# Responses to Questions from Health Canada on Implementation of Dietary Reference Intakes for Calcium and Vitamin D by the Expert Advisory Committee of the Canadian Academy of Health Sciences

*Submitted to Health Canada, January 31, 2012*


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## Terms and Abbreviations

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| 25(OH)D | 25-hydroxy vitamin D |
| AI | Adequate Intake |
| ASBMR | American Society for Bone Mineral Research |
| CAHS | Canadian Academy of Health Sciences |
| CaMos | Canadian Multicentre Osteoporosis Study |
| CDC | Centers for Disease Control and Prevention (U.S.) |
| CCHS | Canadian Community Health Survey |
| CHMS | Community Health Measures Survey |
| D2 | Ergocalciferol |
| D3 | Cholecalciferol |
| DRI | Dietary Reference Intakes |
| EAC | Expert Advisory Committee |
| EAR | Estimated Average Requirement |
| FDA | Food and Drug Administration (U.S.) |
| HC | Health Canada |
| IOM | Institute of Medicine |
| IU | International Units |
| mcg | microgram |
| mg | Milligram |
| NIH | National Institutes of Health (U.S.) |
| NHPD | Natural Health Products Directorate |
| nmol/L | Nanomoles per Litre |
| PTH | Parathyroid Hormone |
| RCT | Randomized Controlled Trial |
| RDA | Recommended Daily Allowance |
| RDI | Reference Daily Intake |
| SES | Socio-economic Status |
| UL | Tolerable Upper Intake Level |
| WHO | World Health Organization |

## EXECUTIVE SUMMARY
## OF THE EXPERT ADVISORY COMMITTEE REPORT TO HEALTH CANADA ON CALCIUM AND VITAMIN D

Calcium and vitamin D are two essential nutrients that have been the subject of previous recommendations by Health Canada. Recently, the Institute of Medicine (IOM) updated these recommendations by reporting Dietary Reference Intakes (DRIs) for these nutrients. Because of their close relationship (vitamin D facilitates intestinal calcium absorption), both nutrients were considered together.

The Canadian Academy of Health Sciences (CAHS) struck an Expert Advisory Committee (EAC), which first convened in January 2011, in order to respond to specific questions posed by Health Canada as a consequence of the IOM report. The following are the questions posed and a summary of the responses and recommendations of the EAC.

### Calcium

#### *1. Potential Approaches to Increase Calcium intakes*

**Q 1.1 – By how much should calcium intake be increased for the various age-sex groups?**
The intake values for calcium in relation to the DRIs vary quite widely by age and sex group. Based on data from the Canadian Community Health Survey (CCHS), the prevalence of inadequacy for calcium is high in older men and women, and in adolescent girls. The extra calcium intake needed in those with low calcium intake is generally around 300 mg but up to approximately 500 mg in the groups mentioned above. This increase, if introduced at the population level, would result in some groups (men and women over age 51) exceeding the Tolerable Upper Intake Level (UL). Furthermore, the UL might well be exceeded in those also consuming supplements. Canadians living in food-insecure households are, by definition, nutritionally vulnerable and this vulnerability includes compromised calcium and vitamin D intakes. Aboriginal communities are globally at higher risk of inadequate calcium intake, especially in the far north, but also in those living off reserves. There is substantial heterogeneity of calcium intake both within and between Aboriginal populations, thus it is currently unclear how much calcium intake should be increased for each of the various age-sex groups. Pregnant and lactating women represent another vulnerable group and nutrition education for women of reproductive age may be helpful to bring their intake to the Recommended Daily Allowance (RDA).

**What are benefits and drawbacks to the general population and vulnerable sub-populations (those with low exposure to calcium through diet) of increasing intake via:**

**Q 1.2 - a) Increased consumption of food sources (without further fortification)?**
*Benefits:* Adolescents are in a period of important bone growth and a rapid increase in body size and are in need of nutrient rich diets for many nutrients including calcium. Most dairy sources of calcium are also good sources of other nutrients so that increasing increased dairy consumption may also have other nutritional benefits. Successful intervention to encourage increased consumption of dairy products in childhood and adolescence may impact lifetime dietary patterns.

*Drawbacks:* There seems to be a strong belief among some people that certain populations are prone to suffer from lactose intolerance, or that milk is only for children, and education may have limited impact on overall diet. Education alone also does not address barriers to improved diet among those with low socio-economic status (SES), where cost is one important barrier to acceptance. Over age 50 it is likely problematic to encourage greater consumption of current calcium rich foods as energy needs decline with advancing age.

**Q 1.3 - b) Supplementation?**

*Benefits:* With supplements, there would be no need to introduce wholesale changes in dietary patterns and the choice to supplement would be based on the individual; as well, the intake of total calcium intake could still be below the UL, provided that only those who need a supplement take it and only at the proper dose.

*Drawbacks:* Supplements, although not very costly are still a cost burden to many, and supplementation often will not reach the most vulnerable Canadians. Promotion of supplement use also has the risk of reducing intake of protein and other nutrients also important to growth and bone health, nutrients that naturally are provided with major food sources of calcium

**Q 1.4 - c) Increased fortification of dietary sources?**

*Benefits:* As long as the foods selected for fortification are foods consumed regularly by Canadians across the socio-economic spectrum, mandatory fortification will reach the entire population. Voluntary fortification (as with orange juice) would provide more consumer choice.

*Drawbacks:* Economic costs may be associated with increased fortification, and perceptions that government is "tampering" with the food supply. Big eaters - adolescent boys and young men - will consume more of all foods, and some could exceed the UL. On the other hand, if fortification is only done at a low level, older people who comprise the group with the highest percent of intake below the Estimated Average Requirement (EAR) and who generally have lower food intake, might then not meet their needs. Voluntary fortification can also be expected to exacerbate our 'income gradient' and the 'education gradient' in food and nutrient intakes.

**Q 1.5 - Given these benefits and drawbacks, and the fact that the food supply provides enough calcium to meet the population's requirements, but that most of the population is not consuming enough, what is the most appropriate approach to increase calcium intake in the general population and vulnerable subpopulations so that there is a low prevalence of inadequate intakes?**

There is likely no single strategy that will appropriately increase calcium intake in both men and women in all age groups in the general population, and in all vulnerable subpopulations, that would ensure a low prevalence of inadequate intakes.

- Voluntary fortification of some non-dairy foods along with better education may be appropriate in the general population, especially for those not consuming dairy products.
- Calcium-rich food offerings in the school environment could be helpful for youth and adolescent females.
- Clear guidance on supplement use might be important for those over age 50.
- Adopting a 'social determinants of health' framework to develop effective interventions that tackle the root causes of this problem might be an important approach for low SES groups, and community-specific responses for Aboriginal groups may be among the strategies for these vulnerable groups.

Therefore a combination of strategies may best serve to reduce the prevalence of low calcium intakes.

**Q 1.6 - What education strategies should be considered?**
Eight conditions representing a behavioural change framework are described that must be present for individuals to perform a given behaviour, including consuming the daily recommended intake of calcium and vitamin D. A well-grounded and well-conducted health education strategy must also aim at compliance, adherence and persistence with supplements. Twelve Health Behaviour Change Strategies are described which could involve the media in designing a health communication campaign focusing on nutrient health.

**Q 1.7 - Are there vulnerable subgroups in need of special guidance?**
Some of the most vulnerable subgroups (e.g. low SES groups, Aboriginal communities) are often the most challenging to engage in health communication campaigns and behaviour change but progress has been reported. There is a need to consider the context of social determinants of health in vulnerable groups, removing barriers to change, and increasing availability and visibility of healthy calcium rich food sources.

**Question 1.8- 1.10**
**If "Increased fortification of dietary sources" (c) is deemed most appropriate:**

**Q 1.8 - should fortification of a staple food be an option for improving calcium intakes?**
If flour or other staple food were fortified, this would ensure that higher levels reached more, but certainly not all, of the vulnerable subpopulations. However, a greater proportion of young men would be at risk of exceeding the UL if calcium is added to frequently eaten staple foods; if fortification were at a low level to prevent this, small eaters would not get the extra calcium in the quantities needed.

**Q 1.9 - If fortifying a staple food is not appropriate, should there be more fortified food choices as part of the general food supply?**
The availability of more calcium-fortified food choices as part of the general food supply might be beneficial, however once a number of different products are fortified there is a risk of a person regularly consuming several sources. Some populations such as young men may become at risk of exceeding the UL for calcium. Education in wiser food selection would be necessary

**Q 1.10 - How do we ensure a balance between fortified food use and the use of supplements, so that the prevalence of intakes above the UL is minimized?**
Accurate labelling on fortified and non-fortified foods must be present. Only then can consumers attempt to balance intake from fortified foods and supplements. Nevertheless, asking people to track their personal calcium intakes relative to their needs and ULs may be difficult. Health Canada must also continue to monitor the total calcium intake of the population, so that in fortification, excess calcium is not added to any particular food and therefore the total intake of fortified food use and supplements does not exceed the UL.

***Question on Drug-Nutrient Interactions Relevant to Calcium:***

**Q 1.11 - Given that the IOM recommendations cover the vast majority of the general population and we know that many in the general population are using prescription medications on a regular basis - are there any drug-nutrient interactions that should be considered with regard to fortification or supplementation?**

Drug-calcium interactions include the potential of calcium to interfere with absorption of medications, or vice versa, and this has been reasonably well documented for the use of calcium supplements. In general terms, dosing instructions given to patients by pharmacists are usually very clear regarding the separation of calcium/food intake and ingestion of a drug. Most drug-calcium interactions should therefore not be a major concern, and should not require any specific actions beyond the overall recommendations for total calcium intake. A summary of the major drug-calcium interactions is provided.

***2. Calcium Supplement for Infants: Levels***

**Q 2.1 - Is calcium supplementation appropriate in infants (0-12 months)?**
**Q 2.2 - If yes, what levels would be recommended?**

There are few situations where calcium supplementation of infants is indicated. Preterm infants have higher calcium requirements than term infants and preterm formulas and human milk fortifiers are accordingly fortified with added calcium.

Calcium supplementation for older infants may be required in situations where dairy foods are eliminated (e.g. dairy allergy or intolerance). However, it is more likely that soy-based infant formula or extensively hydrolyzed infant formula would be substituted, and such formulas would contain appropriate amounts of calcium for infants. Overall, there is insufficient evidence to support a recommendation for calcium supplementation in infants. This conclusion is based on the rationale that the amount of calcium provided by either breast milk or formula will always be sufficient for exclusively breast or formula fed infants.

**<u>Vitamin D</u>**

***3. Vitamin D Intakes and Status***

**Q 3.1 - Is there a need to increase vitamin D intakes in order to achieve a higher prevalence of dietary adequacy?**

Yes. The new EAR for vitamin D has been set at 400 IU and a majority of Canadians have vitamin D intakes below this level.

**Q 3.2 - Should Canada continue to rely on sunlight as a key source of vitamin D for the general population?**

Canada does not rely on sunlight as a key source of vitamin D for the general population but sunlight is an unavoidable contributor to 25(OH)D levels in Canadians and this factor should be taken into consideration for any assessment of 25(OH)D.

**Q 3.3 - By how much should vitamin D intake be increased for the various age-sex groups?**
Approximately 73% of men and 63% of women currently have intakes below the EAR from food and supplements combined (CCHS). In the absence of education programs to increase vitamin D consumption from currently fortified foods, and in the absence of extending food fortification to other foods, to bring the usual intake of the 50$^{th}$ percentile of the Canadian population up to the EAR (400 IU/day) would require increasing the amount of vitamin D introduced into currently fortified foods by over 60%. This is unlikely to resolve the problem of vulnerable groups such as those with low milk consumption for a variety of cultural and other reasons.

**Q3.4 – If Health Canada decided to recommend increased consumption of current food sources of vitamin D (without further fortification or the use of supplements), what would be the benefits and drawbacks to both the general population and vulnerable subpopulations?**
*Benefits:* These would include minimization of the prevalence of inadequacy in the population, while running a limited risk of exceeding the UL on the basis of the quantities of vitamin D in the present food supply.
*Drawbacks:* Many Canadians are not even consuming milk at the current recommendation, and vulnerable subgroups even less so. There are several barriers to increased milk intake, including cultural habits, perceived lactose intolerance, and peer use. In addition, education alone, to increase consumption of current food sources of vitamin D, would not address cost barriers to improved diet among those with low SES. Furthermore, without fortification, there is too little vitamin D in other commonly consumed foods

**Q 3.5 - If Health Canada decided to recommend wider supplementation (to more age-sex groups, to high risk population groups), or increased supplementation to those with current recommendations to take a supplement, or supplementation by season, what would be the benefits and drawbacks to both the general population and vulnerable subpopulations?**
*Benefits:* For supplements**,** benefits would include the lack of requirement to change dietary patterns and to produce changes in the food supply. Supplementation would provide minimal risk of exceeding the UL. Assuming dietary supplements providing vitamin D were consumed at recommended levels, this approach could provide choice to supplement based on the individual, as well as the capacity to target increases in vitamin D intake for those who groups that most require the increases.
*Drawbacks:* Supplementation is more expensive than food fortification for the consumer, and supplementation would require high levels of compliance/adherence by the population. The most vulnerable population groups are the ones least likely to be taking vitamin D supplements because of cost, lack of awareness of the need, and possibly lack of belief in the benefits.

**Q 3.6 - If Health Canada decided to recommend increased fortification of dietary sources with vitamin D, what would be the benefits and drawbacks to both the general population and vulnerable subpopulations?**
*Benefits:* Increased fortification of existing products would have the advantage that an existing mandatory fortification policy is in place and change would mainly be in the level of fortification. Increased fortification of appropriate dietary sources with vitamin D would reach a wider population than supplementation and could address the needs of those with some (but too little) milk intake. Concurrent increased fortification of milk substitutes (e.g. soy beverages) would assure that those who do not drink milk have the same benefit. Increased fortification of new sources of foods might more readily address the global under supply of vitamin D in the food supply.

*Drawbacks:* Mandatory food fortification may be politically contentious because of perceived tampering of the food supply, and there might be an economic cost associated with food fortification. Increased fortification may also be of limited use for those with low energy intake.

**Q 3.7 - Could fortification address recommended intakes without the need to recommend supplements to specific sub-groups?**
If fortification were used one would need to calculate the levels that the population would receive if specific vehicles were used and then examine the data to see who may still not be adequately covered. It is possible that because elderly Canadians have reduced energy intakes, they might still require a supplement as many other vulnerable groups.

In summary, the EAC recommends:

- Increasing the mandatory fortification of already fortified selected foods with vitamin D. This would include increasing vitamin D in milk and milk substitutes (for those not consuming dairy products).
- In addition, Health Canada should explore other fortification options, through modeling exercises, as many adult Canadians drink very little milk and reliance on milk does not reach certain at-risk populations.
- Even fortification may not totally address recommended intakes of vitamin D without the need to recommend supplements to specific sub-groups.

**Q 3.8 - If Health Canada were to decide to recommend increased vitamin D food fortification or the use of supplements, would there be an increased risk of toxicity to people with high sun exposure, considering that there may not be any (or an adequate) feedback mechanism to control serum 25(OH)D levels from oral sources of vitamin D?**
The IOM places the UL at 4000 IU daily, as a long-term average consumption with no known risk of adverse effects. With appropriate increased vitamin D food fortification or the use of supplements the resulting distribution of intake would still fall entirely below the UL level.

**Q 3.9 - Are additional data needed to help answer Question 3.8, and what data would be needed?**
Ideally, a longer-term trial e.g. a 5-year RCT using different doses of vitamin D up to 4000 IU daily and with a defined calcium intake could be helpful to examine both indices of efficacy and of toxicity and potential interaction between vitamin D and calcium intake. There is also a need for social/consumer research to determine if there are preferred scenarios for vitamin D fortification and a need for modeling studies to determine the impact of various modeling scenarios on the distribution of vitamin D intake globally and among populations at risk.

***4. Vulnerable Populations and Vitamin D***

**Q 4.1 -What do we know about the 25(OH)D status of the people who were not covered by The Community Health Measures Survey (CHMS), that is those living in institutions, on reserves or north of the 60th parallel?**
There is very little up-to-date data on serum 25(OH)D levels among Canadians living in long-term care facilities. There is dietary heterogeneity among Aboriginal communities, but present surveys indicate

that all surveyed communities face increased risk of low 25(OH)D status, especially related to dietary transition.

**Q 4.2 - What do we know about the 25(OH)D status of non-white persons?**
The overall prevalence of vitamin D deficiency (25(OH)D < 30 nmol/L) in the CHMS was 16.3% among non-whites compared with less than 5% among whites.

**Q 4.3 - Are there differences in 25(OH)D status among East Asian, South Asian, Middle Eastern and African groups?**
Darker skin pigmentation increases the risk of lower 25(OH)D levels in all groups studied.

**Q 4.4 - If there are insufficient data to draw any conclusions about the status of these groups mentioned in questions 4.1 to 4.3, what is the best way to obtain such data?**
It may be productive to determine whether the CHMS survey of 25(OH)D levels in Canadians could be analyzed in terms of differences among groups with different ethnic origins or to specifically address this issue with a new study. For immigrant groups, it may be useful to do more focused studies within the large metropolitan areas to adequately sample non-white groups, rather than pan-Canadian studies, as the levels of 25(OH)D and the predictors of their status including cultural and dietary factors need to be better understood in order to know what interventions are needed and which are acceptable.

**Q 4.5 - Is there a need to fortify foods only eaten by a vulnerable group; i.e. that are not eaten by the general population, and what would be the appropriate food vehicles?**
Ideally, additional foods to fortify should be foods eaten by the general population and by the sub-groups at risk. However research needs to be done to determine appropriate food vehicles for vulnerable groups and the amount of fortification to use. Modeling various choices might help in identifying the appropriate food vehicle.

**Q 4.6 - Are there vulnerable subgroups in need of special guidance to ensure adequate intakes of vitamin D?**
Yes, vulnerable subgroups include those with malabsorption syndromes, Middle Eastern and other women who wear full-coverage clothing, and Aboriginal groups.

### *5. Infants and Vitamin D*

**Q 5.1 - Are there risks to any subgroups if the current Health Canada recommendation to give a daily vitamin D supplement of 400 IU to breastfed healthy term infants, starting at birth, is promoted? (Note the Canadian Paediatric Society currently recommends a supplement of 800 IU for at-risk infants e.g. living in the far North.)**
The recommendation of 400 IU vitamin D per day may not be adequate in the following subgroups of infants: 1) infants born to mothers with sub-clinical or overt vitamin D deficiency; 2) infants with malabsorptive disorders such as cystic fibrosis or celiac disease; 3) infants in the far north who have dark skin and minimal exposure to sunlight due to latitude of their environment.

**Q5.2 – Are there cases in which there would be a good rationale to recommend a higher dose for infants?**
Yes, in preterm infants, and in term infants living in northern communities (especially those with intermediate or dark skin colour), and at risk of vitamin D deficiency at birth because of maternal vitamin D deficiency during pregnancy.

**Q 5.3 - When a formula-fed infant switches to cow's milk between 9 and 12 months of age, should a vitamin D supplement be recommended given that a child may obtain less than 400 IU vitamin D from cow's milk?**
From a practical perspective, it might be appropriate to recommend continuation of a supplement of 400 IU of vitamin D until two years of age unless it is provided in other foods.

## Vitamin D and Calcium

### *6. Supplement Claims with respect to Vitamin D and Calcium*

**Q 6.1 - Does the current osteoporosis claim on the monographs of Natural Health Products Directorate (NHPD) require revisions to the wording or the addition of a dose threshold based on the information provided in the DRI report and in consideration of recent Food and Drug Administration (FDA) recommendations?**
The committee agrees that 20% of the Reference Daily Intake (RDI), i.e.200 mg calcium and 100 IU vitamin D, would be sufficient to support the claim "adequate calcium (and vitamin D) (throughout life) as part of a healthy diet (along with physical activity) may help prevent bones loss/osteoporosis (in peri and post menopausal women) (in later life)".

### *7. Vitamin D and Calcium Bioavailability and Co-Fortification:*

**Q 7.1 - Are there concerns regarding bioavailability that would lead to recommendations regarding specific forms of vitamin D and/or calcium to be used in foods or in supplements?**
Vitamin D:
1) Bioavailability from various foods:
Based on current evidence, fortification with vitamin D in several foods – milk, cheese, orange juice - appears to yield similar bioavailability as evidenced by response in vitamin D status in adults.
2) The biopotency of the D2 versus D3 form of vitamin D:
Differences in biopotency of D3 versus D2 have only been demonstrated at very high intake levels of supplements, in which case D3 appears more potent. The failure to demonstrate differences at low intake levels may however be because of lack of statistical power. Consideration for inclusion of vitamin D2 should be given due to D2 being a preferred source for vegans. It would be important to provide clear labeling of the form of vitamin D and the quantities.

Calcium:
Bioavailability of calcium varies with the type of calcium salt (e.g. calcium carbonate versus calcium citrate) and the type of food that is the carrier, primarily being lower from plant than animal based foods. Thus, criteria for the amount and type of calcium salts used in fortification are recommended.

**Q 7.2 - Are there concerns regarding bioavailability that should lead to specific dietary advice to enhance absorption?**
Some advice should be provided about the amount of calcium per dose of supplement (i.e. 500 mg would be optimal) and that calcium carbonate is best taken with food or beverages to stimulate acid secretion whereas calcium citrate may be taken without foods or beverages .

**Q 7.3 - When considering addition of calcium or vitamin D to foods should co-fortification be required always, i.e., should it be necessary to add calcium when vitamin D is added and vice versa?**
Although calcium-fortified food should have co-fortification with vitamin D, consideration should also be given to fortification with vitamin D alone.

## Other

### *8: Risk Communication Strategies*

**Q 8.1 - What educational strategies or risk communication strategies should be considered when the policy approaches are decided on?**
A risk communication plan needs to be an integral component of a comprehensive communication and behaviour change campaign. At a minimum, this would include:

- A situational assessment regarding who (individual, sub group, community) is most at risk from under/over utilization of calcium and vitamin D.
- Preventive strategies to address the vulnerable sub groups.
- An evaluation plan including measureable outcomes and quality improvement cycle.

Various organizational and audience constraints that can have major impact on the effectiveness of health communication and behaviour change are described and seven distinct steps for a successful health communication campaign are also described.

### *9. Clinical Standards for 25(OH)D Levels*

**Q 9.1 - What is the most appropriate process by which these cut-points should be established?**
The current recommended thresholds for 25(OH)D of 40-50 nmol/L seem based mainly on levels to prevent or treat bone disease, i.e. rickets, osteomalacia and osteoporotic fractures. Establishing thresholds of vitamin D to prevent the antecedents of these diseases before they become manifest would ideally be more helpful. The EAC suggests a committee of experts be formed to develop a vitamin D (and possibly a calcium) research plan and set priorities for the research questions to be answered in developing clinical standards.

**Q 9.2 - Which parties should be involved in this process and what should their roles be?**
Individuals who are knowledgeable about vitamin D and calcium metabolism and who have expertise in pertinent disciplines: clinical biochemistry and physiology; statistics and epidemiology; clinical

medicine and nutrition; and public policy, and who would be able to address the issues of ethnic and geographic diversity which are prevalent in Canada.

**Q 9.3 - Should efforts be made to establish a common standard with the US?**
Overall this would be a pragmatic approach.

**Q 9.4 - In the absence of an agreed-upon cut-point, what threshold cut-off value should be used (e.g., 40 or 50 nmol/L) by Government agencies when examining the distribution of serum concentrations of vitamin D in order to assess adequacy of vitamin D status in Canada?**
The EAC recommends that a threshold of 50 nmol/L of 25(OH)D should be used by Government agencies when examining the distribution of serum concentrations of 25(OH)D in order to assess adequacy of vitamin D status in Canada.

# DETAILED RESPONSES TO QUESTIONS SETS FROM HEALTH CANADA ON IMPLEMENTATION OF DRIs FOR CALCIUM AND VITAMIN D

## Introduction

Calcium and vitamin D are two essential nutrients, which have been the subject of previous recommendations by Health Canada. Recently, the Institute of Medicine (IOM) updated these recommendations by reporting Dietary Reference Intakes (DRIs) for these nutrients. Because of their close relationship (vitamin D facilitates intestinal calcium absorption), both nutrients were considered together.

In response to a request from Health Canada, an Expert Advisory Committee (EAC) was constituted by the Canadian Academy of Health Sciences (CAHS) in order to respond to specific questions as a consequence of the IOM report. The EAC membership had broad geographical distribution and spanned a wide range of expertise, including: nutrition, growth, and body composition as determinants of health and disease risk; nutritional health of high risk populations in Canada including obese chilren and the elderly; adult and pediatric clinical and investigative medicine; clinical biochemistry and genetics; calcium, vitamin D and bone physiology and biochemistry; epidemiology and biostatistics; health policy and the governance of health care organizations; and behavioural change and organizational improvement.

EAC members were:

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The EAC first convened in January 2011 and deliberated via face to face meetings, conference calls and electronic communication. It responded to several iterations of questions, clarifications and suggestions from Health Canada. This document represents the consensus of the EAC on the questions posed by Health Canada.

Consultants were also included to provide additional expertise in vitamin D and skeletal health in aboriginal communities; social and economic determinants of health and nutrition, and food insecurity; and bioavailability and safety of nutritional supplements
Consultants were:

Frank Rauch
Department of Pediatrics, McGill University
Valerie Tarasuk
Department of Nutritional Sciences, University of Toronto
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(Dr Tarasuk contributed to sections of the document but does not share some of the views expressed in this report.)

One of the major areas considered by the EAC was the issue of fortification policy. In the current social and political environment, it is probable that a policy prescribing an intervention at population level involving supplementation or fortification of food would raise perceptions that government is "tampering" with food, and might therefore face strong resistance [1]. The public's understanding of the precautionary principle too often confuses risk—even if it is truly minimal—with harm, resulting in a bias against new technologies, new activities or new initiatives. The constant debate over fluoridation of the water supply demonstrates that it is not enough to state that an intervention brings high benefits at very low risks [2]. Not only must the science be irreproachable, but also the intervention has to be carefully proportioned to the importance of the public health problem it attempts to remedy and should take into consideration the size of the population affected by the deficiency, whether this population is geographically concentrated or socially defined, what health risks are associated with the deficiency, is it possible to mitigate the risk and what sorts of risks are associated with the mitigation strategy.

Factors such as socio-economic status, age or ethnic origin have a huge influence on the nutritional experience of different groups or sub-groups. Policy choices to address observed deficiencies must necessarily take into account these differences. A small but well-defined population may positively react to a targeted intervention. However, when the population at risk is dispersed within a greater ensemble, like childbearing women for example, the preferred option might be a more encompassing action, given that the intervention presents few risks for the general public.

The severity or intensity of the health outcomes associated with a deficiency is also part of the evaluation process. Relatively benign outcomes will call for voluntary measures, with or without the

support of a health provider. For more severe outcomes or for problems that develop very rapidly, it might be necessary to resort to approaches that leave less to the initiative of the patient or the provider.

Finally, it is important to weigh carefully the costs and benefits or any proposed intervention, both for public health and for the economy. In the first case, a measure that is beneficial for the population at large might in fact cause harm to a particular sub-group—we'll look in the report at the potential impact of excessive calcium supplementation on a few specific age and gender groups, for example. In the latter, one should not be forgetful of the costs associated with the production and distribution of foods; any recommended change has indeed an impact on a large number of stakeholders.

The decision to regulate the fortification of milk with vitamin D provides a good illustration of such an approach. This was a case in which there was a widespread problem with rickets Mandatory fortification of all milks with vitamin D virtually eliminated rickets as a public health problem in the late 1970s, while presenting no significant risk for the public.

A final note: norms emerging from recent legal disputes suggest that decision-making in the health sector is not only "informed" by evidence, but that it must actually follow what scientific evidence points to be a prudent course of action. We believe this report and our recommendations are in good accordance with this framework and could actively contribute to decrease the risk of disease while limiting other risks to public health.

## RESPONSES TO SPECIFIC QUESTIONS

## Calcium

### *1. Potential Approaches to Increase Calcium Intakes*

***Context (provided by Health Canada):***

***According to the CCHS dietary data, a large proportion of Canadians have less than adequate intakes of calcium. Although there is sufficient calcium in the food supply to meet the requirements, people are not choosing to consume foods rich in calcium. One approach to increasing calcium intakes would be to add it to another widely consumed food. In Canada, flour may be fortified with calcium (as calcium carbonate, chalk, ground limestone, or calcium sulphate) at the level of 140 mg per 100 g although this is not done in practice. Mandatory fortification of flour would raise calcium intakes just as it raised folic acid intakes after 1998.***

***There is, however, a narrow margin between the RDA and the UL in persons over 50 years of age and in fact when supplements were considered, there were people exceeding the UL among the 50+ age group in CCHS. The fortification of flour with folic acid raised blood folate levels more than anticipated. There is no comparable measure for calcium exposure to assess the short-term impact of increased calcium fortification of the food supply.***

***For all the following questions, please consider both the general population at large and vulnerable subgroups. Vulnerable subgroups are those with low exposure to calcium through diet, such as those with low socio-economic status; those with alternative diets (e.g., dairy product exclusion) or diets that do not traditionally include milk or dairy products (such as First Nations and Inuit); or those with inadequate intakes of milk products and alternatives (e.g., adolescent girls).***

***Questions on Potential Approaches to Increase Calcium intakes:***

**Q 1.1 – By how much should calcium intake be increased for the various age-sex groups?**

The intake values for calcium in relation to the DRIs vary quite widely by age and sex group. The population health goal is to maximize the proportion of the population distribution that lies between the thresholds of adequacy and excess, or equivalently to minimize the extent to which the tails of the distribution extend beyond the specified thresholds. We have included Table 1a, which presents mean intake and observed prevalence below estimated average requirement (EAR) for food alone and food plus supplements for each age/sex subgroup, to highlight the groups at greatest risk. As there is believed to be underreporting by some in the Canadian Community Health Survey (CCHS) data one must interpret this data with caution. Using Table 1a, we note that it is only in the oldest age groups, especially among women, where supplements help bring up the intake of calcium. Very few Canadians have intakes above the UL and this appears to occur to a small extent among women in the older age groups. As some dosages of calcium may be for therapeutic purposes, the small number above the UL is unlikely to be of concern. For older men and women, and adolescent girls, the prevalence of inadequacy for calcium is however particularly high. For these groups, the total amount of calcium consumed in the diet appears low. For other age groups there are still a considerable number of people not meeting the EAR and additional calcium may be advised for those with lowest intake. The number of people with intakes below the EAR provides an estimate of the number of people not meeting their

needs. Theoretically, if one examines the intake of Canadians at the 10th percentile of intake from food only and wished to increase their intake towards the EAR, the extra intake of calcium needed in the low calcium consumers is generally around 300 mg but up to approximately 500 mg in the groups mentioned above (Table 1b). Adding these amounts to the diet of everyone would not put those in the highest intake group (90th percentile) above the UL even if intake levels from the diet did rise with this increased fortification, but could approach the UL in some groups such as men and women over age 51. Furthermore, the UL might well be exceeded in those also consuming supplements.

Table 1a

Usual intakes of calcium from food alone and from total sources, by DRI age-sex group. Data Source: Statistics Canada, Canadian Community Health Survey, Cycle 2.2, (2004).

| Sex / age group | Mean intake from food (mg/d) | Mean intake from food and supplements (mg/d) | EAR/ UL | % below EAR Food alone | % below EAR Food & Supplements |
|---|---|---|---|---|---|
| Both sexes / 1-3 y | 1051 | 1083 | 500/2500 | 3.2 | 2.6 |
| Both sexes /4-8 y | 1036 | 1076 | 800/2500 | 23.3 | 18.7 |
| Male / 9-13 y | 1219 | 1234 | 1100/3000 | 43.9 | 43.1 |
| Male /14-18 y | 1300 | 1315 | 1100/3000 | 33.4 | 31.9 |
| Male /19-30 y | 1107 | 1137 | 800/2500 | 26.5 | 15.4 |
| Male / 31-50 y | 938 | 977 | 800/2500 | 39.0 | 36.6 |
| Male / 51-70 y | 832 | 921 | 800/2000 | 53.0 | 44.5 |
| Male / >70 y | 762 | 891 | 1000/2000 | 80.1 | 69.4 |
| Female / 9-13 y | 993 | 1013 | 1100/3000 | 66.9 | 65.4 |
| Female / 14-18 y | 917 | 944 | 1100/3000 | 70.0 | 67.8 |
| Female / 19-30 y | 867 | 950 | 800/2500 | 47.5 | 41.6 |
| Female / 31-50 y | 827 | 969 | 800/2500 | 51.9 | 41.4 |
| Female / 51-70 y | 740 | 1063 | 1000/2000 | 82.4 | 56.8 |
| Female / >70 y | 690 | 948 | 1000/2000 | 86.9 | 63.1 |

Table 1b

Usual intakes of calcium from food alone, by DRI age-sex group, showing 10th, 50th and 90th percentiles of intake relative to EAR and UL values. Data Source: Statistics Canada, Canadian Community Health Survey, Cycle 2.2, (2004).

| Sex / age group | Intake (mg/d) | | | EAR/UL |
|---|---|---|---|---|
| | 10th Percentile | 50th Percentile | 90th Percentile | |
| Both sexes / 1-3 y | 650 | 1041 | 1567 | 500/2500 |
| Both sexes /4-8 y | 666 | 1003 | 1472 | 800/2500 |
| Male / 9-13 y | 718 | 1164 | 1827 | 1100/3000 |
| Male /14-18 y | 785 | 1288 | 2001 | 1100/3000 |
| Male /19-30 y | 606 | 1029 | 1691 | 800/2500 |
| Male / 31-50 y | 518 | 893 | 1458 | 800/2500 |
| Male / 51-70 y | 457 | 776 | 1304 | 800/2000 |
| Male / >70 y | 398 | 702 | 1193 | 1000/2000 |
| Female / 9-13 y | 596 | 950 | 1140 | 1100/3000 |
| Female / 14-18 y | 500 | 888 | 1459 | 1100/3000 |
| Female / 19-30 y | 479 | 820 | 1323 | 800/2500 |
| Female / 31-50 y | 457 | 785 | 1287 | 800/2500 |
| Female / 51-70 y | 410 | 702 | 1138 | 1000/2000 |
| Female / >70 y | 397 | 661 | 1060 | 1000/2000 |

The goal at present, therefore would be not so much to increase intake globally, as it would be to bring the lower end of the distribution above the EAR. With this explicit goal, an implicit goal is to narrow the distribution of intake. Thus, a primary concern in addressing the problem is to identify sub-groups at risk of low intake and strategies that would effectively change intake in the at-risk subgroups.

In addition to age and sex subgroups, other demographic groups at possible increased risk of inadequate calcium intake are:

- Those with low socio-economic status (SES);
- First Nations and Inuit;
- Pregnant and lactating women.

*Low SES:*

Canadians living in food-insecure households are, by definition, nutritionally vulnerable [3] and this vulnerability includes compromised calcium and vitamin D intakes. In addition to the nutritional risks associated with food insecurity however, it is important to recognize that the dietary intakes of Canadians vary with income and education levels. In some ways, the nutritional vulnerability associated with food insecurity can be seen as the extreme end of a broader continuum of vulnerability defined by socioeconomic factors. Using data from the 2004 CCHS, Tarasuk et al. [4] examined the relationships between household income and education level and adults' and children's intakes of energy, fibre, micronutrients, and number of servings consumed of food groups from Canada's Food Guide and found a higher household income adequacy and/or higher levels of education were associated with increased consumption of milk and alternatives, and vegetables and fruit, and

significantly higher vitamin, mineral, and fibre intakes among both adults and children. These findings are consistent with the earlier examination of household food expenditure patterns in Canada [5], and the observed associations have profound implications for the design of effective nutrition intervention strategies. Thus, to address the nutritional vulnerability of Canadians facing food insecurity, adopting a 'social determinants of health' framework to develop effective interventions that tackle the root causes of this problem might be an important approach.

*Aboriginal populations:*

A survey of Inuit coastal community households was performed in 2007 and 2008 [6]. A total of 2796 households were approached and 1901 participated in the survey. In this study population, 57.5% consumed traditional foods in the past day. Among those who ate traditional foods, these foods contributed to 29.2% of overall energy. Among those consuming traditional foods in the past day, the mean (interquartile range) of dietary calcium intake was 387 (212-619) mg/d in men and 378 (222, 555) mg/d in women. Among those who had no traditional food, the mean (interquartile range) of dietary calcium intake was 470 (253, 760) mg/d in men and 396 (229, 605) mg/d in women. Thus, the dietary calcium intake is on average less than half that of the mean intake in Canadian population surveyed by the CHMS. It is important to note that these communities are undergoing a dietary transition. Traditional foods are important sources of vitamin D, but fewer traditional foods are important sources of calcium. The dietary transition increases the risk of vitamin D inadequacy, but according to this survey is not offset by similar increases in calcium intake. Dietary patterns and nutrient adequacy were also assessed in a multi-ethnic study of Inuit, Yukon First Nations, and NWT Dene/Metis communities [7]. The median intake over the different age-sex strata for calcium ranged from 397 to 495 mg/d among Inuit, from 481 to 535 mg/d among those of the Yukon First Nations, and from 520 to 750 mg among the Dene/Metis. There was some heterogeneity by age and sex, and clear heterogeneity between different communities. A study of urban and rural Aboriginal Manitoba women found mean calcium intakes close to Canadian population averages, with intakes of 1170 mg/d (rural areas) and 974 mg/d (urban areas) [8]. Milk was the main sources of calcium in all groups in this study, and thus would also be an important source of vitamin D. Of note, the variation in the calcium intake was higher in the Aboriginal population than in urban white women, thus leading to higher prevalence of inadequate calcium and vitamin D intakes despite apparently high average intakes. In summary, Aboriginal communities are globally at higher risk of inadequate calcium intake, especially in the far north, but also in Aboriginal adults living off-reserve [9]. There is also substantial heterogeneity in calcium intake (by age, sex, ethnic group, and over time). Thus, it is currently unclear how much calcium intake should be increased for each of the various age-sex groups among the diverse groups of aboriginal populations

*Pregnant and lactating women:*

Calcium for the pregnant mother and fetus is supplied by maternal dietary intake of calcium-rich foods (dairy products) and/or maternal stores (serum calcium and bones) and calcium for the lactating mother and breastfeeding baby is accessed from the maternal diet. Lack of sufficient calcium during reproduction and lactation may contribute to maternal bone loss and increased risk of low bone mineral density later in life. One study examined the use of vitamin/mineral supplements before and during pregnancy and the use of calcium-based antacids to estimate their contribution to total dietary calcium intake in a Canadian cohort of childbearing women who were prenatal class attendees in Calgary [10]. Almost 20% of pregnant participants did not achieve, from diet alone, the previous AI for calcium (1000 mg/day), which is equivalent to the new RDA for calcium for pregnant or lactating women

greater than 19 years of age (this value is however greater than the EAR of 800). This percent consuming below 1000 mg/day was a smaller percentage than that reported by the CCHS Cycle 2.2. The use of prenatal vitamin/mineral or calcium supplements and calcium-based antacids placed an additional 12.9% (n = 31) above 1000 mg/day. However, even with these additional calcium sources, 5% of participants did not reach 1000 mg/day. This may point to the importance of nutrition education for women of reproductive age.

In a study to assess the diet of Aboriginal women, including a relatively small group of pregnant and lactating women, in the Canadian Arctic in terms of dietary adequacy, and to assess the contribution of traditional food to the diet, it was found that average intakes of calcium did not meet recommended levels (approximately 100 to 500 mg below the recommendation whether compared to the current RDA of 1000 mg per day or to the previous AI of 1000 mg per day for women age 19 through 50 years or of 1300 mg per day for women aged 18 and under). It was concluded, by the authors, that a special emphasis on nutrition is required during pregnancy and lactation, including nutrition education and promotion of supplements as a means to improve nutrient intakes [11] but that intakes above the recommendations are not necessary. Since there is only one report to base recommendation on, reaching the RDA would be a reasonable goal but a specific recommendation regarding by how much intakes should be increased would be premature.

**What are benefits and drawbacks to the general population and vulnerable sub-populations (those with low exposure to calcium through diet) of increasing intake via:**

**Q 1.2 - a) Increased consumption of food sources (without further fortification)?**

The approach to amelioration of low intake by encouraging consumption of more calcium-rich foods (without further fortification) may depend on age. Adolescents are in a period of important bone growth and a rapid increase in body size and are in need of nutrient rich diets for many nutrients including calcium. Most dairy sources of calcium are also good sources of other nutrients so that increasing increased dairy consumption may also have other nutritional benefits. Several ways of promoting calcium intake are possible in this age group including school lunch programs and educational initiatives. School lunch programs and other nutritional programs, for which provincial governments are making policies related to permissible food offerings in schools, may help curb some of the sugar sweetened beverages currently consumed, which is a benefit. Canadian children from two to 18 years consume significant amounts of sweetened beverages that contributed between 2 % and 18% of total energy intake. Of note, girls of age 6-11 year who were in the 'soft drink' cluster had lower calcium intake compared with other clusters in that age-sex group [12]. Lower priced sugar sweetened beverages compared to milk may lead youth from low income households to consume less milk and more sugar sweetened beverages. This represents a potential drawback of trying to increase consumption of current food sources of calcium. Given the growing evidence concerning the deleterious effects of sugar sweetened beverages and their link to obesity, education and some changes in the food environment are likely needed to address this related problem.

As noted before, among the adult population, younger adults are doing somewhat better at meeting their calcium needs but education aimed at younger adults and their families to encourage the

consumption of calcium rich food sources as part of their daily routine may be helpful, and successful intervention in childhood and adolescence may impact lifetime dietary patterns. Care in messaging is needed as there seems to be a strong belief among some people that certain populations are prone to suffer from lactose intolerance [13], or that milk is only for children. These beliefs therefore represent a drawback to attempting to increase consumption of calcium rich foods. There may be an opportunity to promote foods such as yogurt, due to potential gastrointestinal benefits associated with probiotics in yogurt. Also, positive messaging around the role of milk in sports might appeal to young adults as well as children. The drawbacks include that education may have limited impact on overall diet and education alone does not address barriers to improved diet among those with low SES, where cost is one important barrier to acceptance.

Among those over age 50 years, it is likely problematic to encourage greater consumption of current calcium rich foods as energy needs decline with advancing age. This therefore represents a drawback to increasing consumption of food sources of calcium. There is a very high proportion of overweight Canadians in this age group [14] and consuming less energy is important. This group will be discussed further in relation to fortification and supplementation.

**Q 1.3 - b) Supplementation?**

With respect to supplements, benefits include that there would be no need to make wholesale changes in dietary patterns and the choice to supplement would be based on the individual; as well, the intake of total calcium intake could still be below the UL, provided that only those who need a supplement take it and only at the proper dose. Canadians are using calcium supplements, as shown by data from CCHS (Table 1a), however there is only a modest decrease in the prevalence of inadequacy of calcium in most age groups, It is only in the females over age 50 years that there is a marked improvement in calcium adequacy. This phenomenon, of supplements not providing benefit to users, is explained by the fact that supplement users tend to already have a good diet and take supplements primarily for "insurance", not need [15].

Supplements, although not very costly are still a cost burden to many, and supplementation often will not reach the most vulnerable Canadians. Based on CHMS (Canadian Health Measures Survey) data, Vatanparast et al. demonstrated that higher socio-economic status was correlated with higher supplement use [16].

Vulnerable groups include those with low incomes and some new Canadians who hold onto diets from their culture that may be low in calcium. Other vulnerable populations include Aboriginal groups, among which there are cultural differences in traditional foods, and current economic realities which will vary across communities, e.g. limited transportation access due to poor or absent roads may increase the cost of foods that are brought in. While some groups have relatively high calcium intake [8], others do not [6], and it would be inappropriate to summarize the situation for all aboriginal communities. Whether or not these vulnerable groups would embrace supplements is largely unknown. Without the belief that a low calcium intake is harmful to health it is difficult to see the motivation for taking a supplement on a regular basis. We do know that in Cree communities, for example, it is challenging to get families to provide regular iron supplements to anemic infants [17].

In the CCHS data, there is a clear economic gradient to calcium intake in youth, present in both boys and girls aged 9-18, which therefore represents a drawback to supplementation. Further assessment of youth in schools from the Health Behaviour in School-aged Children study also showed an economic gradient where higher SES was positively associated with milk intake, fruit and vegetable intake, and negatively associated with non-diet soft drink intake [18]. Kirkpatrick also found higher levels of nutrient inadequacy in those who self report as food insecure [3]. Supplementation in children seems to be very inconsistently offered, which therefore represents a drawback and only a portion of children (1/3 of males and 2/5 of females according to CCHS cycle 2.2) regularly take a vitamin/mineral supplement which does not provide much calcium. Thus, youth at risk of low calcium intake may be the least likely to use them.

For those over age 50, a supplement of vitamin D is already recommended. If a supplement of calcium (possibly 500 mg) were recommended there would be very little risk of consuming a level higher than the UL. In particular, if one adds 500 mg to the level of intake of the individuals at the 95$^{th}$ percentile of dietary intake, none of the resulting values would surpass the UL. Despite the recommendation for vitamin D supplementation for those over age 50, less than half the population takes a supplement, and Quebec data on autonomous seniors aged 68-82 y show that fewer men than women took the supplements, i.e. 17% of men and 45% of women [19]. Consequently, poor acceptance and adherence to a supplement would also likely be a drawback to calcium supplementation.

Overall, supplementation is not universally accepted and is out of reach for the most vulnerable [15, 16].

**Q 1.4 - c) Increased fortification of dietary sources?**

Increased fortification of dietary sources could be done in two major ways: mandatory fortification or voluntary fortification. Mandatory fortification programs have the potential to benefit the entire population, including those with lower incomes or education levels.

As long as the foods selected for fortification are foods consumed regularly by Canadians across the socio-economic spectrum, mandatory fortification will reach the entire population, e.g. mandatory fortification would ensure higher levels for all if flour or other staple food were fortified. Thus a low dose of calcium in the bread could raise the calcium intake levels for virtually everyone if there were no economic cost associated with this approach. In the current social and political environment, it is probable that a policy prescribing an intervention at population level involving mandatory fortification of food would raise perceptions that government is "tampering" with food, and might therefore face strong resistance [1]. Additional limitations of this approach are discussed under Question 1.8, but one also has the challenge that big eaters, in particular adolescent boys and young men, will consume more of all foods, and some could exceed the UL for calcium. Fortification levels would therefore need to be sufficiently low so as to not provide too much calcium to the "big eaters". However older people who comprise the group with the highest percent of intake below the EAR and who generally have lower food intake, might then not meet their needs through a low level of fortification [20].

The general issue of mineral and vitamin fortification of food is currently under review by Health Canada [21] and the proposed policy would create a new provision for food fortification done at the

"discretion" or "choice" of the manufacturer (within defined limits set by Health Canada) to meet a market demand, a process known as discretionary fortification. Thus, it appears that mandatory fortification is not being considered other than for folic acid in flour and vitamin D in milk and margarine although there are provisions in the proposed policy to permit addition of vitamins/minerals for restoration of losses during processing; to allow nutritional equivalence of substitute foods; and to permit fortification to correct or prevent problems of public health significance.

Voluntary fortification (as with orange juice) would provide more consumer choice but does have some of the same risks as mandatory fortification, i.e. modest increase in average intake with concurrent risk of exceeding UL. Allowable food vehicles, and the option not to fortify, mitigate some of these risks. Those who do not consume any milk can choose fortified orange juice, while those who have adequate milk intake can choose unfortified juice. A more recent paper has assessed various plausible scenarios following discretionary fortification. Again, there were modest reductions in the prevalence of inadequate calcium intake, with concurrent increase in the risk of excess calcium intake [22].

Overall, voluntary fortification of dietary sources would be preferred so that those not consuming dairy products could find other food sources. Voluntary fortification could target female adolescents and adults, and older adults (>50 y, men and women) where the needs are greatest. Currently there are no single-serving versions of calcium fortified juices available in Canada, but their availability could be helpful, and making calcium fortified juice available in schools as an alternative to milk and soft drinks might then be desirable. However voluntary fortification programs, by design, do not affect the population equally. One disadvantage that would need to be overcome is the higher cost of some of the products currently offering added calcium. (For example, the costly fresh orange juice products have some products with added calcium but the more affordable generic frozen concentrate often does not.) Insofar as manufacturers promote fortified foods as 'nutritionally enhanced', they can be expected to bear higher prices. It has been demonstrated that nutritional enhancement has impacted prices in the US [23]. Voluntary fortification can also be expected to exacerbate our 'income gradient' insofar as price-conscious consumers reject or limit their consumption of higher priced products. Thus, in the case of voluntary fortification, policies would have to be developed to keep costs down for the consumer. An additional problem with voluntary fortification is that the consumption of voluntarily fortified foods hinges on individuals choosing to purchase and consume those particular products. This is not simply a matter of affordability, but is also a function of health consciousness, consumer information and education. There is already a documented 'education gradient' in food and nutrient intakes among adults and children in Canada [4]. Voluntary fortification can be expected to exacerbate this gradient insofar as Canadians with higher education will be more likely to select the calcium- or vitamin D-fortified products. Whether more consumer education can overcome this drawback remains to be determined.

**Q 1.5 - Given these benefits and drawbacks, and the fact that the food supply provides enough calcium to meet the population's requirements, but that most of the population is not consuming enough, what is the most appropriate approach to increase calcium intake in the general population and vulnerable subpopulations so that there is a low prevalence of inadequate intakes?**

While the food supply does provide adequate calcium, it is not always readily available to the consumer. Existing calcium rich foods could be made more accessible. An example might be if longer shelf life products such as ultra-high temperature pasteurized milk were available in vending machines. Vending machines suppliers in government funded institutions are free to offer no dairy products (so as to have no products with 'best before' dates) and ultra-high temperature pasteurized milk is not offered. School programs for free or reduced price milk in low income neighbourhoods can contribute greatly to providing greater access. There are many examples of providing more choice to one vulnerable population, teenage girls, because they are in school. The US subsidy programs are long standing programs that affect the school food environment and therefore provide both a precedent and a potential model to examine and improve upon.

Education could be targeted to the most vulnerable groups to increase consumption of calcium containing foods. The messaging could center on a) encouraging the consumption of the number of Milk and Alternatives servings for the target age group as set out in Canada's Food Guide (for those who consume dairy or fortified substitutes such as soy-based drinks); b) encouraging the choice of foods with Health Canada approved health claims for calcium and vitamin D. As the currently existing non-dairy sources of calcium contain amounts relatively equivalent to milk, fortified plant (soy, rice) milks, orange juice and some yogurts, for example, would all meet the requirement for the health claim as it stands now. Nevertheless although processed and canned foods are labeled for the nutrients they contain, fresh fish, vegetables and bulk legumes are not labeled. So any educational strategy that emphasizes "looking at the label" will undervalue whole foods that are a source of many nutrients including calcium. One option is to allow food sellers to highlight certain whole foods as good sources of calcium.

Supplementation may be a useful strategy for older Canadians. Although the advice on vitamin D supplements has not been taken up that widely, certainly it is in this group that the difference between intake from food alone vs. food plus supplements is the greatest. A vitamin D plus calcium supplement for those over age 50 could help some Canadians meet their calcium needs. The profile of Canadians using supplements, suggests they are more affluent and consuming a healthier diet. Consequently the reach of messages advocating supplementation is of concern [24].

For the consumer, voluntary fortification can provide an alternative to supplements if the food is consumed daily but it implies that Canadians know that they need additional calcium and in some cases are willing to pay the higher prices. Even with voluntary fortification one needs to be wary that some groups may exceed the UL (i.e., the teenage boy who regularly consumes large quantities of calcium fortified orange juice and milk). It is important that voluntary fortification only be allowed in nutritious foods, otherwise one risks confusing the consumer about the advisability of consuming a particular non-nutritious food.

Mandatory fortification of some widely consumed food in safe quantities has real drawbacks given that the groups at highest risk of low intake i.e. the elderly are those who consume the least energy and sufficiently increasing fortification to ensure improved calcium intake in the elderly may put big eaters at risk. A serious challenge prior to moving ahead with fortification is to have information on the consequences of excessive calcium intake, which may occur mainly in big eaters such as relatively young men who are very active. The consequences for prostate cancer, kidney stones and calcification of vascular tissues are not sufficiently well explored to date (see chapter 6, [25]). However, secondary analysis of large epidemiological studies have raised concerns with regard to adverse effects of calcium supplements (not dietary calcium) on cardiovascular health [26, 27]. Should these consequences occur in even a small proportion of the population, this could cause some very serious morbidity and mortality. This has to be balanced against inadequacies and their deleterious effects. Recently, however, the Professional Practice Committee of the American Society for Bone and Mineral Research (ASBMR) (www.asbmr.org) has reviewed the evidence and has concluded in a position statement that the weight of evidence is insufficient to conclude that calcium supplements cause adverse cardiovascular events. Nevertheless, the debate continues.

Since 1991, the Province of Quebec has run a program intended to target expectant mothers with low SES, with the specific objective of insuring the adequate consumption of foods rich in calcium, vitamin D, vitamin C, and other minerals and or vitamins [28]. The program is administered by an independent non-profit organization (the OLO Foundation) [29] and is delivered through primary care public institutions (Centre local de services communautaires/Local Community Service Centres and Centres de santé et de services sociaux /Health Services and Social Services Centres). The program currently claims to reach more than 17,000 women per year, for a cost averaging $350 per person (including direct oversight by dietitians and nurses). The cost of the program is shared between government and donors, which include producers of milk and eggs, pharmacy chains, and philanthropic organizations. Most of the food is made available through coupons and vouchers, to be exchanged in stores for milk, eggs, orange juice, and supplements. The duration of the program and the outcomes achieved over more than 20 years of operation are a demonstration of the feasibility and interest of a targeted approach to increase calcium and vitamin D intake in vulnerable subpopulations.

Summary and Recommendations

In summary, there is likely no single strategy that will appropriately increase calcium intake in both men and women and in all age groups in the general population, and in all vulnerable subpopulations, that would ensure a low prevalence of inadequate intakes. Thus, voluntary fortification of some non-dairy foods along with better education may be appropriate in the general population, especially for those not consuming dairy products; calcium-rich food offerings in the school environment could be helpful for youth and adolescent females; clear guidance on supplement use might be important for those over age 50; furthermore, strategies to address the social determinants of health for low SES groups, and community-specific responses for Aboriginal groups may be among the strategies for these vulnerable groups. Therefore a combination of strategies may best serve to reduce the prevalence of low calcium intakes.

## Q 1.6 - What education strategies should be considered?

The evidence is clear that communication campaigns done in isolation of other strategies are limited in effecting sustainable change. A large body of evidence suggests that health communication campaigns relying only on media appeals are not very effective for changing attitudes and behaviour. A more comprehensive, systems approach is needed where media campaigns are one component of a broad community mobilization strategy. These basic principles should apply in order to gain broad adherence to recommended intakes for calcium and vitamin D among diverse subgroups and communities.

Although there is a plethora of theories and models regarding health behaviour change, Fishbein engaged a prominent group of social scientists at a consensus conference to come up with a practical behaviour change framework [30]. They found that one or more of the following 8 conditions must be present for individuals to perform a given behaviour (e.g. daily recommended intake of calcium and vitamin D):

1. The person has formed a strong positive intention (or made a commitment) to perform the behaviour.
2. There are no environmental constraints that make it impossible for the behaviour to occur (e.g. poor communities).
3. The person has the skills necessary to perform the behaviour.
4. The person believes the advantages (benefits, anticipated positive outcomes) of performing the behaviour outweigh the disadvantages (costs, anticipated negative outcomes).
5. The person perceives more social pressure to perform the behaviour than to not perform the behaviour.
6. The person perceives that the behaviour is consistent with their self-image and does not violate their personal standards.
7. The person's emotional reaction to performing behaviour is more positive than negative.
8. The person believes (has confidence) that they can execute the behaviour under a number of difference circumstances (i.e., the person has the perceived self-efficacy to execute the behaviour).

For example, educational strategies could be used under the first condition (positive intention) to raise awareness about the need for change by making the risk of not adhering to recommended daily intake of calcium and vitamin D serious and personally relevant. Regarding condition 2 (environmental constraints), community mobilization strategies could be used to address barriers such as access (not enough money, not available for purchase) by creating a more supportive social and physical environment.

A well-grounded and well-conducted health education strategy must aim at compliance, adherence and persistence. Although initially used with respect to medication use, these terms seem equally applicable to supplement use, e.g. with vitamin D [31]. *Compliance* refers to the extent to which the individual's behaviour matches the recommendations for the supplement in all its dimensions (dosage, frequency, regularity, duration). *Adherence* refers to the extent to which the individual's behaviour matches agreed recommendations for the supplement, implying choice on the part of the individual, however, the definitions and preferred terminology remains a matter of debate. *Persistence* refers to the act of continuing the supplement for the duration it is required. Special consideration needs to be

given to compliance strategies when supplements are encouraged. Better compliance with a supplement-taking regimen could be achieved through improved communication, often with a health care provider, and, incorporating the beliefs and preferences of the individual in the decision-making process.

The media and notably, the "new" media, have an essential role to play, given our social environment, in the success or failure of an education strategy. Stories, anecdotes and so-called "junk" science circulate freely and widely and it is sometimes difficult for a lay person to find an answer to his or her questions among the conflicting voices. Educating the media on health issues must therefore become a priority. In the case of nutrition related issues, it might be important to envision as well a campaign targeted at health care providers. Training in this area is usually limited and non-specific and may leave providers unprepared to support their patients or clients in need of information or intervention.

Listed below are twelve Health Behaviour Change Strategies that can be used to design a comprehensive campaign, according to the Health Communication Unit [32]:

1. Raise awareness about the need for change by making the risk seem serious and at the same time personally relevant.
2. Specify the recommended action in terms of how, where, and when and provide clear directions and training to perform the recommended action.
3. Emphasize likely positive results of adopting the recommended action and downplay negative consequences.
4. Identify or provide role models who have adopted the recommended action and ensure that they are visible.
5. Identify key influencers/role models who are important to the intended audience and make audience feel that they support the recommended behaviour.
6. Determine audience barriers to action and attempt to rectify.
7. Provide suggestions or teach how to find own healthier alternatives/solutions for certain barriers.
8. Create supportive environments whenever possible.
9. Assist with setting quantifiable, realistic, graduated, and moderately difficult goals within the context of pre-existing goals.
10. Teach how to critically and practically assess past failures/current relapse so that lessons can be learnt and progress continues rather than stops.
11. Set up systems of reinforcement through incentives, assistance, and regular updates on the given risk and recommended action.
12. Customize information on risks, benefits, and recommended action and tailor the intervention itself to the intended audience's values, norms, and situation.

**Q 1.7 - Are there vulnerable subgroups in need of special guidance?**

There are a number of vulnerable sub groups that need special and careful attention as noted below in the context which HC has provided for questions 1.8-1.10.

For example:

- Those with low SES with little exposure to calcium through diet.
- Those with alternative diets or diets that do not traditionally include milk or dairy products (e.g. First Nations and Inuit).
- Those with inadequate intakes of milk products (e.g. adolescent girls, women in pregnancy and lactation) [33, 34].

A major challenge is that some of the most vulnerable subgroups (e.g. low SES, Aboriginal communities) are often the most challenging to engage in health communication campaigns and behaviour change but progress has been reported [35]. We first note that one precondition to behaviour change is that there are no environmental constraints (see question 1.6). Thus we reiterate the need to consider the context of social determinants of health, removing barriers to change, increasing availability and visibility of healthy calcium rich food sources. We have briefly outlined the situation for Aboriginal groups in earlier questions. The studies referenced are participatory research, i.e. they involve direct feedback to the communities involved. Research can include focus groups that explore avenues for potential change, thus addressing real world barriers to change [36]. Clearly, as such studies become available, the resulting knowledge can be shared between at-risk communities. Building on the education and health behaviour change strategies outlined under question 1.6, special effort should be directed at engaging health professionals (e.g. curriculum development and continuing education) and health media (e.g. professional development) regarding their important role in providing accurate and personalized information, special guidance and interventions for vulnerable subgroups. An example of this type of work is an 8-week long course that was developed for delivery in January-March, 2004 addressed to prenatal nutrition program workers, community health representatives, their students, home-care workers, Aboriginal Diabetes Initiative workers and public health nurses in Nunavut [37].

**Questions 1.8- 1.10**
**If "Increased fortification of dietary sources" (c) is deemed most appropriate:**

**Q 1.8 - should fortification of a staple food be an option for improving calcium intakes?**

Currently, fortification of foods with calcium is not targeted solely to staple foods, as milk is not consumed in similar amounts by all Canadians. If flour or other staple food were fortified, this would ensure that higher levels reached more, but certainly not all, of the vulnerable subpopulations. Thus, as discussed in Q1.4, a low dose of calcium added to widely consumed staple foods could at least modestly raise the calcium intake levels for virtually everyone. The limitations of this approach are as previously indicated, i.e., that in many models one quickly finds that a greater proportion of young men will be at risk of exceeding the UL if calcium is added to frequently eaten staple foods and small eaters will not get the extra calcium in the quantities needed. Thus fortification of widely consumed

staple foods could pose risks of excessive nutrient intake for some if levels were high enough to be effective, or if levels added are low, would barely help others.

**Q 1.9 - If fortifying a staple food is not appropriate, should there be more fortified food choices as part of the general food supply?**

The availability of more calcium-fortified food choices as part of the general food supply might be beneficial, however once a number of different products are fortified there is a real risk of a person regularly consuming several sources. In order to ensure safety, allowable levels in each food must remain low and exposure must be carefully tracked. Modeling done on fortification with calcium has been conducted in the past [20] using a large national survey of Canadians. Health Canada could do a modeling exercise to examine the best foods to fortify from the CCHS. These foods would need to be healthy food choices so as not to confuse the public about the advantages of consuming certain foods. The availability of more calcium-fortified food choices as part of the general food supply could provide non-dairy sources of calcium for sectors of the population who can afford the fortified food products. Policies would have to be developed however, as indicated in response to Q1.4, to keep costs down for the consumer and facilitate the success of this approach. Better understanding of the dynamics of food production, import, export, and distribution may indicate where these policies would be most effectively introduced. Efforts to expand fortification of foods in lower price ranges may be one option to make calcium rich food sources more widely available.

The availability of more calcium-fortified food choices as part of the general food supply may put some populations such as men at risk of exceeding the UL for calcium. With widespread media reporting on the importance of calcium and vitamin D for health, industry is likely to respond by fortifying more food items. Thus, there is a theoretical risk that the consumption of too many calcium foods might lead to excessive intakes above the UL (which is only 2000-2500 mg calcium per day for adults). Consequently education in wiser food selection to increase calcium intake, thus protecting those at risk of excess intakes, should still be a complementary strategy, even if more calcium-fortified food choices are made available as part of the general food supply.

**Q 1.10 - How do we ensure a balance between fortified food use and the use of supplements, so that the prevalence of intakes above the UL is minimized?**

Accurate labelling on fortified and non-fortified foods must be present. Only then can consumers attempt to balance intake from fortified foods and supplements, however asking people to track their personal calcium intakes relative to their needs and ULs may be difficult. Furthermore this does not account for foods consumed away from home such as in restaurants. Although few studies have addressed the issue of the effectiveness of providing nutrition fact labelling in changing food selection practices, one US study found that models that account for zero away-from-home intakes suggest that the labels increased fibre and iron intakes of label users compared with label nonusers but not the other 11 nutrients (including calcium) that appeared on the labels [38]. This suggested to these authors, that the Nutrition Facts panel mandated by the Nutrition Labelling and Education Act in the US had a beneficial but modest impact on dietary intakes of Americans. As addressed in Q1.5, a reasonable approach to increasing calcium intake would be through educational messaging. Messaging has to be

in terms of total calcium intake. Consumers therefore need to be aware of what their recommended daily allowance should be and they should be trying to achieve the amount in the RDA.

Health Canada must also continue to monitor the total calcium intake of the population, so that in voluntary fortification, excess calcium is not added to any particular food. Indeed in the Health Canada proposed policy document "Addition of Vitamins and Minerals to Foods, 2005", calcium and vitamin D are in risk category B, and it is proposed that the total amount of each of these nutrients (naturally occurring and added) permitted in the food after addition is up to 10% of the Daily Value (DV) per reference amount of the food. This should ensure that excess calcium will not be added to any particular food, however it is not clear that the reference amount is the usual portion for many consumers and the potential for excess intake of calcium remains of concern particularly in young men [22].

Based on the CCHS data, a notable increase in total calcium intake as a result of consuming supplements was only identified in women in the 51-70 year age group. Some of these women may have been using therapeutic doses of calcium supplements alone so this may not be of concern for the healthy Canadian population. The calcium content of a single multivitamin tablet is generally very low, and not likely to harm but will not increase calcium intake substantially either. Health Canada only recommends a vitamin D supplement over age 50 but many people (particularly women) take a multivitamin instead. One caution is that supplemental calcium use across all ages may have increased since the CCHS in 2004-05 due to the huge increase in the number of different supplements containing calcium and/or vitamin D on the market and an increasing emphasis on osteoporosis in men as noted in the new Clinical Practice Guidelines for the Diagnosis and management of Osteoporosis from Osteoporosis Canada [39]. These guidelines made recommendations for higher intakes of vitamin D (400 – 1000 IU for individuals < 50 years and 800 – 2000 IU for individuals ≥ 50 years) but lower calcium intakes (1200 versus 1500 mg/day) from all sources. While supplementation is relatively inexpensive and widely available, compliance to supplementation is poor in many settings (as has been shown for folic acid in young women). For the group with low SES, calcium is just one of the nutrients which is inadequately consumed [3]; however, in youth calcium does seem to be one of the most dependent on income. The other issue to consider with promotion of supplement use is the risk of reducing intake of protein and other nutrients also important to growth and bone health, nutrients that naturally are provided with major food sources of calcium.

***Question on Drug-Nutrient Interactions Relevant to Calcium:***

**Q 1.11 - Given that the IOM recommendations cover the vast majority of the general population and we know that many in the general population are using prescription medications on a regular basis - are there any drug-nutrient interactions that should be considered with regard to fortification or supplementation?**

In general terms, dosing instructions given to patients by pharmacists are usually very clear regarding the separation of calcium/food intake and ingestion of the drug. Most drug-calcium interactions should therefore not be a major concern, and should not require any specific actions beyond the overall recommendations for total calcium intake. The main drug-calcium interaction is the potential of calcium to interfere with absorption of medications, or vice versa, and this has been reasonably well

documented for the use of calcium supplements (see table below). One would not expect food fortification to create a greater problem in this regard than calcium supplements.

The common medications susceptible to this interaction are levothyroxine, bisphosphonates, and the quinolone and tetracycline antibiotics.

Table 2 (modified from Straub et al. [40]) is a typical summary of the interactions of importance:

| *Calcium-drug interactions* | |
|---|---|
| Levothyroxine | Administrations of calcium and levothyroxine should be separated by 4 h; calcium reduces levothyroxine absorption by forming insoluble complexes. |
| $H_2$ blockers and proton-pump inhibitors | $H_2$ blockers and proton-pump inhibitors decrease the absorption of calcium carbonate, which requires an acidic environment. |
| Tetracyclines | Tetracyclines should be taken 2 h before or 4-6 h after calcium supplements or milk; calcium decreases the absorption of tetracycline by forming insoluble complexes. |
| Bisphosphonates | Bisphosphonates should be taken at least 30 min before calcium supplementation. Ideally, calcium should be taken at another time of day, and most osteoporosis experts recommend waiting 45-60 minutes after taking a bisphosphonate before eating. |
| Quinolone antibiotics | Quinolone antibiotics should be taken at least 2 h before or 4-6 h after calcium supplementation or calcium-containing food; calcium decreases absorption of the drug by forming insoluble complexes. |
| | |
| Thiazide diuretics | Thiazide diuretics decrease the excretion of calcium. Calcium supplementation in moderate doses increases the risk of milk-alkali syndrome. Serum calcium levels should be monitored regularly. |
| | |
| Corticosteroids | Corticosteroids in doses of 7.5 mg/d or more can decrease calcium absorption, increase calcium excretion, and inhibit bone formation. They therefore cause significant bone loss . Patients using these drugs should take calcium and vitamin D supplements. |
| Anticonvulsants, phenytoin, fosphenytoin, carbamazepine, phenobarbital | These anticonvulsants decrease calcium absorption by increasing the metabolism and preventing reabsorption of vitamin D. Hypocalcemia and osteomalacia have been identified in patients receiving chronic therapy. Patients receiving these drugs should take calcium and vitamin D supplements. |

Hypothyroidism is a very common condition, and co-ingestion of calcium supplements with levothyroxine has been associated with reduced absorption of thyroid hormone [41], but as noted above, instructions regarding timing of dose are usually made quite clear. The recommendations/cautions given here, however, may be somewhat unrealistic. For example, many people with hypothyroidism take their daily levothyroxine dose in the morning before breakfast, but few are likely to wait 4 hours before consuming milk with their breakfast cereal. Levothyroxine dose is

however adjusted based on the patient's response to the drug (serum TSH measurement) and does not usually require frequent adjustment, particularly if the patient is consistent in the timing of the daily dose.

$H_2$ blockers and the more potent proton-pump inhibitors are widely used to reduce gastric acidity. Proton pump inhibitors have been reported to reduce absorption of calcium carbonate[42] although it is not certain whether there is a similar effect on absorption of other forms of calcium supplements, such as calcium citrate, and it is not known whether calcium absorption from foods is similarly affected. Furthermore although several studies have suggested that there is a deleterious effect of the use of proton pump inhibitors on bone health [43], alterations of calcium absorption may be only one mechanism. Consequently it is currently unclear whether increased calcium intake (dietary and/or supplements) should be recommended for individuals consuming H2 blockers and proton pump inhibitors, and what the appropriate form should be.

The standard dosing regime for tetracycline antibiotics is to avoid taking them with food, however, a study of chlortetracycline absorption with milk vs. calcium citrate suggested the citrate salt was associated with better absorption of the antibiotic [44]. The choice of calcium salt used for fortification may therefore influence the calcium interaction with medications.

Bisphosphonates are the mainstay of osteoporosis therapy [39]. Less than 1% of these drugs will be absorbed when taken by mouth [45], and dosing instructions specifically request the drug be taken with water only, at least 30 minutes before food or any other medications. Poor bisphosphonate absorption is therefore not restricted to consumption with calcium.

The interference with fluoroquinolone antibiotics by fortified orange juice has been documented, but the usual dosing instructions given to patients by pharmacists deal with this risk. The study by Wallace et al. [46], indicates that cereal with milk or a calcium fortified orange juice have roughly equally deleterious effects on absorption of the antibiotic.

Thiazide diuretics reduce calcium excretion, and in the setting of excessive calcium intake from diet, would have the potential to cause hypercalcemia or worsen pre-existing hypercalcemia, but this should not be a problem if individuals follow the calcium intake recommendations of the IOM report. Serum calcium levels should be monitored periodically in thiazide users whether or not they are taking calcium supplements or fortified foods.

In view of decreases in calcium absorption, increases in calcium excretion, and an increased risk for osteoporosis that occur with pharmacological levels of corticosteroids (glucocorticoids), calcium and vitamin D supplementation are generally advised for individuals taking this medication unless there is evidence of adequate dietary calcium and vitamin D intake [47].

A concern regarding potential interference with the absorption of iron by consumption of calcium supplements with meals has been raised [48], but the importance of this interaction remains uncertain. Short-term studies have shown a significant effect of as little as 500 mg of calcium (as a supplement) on iron absorption [49], and Hallberg and Hulthén have developed an algorithm for calculating iron absorption that adjusts for calcium intake [50]. However, Grinder-Pedersen et al. found no effect of milk or calcium fortified foods on non-heme iron absorption in 4-day studies [51]. Long-term studies

have not demonstrated a link between calcium intake and iron deficiency as indicated by anemia or measures of iron status [52-54], suggesting that if there is a short term detrimental effect of calcium on iron absorption, the body has ways of adapting to this by increasing proportional iron absorption. In summary, the clinical importance of this interaction has not been determined.

Theophylline can rarely increase serum calcium, apparently through beta-adrenergic stimulation [55]. Patients on these medications warrant monitoring of serum calcium, but the influence of dietary calcium or calcium food fortification on risk of hypercalcemia with these medications would not merit increased surveillance.

There is potential for increased calcium intake to worsen pre-existing hypercalcemia, but observations in this regard are not consistent. Essentially the consumption of a calcium enriched diet would only worsen hypercalcemia if the cause of the hypercalcemia was enhanced gut absorption, as in vitamin D toxicity or excess production of calcitriol by diseases featuring granuloma formation, like sarcoidosis. When hypercalcemia is caused by increased bone resorption, production of calcitriol and intestinal calcium absorption tend to be reduced. Retinoid therapy for acne and some cancers simulates vitamin A toxicity, increasing bone resorption, which may lead to hypercalcemia [56].

## ***2. Calcium Supplements for Infants: Levels***

***Context (provided by Health Canada):***

***The monographs of the Natural Health Products Directorate (NHPD) do not currently allow calcium supplements to be sold for use by infants. This is because in 1997 the IOM did not set a UL for this life stage group due to the lack of data on adverse effects and concern regarding the lack of ability to handle excess amounts. As such, the IOM (1997) stated that the only source of calcium intake for this group should be from food to prevent high levels of intake.***

***The new DRI report however now includes a calcium UL for infants. As such, NHPD is revisiting the issue of calcium supplements for infants to determine if it is appropriate.***

***Questions on Calcium Supplement Levels for Infants:***

**Q 2.1 - Is calcium supplementation appropriate in infants (0-12 months)?**
**Q 2.2 - If yes, what levels would be recommended?**

The AI's for infants are based on the amount of calcium provided by breast milk. Standard infant formula contains a higher concentration of calcium to account for lower bioavailability from formula vs. breast milk. Because all formulas for infants - whether based on cow milk, soy, protein hydrolyzates, etc. - must meet the minimum for each nutrient outlined in the infant feeding code, any exclusively formula or breastfed infant will always be provided with an appropriate amount of calcium.

There are few situations where calcium supplementation of infants is indicated. Preterm infants have higher calcium requirements than term infants and preterm formulas and human milk fortifiers are accordingly fortified with added calcium [57]. There is no evidence to indicate, once term corrected age is reached, that higher amounts of calcium need be provided as a supplement.

The introduction of solid food can introduce variability in the 54% of calcium intake the IOM report estimates to be derived from solid food in infancy. Calcium supplementation for older infants may be required in situations where dairy foods are eliminated (e.g. dairy allergy or intolerance). However, it is more likely that soy-based infant formula or extensively hydrolyzed infant formula would be substituted, and such formulas would contain appropriate amounts of calcium for infants.

Practically speaking, the only situations where calcium supplementation is required in infancy are pathological conditions such as rickets and the other causes of hypocalcemia of infancy. Therapeutic doses of calcium supplements are required in these conditions and are generally prescribed by specialists. Based on these considerations we believe there is insufficient evidence to support a recommendation for calcium supplementation in infants. This conclusion is based on the rationale that the amount of calcium provided by either breast milk or formula will always be sufficient for exclusively breast or formula fed infants.

*Guidance on elective supplementation of calcium in infants*

Guidance for the amount of calcium that electively may be given to infants that is safe and without risk of adverse effect should be the upper level recommended in the DRI report [25]. For infants 0 to 6 months of age this is 1,000 mg/d and for 7 to 12 months of age this is 1,500 mg/d. As outlined on page 419-20 of the DRI report the UL values were based on only one study of calcium excretion in infants and the UL was set using a cautionary approach. Since infants that are exclusively breastfed or formula fed will receive 202 mg/d (range 159 mg – 248 mg) calcium from their diet [25] (page 4-5), there is scope for HC to safely allow for elective supplementation of up to 800 mg calcium per day (1000 mg/d UL – 200 mg/d from breastmilk=800 mg). Due to the wider range and slightly higher intakes of formula fed infants [58], we propose 700 mg/d (rather than 800 mg) as a conservative, safe, elective supplement level. Older infants 7 to 12 months have a higher UL and therefore could tolerate higher levels of elective supplementation but we believe having 2 different levels for infants would be confusing for some. We therefore recommend the lower level of 700 mg/d as a safe and appropriate elective supplement level for infants 0 to 12 months.

## Vitamin D

### *3. Vitamin D Intakes and Status*

***Context (provided by Health Canada):***

***According to the CCHS dietary data, a large proportion of Canadians have less than adequate intakes of vitamin D. The DRI Committee, however, pointed out the estimated intake data for vitamin D cannot stand alone as a broad basis for public health action. Rather, national policy should consider intake data in the context of measures of serum 25(OH)D, a well-established biomarker of total D exposure (endogenous synthesis and diet including supplements). Based on data from the CHMS, most Canadians appear to be meeting their needs for vitamin D.***

***For all the following questions, please consider both the general population at large and vulnerable subgroups.***

***For vitamin D, vulnerable subgroups are those with reduced sun exposure or cutaneous synthesis of vitamin D (such as those with dark skin, those who use sunscreen or cover the skin with clothing, those who are institutionalized or spend most of their time in indoor environments) and those with low exposure to vitamin D through diet, such as those with low socio-economic status; those with alternative diets (e.g., dairy product exclusion) or diets that do not traditionally include milk or dairy products.***

***Also for consideration are First Nations and Inuit populations. Dairy products are expensive foods, and cost may put them beyond the reach of First Nations and Inuit, particularly those living in more remote communities where food costs and unemployment tend to run higher. Add to this that milk and dairy products were not part of a traditional/country food eating pattern and are consumed in lower amounts than recommended according to surveys; and that there is a real or perceived high rate of lactose intolerance in Aboriginal populations. Dietary intake data is scant and we do not have vitamin D status data for northern populations, although we are aware of concerns over rickets incidence in some areas.***

***Questions on Vitamin D Intakes and Status:***

***Most of our population are not meeting the recommended intake levels for vitamin D since the current levels of vitamin D in the food supply were not intended to provide the amount of vitamin D recommended by the new DRIs. However, the majority of Canadians (as indicated in the CHMS data) have an adequate 25OHD level, most likely due to sun exposure.***

***Given these considerations:***

**Q 3.1 - Is there a need to increase vitamin D intakes in order to achieve a higher prevalence of dietary adequacy?**

Yes. The new EAR for vitamin D has been set at 400 IU and a majority of Canadians have vitamin D intakes below this level. The Canada Food Guide already took the unusual step of advising vitamin D

supplements for adults over age 50. Given that the new RDA is set at to 600 IU, it will be impossible to achieve a higher prevalence of dietary adequacy without increasing intakes of vitamin D.

The IOM established intake levels in order that 25(OH)D levels would reach stated targets with minimal sun exposure. Even though mean population levels of 25(OH)D are higher than these levels, this ignores several important population health considerations. The first is that during the winter Canadians have markedly reduced UVB exposure, and there is a consequent drop in 25(OH)D [59-63]. A second consideration is that there is increasing evidence of certain at risk populations in Canada having low serum 25(OH)D and policy needs to be revised to reflect these risks [64]. These issues and others will be discussed as applicable in later sections.

**Q 3.2 - Should Canada continue to rely on sunlight as a key source of vitamin D for the general population?**

Canada does not rely on sunlight as a key source of vitamin D for the general population, but sunlight is an unavoidable contributor to 25(OH)D levels in Canadians as demonstrated by the seasonal variation in levels of 25(OH)D. Thus, the northern latitude of Canada reduces synthesis of vitamin D from sunlight much of the year, such that serum 25(OH)D levels in Canadians are higher in the summer/fall and lower in the winter/spring [59-61, 63]. This is observed even in Arctic communities, where 25(OH)D levels also increase in summer [62]. The reality therefore is that Canadians acquire at least some of their vitamin D through exposure to sunlight, either during summer or on winter holidays, and will continue to do so. Although the IOM report assumes minimal input from sunshine in its recommendations, in the end, it does advise intakes that require a background input of vitamin D from sun exposure to achieve a 40 or 50 nmol/L level of serum 25(OH)D, as none of the clinical trials quoted by the IOM involved avoidance of sunshine. Even the Smith paper on 25(OH)D levels in Antarctica [65] lasted only 5 months, roughly the period of Canadian winter, thus not truly the minimum levels assuming no exposure; and the 25(OH)D levels achieved with supplements still reflect baseline levels of 25(OH)D prior to withdrawal from sunlight exposure.

In practice, therefore, it is important to acknowledge sunlight as a source of vitamin D for Canadians for 5-6 (or less) months a year. The IOM recommendations are therefore vitamin D intakes suitable for Canadians at all times of the year even if they attempt to avoid sunshine e.g. with sunscreens or clothing. However, persons of non-European ancestry exhibit especially low 25(OH)D levels in winter. According to the IOM, the low vitamin D intakes of persons of non-European ancestry, combined with their less efficient responses to sun exposure, contribute to their low 25(OH)D levels. In Canada, one study showed more rapid losses of 25(OH)D between fall and winter in non-white Canadians than in white Canadians [63]. Thus, sun exposure, while important as a source of vitamin D, cannot be assumed to be an equally effective source of vitamin D for all Canadians. This would logically suggest that persons of non-European ancestry represent a vulnerable group and efforts need to be made to direct food fortification toward this group.

Table 3a
Usual intakes of vitamin D from food alone, by DRI age-sex group, showing 5th, 50th and 95th percentiles of intake, EAR and UL values, and percent of age-sex group below EAR. Data Source: Statistics Canada, Canadian Community Health Survey, Cycle 2.2, (2004).

| Sex / age group | Percentiles of Intake (IU/d) | | | EAR/UL | % below EAR |
|---|---|---|---|---|---|
| | 5th | 50th | 95th | | |
| Both sexes / 1-3 y | 84 | 252 | 500 | 400/2520 | 86.0 |
| Both sexes /4-8 y | 100 | 224 | 432 | 400/3000 | 92.7 |
| Male / 9-13 y | 124 | 264 | 512 | 400/4000 | 84.5 |
| Male /14-18 y | 108 | 288 | 648 | 400/4000 | 74.7 |
| Male /19-30 y | 88 | 208 | 464 | 400/4000 | 91.1 |
| Male / 31-50 y | 92 | 204 | 476 | 400/4000 | 90.5 |
| Male / 51-70 y | 92 | 236 | 692 | 400/4000 | 79.6 |
| Male / >70 y | 88 | 212 | 552 | 400/4000 | 87.1 |
| Female / 9-13 y | 88 | 208 | 428 | 400/4000 | 93.1 |
| Female / 14-18 y | 60 | 176 | 428 | 400/4000 | 93.5 |
| Female / 19-30 y | 68 | 168 | 372 | 400/4000 | 96.4 |
| Female / 31-50 y | 76 | 180 | 480 | 400/4000 | 91.1 |
| Female / 51-70 y | 68 | 176 | 492 | 400/4000 | 90.7 |
| Female / >70 y | 80 | 188 | 460 | 400/4000 | 91.8 |

Table 3b
Usual intakes of vitamin D from food and supplements, by DRI age-sex group, showing 5th, 50th and 95th percentiles of intake, EAR and UL values, and percent of age-sex group below EAR. Data Source: Statistics Canada, Canadian Community Health Survey, Cycle 2.2, (2004).

| Sex / age group | Percentiles of Intake (IU/d) | | | EAR/UL | % below EAR |
|---|---|---|---|---|---|
| | 5th | 50th | 95th | | |
| Both sexes / 1-3 y | 96 | 332 | 820 | 400/2520 | 59.8 |
| Both sexes /4-8 y | 124 | 328 | 748 | 400/3000 | 59.8 |
| Male / 9-13 y | 132 | 308 | 760 | 400/4000 | 66.4 |
| Male /14-18 y | 120 | 308 | 824 | 400/4000 | 67.7 |
| Male /19-30 y | 92 | 232 | 704 | 400/4000 | 78.0 |
| Male / 31-50 y | 96 | 232 | 744 | 400/4000 | 78.0 |
| Male / 51-70 y | 96 | 284 | 1028 | 400/4000 | 64.9 |
| Male / >70 y | 96 | 272 | 1096 | 400/4000 | 66.3 |
| Female / 9-13 y | 100 | 232 | 692 | 400/4000 | 77.4 |
| Female / 14-18 y | 64 | 200 | 620 | 400/4000 | 83.8 |
| Female / 19-30 y | 68 | 192 | 684 | 400/4000 | 81.4 |
| Female / 31-50 y | 84 | 236 | 856 | 400/4000 | 70.6 |
| Female / 51-70 y | 96 | 316 | 1096 | 400/4000 | 57.6 |
| Female / >70 y | 80 | 360 | 1108 | 400/4000 | 54.3 |

**If yes for question 3.1:**

**Q 3.3 - By how much should vitamin D intake be increased for the various age-sex groups?**

Based on the new DRI guidelines, the RDA is 600 IU/day for all non-infant age groups up to age 70. Table 3a shows that roughly 90% of the population has vitamin D intake from food below the EAR of 400 IU (10 mcg) and the 5th percentile vitamin D intake is only about 80 IU (2 mcg). Table 3b shows that even including intake of supplements, the 5$^{th}$ percentile vitamin D intake is still very low at roughly 100 IU (2.8 mcg). It is therefore estimated that, to ensure that 95% of the population consume the EAR for vitamin D, intake in those with the lowest intake will need to increase by about fivefold from current levels. For people beyond age 70, a dietary supplement would likely be required to reach the RDA of 800 IU/day

The prevalence of low 25(OH)D levels in non-white Canadians is high [59, 61, 64] and it is important to understand the factors associated with this higher risk noted in the CHMS data. For vulnerable groups such as non-white Canadians in winter, in whom 25(OH)D levels are lower due to decreased levels derived from sunlight [66] it is likely that more than 600 IU/day of oral consumption would be needed to compensate and achieve a 25(OH)D target level of 40 or 50 nmol/L . Those who avoid sun exposure are also more vulnerable, but the vulnerability of non-white Canadians is a non-modifiable risk factor since their capacity to use ultraviolet light as a source of vitamin D synthesis is reduced [66]. There are also differences in cultural preferences for sun exposure and clothing covering while outdoors, and less ready acceptance of vitamin supplements that would put specific groups at elevated risk. Additional national studies are required in specific cultural and racial groups to understand the practices that lie behind the observed lower levels of 25(OH)D over and above physiologic differences in response to uv light .

To consider baseline intakes without supplements, and assume minimal sun exposure, is quite complex. Measurements of 25(OH)D in 3 month intervals throughout the year in a small population-based study of Calgarians over age 25, taking ≤200 IU of vitamin D supplements per day, showed that about 2/3 of the subjects had 25(OH)D levels below 50 nmol/L at least once during the year, and about 1/3 had levels below 40 nmol/L at least once during the year [67]. In the CaMos study, levels less than 50 nmol/L affected one in 5 Canadian adults 35 years of age or older [60]. Results from the CHMS indicated that 1 in 4 Canadians aged 6 to 79 years had levels less than 50 nmol/L and Table 2 in Whiting et al. [61] shows that during winter, 20% of non-white individuals have 25(OH)D levels below 30 nmol/L. Data on University of Toronto students during winter suggests that this may even underestimate the severity of the problem [64]. This establishes a substantial prevalence of serum 25(OH)D below the levels associated with the EAR or RDA among Canadians overall, and a high prevalence of insufficient serum 25(OH)D (less than 30nmol/L) in non-white Canadians based on present dietary consumption and fortification. Furthermore, according to Table 4 in Whiting et al. [61], non-white Canadians were also less likely to use a dietary supplement containing vitamin D. Therefore, our recommendation would be to increase the amount of vitamin D in foods.

The aim is to increase vitamin D intake such that most Canadians have intakes above the EAR, since this level is set as a threshold for estimating adequacy in a population. According to Table 3, the 50th

percentile for vitamin D consumption from food is approximately 240 IU/day (6 mcg/day). To have sufficient intakes for most of the population to consume levels of vitamin D above the EAR would require a substantial shift in intakes for a large proportion of the population; 73% of men and 63% of women who currently have intakes below the EAR from food and supplements (CCHS). In view of the fact that the gap between the 50$^{th}$ percentile of vitamin D consumption (240 IU) and the EAR of 400 IU is 160 IU, increasing the intake of those in the 50$^{th}$ percentile to the level of the EAR would therefore require an increase of 160/240=67%. Therefore in the absence of education programs to increase vitamin D consumption from currently fortified foods, and in the absence of extending food fortification to other foods, to bring this usual intake up to the EAR (400 IU/day) would require increasing the amount of vitamin D introduced into currently fortified foods by over 60%.

This would be a first and conservative step to ameliorate vitamin D inadequacy leading to deficiency. Even so, those falling below the median, and especially those who do not consume milk would still be at risk. Thus, it is unlikely to resolve the problem of vulnerable groups such as those with low milk consumption for a variety of cultural and other reasons (e.g. Aboriginals that consume less dairy). It would therefore be necessary to monitor the situation and potentially take other steps to address the population at higher risk of deficiency.

**Q3.4 – If Health Canada decided to recommend increased consumption of current food sources of vitamin D (without further fortification or the use of supplements), what would be the benefits and drawbacks to both the general population and vulnerable subpopulations?**

*Drawback:* The main problem with an approach that advises increased consumption of vitamin D-containing foods is that it is likely not feasible. First, without fortification, there is too little vitamin D in commonly consumed foods and an overall limited choice/availability of foods that are a "good or excellent source" of vitamin D. A widespread shift toward existing foods that presently contain vitamin D is not plausible. It is difficult to change dietary habits. From a food-supply perspective, the supply of cost-effective fatty fish is likely not sufficient to meet the needs of the whole population. Further drawbacks to promoting fatty fish consumption are that this food is not consumed by everyone and there is a premium cost for most of these foods relative to other protein sources. Second, there is also a great reliance on dairy as a major food source of vitamin D. The drawback to recommending more fortified milk as the mechanism to increased vitamin D consumption is that many Canadians are not even consuming milk at the current recommendation, and vulnerable subgroups even less so. Thus, there are several barriers to increased milk intake, including cultural habits, perceived lactose intolerance, and peer use. In addition, education alone, to increase consumption of current food sources of vitamin D, would not address barriers to improved diet among those with low SES, where cost is one important barrier to consumption.

*Benefits:* Assuming that on average, by consuming more fortified milk and/or fatty fish, people, could achieve an intake of 400 IU/day (or 600 IU/day in the case of those over 70 years) the benefits would of course be minimization of the prevalence of inadequacy in the population, a limited risk of exceeding the UL on the basis of vitamin D in the present food supply, the capacity to tailor messaging to address issues specific to each at-risk sub-group, and the lack of need to further fortify foods or recommend supplements. The overarching benefit would be the prevention of osteomalacia and rickets, as well as the prevention of osteoporotic fractures as accepted by the IOM.

**Q 3.5 - If Health Canada decided to recommend wider supplementation (to more age-sex groups, to high risk population groups), or increased supplementation to those with current recommendations to take a supplement, or supplementation by season, what would be the benefits and drawbacks to both the general population and vulnerable subpopulations?**

*Benefits:* For supplements**,** benefits would include the lack of requirement to change dietary patterns and to produce changes in the food supply. Assuming dietary supplements providing vitamin D were consumed at recommended levels, this approach could provide choice to supplement based on the individual, as well as the capacity to target increases in vitamin D intake for those who groups that most require the increases i.e. specific age-sex groups and high risk populations rather than exposure of the population as a whole to increased fortification. Recommending a vitamin D supplement may also possibly help health professionals to make the public aware of the prevalent levels of low vitamin D consumption, particularly in certain groups. Vulnerable subgroups such as Aboriginals (including preschoolers), and other Canadians of non-European ancestry, could potentially benefit from supplements all year round [6-8, 62] whereas supplementation by season, i.e., at the time of the nadir of serum 25(OH)D levels in winter/spring months, might be more prudent in others. However, given the low rate of toxicity and the greater likelihood of continued compliance or adherence if supplements are recommended year-round, it is preferable to recommend the latter.

Supplementation would provide minimal risk of exceeding the UL. Thus, the 95$^{th}$ percentile of the usual intake of vitamin D from both dietary sources and supplements varies with age and sex but is highest at 1108 IU/day (27.7µg/day) for females aged 51-70, and males and females over 70 (Table 3a) and the UL is 4000 IU /day (40µg/day). Consequently there is a large gap between the 95$^{th}$ percentile of intake and the UL, and there would be minimal risk to the general population related to toxicity in association with consuming supplements as the source of the recommended intakes. The health benefit would of course be the prevention of rickets, osteomalacia and fractures as accepted by the IOM.

*Drawbacks:* Supplementation is more expensive than food fortification for the consumer, and supplementation would require high levels of compliance/adherence by the population [68]. Convincing educated consumers to take vitamin D in summer may be challenging, as some clearly know that a short amount of sun exposure increases vitamin D production. While some will choose supplements, the concern is that this will be limited to the more "health conscious". In the USA those most likely to consume supplements are white women with higher education, lower BMI, and higher physical activity levels [69]. Another major limitation to the use of supplements is that it seems unrealistic to expect that target populations would embrace supplements [8]. Furthermore, the most vulnerable population groups are the ones least likely to be taking vitamin D supplements because of cost [3], lack of awareness of the need, and possibly lack of belief in the benefits. Many if not most of the population would continue to consume vitamin D below recommended levels if this were the only strategy. Other strategies have noted limitations, in particular changes in the food supply require time, and changes to dietary patterns are not readily achieved. So while there are limitations with recommending supplements, there are identifiable at-risk subgroups, and these subgroups should be included in the Health Canada recommendations.

**Q 3.6 - If Health Canada decided to recommend increased fortification of dietary sources with vitamin D, what would be the benefits and drawbacks to both the general population and vulnerable subpopulations?**

*Benefits:* Increased fortification of existing products would have the advantage that an existing mandatory policy is in place and change would mainly be in the level of fortification. Increased fortification of appropriate dietary sources with vitamin D would reach a wider population than supplementation and could address the needs of those with some (but too little) milk intake. Thus if more vitamin D were permitted in milk, Canadians could continue to target current Food Guide recommendations, rather than have to consume an unrealistically high number of milk servings. However, as mentioned earlier this would not help those who consume little or no milk and these are the most vulnerable [8, 64]. (Presumably other dairy foods and plant-based beverages would be permitted a higher level of fortification). Thus concurrent increased fortification of milk substitutes (e.g. soy beverages) would assure that those who do not drink milk have the same benefit. Increased fortification of new sources of foods might more readily address the global under supply of vitamin D in the food supply. The ability to fortify more kinds of foods with vitamin D would allow people without a cultural preference for, or with an aversion to, milk products, to find a food source of vitamin D in a common food. The best vehicle for vitamin D fortification would need to be worked out through modeling exercises, to find foods where it is technically feasible to supplement with vitamin D at a low cost, and to ensure that the food vehicle is consumed in reasonable amounts by all Canadians. The best long-term solution to the issues being addressed here would therefore likely be appropriate mandatory fortification of some other food, in addition to the continued mandatory fortification of milk. Assuming that individual consumption would reach the EAR, the benefit would of course be the prevention of rickets, osteomalacia and fractures as per the IOM Report.

*Drawbacks:* Mandatory food fortification may be politically contentious because of perceived tampering of the food supply, and there might be an economic cost associated with food fortification. If only currently fortified foods were supplemented it would have limited effect on those who do not drink milk/milk substitutes, and that some groups at high risk (e.g., skin pigmentation and cultural practices) would be least likely to benefit. If new foods were fortified there would be the need to identify an acceptable food vehicle. Increased fortification may also be of limited use for those with low energy intake. Labels would obviously clearly need to indicate whether foods are fortified and to what extent. Nevertheless, the desirability of fortifying food with vitamin D contrasts with the desirability of fortifying food with calcium. In the case of vitamin D, the fact the UL is well above the distribution of current intake means that there is room for further fortification while minimizing the risk of exceeding the UL. In contrast, the proximity of the current distribution of calcium and the UL for calcium intake makes food fortification with calcium as a source of achieving the EAR a less attractive option. The percentiles of vitamin D intake may be viewed as being proportional to increases in fortification under the assumption that fortification is the major source of vitamin D. In practice, there is some vitamin D intake from other sources such as fish, whose intake will not go up. Consequently when calculating the effect of increasing fortification levels in foods, a given percentage rise in vitamin D fortification does not mean that average vitamin D intakes will go up by that percentage.

Summary and Recommendations

Overall, the EAC recommends increasing the mandatory fortification of selected foods with vitamin D. For example, a food such as milk, which is currently subject to mandatory fortification with 400 IU vitamin D per litre, could instead contain 50% more (600 IU per litre). As noted from above, this increase will move the distribution of vitamin D intake, but not so much as to risk exceeding the UL. Likewise, milk substitutes could also be standardized to have 600 IU per litre, to allow for benefits for those not consuming dairy products. Furthermore, Health Canada should explore other fortification options, through modeling exercises, as many adult Canadians drink very little milk and reliance on milk does not reach certain at-risk populations. Even fortification may not totally address recommended intakes of vitamin D without the need to recommend supplements to specific sub-groups.

**Q 3.7 - Could fortification address recommended intakes without the need to recommend supplements to specific sub-groups?**

If mandatory fortification were used one would need to calculate the levels that the population would receive if specific vehicles were used and then examine the data to see who may still not be adequately covered. It is possible that because elderly Canadians have reduced energy intakes, they might still require a supplement. Such modeling can be done with the CCHS data as we have excellent information on nutrient levels and the specific food consumed by different potentially vulnerable groups with the exception of Aboriginals living on reserves.

If voluntary fortification was chosen, only a portion of the population will consume foods that are fortified. Several issues related to the limitations of fortifying foods with calcium as a sole source of intake are discussed in response to questions 1.2, 1.5, and 1.8 apply equally to vitamin D products. For example food with extra nutrients tend to be in the higher cost items and reach a higher SES group that are also more likely to take vitamin and mineral supplements [15, 16]. Thus, it is likely that vitamin D fortification would not reach the lower SES population unless there were financial policies introduced to producers in order to keep costs down. There could be the issue of additional energy intake if consumers chose to increase intakes of specific foods to increase their vitamin D intake. It would therefore be important to introduce educational programs in concert with food fortification in order to enhance the chance of achieving recommended intakes from fortified foods by substituting foods containing vitamin D rather than adding these foods to the diet, so as to not encourage increased energy consumption.

With either mandatory or voluntary fortification, the needs of all Canadians will likely not be totally addressed. The need to recommend supplements to some subgroups will likely remain. This might be most evident in the "small eaters" or those with diets very far removed from mainstream Canadian diets. The risk of not meeting needs with voluntary fortification is likely greater but this may depend on the additional costs to manufacturers of fortifying their food products and therefore the final costs to the consumers. Furthermore, it should also be noted that for those over age 70 years, the higher RDA of 800 IU/day will likely mean that for them, supplements should continue to be recommended, given that Canada's Food Guide already does recommend supplements for older adults.

**Q 3.8 - If Health Canada were to decide to recommend increased vitamin D food fortification or the use of supplements, would there be an increased risk of toxicity to people with high sun exposure, considering that there may not be any (or an adequate) feedback mechanism to control serum 25(OH)D levels from oral sources of vitamin D?**

Physiological mechanisms for vitamin D do exist for both sun-derived and oral vitamin D. Sunlight exposure does not cause vitamin D toxicity [70, 71] and for a given oral dose of vitamin D, the incremental increase in serum 25(OH)D becomes progressively smaller as the pre-treatment 25(OH)D level becomes higher [72].

The IOM places the UL at 4000 IU daily, as a long-term average consumption with no known risk of adverse effects. This level was chosen in part because of the IOM's concern about possible increased risk of some cancers at serum 25(OH)D above 125 nmol/L and the fact that one study of supplementation with 5000 IU/day resulted in a plateau of serum 25(OH)D at around 125 nmol/L after 3 or more months of supplementation in a small number of healthy adults [73]. Toxicity, featuring the classic signs and symptoms of hypercalcemia and hypercalciuria, would not be expected at this level of 25(OH)D [25]. The highest intake of vitamin D from food is shown in Table 3 as 692 IU/day or the 95$^{th}$ percentile for men over age 50. With fortification levels set to a maximum increase of 1500 IU/day among those with the greatest intake (assessed by modeling) and recommended supplement intake at 1000 IU/day the resulting distribution of intake would still fall entirely below the UL level. Finally, the setting of an UL incorporates a substantial uncertainty factor compared to the estimates published by Hathcock et al., that were already subjected to further a margin of safety [74].

*Perceived risks with higher serum 25(OH)D*

Risks of adverse health outcomes exist for almost all biologically active substances at doses that are either excessively low or excessively high. The IOM based its concern about the risks of high serum 25(OH)D and the levels at which these risks occur primarily on the clinical trial of Sanders et al. that gave exceptionally large doses of vitamin D all at once [75] and on epidemiologic data suggestive of U- or reverse J-shaped curves associating serum 25(OH)D with all cause mortality. Higher serum 25(OH)D levels have been related to increased risk of prostate cancer [76], pancreatic cancer [77], and other cancers [78] as well as all cause mortality [79]. However, supplementation with vitamin D in clinical trials has never been related to adverse effects. In fact, the range of vitamin D consumption being discussed here (over 400 IU up to about 1000 IU daily) has resulted in lower mortality than placebo [80] and no excess in adverse event reports [81]. A recent 1-year long randomized clinical trial comparing 800 IU per day versus 6500 IU per day detected no difference in adverse events [82]. Further work will always be helpful to clarify the levels of serum 25(OH)D at which both skeletal/mineral and extra-skeletal effects are deleterious at both the upper and the lower ranges of serum 25(OH)D.

**Q 3.9 - Are additional data needed to help answer Question 3.8, and what data would be needed?**

The information in the published literature about the safety of vitamin D is growing steadily, and to date, there is no clinical trial that has shown adversity related to the supervised consumption of vitamin D. The best of the longer-term studies is by Jorde et al. [83, 84] but these extended to only one year and assessed only selected outcomes. Ideally, a longer-term trial e.g. a 5-year RCT using different doses of vitamin D up to 4000 IU daily and with a defined calcium intake could be helpful to examine both indices of efficacy and of toxicity and potential interaction between vitamin D and calcium intake. There is also a need for social/consumer research to determine if there are preferred scenarios for vitamin D fortification and a need for modeling studies to determine the impact of various modeling scenarios on the distribution of vitamin D intake globally and among populations at risk.

***Vulnerable Populations***

***Context (provided by Health Canada):***

***The IOM Report identified sub-populations or vulnerable groups that could be at higher risk of vitamin D inadequacy. These sub-populations include those with reduced sun exposure or cutaneous synthesis of vitamin D and those with low exposure to vitamin D through diet.***

***The Community Health Measures Survey (CHMS) did not survey Canadians living in institutions, on reserves or north of the 60$^{th}$ parallel. Data on those self-identified as non-White in the CHMS are presented in Tables 6 and 7. Consider, as well, the First Nations and Inuit populations.***

***Questions on Vulnerable Populations and Vitamin D:***

**Q 4.1 -What do we know about the 25OHD status of the people who were not covered by CHMS, that is those living in institutions, on reserves or north of the 60th parallel?**

Elderly: One 1997 report of Toronto elderly in an institution was by Liu et al and showed that 25(OH)D levels averaged 40 nmol/L in winter, and 45 nmol/L in summer [85]. There is an earlier study that examined community-living elderly in Montreal, which showed low levels of 25(OH)D [86]. There is very little up-to-date data on serum 25(OH)D levels among Canadians living in long-term care facilities. This population was not sampled as a part of the CHMS, nor were they sampled in other studies, including the Canadian Multicentre Osteoporosis Study (CaMos). Collection and dissemination of reference data from long-term care facilities should be of high-priority, as it is known that such individuals are at extremely high risk of both falls and fracture. It is likely that serum levels of 25(OH)D have increased over time due to increased awareness of vitamin D needs. First, the 1997 dietary guidelines already raised the vitamin D recommendation for older adults to 600 IU daily, More recent recommendations from Osteoporosis Canada, suggest that for most adults, a vitamin $D_3$ supplement at an initial daily dose of at least 800 IU is appropriate [87]. Other recommendations from the Canadian Cancer Society [88], suggest a vitamin D supplement of 1000 IU daily. . Thus, it is reasonable to assume that serum levels should be higher now. In fact, at a recent presentation at the 2011 annual meeting of the American Society for Bone and Mineral Research, it was reported that in the CaMos study, 25(OH)D levels increased progressively between 1996-97 until 2006-07 in all age

groups and in both sexes [89]. There was also an inverse relationship between PTH and 25(OH)D and therefore a decrease in PTH over 10 years. Concomitant with the increase in 25(OH)D there was a progressive increase in intake of vitamin D supplements over the 10 years in the elderly as well as those less than 70. It is unclear whether there have been similar changes among those in long-term care.

Aboriginal Communities:
Nunavut Child Inuit Health Survey 2007-2008. In Inuit preschoolers living in 16 Arctic communities (51ºN-70ºN) and participating in the 2007-2008 Nunavut Child Inuit Health Survey, 282 children were tested during summer, and 52 of them were re-tested in winter. Plasma 25(OH)D using the Diasorin Liaison assay system (same method as used for CHMS) showed median summertime concentrations and interquartile ranges of 48.3 (32.8-71.3) nmol/L while wintertime values were 37.7 (21.4-52.0) nmol/L. Prevalence of 25(OH)D < 25 nmol/L (overtly rickets range) was 13.6 % [62]. The predictors of vitamin D status were dietary intake and age. Given low traditional food consumption and low consumption of milk by children in these communities, the authors concluded that interventions promoting vitamin D supplementation might be required to prevent low vitamin D status.

In another study performed as part of this survey, the prevalence and correlates of parental-reported oral health among Inuit preschool-aged children in Nunavut was examined. It was found that among these children, only 4.9% (95% CI: 2.4-7.4%) took a vitamin D supplement and only 16% (95% CI: 12.3-20.1) took a multivitamin and multi-mineral supplement containing vitamin D and calcium [90]. This appears to reinforce the concept that promoting vitamin D supplementation may be required in this community.

The assumption that 25(OH)D levels have increased in the Caucasian population as a result of recent guidance about vitamin D supplementation, as found in the recent CaMos study [89], needs to be verified with updated measurements of serum 25(OH)D levels in Northern population groups (as well as in the institutionalized) to determine if there have been changes since the 2008 survey.

A Multi-Community Environment and Health Longitudinal Study in Iiyiyiu Aschii (2005-2008). A cross-sectional age-stratified random sample of people living in five Cree communities in Quebec was used to study various health parameters [91]. Serum 25(OH)D in this study was assessed by RIA using Medicorp IDS RIA kits, and thus, may not be directly comparable to the CHMS. The population consisted of 292 women and 218 men with mean age 36 y. The mean (SD) 25(OH)D levels were 52.4 (16.4) nmol/L, and the prevalence of serum levels below a 37.5 nmol/L threshold was 20%. With noted limitation of different assays, comparison of these results with the Langlois CHMS report [59], show that these communities had lower mean serum 25(OH)D (CHMS mean of 67.7 nmol/L) and higher prevalence of serum levels below 37.5 nmol/L (CHMS estimate 12.9% of males, 8.3% of females). Of note, the Del Gobbo et al. study [91] collected samples in the spring and summer, and thus does not indicate the prevalence of inadequacy during winter.

Canadian IPY Inuit Health Survey (2007-2008). A cross-sectional survey of people living in 33 Inuit coastal communities was used to study multiple health parameters [6]. Serum 25(OH)D was measured using Diasorin Liaison total vitamin D assay. There were 2585 participants from a total of 1901 households out of 2796 households approached to participate; survey respondents had mean age 41 and 62% were female. Among those consuming traditional foods in the past day the mean (interquartile

range) of dietary vitamin D intake was 5.7 (2.2, 11.4) μg/d (90-445 IU/day) in men and 4.8 (2.0, 9.2) μg/d (80-370 IU/day) in women, and the mean 25(OH)D level was 55.2 nmol/L. Among those with reporting having no traditional foods, the mean (interquartile range) of dietary vitamin D intake was 2.3 (1.2, 4.6) μg/d (50-200 IU/day) in men and 1.8 (0.8, 3.6) μg/d (30- 180 IU/day) in women and the mean 25(OH)D level was 40.5 nmol/L. In conclusion, those who did not consume traditional foods had a higher risk of low vitamin D intake, and this was reflected by lower levels of serum 25(OH)D.

A Manitoba study done from 2002-4, comparing rural and urban Aboriginal women to urban Caucasian women found that 32% of rural Aboriginal, 30.4% of urban Aboriginal, and 18.6% of urban white women had serum 25(OH)D concentrations <37.5 nmol/L [8].

As was noted earlier, there is dietary heterogeneity among Aboriginal communities, but present surveys indicate that all surveyed communities face increased risk of low 25(OH)D status, especially related to dietary transition. Non-surveyed communities should be made aware of these important results.

**Q 4.2 - What do we know about the 25(OH)D status of non-white persons?**

Both the statistics Canada CHMS [59] as well as a study focusing on non-white students at the University of Toronto [64] showed that 25(OH)D levels are substantially lower in all groups who are not of European ancestry. Further analysis from the CHMS [61] showed that the overall prevalence of vitamin D deficiency (25(OH)D < 30 nmol/L) was 16.3% among non-whites compared with less than 5% with deficiency among whites. Using the 40 nmol/L threshold among non-whites resulted in a prevalence below the threshold of 30.5% year round, with slightly higher prevalence 33.0% in winter versus 28.3% in summer. Thus, even in summer, non-white Canadians have sub-optimal levels of vitamin D, with apparently high levels of inadequacy. Finally, roughly half of non-white Canadians had 25(OH)D levels less than 50 nmol/L, while this was true of only 1 in 5 white Canadians. This suggested to the authors that current food choices alone are insufficient to maintain 25(OH)D concentrations of 50 nmol/L in many Canadians, especially in winter.

**Q 4.3 - Are there differences in 25(OH)D status among East Asian, South Asian, Middle Eastern and African groups?**

In theory there may be differences among these immigrant groups because of different skin color and cultural and dietary habits. More skin pigment results in more prevention of UVB rays from reaching the vitamin D forming dermis layer of the skin. The non-European-ancestry racial groups of students in Toronto show remarkably similar 25(OH)D levels that were much lower than for the students of European ancestry [64]. Further assessment showed that the lighter-skinned East Asians had significantly higher levels of 25(OH)D during the summer than South Asians (averaging about 50 versus 40 nmol/liter respectively), the levels were similarly low in winter [63]. In Europe, low serum 25(OH)D levels with a high prevalence of vitamin D deficiency has been reported in Turkish immigrants in Germany [92]. In the US non-Hispanic whites were reported to have higher vitamin D status than do non-Hispanic blacks and Mexican Americans [93]. In conclusion, increasing skin pigmentation increases risk of lower 25(OH)D levels in all groups studied.

**Q 4.4 - If there are insufficient data to draw any conclusions about the status of these groups mentioned in questions 4.1 to 4.3, what is the best way to obtain such data?**

Further research is not likely to change the finding that all those classified as non-white, including Aboriginal people, and those of non-European ethnic background possess lower 25(OH)D levels than persons of European ancestry. However, it is necessary to have additional data, since the diet and situation of the different vulnerable groups vary, and thus dietary change, supplementation, and fortification may have different impact depending on the population. There was clear heterogeneity even between different Aboriginal communities, and therefore assessments in one community cannot be extrapolated to other communities. Nevertheless, there is some data on dietary risk factors that may be shared between communities, and thus the existing research is potentially relevant to other communities. It may be productive to see whether the CHMS survey of 25(OH)D levels in Canadians could be analyzed in terms of differences among groups with different ethnic origin or to specifically address this issue with a new study. For immigrant groups, it may be useful to do more focused studies within the large metropolitan areas to adequately sample non-white groups, rather than pan-Canadian studies, as the levels of 25(OH)D and the predictors of their status need to be better understood in order to know what interventions are needed and which are acceptable.

**Q 4.5 - Is there a need to fortify foods only eaten by a vulnerable group; i.e. that are not eaten by the general population, and what would be the appropriate food vehicles?**

Additional foods to fortify should be foods eaten by the general population and by the sub-groups at risk. Fortification of specialty foods would be both expensive, and given the broad spectrum of Canadians with vitamin D intake below the EAR, unnecessary. Nevertheless a variety of foods should be considered in order to meet differing preferences of many cultural, income, and age/sex groups. Unlike the situation for calcium, there is a fair gap between the current distribution and the UL, so there is essentially no risk if more than one kind of food were fortified. It is appropriate to diversify the types of foods that contain vitamin D. Traditional Inuit foods are high in vitamin D, and as these populations move away from their traditional diet they are particularly vulnerable. European ancestry individuals are more likely to consume milk and dairy products. Some soy beverage is already fortified with vitamin D, but there are many different cultural groups in Canada and targeting foods to specifically fortify foods for each would be complex. Research needs to be done to determine appropriate food vehicles and the amount of fortification to use. Modeling various choices might help in identifying the appropriate food vehicle. In order to be effective, however, it is important that these foods not be more expensive than the usual food in the category (e.g. refrigerated orange juice vs. many frozen orange juice concentrates), i.e. the considerations regarding fortification of foods with vitamin D overlap with those already considered regarding fortification of foods with calcium and which are discussed in the response to Question 1.8.

**Q 4.6 - Are there vulnerable subgroups in need of special guidance to ensure adequate intakes of vitamin D?**

One obvious group, identified by the IOM, includes individuals with malabsorption syndromes. Middle Eastern and other women who wear full-coverage clothing would be another vulnerable group [94]. Even when living at 30 degrees latitude in the Middle East some women have remarkably low 25(OH)D concentrations, consistent with osteomalacia, and low 25(OH)D is associated with myopathy and back pain [95].

In addition, an extremely disproportionate amount of the rickets in Canada is seen in Aboriginal populations [34]. Aboriginal people who rely on traditional foods should be made aware of the richest sources of vitamin D and how to select market foods if they transition to subsistence based mainly on market food. Since 94% of cases of infant rickets occur in infants who were breastfed [34], and since infant vitamin D supplements to Aboriginal groups are publicly provided, food policy related to vitamin D is very likely appropriate for infants, especially Aboriginal infants but the problem appears to lie in low rates of adherence to policy recommendations. One target for research would therefore be how to improve adherence.

Vitamin D deficiency in early infancy may also be directly related to sub-clinical vitamin D deficiency in the mother during pregnancy [96]. Consequently even the amount of supplement required for women during pregnancy requires further assessment.

Individuals who are incarcerated in prisons could represent another vulnerable group, but little data exists around this group.

## ***5. Infants***

***Context (provided by Health Canada):***

***Health Canada currently has a recommendation to give a daily vitamin D supplement of 400 IU to breastfed healthy term infants, starting at birth. (Infants fed commercial infant formula get sufficient supplemental vitamin D from the formula.) Based on the new DRIs, Health Canada will likely propose continuing the recommendation for 400 IU of supplemental vitamin D during the first 2 years of life.***

***Questions on Infants and Vitamin D:***

**Q 5.1 - Are there risks to any subgroups if this recommendation is promoted? (Note the Canadian Paediatric Society currently recommends a supplement of 800 IU for at-risk infants e.g. living in the far North (CPS statement included as an attachment).)**

Adherence to administering the current recommendation of 400 IU/day is effective at sustaining serum 25(OH)D above 50 nmol/L in infants [97]. As for risks caused by promoting vitamin D supplementation of breastfed infants, we are not aware of any, other than that is probable that some parents may misuse supplements if they are not following the instructions on the product label.

The recommendation of 400 IU vitamin D per day may not be adequate in the following subgroups of infants: 1) infants born to mothers with sub-clinical or overt vitamin D deficiency due to inadequate placental transfer of vitamin D in utero to build the infant body stores of 25(OH)D [34]*. Such mothers include those who do not consume vitamin D-fortified cow milk or other beverages, who do not take vitamin supplements in pregnancy containing vitamin D, those with liver or renal disease [98], with inflammatory bowel disease [99] or who have moderate to severe obesity [100], and those with intermediate or dark skin, who avoid exposure to sun or who cover the majority of their skin outside the home [101]; 2) infants with malabsorptive disorders such as cystic fibrosis or celiac disease; 3) infants in the far north who have dark skin and minimal exposure to sunlight due to latitude of their environment[34].

*Note that in a recent Canadian survey describing characteristics of mothers with children manifesting vitamin D deficiency, 75% of the mothers did not drink milk while only 12% received vitamin D supplementation pre-natally and even fewer (5%) took vitamin D following birth [34].

**Q 5.2 – Are there cases in which there would be a good rationale to recommend a higher dose for infants?**

Term Infants. While clinical evidence is scant to support recommendations for vitamin D intakes above 400 IU/day for infants 0 to 12 months, some consensus statements have made recommendations of 800-1000 IU/day for specific sub-groups. It should be noted that no known risks have been associated with vitamin D intakes of 800 IU/day in infants [102, 103]. The new DRIs recommend an upper level (UL) of 1000 IU/day for infants to 6 months and 1500 IU/day for infants 6-12 months [25]. Groups of infants who may benefit from vitamin D intakes above 400 IU/day include:

*1) Infants living in northern communities especially those with intermediate or dark skin colour.*
The Canadian Pediatric Society Nutrition Committee supports the recommendation to supplement term infants with 400 IU/day of vitamin D, but further recommends that infants living in the far north be supplemented with 800 IU/day of vitamin D [104]. This recommendation is not based on clinical trial evidence. However, risk of vitamin D deficiency has been implied from observational studies such as Weiler et al. [8] in Winnipeg area Aboriginal populations.

*2) Infants at risk of vitamin D deficiency at birth.*
If mothers have sub-clinical vitamin D deficiency during pregnancy then the infant will be born with vitamin D insufficiency or deficiency (as detailed in question #1). Although no clinical trial evidence is available in such infant groups, it may be prudent to provide 800 IU/day supplementation at least for the first six months in such infants, though it should be noted that even higher doses may be required in severe cases, to rescue the infants from the vitamin D deficient state [34].

Preterm Infants. The vitamin D status of premature infants at birth is dependent on placental transfer of maternal vitamin D during pregnancy [105]. Premature infants are at risk of poor vitamin D status due to low nutrient stores at birth, low content of vitamin D in human milk and prolonged hospitalization, which prevents endogenous production of vitamin D [105]. Recommendations for vitamin D intake for premature infants vary among international sources. The 1995 Canadian Pediatric Society Preterm Recommended Intake (P-RNI) for vitamin D is 400-800 IU/day [104]. The European

Society for Paediatric Gastroenterology, Hepatology and Nutrition Committee on Nutrition recommends 800-1000 IU/day for enterally fed preterm infants [106]. The consensus recommendations published by Tsang et al. recommend an enteral intake of 200-1000 IU vitamin D/day [105]. For preterm infants or very low birth weight preterm infants, there are 3 randomized trials supporting the position that 400 IU per day is sufficient supplemental vitamin D for both short-term (about 3 months) [107] and long-term (9-11 years) normal bone health [108, 109]. After discharge from hospital, premature infants should receive vitamin D supplements as recommended for term infants.

Premature infants fed premature formula or expressed breast milk fortified with human milk fortifiers that have vitamin D added require a vitamin D supplement until they are being fed at least 300 – 400 mL/day, depending on the product being used. This volume of formula or fortified expressed breast milk is the amount that would supply 400 IU/day of vitamin D.

**Q 5.3 - When a formula-fed infant switches to cow's milk between 9 and 12 months of age, should a vitamin D supplement be recommended given that a child may obtain less than 400 IU vitamin D from cow's milk?**

Once solid foods are introduced the total volume of milk consumed by the infant may decline. In setting the DRIs, it was estimated that breastfed infants consume 600 ml of milk per day. If the infant is fed formula or cow milk (both containing 400 IU vitamin D/L), at similar volumes of intake, then they would only receive about 240 IU vitamin D/day, assuming vitamin D was not provided through any other food sources (some yogurts are made with vitamin D fortified milk but the total amount in a serving of yogurt is small). Based on one observational study in the Montreal area, when infants are transitioned from breast feeding to partial feeding with formula before six months of age, continuation of vitamin D supplementation is not widely practiced [110]. In this study, 50% of infants receiving mixed feeding had vitamin D intakes below recommendations. To meet the likely Health Canada recommendation of 400 IU vitamin D intake for the first 2 years of life, infants would require a supplement of about 200 IU per day. From a practical perspective, it might be appropriate to recommend continuation of a supplement of 400 IU of vitamin D to two years unless it is provided in other foods. The answer to this question is therefore partly contingent on the issues raised in questions 7.1-7.3 since the efficacy of provision of vitamin D via other foods would depend in part on its bioavailability in those substances.

## Vitamin D and Calcium

***6. Supplements: Claims***

***Context (provided by Health Canada):***

***The claim on the NHPD monographs is: Adequate calcium (and vitamin D) (throughout life) as part of a healthy diet (along with physical activity) may help prevent bones loss/osteoporosis (in peri and post menopausal women) (in later life)***

***Note: "May reduce the risk of developing osteoporosis" is an acceptable alternative to "May help prevent osteoporosis".***

***Note: The information in parenthesis is optional.***

***In order to qualify for the above claim, the vitamin D and calcium dosages must meet the minimum on the NHPD multi-vitamin and mineral supplements monograph. The minimum dose is 65 mg for calcium and varies for vitamin D according to the indicated subpopulation (i.e. 0.8 mcg for children and adolescents 1-13 years and 1.0 mcg for adolescents and adults 14 and over).***

***The Food and Drug Administration (FDA) also permits the claim "Adequate calcium (and vitamin D) (throughout life) as part of a well balanced/healthful diet, (along with physical activity), may reduce the risk of osteoporosis (in later life)" is permissible on foods. However, the minimum dose for the FDA claim is based on 20% of the Reference Daily Intake per reference amount customarily consumed of the food. This is equivalent to 200 mg calcium and 2mcg vitamin D (if vitamin D is included in the claim).***

***Currently, NHPD is considering recommending that the threshold dose for the monograph claim be consistent with the FDA recommendations (e.g. 200 mg calcium and if applicable 2 mcg vitamin D). All supplement products would be required to provide 200 mg calcium to carry this claim. Products carrying a claim which mentions vitamin D would also be required to meet the vitamin D minimum.***

***Question on Supplement Claims with respect to Vitamin D and Calcium:***

**Q 6.1 - Does the current osteoporosis claim on the NHPD monographs require revisions to the wording or the addition of a dose threshold based on the information provided in the DRI report and in consideration of the Food and Drug Administration (FDA) recommendations summarized above?**

Calcium and vitamin D are essential for normal bone formation and maintenance, and as such have been a staple for primary prevention of osteoporosis. In adults age 65 and above, daily vitamin D3 (up to 17.5 or 20 mcg i.e. 700 or 800 IU) with calcium supplements resulted in small but significant increases in bone mineral density in the lumbar spine and hip relative to placebo [111-113]. Therefore, the initial wording, the "acceptable alternative" wording and the FDA's approved wording, of the claim were felt to be appropriately conservative, and acceptable to the committee. Thus, a claim by a NHPD monograph that "Adequate calcium and vitamin D throughout life as part of a healthy diet, along with physical activity, may reduce the risk of developing osteoporosis in later life" would be acceptable wording. A cure is not claimed, and the possibility that calcium and/or vitamin D may be helpful in protection against osteoporosis seems reasonable. Nevertheless the precise doses of calcium and vitamin D that would reduce the risk of developing osteoporosis are not known. Osteoporosis is

believed to have its inception in infancy and childhood [114] but the optimum dose of calcium and vitamin D to minimize the future risk of osteoporosis is unknown. In older adults, there is controversy about the efficacy of calcium supplementation for reducing osteoporotic fractures, especially hip fractures [115, 116], and there is also controversy about the potential adverse effects of calcium supplementation on increasing the risk of myocardial infarction and cardiovascular events [26]. Despite the important role of vitamin D in enhancing calcium absorption, however, studies that have examined doses of calcium that might be harmful, have not generally controlled for prevailing 25(OH)D levels. Consequently it is not clear that doses of calcium that might be harmful at one level of serum 25(OH)D would also be harmful at other levels of serum 25(OH)D.

The committee believes that 20% of the RDI, (200 mg calcium and 100 IU vitamin D) would be sufficient to support the claim as worded above, for a food or supplement[117-119]. The initial minimum doses recommended in the NHPD monograph were 65 mg calcium and 0.8-1.0 mcg vitamin D. The current recommendations of 20% of the RDI are higher than the threshold values required by Canadian Food Inspection Agency and as such, they also meet the criterion for making a claim that the food "contains" or "is a source of" the mineral or vitamin in question[120].

Although there is no evidence, based on the current available literature, to suggest that a single dietary supplement dosage threshold of 200 mg calcium and 100 IU vitamin D, would be sufficient to provide a threshold dose for "adequate calcium and vitamin D throughout life", one can assume that a supplement or food item containing this amount would be consumed in the context of other dietary and supplement sources, so it is also reasonable to make the claim as outlined above. On the other hand, it is difficult to make the same assumption regarding a source that contains only 65 mg calcium and 0.8-1.0 mcg vitamin D. Therefore, the committee would favour raising the minimum standard for supporting the NHPD osteoporosis claim to that of the FDA (20% of the RDI for vitamin D and calcium).

## ***7. Bioavailability and Co-Fortification***

***Context (provided by Health Canada):***
***Currently in Canada, guidance is not provided to the food industry on the forms of vitamin D and calcium that may be added to foods.***

***Questions on Vitamin D and Calcium Bioavailability and Co-Fortification:***

**Q 7.1 - Are there concerns regarding bioavailability that would lead to recommendations regarding specific forms of vitamin D and/or calcium to be used in foods or in supplements?**

Vitamin D

The issues with respect to fortification of food with vitamin D relate to 1) bioavailability including the absorbability from the food (does the amount of fat contained in the food alter absorption since vitamin D is fat soluble); and 2) the biopotency of vitamin D2 (ergocalciferol derived from fungal, i.e. mushroom and yeast sources) versus vitamin D3 (cholecalciferol derived from animal sources).

1) Bioavailability from various foods: As detailed in the IOM on page 83-84, vitamin D is dependent upon the presence of fat in the lumen and subsequent steps in fat digestion and absorption [25]. Thus, vitamin D absorption is known to be impaired in clinical conditions of fat malabsorption (e.g. cystic fibrosis) and with use of weight-loss agents that block fat absorption. The quantity of dietary fat needed to be present for a given "dose" of vitamin D is not known.

There is evidence than in addition to milk, fortification of foods such as orange juice [121] and cheese [122] may offer effective vehicles for dietary vitamin D. Overall food fortification has worked to improve vitamin D status as shown by a systematic review analysis by O'Donnell S. et al. [123].

The bioavailability of vitamin D from orange juice, as measured by serum 25(OH)D response, was similar to that from whole and skim milk and corn oil on toast [121]. However, the dose delivered was 1000 IU whereas the current level of fortification of vitamin D in orange juice in Canada is 400 IU/L. In a RCT in healthy adults (although 60% of subjects had serum 25(OH)D concentrations <60 nmol/L), D2 (ergocalciferol) and vitamin D3 (cholecalciferol) were shown to be equally bioavailable in orange juice and capsules [124]. Also, no differences in serum PTH were observed between groups. It is unclear, however, whether the trial may have had the statistical power to be meaningful. A recent meta-analysis concluded that a substantial difference exists [125].

Cheese proved to be a good vehicle for vitamin D fortification in a study in human adults randomized to weekly servings of fortified cheddar cheese (34 g; n = 20); fortified low-fat cheese (41 g; n = 10); liquid vitamin D supplement (1 mL), taken with food (n = 20) or without food (n = 10); placebo cheddar cheese (n = 10); or placebo supplement (n = 10). The response in serum 25(OH)D was similar across treatment groups and greater than in the placebo group [122]. Also, compared with baseline, serum parathyroid hormone decreased with both fortification (P = 0.003) and supplementation (P = 0.012). Based on the data reviewed, vitamin D is bioavailable from fortified hard cheeses and orange juices in similar amounts to supplements, making these foods suitable for vitamin D fortification.

Other fortified foods are currently available in the USA without supporting publications that are available to the public (presumably information was presented to the FDA). Such foods include fortified yogurt (as opposed to yogurt made with fortified milk) and fortified cheese.

Of particular note, there are several new products on the market in the USA: yeast products such as bread made from irradiated yeast, and irradiated mushrooms. Requests to allow these foods in Canada have been made. The irradiated mushrooms are considered equivalent to wild mushrooms, as irradiation by ultraviolet B (UVB) can occur naturally, e.g., in shitake mushrooms. Vitamin D2 is made during irradiation of mushrooms [126]. A serving of portabella mushrooms without light exposure contains very little natural vitamin D2 - approximately 0.3 µg (12 IU) in 100 g of raw mushroom. A serving of UV light-exposed portabella mushrooms can supply a fixed amount of vitamin D2, for example 11.5 µg (460 IU) of vitamin D2 in a serving by manipulating the length of time of UV exposure. This could represent an important natural food source of vitamin D2 for vegetarians and vegans. In vitamin D-deficient rats, vitamin D2-rich yeast baked into bread was shown to be bioavailable and to improve bone quality [127]. The second product is irradiated yeast, a process that was done originally to provide vitamin D for fortification purposes in the early twentieth century. The company Lallemande (www.lallemande.com) has a (patent pending) process to convert ergosterol

in the yeast to ergocalciferol (Vitamin D2) while allowing the baker's yeast to maintain leavening and flavour properties. Many different kinds of baked goods leavened with yeasts irradiated in this process may be produced, and these are in compliance with the regulatory levels of vitamin D allowed in grain products in the USA. According to Health Canada (personal communication to S. Whiting, August 2011), an Interim Marketing Authorization was published in February 2011, to permit the sale of bakery products containing vitamin D-enhanced yeast (90 IU vitamin D2/100g baked product). The Food Directorate at Health Canada would agree to the use of this source of vitamin D2 in other foods where addition of vitamin D is permitted, if yeast is an acceptable ingredient in that food.

2) The biopotency of the D2 versus D3 form of vitamin D has been variably reported as four-fold higher for D3 to equipotent [128]. In Canada, the D3 form is the primary source used in both food fortification and vitamin supplements.

Existing evidence on the relative biopotency of vitamin D3 and D2 in humans is conflicting as outlined in the IOM report ([25],p 92-93). In a very recent trial consisting of a single-blind, randomized design in 33 healthy adults dosed with 50,000 IU/wk of vitamin D supplement for 12 wk, a significantly greater rise in serum 25(OH)D3 than in serum 25(OH)D2 was observed [128]. This was computed as D3 being about 87% more potent than D2. This supports previous observations using high dose vitamin D supplementation [129]. Analysis of subcutaneous fat stores demonstrated a 2-3 fold greater storage of D3 compared to D2, with no evidence of sequestration of the vitamin in the fat. However, when lower doses of supplemental vitamin D (e.g. 1000 IU per day) were given [130], the response in serum 25(OH)D was not statistically different for D2 and D3. Nevertheless, with lower doses, the effect size was small, and fewer subjects were included, resulting in lower statistical power to detect changes. Just how this information on biopotency of the vitamin D forms can be translated to food fortification policy remains undetermined. Therefore, it appears reasonable to continue to recommend vitamin D3 over vitamin D2 as the preferred chemical form for use in fortified foods and supplements. However, in the marketplace there are vegan sources of D2 (e.g. soy beverages fortified with vitamin D2), and there should be consideration of new sources that might appeal to those seeking non-animal sources of D which either are either made with irradiation of yeast or with addition of a chemical source of vitamin D2.

As there are two sources of vitamin D i.e. animal –derived vitamin D3 and yeast –derived vitamin D2, the need to distinguish vitamin D3 from vitamin D2 on a label may arise. Currently, the practice for fortification of milk, margarine and selected yogurts display the form of vitamin D, i.e. D3, clearly on the label. For plant-based beverages that are fortified with vitamin D2, again, this form is clearly identified on the label. There is divided opinion about the use of vitamin D2. In a commentary as well as in a recent book chapter [131, 132], Vieth argued that all use of vitamin D should be as D3 based on differences in their efficacy at raising serum 25(OH)D, diminished binding of vitamin D2 metabolites to vitamin D binding protein in plasma, and differences in their metabolism. On the other hand, the Vegan Society recommends its own supplement which contains 400 IU of vitamin D2 [133], and has put vitamin D3 on its "Animal-derived or possibly animal-derived substances" list. Similar advice (to use vitamin D2) is found at another vegan site [134]. Thus, consumers may feel they have the right to know the source of the vitamin D in the fortified food or supplement, whether to avoid vitamin D2 as being "unnatural" or to seek it as a non-animal source.

Summary and Recommendations - Vitamin D

Based on current evidence, fortification with vitamin D in several foods – milk, cheese, orange juice - appears to yield similar bioavailability as evidenced by response in vitamin D status in adults. Demonstration of differences in biopotency of D3 versus D2 is inconsistent and only demonstrated at very high intake levels of supplements when D3 appears more potent. Consideration for inclusion of vitamin D2 should be given due to D2 being a preferred source for vegans and also the emerging availability of higher vitamin D content in mushrooms and yeast through irradiation producing vitamin D2. It would be important to provide clear labelling of the form of vitamin D and the quantities in order to allow those who prefer not to consume animal products to make their choice.

Calcium

Calcium absorption from milk-based products is usually about 25-35% in adults. Absorption of calcium in the form of the insoluble calcium carbonate or various organic sources is similar to that from milk [135]. However, some calcium salts such as calcium citrate malate may be more available in moist foods and beverages [136]. Nevertheless, they are more expensive than other salts such as calcium carbonate and tricalcium phosphate. When added to commercially marketed calcium-fortified (500 mg dose) orange juices in a cross-over study in 25 healthy pre-menopausal women, calcium citrate malate was more bioavailable that the combination of tricalcium phosphate and calcium lactate (tricalcium phosphate/calcium lactate) as measured by a rise in serum calcium [137].

Plant-based products such as soy may require higher amounts of calcium to be added due to lower absorption caused by mineral-phytate interactions [137]. Calcium absorption from calcium-fortified soy beverages using tricalcium phosphate as the source of calcium is 75% of the calcium absorbed from cow's milk [138]. Using an in vitro beverage scoring system, defining 100 for the beverage with the maximum absorbability of calcium (cow's milk= 99.5), three soy beverages scored between 57.5 and 70.6 [139]. Products using calcium carbonate are equivalent to cow’s milk [140].

Fortification of some foods may change the appearance or taste and thus consumer acceptance of the foods. In a study using all-purpose wheat-flour tortillas fortified with calcium lactate, calcium carbonate, or calcium citrate (114 mg elemental calcium per standard serving [48 g tortilla]), consumers found some differences in appearance and aftertaste of fortified and non-fortified tortillas but (this) did not influence their willingness to purchase the fortified tortillas [141].

Summary and Recommendation - Calcium

Based on the available research, bioavailability of calcium varies with type of calcium salt and type of food that is the carrier, primarily being lower from plant than animal based foods. Thus, criteria for the amount and type of calcium salts used in fortification are recommended.

**Q 7.2 - Are there concerns regarding bioavailability that should lead to specific dietary advice to enhance absorption?**

Calcium absorption is highly regulated according to need (reviewed the IOM report [25], p 40-42). As a % of intake, absorption is higher in infancy and childhood compared to older ages, and rises in pregnancy to support fetal needs. For most calcium taken as a supplement, it is best to not exceed 500 mg per dose and to take the supplement (if it is a carbonate salt) with meals[142]. Calcium citrate appears to be better absorbed than calcium carbonate in achlorhydric patients and in those on proton pump inhibitors [42, 136]. Food, which may stimulate acid secretion, should make calcium carbonate sources more available especially to older adults. Calcium as citrate may be more effective than calcium as carbonate in suppressing parathyroid hormone (PTH) and bone resorption when taken without foods [143], however in these studies, the calcium supplements were not administered with food. Overall, calcium supplements, and in particular calcium carbonate, should be administered with food to facilitate absorption.

**Recommendations for Q 7.2**

Some advice should be provided about the amount of calcium per dose of supplement and whether it is best taken with or without foods or beverages.

**Q 7.3 - When considering addition of calcium or vitamin D to foods should co-fortification be required always, i.e., should it be necessary to add calcium when vitamin D is added and vice versa?**

For bone health, from a functional standpoint it is best to have both calcium and vitamin D together. However, calcium requirements, but not necessarily D requirements, appear to be met by Canadian men, in part likely due to higher food intakes [144]. Furthermore, it may be generally more difficult to meet the new vitamin D RDA of 600 to 800 IU daily than the calcium requirements of 1000 to 1300 mg daily. Consequently, although calcium fortified food should have co-fortification with vitamin D, consideration should also be given to fortification with vitamin D alone. Vitamin D fortification might not be subject to restrictions of taste for example, which could limit calcium addition to some foods.

## Other

***8. Risk communication strategies***

***Context provided by Health Canada:***

***Government information must be broadly accessible throughout society. A variety of ways and means to communicate are available to provide the public with timely, accurate, clear, objective and complete information about policies and programs.***

***Question on Risk Communication Strategies:***

**Q 8.1 - What educational strategies or risk communication strategies should be considered when the policy approaches are decided on?**

As part of a comprehensive communication and behaviour change campaign for adhering to recommended daily intake of Calcium and Vitamin D, a risk communication plan needs to be an integral component. At a minimum, this would include:

a) A situational assessment regarding who (individual, sub group, community) is most at risk from under/over utilization of Calcium and Vitamin D.
b) Preventive strategies to address the vulnerable sub groups.
c) An evaluation plan including measurable outcomes and quality improvement cycle.

Various organizational and audience constraints can have major impact on the effectiveness of health communication and behaviour change. According to Lundren and McMakin[145] organizational constraints can include:

- Inadequate resources
- Management hostility or apathy
- Difficult review or approval processes
- Conflicting organizational requirements
- Insufficient information to adequately plan and set schedules
- Managements unwillingness to see the public as an equal partner
- Managements unwillingness to acknowledge the feelings and values of the public
- Managements belief that the public cannot understand science

Similarly, audience constraints can include:

- Hostility and/or outrage
- Apathy
- Mistrust of risk assessment
- Expert disagreements on acceptable magnitude of risk
- Mistrust in the responsible organization

A recent review of the literature and interviews with 29 leading scholars and practitioners, compiled by the Heath Communication Unit, concludes that a successful campaign must comprise seven distinct steps or tasks[146]. The following list summarizes these results.

1) *Get Started: Revisit Your Health Promotion Strategy*
    a. involve key power figures and groups in mass media organizations and in government bodies in its design and implementation
    b. use commercial marketing and social marketing strategies to increase effectiveness

2) *Audience Analysis and Segmentation*
    a. carefully target or segment the audience you intend to reach
    b. segment audiences using psychographic variables based on attitudes, values and beliefs, since demographic segmentation has been found to be relatively ineffective
    c. use formative evaluation techniques to appraise and improve approaches during planning and in implementation
    d. use pretesting to ensure messages have the expected effects on priority audiences
    e. address the existing knowledge and beliefs of priority audiences that are impeding adoption of desired behaviours

3) *Set Goals and Objectives*
    a. set fairly modest, attainable goals for behaviour change
    b. address the larger social, structural and environmental factors influencing the health problems being addressed by the campaign or activity

4) *Select Channels and Vehicles*
    a. use multiple media (TV, radio, print, etc.)
    b. combine mass media approaches with community, small group and individual activities
    c. use celebrities to attract public attention to a health communication issue
    d. embed a health communication message in an entertainment program
    e. coordinate with direct service delivery components (e.g., hotline numbers for information or counselling) so that immediate follow through can take place if behaviour change begins to occur
    f. direct messages to people linked to the priority audience, especially those with interpersonal influence such as peers and parents
    g. choose positive role models for social learning carefully, as these individuals may become negative role models through their actions
    h. combine public service announcements (PSAs) with other campaign activities since PSAs alone generally do not effectively bring about behaviour change
    i. use the news media as a means of increasing visibility
    j. use government as a source of funding and appropriate leadership on controversial issues

5) *Combine and Sequence Your Activities*
    a. repeat a single message
    b. carefully consider timing (e.g., when health communication activities are introduced, what other events are happening during their implementation, etc.)

*6) Develop the Message*

a. emphasize positive behaviour change rather than the negative consequences of current behaviour (fear arousal is rarely successful as a campaign strategy)
b. couple fear appeals (when used) with mechanisms for reducing the anxiety they create
c. emphasize current rewards rather than the avoidance of distant negative consequences
d. communicate incentives or benefits for adopting desired behaviours that build on existing motives, needs and values of the priority audiences
e. focus priority audiences' attention on immediate, high probability consequences of healthy behaviour

*7) Complete Campaign*

a. make deliberate efforts to resolve potential conflicts between evaluation researchers and message creators

***9. Clinical Standards for 25(OH)D Levels***

***Context provided by Health Canada:***

***On page S-11 of the Summary, the IOM Committee Report states:***

***"Serum levels of 25(OH)D have been used as a measure of adequacy for vitamin D, as they reflect intake from the diet coupled with the amount contributed by cutaneous synthesis. The cutpoint levels of serum 25(OH)D intended to specify deficiency for the purposes of interpreting laboratory analyses and for use in clinical practice are not specifically within the charge to this committee. However, the committee noted with some concern, that serum 25(OH)D cut-points defined as indicative of deficiency for vitamin D have not undergone a systematic, evidence-based development process.***

***"From this committee's perspective, a considerable over-estimation of the levels of vitamin D deficiency in the North American population now exists due to the use by some of cut-points for serum 25(OH)D levels that greatly exceed the levels identified in this report as consistent with the available data. Early reports specified a serum 25(OH)D concentration of at least 27.5 nmol/L as an indicator of vitamin D adequacy from birth through 18 years of age, and a concentration of at least 30 nmol/L as an indicator of vitamin D adequacy for adults 19 to 50 years of age. In recent years, others have suggested different cut-points as determinants of deficiency and what has been termed "insufficiency." In the current literature, these include values ranging from less than 50 nmol/L to values above 125 nmol/L. Use of higher than appropriate cut-points for serum 25(OH)D levels would be expected to artificially increase the estimates of the prevalence of vitamin D deficiency.***

***"The specification of cut-points for serum 25(OH)D levels has serious ramifications not only for the conclusions about vitamin D nutriture and nutrition public policy, but also for clinical practice. At this time, there is no central body that is responsible for establishing such values for clinical use.***

***"This committee's review of data suggests that persons are at risk of deficiency at serum 25(OH)D levels of below 30 nmol/L (12 ng/mL). Some, but not all, persons are potentially at risk for inadequacy at serum 25(OH)D levels between 30 and 50 nmol/L (12 and 20 ng/mL). Practically all persons are sufficient at serum 25(OH)D levels of at least 50 nmol/L (20 ng/mL). Serum 25(OH)D concentrations above 75 nmol/L (30 ng/mL) are not consistently associated with increased benefit. There may be reason for concern at serum 25(OH)D levels above 125 nmol/L (50 ng/mL).***

***"Given the concern about high levels of serum 25(OH)D as well as the desirability of avoiding mis-classification of vitamin D deficiency, there is a critical public health and clinical practice need for consensus cut-points for serum 25(OH)D measures relative to vitamin D deficiency as well as excess.***

***"The current lack of evidence-based consensus guidelines is problematic and of concern because individuals with serum 25(OH)D levels above 50 nmol/L (20 ng/mL) may at times be classified as deficient and treated with high-dose supplements of vitamin D containing many times the levels of intake recommended by this report."***

***At least one clinical laboratory in Ontario currently uses 75 nmol/L as the standard for adequacy.***

***Questions on Clinical Standards for 25(OH)D Levels:***

**Q 9.1 - What is the most appropriate process by which these cut-points should be established?**

The appropriate reference range (both the lower limit and the upper limit) for any laboratory test comprises the values that minimize evidence of ill health. The latest IOM report concluded that a serum 25(OH)D level of 40 nmol/L was consistent with the median requirements and that 50 nmol/L coincides with the level that would cover the needs of 97.5% of the population [25]. However, those values were determined partly based on placebo-controlled clinical trials of reduction in bone fractures which were interpreted as showing no further reduction in fracture incidence could be attributed to vitamin D when 25(OH)D was above 50 nmol/L. The IOM report also placed emphasis on a study identifying histologic evidence of osteomalacia in autopsy-obtained bone biopsies and blood specimens for 25(OH)D, which the IOM interpreted as showing that 97.5% of the histological evidence of osteomalacia occurred below 50 nmol/L and 50% below 40 nmol/L [81]. Other studies, such as those associating 25(OH)D levels with serum PTH levels were felt to be too inconsistent or lacking to be helpful. However, parameters such as increased serum PTH would be expected to occur earlier in the evolution of vitamin D (and 25(OH)D) deficiency than fractures and osteomalacia, and the latter would only be expected to occur at later stages of vitamin D deficiency. If absence, in 97.5% of the general population, of clinical manifestations of severe deficiency such as rickets, osteomalacia or fractures is to be accepted as the definition of adequate intake, then 50 nmol/L seems to be an appropriate conservative target. However, absence of a clinical deficiency state does not necessarily define a desirable level for optimal health.

Even if we accept that 50 nmol/L (see discussion in Q9.4) would be an appropriate cut-point for serum 25(OH)D in relation to skeletal health, a substantial number of Canadians still fall below that level. The current increased interest in vitamin D and use of vitamin D supplements probably has resulted in higher 25(OH)D levels than what has been documented in studies done in the late 1990's or earlier in this century. However a recent published report using CHMS data still found that 25% of the population fell below 50 nmol/L [61].

The current recommended cut-offs for 25(OH)D of 40-50 nmol/L therefore seem based on levels to prevent or treat disease, i.e. rickets, osteomalacia and osteoporotic fractures. Establishing thresholds of vitamin D to prevent these diseases before they become manifest would ideally be more helpful. We should therefore be supporting studies to better define the 25(OH)D levels required to prevent the antecedents of these diseases e.g. the relationship between vitamin D intake and calcium absorption, the development of secondary hyperparathyroidism, bone resorption, or other biomarkers which may antedate and predict optimal bone health. Additionally, in view of the increasing diversity of the Canadian population and the increasing proportion of non-Caucasians, we should also attempt to better define the current levels of 25(OH)D in subgroups referred to in question 4 above to determine where they stand with respect to the current cut-offs and what the implications for skeletal outcomes are in these populations. For example: The relationships between 25(OH)D, bone mineral density (BMD), and PTH have been reported to differ by race among US adults, suggesting that race-specific ranges of optimal 25(OH)D may be needed to appropriately evaluate the adequacy of vitamin D stores in minorities [147]. African-Americans and Asians have lower levels of 25(OH)D than white Americans,

yet have lower annualized rates of fractures [148]. Additionally there are many questions with respect to optimal calcium intake, and it is frequently difficult to dissociate vitamin D effects from calcium effects. For example, in one small study, dietary calcium absorption appeared to be more efficient in Inuit children with low dietary calcium intake, but was associated with an increased frequency of hypercalciuria [149]. The authors concluded that this may represent a genetic adaptation (possibly related to polymorphisms of the vitamin D receptor) to dietary constraints and may predispose to nephrolithiasis or nephrocalcinosis if standard nutritional guidelines are followed. The relationship of calcium intake to other untoward events also warrants further study.

We would suggest a committee of experts be formed to develop a vitamin D (and possibly a calcium) research plan and set priorities for the research questions to be answered in developing clinical standards. This committee would include, but not be restricted to representation from government, from the academic sector, learned societies of health professionals, and industry. The aim of the committee would be to establish a research agenda. One primary area of interest would be to establish a reference range for 25(OH)D not based on apparently healthy people, but rather a reference range for 25(OH)D with the primary prevention of chronic disease as its goal. Early and sub-clinical disturbances in metabolism may have many long-term implications for chronic disease.

**Q 9.2 - Which parties should be involved in this process and what should their roles be?**

The outcome of any committee hinges largely on who is selected to be on that committee. Ideally, an objective committee should be struck, containing experts reflecting a diversity of opinion, but with willingness to compromise to achieve a meaningful consensus. These should be individuals who are knowledgeable about vitamin D and calcium metabolism and who have expertise in pertinent disciplines: clinical biochemistry and physiology; statistics and epidemiology; clinical medicine and nutrition; and public policy, and who would be able to address the issues of ethnic and geographic diversity which are prevalent in Canada. Consequently, either Health Canada, the Public Health Agency of Canada, or the Canadian Institutes of Health Research should take the lead in this regard. The committee to address this topic should include representatives from the Canadian Academy of Health Sciences, societies of health professionals such as the Canadian Society of Endocrinology and Metabolism, the Canadian Society of Nephrology, the Canadian Nutrition Society, the Dietitians of Canada, the Canadian Paediatric Society, the Canadian Society of Clinical Chemists and the Canadian Public Health Association, and from groups such as Osteoporosis Canada which could represent lay opinion. This committee should include representatives from industry because of their importance in providing vitamin D fortification and supplementation. It would also be extremely important to have experts in health policy included.

**Q 9.3 - Should efforts be made to establish a common standard with the US?**

Although this seems logical, it is not essential. It would clearly be advantageous to establish comparable 25(OH)D cut-off values in terms, for example, of having similarly fortified North American food products and supplements to reach those values and in terms of developing similar clinical guidelines and public health messaging. The disadvantages of common standards are largely due to real differences in demographics, with very different risk profiles and in particular different

high-risk populations. The northern climate and higher latitude lead to long periods of limited cutaneous synthesis of vitamin D among all Canadians. The demographics specific to Canada are First Nations, Metis and Inuit communities living in remote northern locations who are experiencing a period of dietary transition and growing multi-ethnic communities living in the major metropolitan areas with a high percentage of recent immigrants from geographically diverse locations, while the demographics specific to the United States are their larger minority black and Hispanic population. As noted earlier in the report, skin-color and cultural dietary practices all impinge on levels of 25(OH)D, but consequent risk of chronic disease, including fracture might also be different. Nevertheless, although the impact of similar levels of 25(OH)D in different ethnic groups may be different, it is unlikely that it would be practical or even desirable to establish different clinical reference ranges for different ethnic groups. Consequently despite the different demographics and other issues mentioned, interaction with the US in establishing clinical reference standards for 25(OH)D would be a pragmatic approach.

**Q 9.4 - In the absence of an agreed-upon cut-point, what threshold cut-off value should be used (e.g., 40 or 50 nmol/L) by Government agencies when examining the distribution of serum concentrations of vitamin D in order to assess adequacy of vitamin D status in Canada?**

The RDA equivalent of 50 nmol/L and EAR of 40 nmol/L, proposed by the IOM report, were based on cross-sectional data [81]. A serum 25(OH) D value of 50 nmol/L was regarded by the IOM as a level above which only 2.5% of the population would be regarded as insufficient in vitamin D, and 40 nmol/L was regarded as the value above which 50% of the population would be regarded as sufficient [25]. The study on which these values were derived however has been highly controversial [150] and to date no official body, including the US government has adopted 40 nmol/L as a cut-off for population assessment. The EAC recommends that 50 nmol/L would be appropriate to be used by Government agencies when examining the distribution of serum concentrations of vitamin D in order to assess adequacy of vitamin D status in Canada.

This is based upon the following rationale:

1) There is an on-going debate as to whether 50 or 75 nmol/L is an appropriate level to aim for to achieve vitamin D sufficiency. Expert groups such as the International Osteoporosis Foundation [151] and the new guidelines of the Endocrine Society [152] seem willing to accept the value of 50 nmol/L for the general population but emphasize that if a person is at risk for vitamin D deficiency or has a condition that would be worsened by vitamin D deficiency, then a clinical target 25(OH)D level of >75 nmol/L would be more appropriate, and certainly safe. Others, including Osteoporosis Canada, favour a minimum threshold for health of 75 nmol/L [87]. The Standing Committee of European Doctors or Comité permanent des médecins Européens (CPME) in a statement on "Vitamin D nutritional policy in Europe" concluded that "the greatest risk for bone and several major human diseases and preventable human health conditions are associated with 25(OH)D levels below 20 ng/ml (or 50 nmol/L)" [153].

Just as important as the decision regarding the value per se, is the type of evidence that is allowed for consideration. The IOM preferred placebo-controlled clinical trials as the basis for a health effect, but eventually accepted cross-sectional data to derive the levels of 25(OH)D corresponding to the EAR and RDA of vitamin D intake. Thus, the evidence applied to the derivation was not based on all possible outcomes, but to the narrow group consisting of those with RCT trials, or those with

concurrent association with identifiable phenotypes. The data for evidence of early disturbances in bone mineral metabolism and likely precursors of clinical outcomes was regarded in general as insufficient.

2) While the IOM reported that 40 nmol/L was consistent with an EAR type reference value, we know of no governmental or non-governmental agency outside the IOM committee that has adopted this value as a cut-off value for assessing population prevalence of deficiency. The IOM report points out that there seems little evidence of widespread vitamin D deficiency given an apparent median requirement level for serum 25(OH)D of 40 nmol/L compared to an average U.S. population serum 25(OH)D of slightly over 50 nmol/L, but also recommended that discussions be held about the proper statistical approach to be used in determining prevalence levels of inadequacy for vitamin D given that the measure in question is a serum value rather than an estimate of intake. In a recent report, the US Center for Disease Control (CDC) determined on its own to use a cut-point of 50 nmol/L, declaring sufficient based on the use of that cut-point, while those between 30 and 50 nmol/L were "at risk of insufficiency" and those below 30 nmol were "at risk of deficiency" [154].

The following is an excerpt of a personal communication with Drs. C Taylor and C Rosen of the IOM: "The IOM report does indeed state that 40 is consistent with the median requirement, and that 50 covers approximately 97.5% of the population. The U.S. government has no official position at this point on vitamin D, but has in the past used the median intake value with the statistical algorithm and not a cut-point for estimating prevalence of inadequacy for other nutrients. However, because the median value in the case of 25(OH)D is a biomarker of nutrient status for vitamin D rather than an estimate of vitamin D intake, there is some concern as to how to proceed statistically. The NIH is considering a workshop to address this. The controversy became magnified recently when others in the government (as well as members of the IOM committee on vitamin D) have expressed concern about CDC's using a cut-point rather than the statistical algorithm and the median value [154]. Thus the derivation of 40 nmol/L as the 25(OH)D level corresponding to the EAR for vitamin D intake does not follow DRI terminology which should be the amount of the nutrient intake i.e. dietary vitamin D to bring 50% of the population to vitamin D sufficiency.

3) The IOM-derived upper level for serum 25(OH)D of 125 nmol/L is sufficiently high to provide a good margin of safety even if 50 rather than 40 nmol/L is taken as the threshold cut-off value. While 75 nmol/L might be an appropriate minimum level of 25(OH)D for a physician to advise for patients at risk or being treated for osteoporosis or other conditions made worse by low levels of 25(OH)D, the principles for medical care are different from the considerations for public guidance; thus a more conservative view point is needed for population intervention. The 25(OH)D level of 50 nmol/L, corresponding to the RDA for vitamin D intake is therefore seen as a good first step for guidance to the public.

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