Sri Lankan-Canadians are deficient in vitamin D

Potential Implications for bone health and COVID-19

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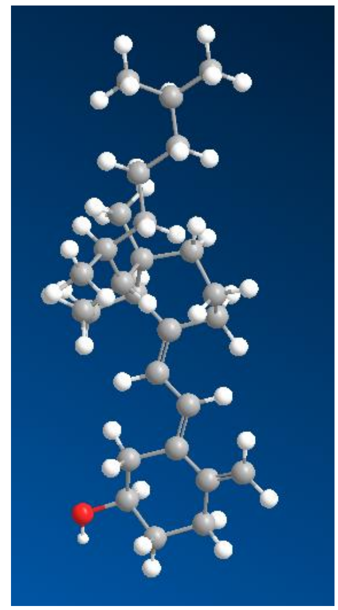
Vitamin D commonly known as the sunshine vitamin, is an essential vitamin to human health. It is produced in the skin by exposing the body to sunlight. Decades of research have established that adequate levels of circulating vitamin D are required for maintaining bone health and preventing rickets in children and bone fractures in adults (1- 4). Recent research has shown that vitamin D also plays a role in preventing respiratory infections, which could have an important implication for the fight against COVID-19 (coronavirus) (5-13). I recommend Sri Lankans note this newly discovered positive health benefit of vitamin D because recent Health Canada studies have shown that vitamin D deficiency is more common in Sri Lankans and other South Asians living in the National Capital Region of Canada (14,15)

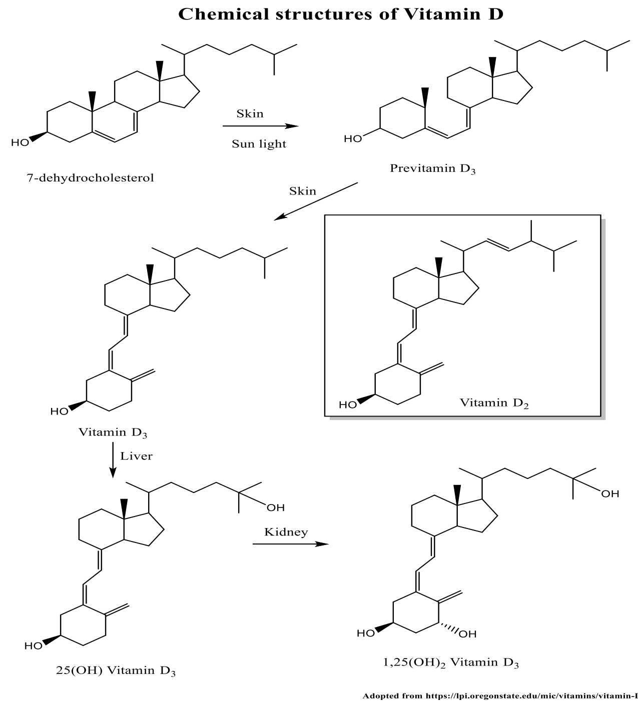
This article examines some potential health benefits of vitamin D, threshold values for blood Vitamin D status related to deficiency as well as adequacy and summarizes the results of the Health Canada studies on the vitamin D status of South Asian Canadians inhabiting the National Capital Region of Canada. The information given in this article might be helpful to Sri Lankan Canadians mitigating the negative health consequences associated with vitamin D deficiency.

What is Vitamin D?



Vitamin D is technically a hormone, not a vitamin. Vitamin D has been known for many centuries as an effective antirachitic agent. Rickets was first described in 1645, and its association with lack of sunlight was realized in 1890. Several decades later, it was observed that rickets is due to inadequate production of vitamin D in the skin and that the human body can make vitamin D from sunlight on the skin (1-4). In 1969, it was finally discovered that the vitamin D was ultimately metabolized to a calcium-controlling hormone. When the skin is exposed to sunlight, it makes vitamin D from a cholesterol precursor (7-dehydroxycholesterol) on the skin. The sun's ultraviolet (UVB) light hits 7-hydroxycholesrol on the skin cells, providing energy for vitamin D synthesis to occur.

In nature, vitamin D is present primarily in two forms, D_2 and D_3, which are sterols, differ chemically in their side chains (Figure). Vitamin D_3 is known as cholecalciferol and present primarily in animal tissues and to a lesser extent in some plants. Vitamin D_3 (derived from 7-dehydroxycholesterol) is the form made naturally in human skin and can also be found in fatty fish like salmon, mackerel, and herring (1-4). Vitamin D_3 is the form commonly added to fortified foods such as milk, and margarine. Ergocalciferol, or vitamin D_2, is the form found in some plants, especially in mushrooms, and is sometimes added to fortified foods, such as soy beverages. At one time the biological activity of the two forms of vitamin D were thought to be comparable and however, that is not the case (3). Vitamin D_2 is less potent and has a shorter duration of action than its counter part vitamin D_3. In general, both forms are technically referred to as vitamin D.



Major physiological roles of vitamin D

Vitamin D obtained from sun exposure, food, or supplements is biologically inactive and must undergo changes in the chemical structure in the body for activation (Figure). Initial metabolism occurs in the liver and converts vitamin D (both D_2 and D_3) to 25-hydroxycholecalciferol [25(OH)D; also known as calcidiol], which is the principal circulating form of vitamin D. 25(OH)D is further metabolized to 1,25-dihydroxycholcalciferol [1,25$(OH)_2$D; also known as calcitriol] principally in the kidney. 1,25$(OH)_2$D is the physiologically active form of vitamin D, whereas 25(OH)D is not biologically active, unless it is metabolized to 1,25$(OH)_2$D. However, the blood level 25(OH)D gives a measure of the vitamin D status, because of its longer life span than that of 1,25$(OH)_2$D (see Section on Vitamin D Status)

1,25$(OH)_2$D promotes calcium absorption and transportation from the intestine and maintains adequate serum calcium and phosphate concentrations to enable normal mineralization of bone. 1,25$(OH)_2$D is also needed for bone growth and bone remodeling by osteoblasts and osteoclasts (1-4). Without sufficient vitamin D, bones can become thin, brittle, or misshapen. Vitamin D sufficiency prevents rickets in children and osteomalacia (softening of the bones) in adults (3). Rickets is a disease of children caused by vitamin D and calcium deficiencies, characterized by softening and distortion of bones resulting in skeletal deformation, including out of shaped skull or legs that bow out (i.e., bowlegs). These days, in most developed countries occurrence of rickets is rare, but commonly seen in children with relatively more pigmented skin from the Indian subcontinent (16). Insufficiency of both dietary calcium and vitamin D are thought to be the underlying cause of rickets in Indian subcontinent children.

Together with calcium, vitamin D also helps protects older adults from osteoporosis (3).

Adults who have been deficient in vitamin D and calcium for a long period of time in their life, are more prone to have fragile bones and consequently, more susceptible to falls, bone fracture and bone pain (3,4). These ailments can be corrected with regular intakes of vitamin D, from food, supplements, or exposure to sunlight.

Vitamin D and Other Health Outcomes

In addition to boosting bone mineral density, a growing body of research suggests that vitamin D plays some role in preventing or lessening the negative health outcomes of a host of other diseases and conditions such as type 1 (17), and type 2 diabetes (18), hypertension (19), glucose intolerance (20), multiple sclerosis (21), and colon, prostate and breast cancers (22,23). However, most evidence for these roles comes from in vitro, animal, and epidemiological studies, not the randomized clinical trials considered to be more definitive (3). Until such trials are conducted, the implications of the available evidence for public health and patient care will be debated.

The largest clinical trial conducted so far to examine the effects of vitamin D on the primary prevention of cancer and cardiovascular events was the VITamin and OmegA-Trial (VITAL) (24,25) by Brigham and Women's Hospital, an affiliate of Harvard Medical School in Boston, Massachusetts. This clinical trial examined the effects of vitamin D_3 supplementation [2000 international units (IU)/day], compared to a placebo for a median of 5.3 years in 25,871 men aged ≥50 years and women aged ≥55 years with no previous incidence of cancer, heart attacks, or strokes (25). The results were published recently (24,25). The study showed that supplementation with vitamin D did not result in a lower incidence of breast, prostate, and colorectal cancers or cardiovascular events (myocardial infarction, stroke, and cardiovascular mortality) than placebo. The authors concluded that, daily supplementation of vitamin D is not helpful in reducing the incidence of cancer or major cardiovascular events among initially healthy adults (25).

Over the last 30 years, there have been many population-based cohort studies showing that persons with depression, psychiatric disorders, and other mental disorders, were associated with low serum vitamin D status (26,27). Some studies have shown that vitamin D supplementation impacted depression ratings in major depression with a moderate effect size (27). However, many of the studies have had mixed results and are limited by study type, sample size, and study duration, which suggests that more research is needed to further understand how vitamin D supplementation might impact someone's mood (26,27).

Vitamin D Status: Cut point values of blood vitamin D for bone health

The level of vitamin D in the body is checked by a blood test that measures 25-hydroxyvitamin D [25(OH)]. This is the form of vitamin D that the human body makes after converting vitamin D received from sunlight on skin, supplements, or food sources (1-4). Furthermore, 25(OH)D has a long circulating half life of 15 days, which makes it a reliable indicator of vitamin D status, whereas the other circulating vitamin D metabolite, $1,25(OH)_2D$, has a half-life of only 15 hours (28). A short half life does

not fully reveal actual vitamin D status. In this article the serum levels of 25(OH)D is simply referred to as blood (or serum) vitamin D.

Currently there is no agreement among the vitamin D researchers, professional health associations and national health agencies on the ideal serum concentrations needed for optimal overall health. Cut point values have not been developed by a scientific consensus process because of lack of high-quality clinical data. Despite this drawback, in late 2000, the US

Institute of Medicine (IOM), with support from the US Food and Drug Administration, and Health Canada, reviewed all the scientific literature data available at the time and established some cut points for serum concentrations of vitamin D most likely associated with deficiency (e.g., rickets), adequacy for bone health, and optimal overall health (3) (Table 1) . Persons are at risk of deficiency, at serum vitamin D concentration of <30 nmol/L (<12 ng/mL). Persons are potentially at risk for adequacy at levels ranging from 30-40 nmol/mL (12-16 ng/ml). For some people, levels above 40 to below 50 nmol/L might be sufficient for maintaining good bone health, but most of the general population are potentially at risk of bone and overall health. Practically all people are sufficient at levels ≥50 nmol/L. IOM stated that 50 nmol/L is the serum 25(OH)D level that covers the needs of 97.5% of the population. These cut-point values were based on proven benefits for bone health, as the IOM did not find convincing evidence about causal outcomes with other health outcomes (3)

Table 1: Serum Concentrations of Vitamin D and Health Status as Established by IOM (3).

Serum Vitamin D Concentration		**Health Status**
nmol/L	ng/mL	
<30	<12	Associated with vitamin D deficiency, leading to rickets in infants and children and osteomalacia in adults
30 to <40	12 to <16	Inadequate for bone and overall health
40 to <50	16 to <20	Some are potentially at risk for bone and overall health
≥50	≥20	Adequate for bone and overall health for 97.5% population
>125	>50	Toxic level. Associated with potential adverse health effects

According to IOM, the current recommended intake of 600-800 IU (15-20 µg) for those from 1 year to 70 years and 800-1000 IU (20-25 µg) for persons over 70 years is sufficient to meet the needs of 97.5% of the population in the US and Canada and who have minimal sun exposure. The IOM, noted a concern for attaining serum concentrations above 125 nmol/L (>50 ng/mL), because these extremely high levels are associated with potential adverse effects (e.g., elevated blood calcium levels, kidney failure, kidney stones) and therefore, IOM designated 4,000 IU daily as the tolerable upper intake limit. IOM, however, cautioned that 4,000 IU is not to be interpreted as a target intake level.

In summary, IOM recommends maintaining a serum vitamin D concentration above 50 nmol/L for bone and overall health, but it should not exceed 125 nmol/L.

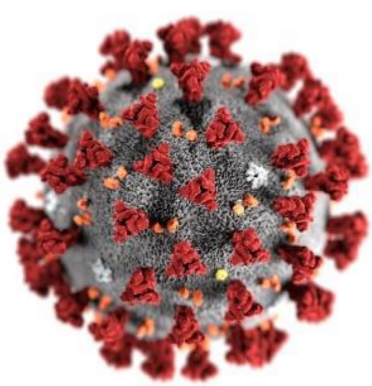
Recent Findings: Post IOM Report. Vitamin D and acute respiratory tract infections

Acute respiratory tract infections (ARTIs), often caused by bacteria or viruses, are a major cause of illness worldwide causing about 2.5 million deaths per year (5). These infections disrupt normal breathing, and come with symptoms like congestion, runny nose, cough, sore throat, muscle aches, and fatigue. The common cold, asthma, and pneumonia also fall under this umbrella (5).

In 2017, a meta-analysis of 10,933 people from 25 clinical trials conducted in 14 countries in four continents (Europe, North America, Asia, and Australia) looked at whether taking vitamin D supplements reduces the risk of ARTIs (5). This meta-analysis included people of all ages, healthy individuals, as well as those with respiratory conditions like asthma or chronic obstructive pulmonary diseases (COPD). In most cases, vitamin D was taken by mouth as vitamin D_3 pills for seven weeks to one-and-a-half years. Supplements were consumed at lower doses (generally 0.02 to 0.05 mg) daily or weekly, or higher doses (generally 2.4 to 3 mg) once monthly to every three months, or through a combined effort of frequent low-dose and infrequent high-dose schedules.

The results were positive. The review found that vitamin D_3 supplementation reduced the risk of developing ARTIs, with no serious side effects. The greatest benefit was seen with weekly supplementation, especially in people who had profound vitamin D deficiency at baseline. However, those with higher baseline serum vitamin D concentrations also experienced benefits. Interestingly, people who received one or more large doses of vitamin D (e.g. once monthly or every two months) did not experience these benefits. The results of the study strongly demonstrate that daily supplementation with vitamin D can prevent acute respiratory tract infections, particularly in people with profound vitamin D deficiency (5).

Vitamin D Supplementation-Potential Implications for COVID-19



A new study published by the Irish Longitudinal Study on Ageing (TILDA) at Trinity College Dublin provides further evidence that vitamin D plays a role in preventing respiratory infections (6). Interestingly, the TILDA researchers suggested that vitamin D could have important implications for the fight against COVID-19 (coronavirus) (6,7).

TILDA is an ongoing study of the health of people over the age of 50 years in the Republic of Ireland. According to its most recent reports (6,7), vitamin D plays an essential role in preventing respiratory infections, reducing antibiotic use, and boosting the immune system's response to illness. The TILDA study results revealed that of those aged 55+ years, 1 in 5 are vitamin D deficient (< 30 nmol/L) during the winter and 1 in 12 during the summer. An important concern is that nearly 30% of those aged 70+ to 85 and 47% of those 85+ are deficient in vitamin D. These are the age groups considered to be 'extremely medically vulnerable' to the adverse health outcomes of COVID-19 and have been advised to participate in 'cocooning' during the COVID-19 public health emergency (6,7). Moreover, of heightened to the TILDA researchers is the fact that only 10.5% of those 70+ report taking a vitamin D supplement. This low use of supplements, combined with 'cocooning' indoors which may not allow an opportunity for sun exposure, may put many of the 70+ group at exceedingly high risk of vitamin D deficiency. The TILLDA research team recommends that adults take 15-20 micrograms (μg) (800-1,000 IU) of vitamin D per day to reap the health benefits of vitamin D and to minimize the complications from the coronavirus (7).

In another study published recently (April 2020), a US team observed that COVID-19 outbreak occurred in winter, a time when 25(OH)D concentrations are lowest. The team also observed that the number of COVID-19 cases in the Southern Hemisphere near the end of summer are low (8). Summer months contribute to maximum skin production of vitamin D. It is known now that hot summer weather has no effect on epidemic growth of COVID-19 (13). Furthermore, the US research team observed that COVID-19 case-fatality rates increase with age and with chronic disease comorbidity, both of which are associated with lower 25(OH)D concentrations. The authors recommended that, people at risk of influenza and COVID-19, consider taking 10,000 IU/d of vitamin D_3 for a few weeks to rapidly raise serum vitamin D concentrations, followed by 5000 IU/d (8). The goal is to raise 25(OH)D concentrations above 40-60 ng/mL (100-150 nmol/L).

The US research team suggested that, randomized controlled trials and large population studies should be conducted to evaluate these recommendations (8). In fact, currently, researchers from universities around the UK launched a study (code name: COVIDENCE UK) to investigate how diet and lifestyle factors might influence severity of COVID-19 symptoms, speed of recovery, and long-term effects (9). They aim to recruit at least 12 000 people and obtain interim results by the summer. University of Alberta is also preparing to launch a study of at least 70 Albertans who contracted COVID-19 to see if their vitamin D levels put them at risk of severe infection and whether boosting these levels will help their conditions (10).

In May 2020, the Irish researchers published results of a literature search on PubMed of vitamin D status (for older adults) in countries/areas of Europe affected by COVID-19 infection and presents further circumstantial evidence linking outcome of COVID-19 and vitamin D status (11,12). The study found that, across Europe, COVID-19 mortality was significantly associated with vitamin D status in different populations (12). COVID-19 emerged and started its spread in Northern European countries at the end of 2019 (winter) when levels of 25(OH)D are at their nadir. The consequence was that Northern European countries have borne much of the burden of cases and mortality. Nordic countries, however, were exception to the poorer outcomes, because populations are relatively sufficient in vitamin D owing to widespread vitamin D fortification of foods. Italy and Spain were also severely affected by COVID-19 and in these populations vitamin D deficiency are common. This is not a surprise, because these two countries have no vitamin D fortification policies. This study also found that, black and minority Asian ethnic people living in Europe-who are more likely to have vitamin D deficiency because of their darker skin-seem to be worse affected than white people by COVID-19 (11). Data from the UK office for National Statistics also show that black people in England and Wales are more than four times more likely to die from COVID-19 than are white people (9).

Vitamin D status of Sri Lankan and other South Asian ancestry Canadians living in the National Capital Region

Two cohort studies, primarily designed to explore vitamin D status in relation to skin colour, dietary and supplementary vitamin D intake in Canadian adults and children of South Asian Ancestry residing in the National Capital Region of Canada, were conducted by Health Canada (14,15). The two studies included age and sex matched Canadians of European Ancestry as the control group. The adult study (20 to 79 years age group) was performed in spring and fall 2012 and the children (9 to 19 years age group) study in winter 2014. The South Asian Ancestry group included people with origin in India, Pakistan, Bangladesh, Sri Lanka, and Nepal. Sri Lankans accounted for approximately 65% of the South Asian Ancestry cohort.

The results revealed that blood vitamin D [25(OH)-D] deficiencies are common in South Asians (Tables 2-4) (14,15). The deficiencies are alarmingly prevalent especially among the young adults in the 20-39 y (Table 2) and children in the 6-19 y (Table 4) age groups. Serum 25(OH)D values tended to increase with age but this dependent on ethnic background (Table 2). For example, significantly higher 25(OH)D values were observed in the oldest among European participants. However, both the middle and the oldest groups were higher among South Asian participants. Differences between seasons were significant only for those of European ancestry while no difference was noted for those of South Asian ancestry (Table 4).

An important finding of this study is that Canadians of South Asian ancestry were more likely than Canadians of European ancestry to fall short of the IOM recommended 25(OH)D levels for the prevention of deficiency and inadequacy that are based on bone health (Table 3). 29-44% of South Asian participants had serum 25(OH)D <40 nmol/L, the cut point for inadequacy, while approximately 10% European participants fell below this cut point. A serum concentration ≥50 nmol/L is considered to provide overall health benefits. Only 31 to 49% of South Asian participants had this healthy serum 25(OH)D level whereas 81.2-91.9% European participants met this healthy level. South Asian children displayed dangerously lower levels of vitamin D status than their adult counterparts and European ancestry children (Table 4). 56.9% of South Asian children had inadequate levels (<40 nmol/L) while only 8.6% European children were below this cut point.

Investigation of the factors related to serum 25(OH)D levels showed that supplement intake, ethnic background coupled with a lack of response to summer-related vitamin D synthesis were important factors related to lower blood vitamin D levels in South Asians (14). In South Asian children, obesity was an additional factor contributing to insufficient vitamin D status (15). These studies reinforce the importance of public health actions towards meeting vitamin D status and reducing adiposity, both of which are anticipated to improve vitamin D status of South Asian Canadians.

These findings are consistent with previous work in Canada showing a high prevalence of low vitamin D levels among South Asian ancestry living Southern Ontario (29). In that study, 35.5% of South Asian participants had 25(OH)D concentrations <25 nmol/L. This high prevalence of vitamin D deficiency in South Asians Canadians is alarming, given its role (along with calcium) in bone accretion and there is evidence that increased bone mineral density can prevent bone fractures (30).

A study done in Norway compared the vitamin D status of Sri Lankans living in Oslo, Norway with those living in Kandy, Sri Lanka (31). Sri Lankans living in Norway had substantially lower vitamin D levels (mean 31.5 nmol/L) compared to those living in Sri Lanka (mean 54.2 nmol/L). The prevalence of vitamin D <50 nmol/L was considerably higher among Sri Lankans living in Oslo (90.3% in men and 90.8% in women) than that among Sri Lankans living in Kandy (34.1% in men and 58.6% in women) (31). These findings in Norway are consistent with those studies from Ottawa (14,15) and Southern Ontario (29) and illustrates that vitamin deficiency is common in Asian immigrant groups living in Western countries.

Vitamin D status of Sri Lankans living in Sri Lanka

Sri Lanka being near the equator receives almost 12 hours of sunlight per day throughout the year. This gives a false impression that all Sri Lankans are exposed to sunlight and therefore have adequate vitamin D status. However, sun-bathing culture is uncommon in Sri Lanka due to hot and humid climate. The Norwegian study discussed above (31) should not be regarded as normal levels for all Sri Lankans, because there are several other observational studies that have shown high prevalence of low vitamin D (<50 nmol/L) in Sri Lanka. For example, Rodrigo et al. (32) have reported that 56% of premenopausal women have vitamin D level ≤35 nmol/L in the Southern coastal belt of the country. In recent years, vitamin D insufficiency (level <50 nmol/) was reported among 35% pre-schoolers (33), 72% pregnant mothers (34), 55%

lactating mothers (34), 99% infants (34) and 88% adults residing in urban areas (35).

Message to Sri Lankans

All Sri Lankans, including those in Sri Lanka as well as Sri Lankans living in Western countries need to take immediate action to boost their vitamin D status**. This is especially true during the Coronovirus pandemic where many people are staying indoors home, particularly the elderly during long-term care lockdowns.** Moreover, the available scientific data suggest that boosting the vitamin D status may help to enhance the immune system and minimize the risk of acute respiratory tract infections (ARTIs) (5). Weak immune system and ARTIs are two major causes of hospitalization and death due to COVID-19 (8).

For those with darker skin tones, research has shown that exposure to sunlight does not provide enough vitamin D (1-4), and it is therefore advisable for these people to eat on a regular basis vitamin D containing foods (e.g., oily fish, eggs) and foods fortified with vitamin D (e.g., breakfast cereals, most margarines (Table 5). Supplements are an alternative source of vitamin D, especially for the elderly population and vegetarians. To maintain healthy vitamin D status [serum 25(0H)D level >50 nmol/L], people of age 1 to 70 years need to intake daily 600 IU (15 µg) and those above 70 years 800 IU (20 µg) of vitamin D.

Occasionally, it will be helpful to do a blood test for vitamin D which would be helpful in assessing whether the intake levels are sufficient in meeting a healthy vitamin D levels. In Ontario, vitamin D test cost about $25-30 but well worth to check considering the benefits.

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Table 2: Serum 25(OH)D concentration in adults of South Asian and European ancestry by age. Both seasons and sexes combined

Age	South Asian Ancestry		European Ancestry	
	N	nmol/L	N	nmol/L
20-39	174	42.7	233	70.8[a]
40-59	287	49.5	272	71.3[a]
60-79	125	57.2	147	76.9[a]
20-79	586	49.1	652	72.4[a]

a-significantly different from South Asians

Table 3: Percentages of adults of South Asian and European ancestry with 25(OH)D values falling IOM cut points

Gender	Season	South Asian Ancestry			European Ancestry		
		<30 nmol/L	<40 nmol/L	<50 nmol/L	<30 nmol/L	<40 nmol/L	<50 nmol/L
Female	Spring	7.1	29.1[a]	51.1[a]	3.5	9.1	19.8
Male	Spring	20.6[a]	44.2[a]	67.3[a]	2.8	10.4	18.9
Female	Fall	12.1[a]	27.3[a]	51.5[a]	0.0[b]	1.4[b]	8.1[b]
Male	Fall	14.9[a]	36.5[a]	68.9[a]	1.0	3.9[b]	13.6

[a] Significantly different from the corresponding value for participants of European ancestry.
[b] Comparison between fall and spring. Significantly differences were observed only for participants of European participants.

Table 4: Percentage of children (9-19 years) of South Asian and European ancestry with 25(OH)D falling below 40 nmol/L cut point

Serum total 25(OH)D	South Asian	European
<40 nmol/L	56.9[a]	8.6
≥40 nmol/L	43.1[a]	91.4

Superscripts show significant difference from the corresponding value for participants of European ancestry.

Table 5: Selected Food Sources of Vitamin D

Food	IU
Rainbow trout, cooked, 100 g	645
Atlantic salmon (sockeye), cooked 100 g	526
Farmed salmon, cooked 100 g	250
Atlantic herring, 100 g	112
Canned sardines, 100 g	177
Halibut, 100 g	384
Mackerel, 100 g	360
Canned tuna, 100 g	268
Egg, one whole egg	44
Liver, beef, 100 g	42
Milk, 2% milk fat, vitamin D fortified, 1 cup	120
Soy, almond, and oat milks, vitamin D fortified, 1 cup	100-144
Ready-to-eat cereals, fortified with vitamin D, 1 cup	80
Mushroom, white, raw, ½ cup	570
Mushroom, portabella, raw, ½ cup	4
Cheese, cheddar, 100g	12
Canadian margarines, fortified with Vitamin D, 10 g	53

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