCT are currently underway, one in Canada with dosages ranging from 400 to 1600 IU beginning at 1 month of age¹² and the other in the USA using 200 to 600 IU also beginning at 1 month of age.¹³

¹² www.clinicaltrials.gov; Identifier NCT00381914
¹³ www.clinicaltrials.gov; Identifier NCT00494104
2. Childhood

A. Dietary Vitamin D Intake of Canadian Children

Assessment of the vitamin D intake of Canadian children is limited as a primary outcome, but there are several studies (published and unpublished) that have included dietary assessment with either direct (IU vitamin D/d) or indirect (servings of milk) evidence of vitamin D intake. In Canada, the majority of data emanates from Quebec. For preschoolers in Quebec (n=98), vitamin D consumption was ~280 IU/d, based on 24-hour recall data, or 425 IU/d based on food frequency questionnaires (150). Another study in preschool children showed that vitamin D intake was lower if dietary fat was low (151). Likewise, a report on Montreal children approximately 10 years of age indicated that only 78% consumed milk each day (the volume consumed was not quantified) (152). In Alberta, a school intervention program revealed that girls aged 10 to 12 years are at high risk of not meeting the recommended intake of vitamin D (153). In First Nations children 10 to 12 years of age, intake of vitamin D from both traditional foods and non-traditional foods ranged from 100 to 128 IU/d (154). This complements older reports of inadequate consumption of vitamin D in First Nations children from the early 1980s (155). In addition many obese and non-obese children do not meet the AI (156). Lastly, in a school milk promotion program, many females 10 to 12 years of age and inner-city students were at greatest risk of not meeting the AI (153). Similarly in the Food Habits of Canadians survey, teens 13 to 17 years of age consumed, on average, 3 servings of milk per day or approximately 264 IU of vitamin D (157).

These Canadian data are very similar to those in the USA. The 24-hour vitamin D intake for a sample of 27,045 children 1 to 18 years of age in the 1988-1994 U.S. National Health and Nutrition Examination Survey (NHANES III), and data from two separate 24-hour recall assessments (Continuing Survey of Food Intakes by Individuals [CSFII] 1994-1996, 1998), suggested that vitamin D intake for all ages, except for females 14 to 18 years of age, was >200 IU/d (from a low of 208 IU/d for females 9 to 13 years to a high of 280 IU/d for males 14 to 18 years) (158). Values for females 14 to 18 years of age were 156 IU/d (3.9 µg/d from CSFII) and 172 IU/d (4.3 µg/d from NHANES III) (158).

Overall, most children in Canada and the USA seem to meet the current recommendation of 200 IU/d. Groups at higher risk for not achieving adequate intake include teenage girls (158) and First Nations children (154). If the recommendation is increased, however, many if not most children will be unable to achieve higher intakes unless food fortification policy and supplementation practices change.

B. Vitamin D Status of Canadian Children

Children in Canada do not appear to have serum 25(OH)D levels consistent with the hypothesized optimal concentration (i.e. 75–80 nmol/L). Further research is required to prove that 75–80 nmol/L is the optimal target for 25(OH)D levels in children.

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14 NHANES III was conducted on a nationwide probability sample of approximately 33,994 persons 2 months and older by the Centers for Disease Control and Prevention in the United States. The survey was designed to obtain nationally representative information on the health and nutritional status of the population of the United States through interviews and direct physical examinations.

15 Further research is required to prove that 75–80 nmol/L is the optimal target for 25(OH)D levels in children.
significant proportion have 25(OH)D consistent with vitamin D deficiency. In a 1993 study in a northern Manitoba community, 43% of infants aged 3 to 24 months had vitamin D levels below the normal range (146). In the Quebec preschooler study, data on a subset (n=61) of the cohort have been published as an abstract and include data on vitamin D status in winter and summer. The overall range of 25(OH)D levels was 41.4 to 158.7 nmol/L, and therefore above the deficiency level. The intake in this sub-sample was ~380 to 444 IU/d of vitamin D which, combined with endogenous synthesis, supported vitamin D status above the deficiency cut-off and in some cases into the optimal range (159). An Edmonton study suggests that children 2 to 16 years of age in Canada are at high risk for low 25(OH)D concentrations. In this study the definition of deficiency was <25 nmol/L and insufficiency <40 nmol/L (160). Overall, if the results are combined 40% had values <40 nmol/L. If examined by age and sex, 69% of males 9 to 16 years of age had insufficient status while only 8% of girls aged 2 to 8 years had insufficient status. Thus, male children might have higher risk for inadequate vitamin D status. The children in the study were recruited through a hospital emergency department and thus may not represent children in the general population or unique groups. First Nations children in 1978 were reported to be deficient in vitamin D (161), but more recent reports are not available.

No other Canadian data for vitamin D status in children exist at present. However, in Alaska, infants between 6 and 22 months of age enrolled in the Women, Infants and Children program were studied for vitamin D status and feeding practices. While the study spanned 13 months that included the summer, 11% of infants had a vitamin D deficiency defined as a 25(OH)D <37.5 nmol/L. Infants who were breastfed had a 12-fold higher likelihood of having a deficiency and only 34% received vitamin D supplementation at least occasionally (147). In another USA report, children aged 11 to 18 years in Boston (n=307) were assessed for vitamin D status during their regular annual physical examinations; 43% were deemed to be vitamin D deficient, with 25(OH)D levels <50 nmol/L(162). Thus the problem of vitamin D deficiency is not unique to Canada.

C. Evidence of Vitamin D Related Health Issues in Canadian Children

Reports of rickets that include children over 1 year of age have been published for many years (67, 68, 163). The recent pediatric surveillance assessment of rickets in Canada reported a prevalence rate of 2.9 cases per 100,000 in those ranging in age from 2 weeks to 6 years (69). The risk factors for children are the same as for infants aside from breastfeeding without supplementation. Reports of rickets in older children (i.e. >6 years old) are lacking in Canada, suggesting that either intakes or endogenous synthesis are sufficient to prevent severe deficiency.

D. Solutions for Improving Vitamin D Nutrition in Canadian Children

During the winter months in Canada, in the absence of sunlight or safe exposure to UVB, it is unclear how much oral vitamin D is required to achieve and maintain optimal 25(OH)D levels in children. A school milk program did improve intakes (153), but status was not assessed. Some research has been conducted in other countries as summarized below.

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16 Note that the definition of deficiency used in this study differed from the level recommended by the IOM (see Table 3).
Daily dosages of vitamin D₂ and D₃ isoforms greater than 400 IU require testing.

- In Finland, researchers analyzed the amount of vitamin D₂ required to normalize vitamin D status in girls 9 to 15 years of age (n=171). A dosage of 400 IU was adequate in many individuals in terms of elevating serum 25(OH)D >37.5 nmol/L; supplemented versus unsupplemented girls had 25(OH)D levels of 45.5 versus 31.8 nmol/L (164). Clearly, 400 IU was not enough to support the suggested optimal 75 nmol/L.

- Daily intake of 624 to 1000 IU (15.6–25 µg) of vitamin D₂ (ergocalciferol) in children 5.2 years of age with maple syrup urine disease resulted in serum 25(OH)D values >90 nmol/L (165).

- A study in France suggested that optimal vitamin D status can only be achieved through supplementation: 100,000 IU of oral vitamin D₃ given every 3 months during the winter achieved 25(OH)D levels >50 nmol/L (not deficient) in all participants (10–15 years of age). Without the supplement, the prevalence of deficiency was maintained at 62%. This study suggests that 1000 IU of vitamin D is required daily in the winter to correct deficiency and maintain 25(OH)D concentrations (12).17

- In Spain, elevation of 25(OH)D levels from 32 to 114 nmol/L and significant reductions in PTH occurred when children 7 to 10 years of age were given 1600 IU of daily vitamin D supplements for one week in March (166).

Overall, if 75 nmol/L is adopted as the optimal target for all ages, the current AI of 200 IU/d seems inadequate. It is more likely that RCT designed to test for the dietary intake required to optimize 25(OH)D will be successful in using dosages over 600 IU/d.

### 3. Young Adulthood

#### A. Dietary Vitamin D Intake of Canadian Men and Women 18–50 Years of Age

There are a few reports regarding vitamin D status of men and women 18 to 50 years of age in Canada. Assessing vitamin D intake is difficult as not many foods contain vitamin D. In Toronto, Vieth’s work shows that women frequently do not achieve the 200 IU/d AI (106). Other reports echo this low intake in Punjabi men and women where the intake was 140 and 132 IU/d, respectively (167). In Dene Métis and Inuit adults, Kuhnlein et al. (168) showed that vitamin D intake ranges from 1405 to 1000 IU/d. Data were not separated based on sex or age. In the First Nations Bone Health Study (169), which included a group of women 25 to 50 years of age, vitamin D intake was on average 440 IU/d in First Nations and 344 IU/d in white women. From a study of mammary density in Quebec, vitamin D intake of premenopausal women was ~188 IU/d from food and 394 IU/d from supplements (170). Based on milk intakes from the CCHS dataset (171) and the Food Habits of Canadians studies (172), most men and women do not consume even 2 servings of milk and thus vitamin D intake is most likely <200 IU/d.

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17 The maximum level of vitamin D intake likely to pose no risk of adverse effects is 2000 IU/d for children. (2)
B. Vitamin D Status of Canadian Men and Women 18–50 Years of Age

There are more reports on the vitamin D status of healthy men 19 to 50 years of age than on their dietary intake. In Calgary, for men and women aged 27 years and older, vitamin D deficiency was common and it was found that 34% have low vitamin D status in at least one season (107). For Punjabi immigrants to Canada, men had serum 25(OH)D of 36±13 nmol/L (167) and women had values of 31±8 nmol/L (167). In Toronto, deficiency is prevalent in 14.8% of white women and 25.6% of non-white non-black women, even if they consume 200 to 400 IU of vitamin D daily (106). During the winter months, the prevalence was not significantly affected by dietary or supplemental vitamin D intakes at values similar to the AI of 200 IU/d (5 µg/d) (106). Recent results of the 1988-1994 NHANES III indicate that the prevalence of hypovitaminosis D (defined as 25(OH)D <37.5 nmol/L) was 42.4% among African Americans and only 4.2% among white American women of reproductive age (173). However, vitamin D status at the most northern latitudes was not assessed in the winter months, and this likely led to underestimation of the problem in the white women. Recent research out of the University of Toronto shows that 25(OH)D <50 nmol/L, consistent with insufficiency, is observed in university students based on ethnic background: 100% of Black, 85% of Asian, 93% of South Asian and 34% of European students were insufficient in vitamin D.18

C. Evidence of Vitamin D Related Health Issues in Canadian Men and Women 18–50 Years of Age

Most health outcomes related to vitamin D are chronic in nature. Within Canada research related to multiple sclerosis (113), prostate cancer (174) and breast density (142, 170, 175) show that individuals with higher 25(OH)D have better odds of achieving improved health.

D. Solutions for Improving Vitamin D Nutrition in Canadian Men and Women 18–50 Years of Age

From studies examining the risk of cancer, the food that most commonly is associated with better vitamin D status is milk (142, 175). Even in the First Nations Bone Health Study, the foods contributing the most vitamin D were milk, whether as pasteurized or condensed milk, and margarine (169). Thus, the mandated food fortification of milk and margarine in Canada (15) makes significant contributions to vitamin D status. Many of the reports show that vitamin D supplements are consumed by many Canadians. To achieve higher 25(OH)D, selection of foods containing vitamin D is important and supplementation required during the winter to achieve 25(OH)D >75 nmol/L (175). In order to achieve 25(OH)D concentrations of 75 nmol/L, Canadian data suggest that 200 IU/d is inadequate and that intakes of 1000 to 4000 IU/d might be required in some individuals during the winter months (29).


A. Dietary Vitamin D Intake of Canadian Women during Reproduction

National surveys regarding vitamin D intakes from diet and supplements are lacking in Canada. In a small-scale study of 50 women from mixed ethnic backgrounds in Winnipeg, only 78% of the women reported taking multi-nutrient supplements during pregnancy and 46% had 25(OH)D

18 The research findings were released in the Globe and Mail on December 17, 2007, prior to publication.
in the deficient range (49). Only 61% of the mothers with deficiency had taken a supplement, while almost all of the women without a deficiency had taken a supplement (93%). Dietary intake from food sources was somewhat lower as well in the deficient women (149 vs 242 IU/d) (49). No other recent Canadian studies with combined assessment of dietary and supplemental intake and status of vitamin D exist. In an earlier report, a predicted prevalence of deficiency was estimated at 48.4% in Native mothers taking a vitamin D supplement and 88.6% in mothers not consuming a supplement (145). For non-Native mothers taking a supplement, the prediction was 15.1% and without a supplement 63.5% (145). Similarly, Lebrun et al. (146) reported that 76% of Northern Manitoban women and 43% of the children (3–24 months) had 25(OH)D below the normal range. Access to food and supplemental sources of vitamin D was limited, forcing reliance on endogenous synthesis that itself is limited due to latitude and UVB exposure. Clearly, the cause of vitamin D deficiency in many Canadians is rooted in inadequate endogenous synthesis combined with exogenous intakes that are not sufficient alone to support vitamin D status.

Inadequate sources of vitamin D are not unique to Canada. In the Northern USA, 90% of one cohort (n=400) of pregnant black and white women took a prenatal vitamin supplement at least once per week in the third trimester, presumably with some vitamin D (176). Despite the supplementation, approximately 20% of the women had vitamin D deficiency (176). A relatively recent review paper summarizes the literature on vitamin D status in pregnancy throughout the world (177). That review covered the periods 1966 up to 2002 and revealed that 35 of 76 (46%) reports included women with 25(OH)D concentrations <35 nmol/L; the majority of reports emanated from Europe and the UK. Thus, vitamin D deficiency during pregnancy is common in industrialized nations. The ongoing deficiency in pregnant women through the 21st century needs to be resolved in view of the early life programming hypothesis and recent evidence linking vitamin D status to pregnancy outcome for the mother as well. It is clear that dietary sources of vitamin D and de novo synthesis in today’s environment are not enough to support optimal vitamin D status (potentially 75 nmol/L (178)) in maternal–infant populations in Canada.

B. Vitamin D Status of Canadian Women during Reproduction

The total amount of vitamin D transferred from mother to fetus is thought to be small relative to maternal stores (2). Fetal vitamin D concentrations are frequently lower than maternal concentrations, with correlations ranging from 0.6 to 0.8 (2, 49), although they can be almost identical. For example in one study, maternal 25(OH)D pre-delivery correlated with cord blood 25(OH)D with a correlation coefficient of 0.97, meaning the relationship was just under 1 to 1 with values in the infant slightly lower (132). These relationships imply that maternal–fetal transfer must exist through a passive route (i.e. transfer down a concentration gradient). To date, the exact mechanism(s) of placental transfer is not known, but likely can be accommodated through transfer of existing maternal 25(OH)D or placental hydroxylation of maternal dietary vitamin D (179) that has not been metabolized already by the liver.

Some clinicians suggest that 25(OH)D concentration might decline over pregnancy as a result of hemodilution and expansion of the plasma volume. One study, however, conducted in Tehran (35.7°N) demonstrated that 25(OH)D concentrations actually improved on average from the first (60% deficient defined as 25(OH)D <50 nmol/L) to third (47% deficient) trimester spanning
summer to winter (180). This suggests that vitamin D status is not necessarily worsened during pregnancy as a result of the maternal–fetal relationship. For studies in which 25(OH)D declined, it is possible that utilization by the placenta and fetus might contribute at least to some of the reduced concentration. However, changes in vitamin D status over pregnancy are more likely attributed to reductions in both endogenous and exogenous sources rather than a high demand for fetal vitamin D requirements.

While little data exist in Canada, it appears that individuals who are at high risk for suboptimal and deficient vitamin D status attributed to low endogenous synthesis include individuals who reside: (a) predominantly indoors (181, 182), (b) in the far northern or southern hemispheres (183-185), and/or (c) in moderate latitudes, but who remain fully clothed while outdoors (186-189) or use sunscreens with SPF >8 and fail to achieve daily exposure >15 minutes (17). Some evidence is building that pollution may be emerging as a contributing factor to poor dermal synthesis of vitamin D (190) and there is another more recent study in New Zealand suggesting that veiled women are at high risk of vitamin D deficiency (191). However, these researchers also noted that while only 22% of the women wore veils, 87% of the pregnant women had 25(OH)D concentrations <50 nmol/L and 61.2% had values <25 nmol/L (191), suggesting that other factors contribute to the deficiency.

Dark skin pigmentation or concealing clothing also yields higher prevalence of deficiency in infants (63 vs 16%) and higher alkaline phosphatase (192). In Winnipeg, Canada, about 75% of non-white and 30% of white pregnant women were vitamin D deficient, defined as serum 25(OH)D <37.5 nmol/L (49). In these women, sampled 1 to 2 days postpartum, only five (10%) had a 25(OH)D concentration >75 nmol/L, with two (4%) having values >100 nmol/L (49). In another report, up to 80% of women and their infants were at risk of vitamin D deficiency if they were non-white (145). Not taking supplements can exacerbate this problem. Infants of mothers with these characteristics are often vitamin D deficient by 3 months of age (193). Even in warmer countries closer to the equator, infants of darker skin are frequently diagnosed with rickets (65, 194).

Additionally, low 25(OH)D might be related to maternal weight. There is now evidence that the relationship between vitamin D intake and vitamin D status may be modified by obesity. Pre-pregnant BMI <25 is associated with higher adjusted 25(OH)D concentration at 4 to 22 weeks compared to women with BMI >30 (57 vs 63 nmol/L) (138); the prevalence of deficiency was 61% for the obese and 36% for those with a healthy BMI (138). Interestingly in this same study, supplementation was more frequent in those with normal pre-pregnancy BMI and not in the deficient women (176). Thus, it is most likely that supplementation is more important than screening on the basis of BMI.

C. Evidence of Vitamin D Related Health Issues in Canadian Women during Reproduction

Within Canada, the consequences of low 25(OH)D are not clear. It is assumed that the consequences would be the same as those observed in other countries as previously reviewed and for Canadian women in general. These include bone loss, tetany, gestational diabetes, and preeclampsia.
D. Solutions for Improving Vitamin D Nutrition in Canadian Women during Reproduction

It is clear that adequate dietary intake is absolutely required if UVB exposure is limited. In Canada, the main fortified sources of vitamin D are cows milk, margarine, and more recently fortified soy and rice beverages, orange juice, and yogurt made from fortified cows milk. Natural sources include fatty fish, eggs and some mushrooms. A pregnant woman who drinks 2 cups of fortified milk would meet the recommendation of 200 IU/d. Inclusion of 2 cups of fortified orange juice and regular consumption of eggs would approximately double this to 400 IU/d. In an RT with either no intervention (control), or increased dietary calcium using orange juice or milk products, adolescent mothers who consumed the milk had significantly higher 25(OH)D than control (58 vs 108 nmol/L) and those consuming orange juice (195). Intakes in the milk group approximated 10 µg/d (400 IU/d). The infants in the milk group were also heavier at birth (240 g) and had higher total body calcium. However, as is discussed earlier in this chapter, there is great debate regarding the adequacy of an intake of 200 to 400 IU/d. Many women who achieve this intake have serum 25(OH)D concentrations consistent with vitamin D deficiency (<37.5 nmol/L 25(OH)D). In the study by Chan et al., the control group had 25(OH)D well above 37.5 nmol/L (195), suggesting that 400 IU/d in those with relatively good vitamin D status is still beneficial. Whether higher intakes in the order of 1000 IU/d would be beneficial to deficient populations is not clear without further research. Nonetheless, 400 IU in addition to a normal diet appears safe and able to elevate 25(OH)D well into the proposed target range of >75 nmol/L.

With addition of a pregnancy supplement, an additional 400 IU of vitamin D would be possible with most supplements. Since formulations contain variable amounts of vitamin D, the brand names of vitamins should be solicited when advising parents or health care professionals about supplementation strategies.

The challenge to obstetric care is to find approaches that ensure pregnant women regularly select vitamin D containing foods and rigorously practice vitamin D supplementation. The magnitude of this problem is demonstrated by Thomson et al. who followed women postpartum (196). All of the women studied had a vitamin D deficiency (<50 nmol/L) at delivery despite the recommendations to take supplements containing vitamin D during pregnancy. Either the supplement was not adequate to improve vitamin D status or the supplement was not taken as prescribed. Both are likely underlying problems since 19 of 35 women reported taking the supplement as prescribed (196). Even in RT, compliance is difficult (197) suggesting that other strategies might be required to achieve vitamin D status within the optimal range during pregnancy.

A number of other maternal characteristics associate with low vitamin D status; these are age, education and smoking. In Finland, where the recommendation is for pregnant women to consume 10 µg/d (400 IU/d), a survey of 804 women (198) showed that only 40% of pregnant women took a supplement containing vitamin D, but 85% had intakes below the recommendation. Results showed that increased intake of a nutrient supplement was associated with older age, higher education level, leaner pre-pregnancy weight and non-smoking (198). Low income mothers tend to limit their own intake of food in order to feed their children (199,
200) and thus their vitamin D intake is likely limited as well. Low educational attainment seems a stronger predictor of low vitamin D status than socioeconomic status (60).

There are no clinical trials or RT of vitamin D intake in pregnant or lactating women in Canada. However, trials exist from other countries from which we can gain appreciation of the relationship between vitamin D intake and status. The few RCT of vitamin D supplementation in pregnancy that exist were conducted in the 1980s; debate continues regarding optimal intakes as disagreement exists among studies.

For pregnancy, in a 2001 Cochrane Database systematic review (201), only two (202, 203) trials reviewed at that time met inclusion criteria. Both trials were based on the administration of 1000 IU/d supplementation of vitamin D₂ in the third trimester. These studies reported elevated maternal 25(OH)D, but one trial (202) showed improved birth weights while the other (203) showed reduced birth weights in the intervention groups relative to the control groups. Seven other trials (13, 14, 135, 197, 204-206), some conducted since the systematic review, are summarized in Table 4. It is clear that no two studies agree in regard to elevations in 25(OH)D at a specific dosage of vitamin D during pregnancy. For example, one trial using 1000 IU/d in the third trimester documented very high concentrations of 25(OH)D in the order of 168 nmol/L (202), while others (203, 206) using the same dosage failed to yield 25(OH)D above the deficient cut-off of 37.5 nmol/L. This discrepancy would suggest that other factors such as geographic location and exogenous synthesis, endogenous stores of vitamin D and supplement compliance contributed to the outcome. Moreover, not every trial measured vitamin D status since assays for measurement of 25(OH)D were not as routinely available in the 1980s. Given the limited number of studies on vitamin D supplementation in pregnancy, the ideal level of supplementation in pregnancy is not known. It is for this reason that newer trials are underway to establish if 1000 IU/d is sufficient to achieve and maintain vitamin D status throughout pregnancy. Thus, while clinicians await the results of new RCT in pregnancy, they should be aware that the theoretical optimal concentration of 25(OH)D of 75 nmol/L can be achieved in pregnancy. In one study where vitamin D status was measured before and after the supplement was taken, serum 25(OH)D in some women reached 80 nmol/L after the supplement (14).

Regarding lactating women, there are now four RT of vitamin D supplementation, with dosages ranging from 1000 IU to 6000 IU/d (Table 5). Two studies are from the USA (207, 208), one from Finland (209) and one from the United Arab Emirates (210). From these studies, it seems that 4000 IU/d is required to elevate maternal 25(OH)D into the 75 nmol/L range (207, 209) and that women with darker skin pigmentation consuming 2000 IU for 3 months do not fully optimize vitamin D following a deficiency (210). Information regarding 25(OH)D in the infant also shows values of ~75 nmol/L when the mother consumes 2000 IU/d (207, 209). It is likely for this reason that the recent recommendation by the Canadian Paediatric Society is set at 2000 IU for lactating women (4).

19 www.clinicaltrials.gov; Identifier: NCT00292591
<table>
<thead>
<tr>
<th>Study</th>
<th>Location</th>
<th>Vitamin D Intervention</th>
<th>Key 25(OH)D Outcomes</th>
<th>Other Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brooke et al. (202)</td>
<td>1980 Asian women in UK</td>
<td>Double blind in last trimester:</td>
<td>Higher 25(OH)D in mothers of intervention group at delivery (16 vs 168 nmol/L).</td>
<td>Control group associated with symptomatic hypocalcaemia, growth restriction and larger fontanelles in infants.</td>
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<tr>
<td></td>
<td></td>
<td>▪ Control (n=67)</td>
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<tr>
<td></td>
<td></td>
<td>▪ 1000 IU D2/d (n=59)</td>
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<tr>
<td>Maxwell et al. (204)</td>
<td>1981 Asian women in London</td>
<td>Double blind in last trimester:</td>
<td>Higher intakes associated with higher vitamin D status as indicated by alkaline phosphatase. 25(OH)D not reported.</td>
<td>Improved maternal weight gain and infant birth weights.</td>
</tr>
<tr>
<td>(companion paper to</td>
<td></td>
<td>▪ Control (n=67)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brooke et al. (202))</td>
<td></td>
<td>▪ 1000 IU/d (n=59)</td>
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<tr>
<td>Marya et al. (205)</td>
<td>1981</td>
<td>Third trimester:</td>
<td>Birth weights higher with supplementation.</td>
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<td></td>
<td></td>
<td>▪ Control (n=75)</td>
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<td></td>
<td></td>
<td>▪ 1200 IU/d (n=25)</td>
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<tr>
<td>Mallet et al. (203)</td>
<td>1986 Winter pregnancy</td>
<td>Last trimester:</td>
<td>Both supplements improved 25(OH)D over control. Reduced birth weights in supplemented groups.</td>
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<tr>
<td></td>
<td>Northwest France</td>
<td>▪ Control (n=29)</td>
<td>Delivery</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>▪ 1000 IU D3/d for 3 mo (n=21)</td>
<td>Control: 9.4 nmol/L</td>
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<td></td>
<td></td>
<td>▪ 200,000 IU single oral dose (n=27)</td>
<td>Daily: 25.3 nmol/L</td>
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<td></td>
<td></td>
<td></td>
<td>Single dose: 26.0 nmol/L</td>
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<tr>
<td>Delvin et al. (206)</td>
<td>1986 France</td>
<td>From 6 mo pregnancy onward:</td>
<td>Maternal and newborn infant 25(OH)D improved by supplement.</td>
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<tr>
<td></td>
<td></td>
<td>▪ Control (n=20)</td>
<td>Term: Elevated 25(OH)D from ~10 to 25 nmol/L (estimated from graphed data).</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>▪ 1000 IU vitamin D3/d (n=20)</td>
<td></td>
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<tr>
<td>Marya et al. (135)</td>
<td>1987</td>
<td>20 to 24 wk:</td>
<td>32 to 36 wk lower blood pressure in supplemented group.</td>
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<tr>
<td></td>
<td></td>
<td>▪ Non-supplemented (n=200)</td>
<td></td>
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<td></td>
<td></td>
<td>▪ Supplemented (n=200) to 375 mg calcium and 1200 IU vitamin D/d</td>
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<tr>
<td>Marya et al. (13)</td>
<td>1988 Rohtak</td>
<td>Third trimester:</td>
<td>Vitamin D status not reported.</td>
<td>Supplemented group had larger infants: weight, length, head circumference and skin fold thicknesses.</td>
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<tr>
<td></td>
<td></td>
<td>▪ Comparison (n=100)</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>▪ 600,000 IU vitamin D at each of 7 and 8 mo (n=100)</td>
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<tr>
<td>Madelenat et al. (14)</td>
<td>2001 France</td>
<td>27 to 32 wk pregnancy in winter:</td>
<td>All women but one had serum 25(OH)D &gt;25 nmol/L. Range from to 12 to 80 nmol/L.</td>
<td>No comparison group.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>▪ 80,000 IU vitamin D single oral dose</td>
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<tr>
<td>Datta et al. (197)</td>
<td>2002 Ethnic women in UK</td>
<td>n=80 women 25(OH)D &lt;20 nmol/L:</td>
<td>Mean elevation of 12 nmol/L 25(OH)D.</td>
<td>Compliance not assessed. No comparison group.</td>
</tr>
</tbody>
</table>
Table 5. Summary of Vitamin D Supplementation Studies in Lactating Women

<table>
<thead>
<tr>
<th>Study</th>
<th>Location</th>
<th>Vitamin D Intervention</th>
<th>Key 25(OH)D Outcomes</th>
<th>Other Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ala-Houhala et al.</td>
<td>1986 Finland</td>
<td>Mothers supplemented from delivery to 8 wk postpartum. Only infants in placebo group received vitamin D2 400 IU/d. 0 IU vitamin D3 (n=16) 1000 IU vitamin D3 (n=16) 2000 IU vitamin D3 (n=17)</td>
<td>Extracted from graphed data: Maternal 25(OH)D increased in both supplement groups while it remained relatively stable in the placebo group. The 2000 IU group had mean 25(OH)D &gt;75 nmol/L by 15 wk.</td>
<td>Infants receiving 400 IU directly had 25(OH)D ~75 nmol/L by 15 wk. Infants in the 2000 IU maternal group had similar values as the infants in the 400 IU infant group, while those in the maternal 1000 IU group had values consistent with deficiency.</td>
</tr>
<tr>
<td>Hollis and Wagner</td>
<td>2004 USA</td>
<td>Randomized at 1 mo postpartum to 4 mo: 2000 IU total (n=9) 4000 IU total (n=9)</td>
<td>In both groups total 25(OH)D increased between 1 and 4 mo of study. From graphed data: 2000 IU ~36 ng/ml (~90 nmol/L) 4000 IU ~44.5 ng/ml (~111 nmol/L)</td>
<td>Infant 25(OH)D from graphed data: 2000 IU ~27.5 ng/ml (~69 nmol/L) 4000 IU ~30 ng/ml (~75 nmol/L)</td>
</tr>
<tr>
<td>Wagner et al. (208)</td>
<td>2006 USA</td>
<td>From 1 to 7 mo postpartum (n=19): 0 or 6000 IU/d plus prenatal supplement with 400 IU vitamin D. Infants in placebo group received 300 IU/d.</td>
<td>Significant elevation in 25(OH)D.</td>
<td>Infant 25(OH)D similar among groups.</td>
</tr>
<tr>
<td>Saadi et al. (210)</td>
<td>2007 United Arab Emirates</td>
<td>Randomized at first postnatal visit for 3 mo: 2000 IU/d 60 000 IU/mo oral</td>
<td>Baseline 25(OH)D ~25 nmol/L. Significant elevations in 25(OH)D but not &gt;50 nmol/L on average. Only 21% &gt;50 nmol/L.</td>
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</tbody>
</table>
5. Aging and Advanced Aging (50 Years of Age and Older)

A. Dietary Vitamin D Intake of Aging Canadian Adults

For aging, information pertaining to vitamin D is more easily combined for men and women from many countries. However, in Canada there are very few reports on vitamin D intakes in free living individuals. First Nations women over 50 years of age and white women from Winnipeg have intakes in the order of 450 and 544 IU/d, respectively (169). These intakes are consistent with the AI of 400 to 600 IU/d for adults over 50 years of age. Additionally, for Dene and Inuit, intakes approximate 316 to 1000 IU/d from traditional and market foods (154). Institutionalized elderly have low dietary intakes of vitamin D of ~450 IU/d (211). One study shows that novel foods for dysphagia management in long-term care improve vitamin D intakes to approximately 600 IU/d (212).

B. Vitamin D Status of Aging Canadian Adults

Excellent reports exist regarding vitamin D status, but the relationship with diet remains unclear. For example, in Canada, deficient vitamin D status is observed in at least one season in 34% of Calgary residents ~64 years of age (107), but determining the relationship between supplement use and vitamin D status was not possible since use of supplements was an exclusion criterion. Some data exist for institutionalized elderly and suggest low vitamin D status (213) despite a controlled feeding environment. However, the state of community dwelling seniors is far less clear. In a Montreal study, using a conservative cut-off value for normal 25(OH)D concentration (25 nmol/L), 36.4% of the ~70-year-old population was deficient (214). A clear seasonal variation was observed in both 25(OH)D and PTH. However, this study did not address dietary intake of vitamin D or other biomarkers of bone health. Another study, of thyroid patients in Toronto, also shows deficiency in adults >70 years of age, but details of nutrition were not clearly available and complete demographics of the study population not presented (215).

C. Evidence of Vitamin D Related Health Issues in Aging Canadian Adults

The consequences of the vitamin D deficiency observed in Canada are not clear. Much of the research regarding vitamin D deficiency has focused on bone health and osteoporosis. More recently, vitamin D deficiency has been associated with other chronic diseases. However, even for osteoporosis and fractures, a direct linkage to vitamin D status in Canadians is not available.

D. Solutions for Improving Vitamin D Nutrition in Aging Canadian Adults

Unless food fortification policy changes, aging adults will not be able to achieve intakes of 600 IU/d and higher in support of year-round optimal vitamin D status. The new Canada’s Food Guide recommends a supplement of 400 IU/d for adults over the age of 50 years (6). Supplementation trials in Canadians over 50 years of age show that both 600 and 4000 IU/d dosages given over 6 months elevate 25(OH)D to >75 nmol/L (216). For those who are over 70 years of age, however, the suggested target for 25(OH)D might be higher and thus higher intakes would be required. From the meta-analysis component of the NIH systematic review of vitamin D (8), it appears that for every 100 IU elevation in vitamin D intake, serum 25(OH)D will increase by 1 to 2 nmol/L. If this is the case and if 75 nmol/L is the minimum optimal target, Canadians deficient in vitamin D (i.e. serum level <37.5 nmol/L) would require anywhere from 3750 IU/d to 7000 IU/d. Whether such dosages are warranted in Canada requires further study. Once deficiency is corrected, lower intakes might possibly provide coverage in the longer-term.
IV. Implications

1. General Implications

The underpinning philosophy of dietary recommendations is to meet the needs of the majority of people. In 1997, the IOM published DRI values for vitamin D (2) to be used by both the USA and Canada. For most age groups, the AI for vitamin D was set at 200 IU/d (2). The IOM acknowledged that exposure to sunlight may not be the best approach to ensuring adequate vitamin D status of populations as this can be dependent on culture, skin pigmentation, and/or behaviour related to use of sun block (2, 3). Thus, the AI is designed to cover the needs for vitamin D in the absence of exposure to UVB. Other institutions and associations have put forth recommended intakes for vitamin D ranging from 400 IU/d for infants to 2000 IU/d for pregnant and lactating women.

The state of vitamin D nutrition in Canada suggests that vitamin D intakes are close to the AI across all ages, but that vitamin D deficiency is very common among all groups studied. The implication of these observations is that Canada’s current health policy, food fortification policy and food supply require updating if optimization of vitamin D status is to be achieved. Additionally, the AI is most likely too low to prevent vitamin D deficiency in most individuals, regardless of ethnicity, although many ethnic groups have high prevalence of deficiency (as high as 100% in some studies). While newer recommendations exist for Canadians, these are not yet all part of Health Canada’s policy update. Only the 400 IU/d for infants has been accepted by Health Canada (3). Furthermore, if a serum 25(OH)D of 75 nmol/L is accepted as the target indicative of optimal vitamin D status, further research is required to establish how much daily dietary vitamin D is required to support healthy outcomes.

Establishment of public policy recommendations is critical to ensuring safety for the public at large. With the expanse of vitamin D deficiency, the risks of updating the recommendations for pregnant women without multiple sound intervention trials might be smaller than the risk of not correcting vitamin D deficiency. Not only are there acute and chronic implications for maternal health, but also the consequences of missing critical windows for programming of fetal health and prevention of chronic disease may manifest as an increased burden of chronic disease.

Lastly, the implication of not clarifying the best dietary intake is that the public will receive a multitude of recommendations and possibly not have confidence in dietary advice. Many will self-medicate with respect to vitamin D without sound knowledge or medical supervision, and will thus be less likely to achieve healthy outcomes.

2. Implications for Doctors and Other Health Care Professionals

Since health policy is not readily altered due to the responsibility to ensure public safety and since many knowledge gaps exist, the responsibility of medical and other health care professionals to know the facts about vitamin D is most important. To date, there are few reports of the practices of Canadian health professionals with regard to vitamin D nutrition, and these only deal with adult clients. From other countries, it seems that vitamin D intakes in children can be improved with counseling. For example, according to Christie et al. in Arkansas, vitamin D intake in children with allergies is higher with counseling than without (217). This research group recommends that children with diagnosed food allergy be counseled yearly and...
that their annual nutritional assessments include the status of vitamin D nutrition. Two other American references report that physicians and nurse practitioners recommend vitamin D supplements for breastfed infants less than 50% of the time. Physicians and nurse practitioners are more likely to recommend supplements if they were either trained at a time when rickets was prevalent or have worked in geographic regions where the risk of rickets is high (218, 219). From Finland, it seems that while health care professionals feel they educate women on giving vitamin D to their infants, most women state they have not received this information (220). From within Canada, 75% of medical professionals are interested in vitamin D and are open to receiving more education on this topic (221). However, current practice related to use of vitamin D in treatment of osteoporosis does not match guidelines (222, 223).

From the above reports, it is clear that health care professionals know that vitamin D nutrition is important, but need to seek further education about current recommendations and follow these recommendations carefully.

3. Implications for Industry

In Canada, fortification has been questioned for quality control (224). Thus, it is in industry’s best interest to prove that fortification is under high-level quality control to ensure the food supply delivers reliable sources of vitamin D. In some studies, milk products are not linked to vitamin D status in young adults in Canada (106), while in others milk and margarine are clearly the foods with greatest impact on vitamin D status (142, 169, 175). Newer foods on the market including orange juice have not yet been assessed for contribution to vitamin D intake and status in Canada.

For the pharmaceutical industry, there also are implications of this research in that the optimal intakes of vitamin D associated with optimal outcomes are not clear. It is in industry’s best interest to clarify the best dosage of vitamin D from all sources that elicits the optimal response including safety assessments.

Lastly, for all industry clear food labeling is critical for public acceptance of vitamin D. Whether the product contains vitamin D₃ or D₂ is important to some segments of the population, regardless of the dosage.

4. Implications for Consumers

Ultimately, consumers are responsible for their dietary intakes and well-being. Individuals must seek education as to which foods are the best sources of vitamin D and what are appropriate serving sizes and frequencies. Compliance in taking supplements and consistency in selecting foods containing vitamin D are likely critical to achieving better vitamin D status. Consumers must seek nutritional or medical counseling to learn of the benefits of foods and supplements while ensuring safe intakes for themselves and any people for whom they are the primary caregiver. The consumer must be educated upon valid sources of nutrition information and become skilled in reading food labels.
5. Implications for Research—Knowledge Gaps for Canada

There are a number of knowledge gaps in the area of vitamin D nutrition for healthy outcomes in Canada. These include:

- The cause of vitamin D deficiency. Is it low food sources and lack of adherence to supplementation guidelines, or is the target too low given lifestyle and health risks related to exposure to UVB?

- The consequences of a high rate of vitamin D deficiency for all age groups.

- Definition of optimal vitamin D status in all age groups and among different ethnic groups. This is critical to harmonization of the various recommended intake values and to harmonization of policy with public education.

- Determination of optimal vitamin D intake in all age groups. How much dietary vitamin D from diet or supplements is required to achieve optimal vitamin D status?

- The nature and safety of supplementation. Is a bolus dosage safe and effective? What is the maximum amount of vitamin D supplementation that is safe?

- Efficacy of food fortification programs. Can food fortification programs safely and successfully enhance vitamin D status?
V. References


207. Hollis BW, Wagner CL. Vitamin D requirements during lactation: high-dose maternal supplementation as therapy to prevent hypovitaminosis D for both the mother and the nursing infant. Am J Clin Nutr 2004;80:1752S-8S.