Vitamin D Fact Sheet

What is vitamin D and what does it do in the body?

Vitamin D is a fat soluble essential nutrient that plays a number of important functions in the body to maintain health and prevent disease[1]. Vitamin D is naturally found in two forms: D_2 (ergocalciferol) and D_3 (cholecaciferol); of the two, vitamin D_3 is the form produced by our skin upon exposure to sunlight (more about this in the next section). Both forms of vitamin D are considered pro-hormones and are biologically inactive: they must undergo two transformation steps in the body before they can become activated and carry out their biological functions.

The first step occurs primarily in the liver and involves adding a pair of atoms to vitamin D to become 25-hydroxyvitamin D, or 25(OH)D for short. The concentration of 25(OH)D in the blood is the best indicator of **vitamin D status**; it reflects the amount of vitamin D obtained from all sources and, unlike vitamin D, remains in the blood for a relatively long period of time. The second conversion step occurs primarily in the kidney, where a second hydroxyl group is added to turn it into 1 alpha, 25-hydroxyvitamin D, or $1,25(OH)_2D$ (also called calcitriol) which is the biologically active, hormonal form. Since this form doesn't last very long in the blood before being used up, it is not a great indicator of vitamin D status.

Vitamin D status is measured using a simple laboratory blood test. The test results give you a number in units of nmol/L (nanomoles per litre); that number will fall into a range that will tell you whether you're severely lacking (deficient), somewhat lacking (insufficient), or getting enough vitamin D (sufficient). There is some disagreement about the levels needed to produce vitamin D sufficiency but most vitamin D experts agree that levels above 75 nmol/L are sufficient.

What are the sources of vitamin D?

The three sources of vitamin D are through sun exposure, diet and supplementation[1].

Sun: For most people, sunlight is the most important source of vitamin D, lending it the nickname "sunshine vitamin". Ultraviolet B (UVB) radiation from the sun converts a cholesterol precursor in the skin (7-dehydrocholesterol) into vitamin D_3, which then goes on to be converted into the active form (see above).

In Canada, vitamin D from sunlight exposure can only be synthesized in your bare skin during the late spring, summer and early fall months, from around 10am – 2pm, when the UV index is above 3. The amount of time necessary to make sufficient vitamin D depends on many factors –

including clothing coverage, use of sunscreen, skin pigmentation, and age – and there is no one-size-fits-all guideline for the right amount of sun exposure. Generally, casual sun exposure during the appropriate time of year (5 – 15 minutes around midday, several times a week, without the use of sunscreen) is thought to be enough to produce enough vitamin D, and is less than the time required for your skin to redden and burn. It is important to keep in mind, however, that UVA and UVB radiation from the sun have been linked to an increased risk of skin cancer[2], and sensitivity to the sun can depend on a number of factors such as skin type, taking certain medications, and others. As a result, caution is recommended during sun exposure for any amount of time.

Diet: Vitamin D_3 can be naturally found in several foods, including fatty fish (e.g. salmon, tuna, mackerel), fish liver oil, beef/pork liver, egg yolks, and some cheeses. Mushrooms are the primary source of vitamin D_2. In Canada, certain foods are also fortified with vitamin D, including milk, margarine, and infant formula as well as some types of orange juice, yogurt, and breakfast cereals. Overall, the quantities of vitamin D present in food are fairly small, and vitamin D obtained from diet alone is not enough to maintain adequate vitamin D status for the vast majority of people[1].

Supplementation: Dietary supplements are potentially a major source of vitamin D and are regarded as the best way to obtain vitamin D during the colder seasons in Canada when sunlight exposure is low. Vitamin D supplements are available in both the D_2 and D_3 forms; although there is no universal consensus over which form is more conducive to better health, greater evidence points towards vitamin D_3 as being the more bioavailable and bioactive form[3]. Supplements are measured in international units (IU), and vitamin D supplements are typically sold in bottles of 400, 500, 600 or 1000 IU tablets. Multivitamins often contain between 200 – 600 IU vitamin D.

The **Recommended Dietary Allowance (RDA)** for vitamin D, which is the average daily intake from dietary sources (i.e. diet and supplements) sufficient to meet the nutrient requirements in nearly all people in a particular demographic group, was adopted by Health Canada following a report by the Institute of Medicine (IOM) that aggregated and analyzed data from a variety of studies, and is listed in *Table 1*.

What role does vitamin D play in health and disease?

Vitamin D plays many important roles in the body, and vitamin D deficiency can have a severe impact on health. One of the most important functions of vitamin D is to promote calcium absorption in the gut and to maintain normal levels of calcium and phosphates in the blood for

bone formation and remodeling[4]. The link between vitamin D (and calcium) and bone health was established in the early 20th century, when diseases characterized by bone softness and skeletal deformity like rickets in children and osteomalacia in adults were shown to be related to vitamin D deficiency[1]. Vitamin D and calcium deficiencies have also been linked to the development of osteoporosis in the elderly[5].

In addition to bone health, vitamin D has a variety of other roles in the body, such as protecting against the risk of cardiovascular disease[6] and colorectal cancer[7], and regulating the immune system with potential implications for type I diabetes[8] and MS (see below). Receptors that bind to vitamin D are ubiquitous throughout the tissues of the body, and vitamin D can influence genes that regulate the multiplication, maturation and turnover of a wide variety of cells[9]. However, most of the data linking vitamin D deficiency to chronic disorders beyond bone health are based on studies in cells and animals as well as population-based observational studies; while these findings can be quite compelling, the strongest evidence comes from controlled, randomized clinical trials (RCTs). Typically, policy makers require RCT evidence to implement changes to policies and guidelines for public health and patient care.

Can vitamin D cause toxicity?

Long-term intake of excessive vitamin D can increase the risk of adverse health effects, although cases of dangerous toxicity are fairly rare[10]. Among the most serious side effects of excessive vitamin D consumption is hypercalcemia, a condition in which calcium builds up in the blood and can cause damage to the heart, blood vessels and kidneys[11].

In general, vitamin D toxicity occurs at 25(OH)D blood levels over 500 nmol/L or at a daily intake exceeding 30,000 IU/day over an extended period of time. Supplements taken as directed and up to 4000 IU/day for adolescents and adults (age 9 and up) would not lead to toxicity. Individuals with liver and kidney conditions may have a lower threshold for vitamin D toxicity than the general population[1].

There is no risk of vitamin D toxicity through sunlight exposure, since the production of vitamin D in the skin upon exposure to UVB light is limited by the amount of the “pre-“ vitamin D molecule in the skin; thus, a “ceiling effect” occurs, effectively limiting production[1]. Similarly, since very few foods contain any vitamin D and because the concentration of vitamin D in those foods is relatively low, it is virtually impossible for someone to ingest sufficient vitamin D from their diet to cause vitamin D-related toxicity.

What is the link between vitamin D and MS?

Vitamin D status – or 25(OH)D levels – may have an effect on MS risk. Evidence has shown vitamin D has immunoregulatory and anti-inflammatory properties, and recent findings point towards a role for vitamin D as a promoter of **remyelination**[12-14]. Research into the association between MS and vitamin D was prompted by findings that showed a correlation between increasing latitude – resulting in decreased exposure to sunlight and thus decreased 25(OH)D concentrations – and increasing MS frequency[15]. Observational evidence has suggested the risk of developing MS is decreased with greater levels of 25(OH)D in the blood and higher levels of vitamin D intake, which points to 25(OH)D levels as a risk predictor for developing MS[16,17]. These observations were supported by a recent genetic epidemiology study showing that genetically lowered 25(OH)D levels were associated with an increase in the risk of MS in people of European descent[18]. Recent research suggests vitamin D deficiency may not only increase the risk of developing MS, but may also affect the clinical course of MS[19]. Researchers have found an inverse association between 25(OH)D levels and brain lesion activity, providing support for further investigations into the link between vitamin D and MS[20].

To date, only a handful of controlled **clinical trials** have been conducted to determine whether vitamin D supplementation can improve disease outcomes in people living with MS, and the results thus far have been inconclusive. Of the completed and published clinical trials, three studies revealed no significant effect of vitamin D treatment compared to the placebo control group[21-23], and one study found no significant effect of high dose over low dose vitamin D_2 supplement[24]. On the other hand, three studies have demonstrated some benefit of vitamin D supplementation on MS outcomes, although the type of benefit (reduction in brain lesions vs. fewer relapse events) varied depending on the study[25-27]. In terms of safety, none of the clinical trials have reported adverse events such as toxicity at any of the tested doses of vitamin D_2 or D_3, and only one study showed mild adverse events in some participants when given the active hormonal form (calcitriol)[28]. Further clinical trials to determine the efficacy and safety of vitamin D as a treatment for MS are ongoing.

What does this mean for me?

There are a few proactive things that all Canadians can do to maintain healthy levels of vitamin D:

- Talk to your physician about having your vitamin D levels checked. Your physician will also be able to provide you guidance on acceptable levels of vitamin D intake for your specific health circumstances.

- If you are an adult (age 9 and up), consider taking up to 4000 IU supplement of vitamin D per day during the winter or if you are at risk of low sun exposure. The risk of vitamin D toxicity is extremely rare, however, with supplements, there is the potential that vitamin D could build up to toxic levels. Supplements taken as directed and up to 4000 IU/day for adults would not lead to toxicity. This is not intended as medical guidance, so it is recommended that you speak with your physician about appropriate levels of vitamin D intake.

- Enjoy the sun safely. Sun exposure is an important source of vitamin D, but excessive sun exposure is the main cause of skin cancer. Exposure time required to make sufficient vitamin D is less than the amount of time needed for skin to redden and burn. In Canada, vitamin D from sunlight can only be synthesized in your skin during the spring and summer months, around midday, from 10am – 2pm, when the UV index is above 3 and your shadow is shorter than your height. Regularly going outside for a matter of minutes around the middle of the day without sunscreen for a 'D-Break' should be enough. It is important to note that vitamin D produced in the skin from solar UVB exposure does not lead to vitamin D toxicity.

- Eat foods that are natural sources of vitamin D: fortified products such as milk, egg yolks, and oily fish like salmon, trout and sardines.

Table 1: Recommended Dietary Allowances (RDA) and 25-hydroxyvitamin D blood levels per day, as well as recommended intakes and target levels by various disease organizations

	Institute of Medicine/ Health Canada	Endocrine Society	Canadian Cancer Society	Osteoporosis Canada	American Geriatrics Society
Infants * (0–12 months)	400 IU	400-1000 IU			
Children/ Adolescents (1-18 years)	600 IU	600-1000 IU			
Adults (18-70 years)	600 IU	1500-2000 IU	1000 IU	400-1000 IU	
Seniors (>70 years)	800 IU	1500-2000 IU	1000 IU	800-2000 IU	4000 IU
Target 25(OH)D levels	>50 nmol/L	>75 nmol/L		>75 nmol/L	>75 nmol/L

** for infants, **Adequate Intake** (AI) values are provided rather than RDA due to a relative lack of scientific evidence in infants to date.*

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Glossary

- **Adequate Intake (AI):** recommended average daily nutrient intake level based on observed or experimentally determined approximations or estimates of nutrient intake by a group (or groups) of apparently healthy people who are assumed to be maintaining an adequate nutritional state. Calculated when sufficient scientific evidence is not available to set a recommended dietary allowance.
- **Clinical trial:** a research study in which human volunteers (participants) receive a specific intervention or interventions – such as medical products, procedures, or changes to behaviour – to test their safety and efficacy.
- **Recommended Dietary Allowance (RDA):** the average daily dietary intake of a nutrient that is sufficient to meet the requirement of nearly all (97-98%) healthy persons. The RDA is a reference value that comprises the dietary reference intake system of nutrition recommendations.
- **Remyelination:** process during which myelin is re-added to nerve fibres by specialized cells.
- **Ultraviolet (UV) B radiation:** a specific part of the light spectrum that is emitted by the sun and reaches the earth. UV radiation is invisible to the naked eye. UVB radiation is responsible for the synthesis of vitamin D in the skin; however, excessive exposure also plays a role in sunburn and the development of skin cancer.
- **Vitamin D status:** describes the amount of circulating vitamin D in the blood obtained from sun exposure, diet and supplementation, and is best measured by assessing the concentration of 25(OH)D in the blood's plasma or serum.

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