

Longitudinal changes in calcium and vitamin D intakes and relationship to bone mineral density in a prospective population-based study: the Canadian Multicentre Osteoporosis Study (CaMos)

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Abstract

Objectives: Our objective was to study changes in calcium and vitamin D intakes over time, and their cross-sectional and longitudinal associations with bone mineral density (BMD). **Methods:** We followed 9382 women and men aged ≥ 25 and 899 aged 16-24, for 10 and 2 years respectively. **Results:** Calcium and vitamin D intakes increased over time in adults, but decreased in women aged 16-18. The increased intakes in adults were largely attributable to the increased use of calcium and/or vitamin D supplements. Both the percentage of supplement users and average dose among users increased over time. There was nevertheless a high prevalence of calcium and vitamin D intake below the estimated average requirement. At baseline, higher calcium and vitamin D intakes were associated with higher total hip and femoral neck BMD in young men, and cumulatively high levels of calcium and vitamin D intakes over time contributed to better BMD maintenance at lumbar spine and hip sites in adult women. **Conclusions:** Although total intakes, particularly of vitamin D, frequently fell below the Institute of Medicine recommendations despite an increase over time in supplement use, we found some positive associations between total calcium and vitamin D intake and bone health.

Keywords: Calcium, Vitamin D, Intakes, BMD, Longitudinal

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Introduction

Calcium and vitamin D are essential nutrients for maximizing peak bone mass, retaining acquired bone mass, preventing bone loss in later life, and thus potentially reducing the risk of osteoporosis¹⁻⁴, which is a growing health and economic problem in Canada and in other countries.

Calcium and vitamin D intake is not only associated with prevention of osteoporosis and fractures, but it also affects general health and well-being^{2,5,6}. Low calcium intake has been implicated in the development of hypertension, colon cancer

and premenstrual syndrome². Vitamin D promotes the absorption of calcium and enhances bone mineralization⁷. Vitamin D deficiency may be associated with increased risk of diabetes, multiple sclerosis, rheumatoid arthritis, autoimmune diseases, hypertension and cardiovascular heart disease, and many common cancers^{5,6,8,9}, although to date randomized trial evidence supporting these associations is lacking. However, recent meta-analyses suggested that calcium supplements may be associated with cardiovascular risks¹⁰ and high annual dose of oral vitamin D may increase the risk of falls¹¹ and fractures¹², although there are limitations of evidence.

In 2011, the Institute of Medicine (IOM) Committee released new Dietary Reference Intakes (DRI) for calcium and vitamin D¹. Previous recommendations for both of these nutrients had been Adequate Intakes (AI), which were set when the distribution of the requirements across the population could not be ascertained¹³. The AI represented a recommended intake for individuals, which was thought to be adequate to meet the needs of most members of a population group. However, it could not be used to determine the prevalence of 'adequate' or 'inadequate' intakes in terms of meeting requirements. In 2011, the IOM established Estimated Average Requirements (EAR) and Recommended Dietary Allowance (RDA) for calcium (from diet plus supplements) and for total oral intake of vitamin D (from diet and supplements). Identifying an EAR meant that it was theoretically possible to assess the prevalence of dietary adequacy/inadequacy for these nutrients, although it was recognized that the confounding contribution of sunlight exposure meant that vitamin D adequacy might be more appropriately assessed using the surrogate measure of serum 25 hydroxyvitamin D [25(OH)D] inasmuch as 25(OH)D concentrations in serum appear to provide the best integrated measure of vitamin D from both cutaneous and dietary sources.

The calcium and vitamin D intakes of Americans have been reported using data from the National Health and Nutrition Examination Survey (NHANES) over the past several decades. However, until the Canadian Community Health Survey Cycle 2.2 (CCHS 2.2) was conducted in 2004¹⁴, no nationally-representative data on Canadians' intakes had been collected since the Nutrition Canada survey in the early 1970s¹⁵, although provincial surveys had been conducted between 1990 and 1999. Vatanparast et al. reported the calcium intake from food in Canadian adults in these surveys¹⁶, and indicated that the mean calcium intake in Canadians appeared to have increased modestly over time, but remained below recommended intakes, despite fortification and supplement use. Although the prevalence of inadequacy could not be assessed at that time, inspection of the CCHS data relative to the 2011 IOM EAR indicated a high prevalence of inadequacy in most age/sex groups based on intake from food sources. Longitudinal data on changes in intake and the prevalence of vitamin D and calcium supplement use are not available for Canadians, although longitudinal data on serum 25(OH)D levels have been recently reported¹⁷.

Therefore, the objectives of this study were to describe calcium and vitamin D intakes and their longitudinal change in a population-based prospective cohort of both youth and adults,

as well as to compare calcium and vitamin D intakes against the 2011 IOM EAR. We also examined the association between calcium and vitamin D intakes and bone mineral density (BMD), an important parameter of bone health and fracture risk.

Methods

The Canadian Multicentre Osteoporosis Study (CaMos) consists of both an adult and a youth cohort. The adult cohort was recruited in 1995-1997, and included 9423 women and men aged 25 and older living within 50 km of one of nine CaMos study centres: Vancouver, Calgary, Saskatoon, Hamilton, Toronto, Kingston, Quebec City, Halifax, and St. John's. In 2004-2006, the CaMos youth cohort was recruited: 1001 women and men aged 16-24 years. The sampling frame and recruitment strategy used to recruit both cohorts were similar and are described elsewhere^{18,19}. Briefly, households were randomly selected from a list of residential telephone listings, and one eligible participant was randomly selected from each household, using a sex- and age-stratified design. Data collection at baseline employed an extensive interviewer-administered questionnaire which included socio-demographic information, medical and fracture history, family history of osteoporosis and fractures, physical activity, tobacco smoking, use of medications and supplements, and food intake. Clinical assessments included height, weight, and BMD by Dual-energy X-ray absorptiometry (DXA). Ethics approval for the study was obtained from the ethics review board at each institution involved in the study, and all participants, as well as at least one parent for those under 18 years of age in the youth cohort, gave written informed consent in accordance with the Helsinki declaration. Year 5 (2000-2002) and 10 (2005-2007) follow-ups of the adult cohort as well as Year 2 (2006-2008) follow-up of the youth cohort, included again an extensive interviewer-administered questionnaire with clinical measurements of height, weight and BMD.

This study included 9382 (6518 women and 2864 men) participants aged 25 years and older and 999 (526 women and 473 men) young participants aged 16 to 24 years, all with available baseline calcium or vitamin D intakes. At Year 10 follow-up of the adult cohort, there were 3999 women and 1570 men in the sample; and at Year 2 follow-up of the youth cohort, there were 395 women and 347 men in the sample.

Calcium and vitamin D intake

Details related to food and supplement data collection were previously reported^{17,20}. Briefly, information on dietary calcium intake was obtained from an interviewer-administered abbreviated semi-quantitative Food Frequency Questionnaire (FFQ), which was completed at baseline, Year 5 and Year 10 for the adult cohort and at baseline and Year 2 for the youth cohort. The semi-quantitative FFQ queried "how often, on average, have you eaten the following items during the last 12 months?" and included only the foods considered to be major sources of calcium. To improve reporting at the time of the interview, the interviewers were provided with food models to

assist participants in estimating the portion size of each food. Dietary vitamin D intake was estimated from reported usual intake of vitamin D-fortified fluid milk, fortified soya beverage (adult Year 10, youth baseline & year 2), and fortified yogurt (adult Year 10 and youth year 2). Note that yogurt was not vitamin D-fortified in Canada until just before our Year 10 examination in this study. An estimate of calcium and vitamin D intake from non-food sources was obtained from a direct inventory (from bottle or package labels) of all medications and supplements. Regarding vitamin D supplement use, although almost all vitamin D supplements in Canada are vitamin D3 (in contrast to the USA, where most are vitamin D2), the type of vitamin D was not always included in the database and precluded us from obtaining the exact proportion of Vitamin D2 versus Vitamin D3 use.

Bone Mineral Density (BMD)

BMD was measured at the lumbar spine (L1-L4), femoral neck, and total hip by DXA using Hologic QDR (Marlborough, MA, USA) 1000, 2000, or 4500 or Lunar DPX (Piscataway, NJ, USA) densitometers. At baseline for the adult cohort, two of the nine centres in CaMos used GE Lunar machines and seven used Hologic machines. At Year 10 for the adult cohort and in the youth cohort, five centers used GE Lunar densitometers, and four used Hologic densitometers. Longitudinal stability was monitored using a spine phantom, local to each centre. Lunar data were converted into equivalent Hologic values by standard methods²¹⁻²⁴. All densitometers were calibrated using the Bio-Imaging Bona Fide Phantom (Bio-Imaging Technologies, Newtown, PA, USA) circulated among centers. A detailed description of BMD quality control appears elsewhere²⁵. All measurements were re-analyzed centrally.

Statistical analyses

All analyses were done separately for the youth and adult cohort, and separately for women and men. Estimates of mean daily intakes for total calcium and total oral vitamin D were stratified by age into the following categories (youth: 16-18, 19-24; adult: 25-50, 51-70, >70 years old). The intake distributions were then compared to the age- and sex-specific EAR, to estimate the prevalence of intakes below requirements, and intakes above tolerable upper intake levels (UL)²⁶ were estimated as well. Longitudinal changes in calcium and vitamin D intakes were calculated by subtracting the baseline value from the last follow-up value (Year 10 for the adult cohort and Year 2 for the youth cohort) and dividing by the time between measurements. Therefore, increases are represented by positive values and decreases by negative values.

The distributions of total calcium and of total oral vitamin D intakes were not normal, thus categorical variables were used in the regression models. Daily calcium intake was stratified into the following categories (low: <600 mg, moderate: ≥600 and <1100 mg, high: ≥1100 and <1500 mg, and very high: ≥1500 mg). Daily vitamin D intake was stratified into the following categories [no intake, low intake: <5 µg (200 IU), moderate intake: ≥5 µg (200 IU) and <10 µg (400 IU),

high: ≥10 µg (400 IU)]. The moderate intake of calcium and low intake of vitamin D were used as reference categories. In the youth cohort there were very few participants with no intake of vitamin D and therefore “no intake” and “low intake” categories were combined into a single stratum.

Multivariable linear regression models were constructed to assess the baseline cross-sectional association between total calcium and total oral vitamin D intake with BMD, adjusting for potential confounders: age, height, body mass index, centre, cigarette use (yes/no), alcohol intake, cola intake, regular activity (yes/no), sedentary hours per day, personal history of fracture, family history of osteoporosis and fracture, inflammatory bowel disease, and antiresorptive use (adult cohort only). Each potential confounder was screened to assess its statistical and clinical importance, first using bivariate models and then in the full model. Baseline BMD estimates for associations with baseline total calcium and vitamin D intakes were adjusted for all the covariates, removing any for which there was little support for inclusion either clinically or statistically.

Multivariable linear regression models were also constructed to assess longitudinal associations between total calcium and vitamin D intake with BMD change over 10 year in adults and over 2 years in youth, adjusting for potential confounders. The main exposure variables were the average calcium and vitamin D intake. In the youth cohort the average intake was calculated from baseline and Year 2, and in the adult cohort the average intake was calculated based on the baseline, Year 5, and Year 10 measures. Average intakes were assessed by the same categories as baseline intakes described in the previous paragraph.

SAS (version 9.2) for Windows (Cary, NC) and R (version 2.13.0) were used for all analyses.

Results

Calcium intake

The mean daily intakes of calcium from all sources (diet and supplement) are presented (by sex, age, and time period) in Table 1, together with the longitudinal changes. In the youth cohort, the estimated annual change in dietary and total calcium intakes over two years differed by age and sex, with decreases noted in young women aged 16-18 and young men aged 16-24 although the 95% confidence interval (CI) for the latter estimates included zero. The decrease was mainly attributable to a decrease in milk consumption. In the adult cohort, total calcium intake increased over ten years in all sex and age groups, with estimated mean annual increase of 32 (95% CI: 29, 34) mg/day in women and 19 (95% CI: 15, 23) mg/day in men. Among women, small but statistically significant increases were found for calcium intake from diet alone, whereas for men, although slight increases were observed, the 95% CI for the estimates included zero except for men 25-50.

The overall prevalence of supplemental calcium use in CaMos was 35% at baseline, and increased to 52% at the last follow-up, paralleled with an increase in mean daily supplement dose among adult supplement users. Table 2 shows de-

Age (year)	Women			Men		
	n	Diet alone ¹	Total intake ¹	n	Diet alone ¹	Total intake ¹
Baseline						
16-18	206	1183 (49)	1189 (49)	201	1483 (61)	1487 (61)
19-24	317	975 (31)	988 (32)	271	1255 (46)	1262 (46)
25-50	1040	811 (15)	961 (18)	735	75 (21)	918 (23)
51-70	3447	790 (8)	1062 (11)	1345	817 (14)	906 (16)
71+	1915	776 (11)	1034 (14)	726	774 (18)	884 (21)
Youth Year 2						
18	49	909 (89)	956 (86)	42	1286 (113)	1338 (120)
19-26	346	1039 (35)	1101 (36)	305	1233 (47)	1267 (48)
Adult Year 10						
35-50	274	927 (33)	1147 (42)	202	1038 (64)	1150 (65)
51-70	1623	879 (13)	1353 (18)	708	840 (19)	1044 (24)
71+	2100	890 (12)	1416 (17)	660	821 (20)	1105 (25)
Change per year²						
Age at baseline	n			n		
16-18	167	-104 (-161, -47)	-85 (-143, -28)	149	-58 (-126, 10)	-42 (-113, 38)
19-24	225	13 (-32, 58)	42 (-6, 91)	197	-29 (-81, 23)	-16 (-68, 36)
25-50	816	8 (4, 12)	30 (24, 35)	484	8 (2, 15)	19 (12, 26)
51-70	2416	9 (7, 11)	34 (31, 37)	843	2 (-1, 6)	19 (14, 23)
71+	684	5 (1, 9)	24 (18, 30)	201	4 (-2, 11)	20 (11, 29)

¹ Data are mean (SEM).

² Data are mean (95% CI).

Note: The estimated average requirement (EAR) for calcium for women age 25-50 and men age 25-70 is 800 mg/day; and for women age 51+ and men 71+ is 1000 mg/day.

Table 1. Calcium intake (mg/day) from diet and all sources by sex and age group in the Canadian Multicentre Osteoporosis Study.

Age (year)	Women			Men		
	n	Users, ¹ %	Supplement, ² mg/day	n	Users, ¹ %	Supplement, ² mg/day
Baseline						
16-18	3	1.5 (0.9)	258 (123)	3	1.5 (0.9)	249 (76)
19-24	12	3.8 (1.1)	359 (97)	6	2.2 (0.9)	340 (179)
25-50	324	30.5 (1.4)	486 (24)	119	16.0 (1.3)	275 (30)
51-70	1623	46.4 (0.8)	587 (11)	342	24.9 (1.2)	362 (18)
71+	908	46.4 (0.8)	555 (13)	189	25.4 (1.6)	424 (31)
Youth Year 2						
18	8	16.3 (5.3)	284 (86)	4	9.5 (4.6)	541 (236)
19-26	58	16.7 (2.0)	367 (35)	48	15.7 (2.1)	219 (31)
Adult Year 10						
35-50	104	37.8 (2.9)	580 (44)	61	30.2 (3.2)	368 (49)
51-70	1073	66.1 (1.2)	718 (14)	280	39.5 (1.8)	516 (23)
71+	1406	67.0 (1.0)	786 (14)	319	48.3 (1.9)	589 (27)

¹ Data are percent (SEM)

² Data are mean (SEM)

Table 2. Prevalence of use and daily contribution for users of calcium supplements by sex and age group in the Canadian Multicentre Osteoporosis Study.

Age (year)	Women			Men		
	n	Diet alone ¹	Total intake ¹	n	Diet alone ¹	Total intake ¹
Baseline						
16-18	206	4.8 (0.3)	5.0 (0.3)	201	7.2 (0.4)	7.3 (0.5)
19-24	320	3.3 (0.2)	3.4 (0.2)	272	5.2 (0.3)	5.4 (0.3)
25-50	1061	2.6 (0.1)	4.9 (0.2)	746	3.3 (0.1)	5.4 (0.7)
51-70	3499	2.6 (0.1)	7.2 (0.3)	1373	2.9 (0.1)	5.1 (0.2)
71+	1958	2.7 (0.1)	7.7 (0.4)	745	2.9 (0.1)	5.3 (0.3)
Youth Year 2						
18	49	3.6 (0.5)	4.7 (0.7)	42	6.6 (0.8)	7.5 (1.1)
19-26	346	3.8 (0.2)	5.2 (0.3)	305	5.2 (0.3)	6.4 (0.4)
Adult Year 10						
35-50	275	2.7 (0.2)	6.6 (0.5)	202	4.1 (0.4)	7.1 (0.6)
51-70	1624	2.8 (0.1)	13.9 (0.5)	708	2.7 (0.1)	9.0 (0.7)
71+	2100	3.0 (0.1)	18.8 (1.0)	660	3.0 (0.1)	10.9 (0.7)
Change per year²						
Age at baseline						
16-18	156	-0.55 (-0.87,-0.23)	-0.22 (-0.62, 0.19)	145	-0.41 (-0.83, 0.00)	0.09 (-0.42, 0.60)
19-24	20	0.05 (-0.16, 0.27)	0.83 (0.45, 1.21)	190	-0.21 (-0.53, 0.10)	0.39 (-0.02, 0.80)
25-50	834	0.00 (-0.02,0.02)	0.53 (0.42, 0.65)	491	0.01 (-0.03, 0.04)	0.13 (-0.10, 0.36)
51-70	2453	0.03 (0.02, 0.04)	0.97 (0.84, 1.10)	860	0.00 (-0.02, 0.02)	0.53 (0.42, 0.65)
71+	700	0.03 (0.01, 0.05)	1.15 (0.73, 1.57)	207	0.03 (-0.01, 0.08)	0.53 (0.31, 0.74)

¹ Data are mean (SEM).

² Data are mean (95% CI).

Note: The estimated average requirement (EAR) for vitamin D for women and men age 25+ is 10 µg/day.

Table 3. Vitamin D intake (µg/day) from diet and all sources by sex and age group in the Canadian Multicentre Osteoporosis Study.

tailed use of supplements by sex and age group. The prevalence of calcium supplement intake was higher in women vs. men, and higher in older vs. younger age groups. At baseline, the prevalence of supplement use among women ranged from 1.5% for 16-18 year olds to 46.4% for those over 70 years old, and among men ranged from 1.5% for 16-18 year olds to 25.4% for those over 70 years.

In youth, the proportion below the EAR stayed stable over two years. In adults, the prevalence of inadequacy in CaMos was high at baseline, 52% (95% CI: 51%, 54%) in women and 56% (54%, 58%) in men, and decreased to 33% (95% CI: 32%, 35%) and 46% (44%, 49%) at Year 10 in women and men, respectively.

The proportion of youth with total calcium intakes above UL was 4% (95% CI: 3%, 5%) at baseline and stayed stable over 2 years. At baseline, 6% (95% CI: 6%, 7%) of adult women and 4% (3%, 5%) of adult men had calcium intakes above the UL, and the percentage exceeding the UL increased to 17% (95% CI: 16%, 19%) of women and 8% (7%, 10%) of men by Year 10 (data not shown).

Vitamin D

The mean daily intakes of vitamin D from all sources (diet and supplement) are presented (by sex, age, and time period) in Table 3, together with the longitudinal changes. In the youth

cohort, the estimated annual change of dietary vitamin D intake over two years differed by age and sex, with decreases noted in young women aged 16-18 years and young men aged 16-24 years, although the latter estimates were not statistically different from zero. In the youth cohort, when supplement use was included there were no statistically significant decreases, but in young women aged 19-24 years there was increased total intake. In the adult cohort, total vitamin D intake increased over ten years in all sex and age groups except men aged 25-50.

The overall prevalence of supplemental vitamin D use in CaMos was 26% at baseline, and increased to 52% at the last follow-up, while among adult users, the mean daily supplement dose also increased. Table 4 shows detailed use of supplements by sex and age group. The prevalence of vitamin D supplement intake was higher in women vs. men, and higher in older vs. younger age groups in both sexes.

The prevalences of inadequate vitamin D intake (proportion below the EAR) at baseline were 91% (95% CI: 89%, 94%) and 76% (72%, 80%) in young women and men, respectively, and remained high after 2 years. In the adult cohort, the prevalences at baseline were 74% (95% CI: 73%, 75%) in women and 80% (79%, 82%) in men, and decreased over 10 years to 46% (45%, 47%) in women and 62% (60%, 65%) in men.

In youth cohort no participants reported total vitamin D intakes above UL. The proportion of adults with total vitamin D intakes

Age (year)	Women			Men		
	n	Users, ¹ %	Supplement, ² µg/day	n	Users, ¹ %	Supplement, ² µg/day
Baseline						
16-18	4	1.9 (1.0)	10.8 (5.0)	2	1.0 (0.7)	10.0 (-)
19-24	11	3.4 (1.0)	5.3 (1.2)	5	1.8 (0.8)	11.0 (1.0)
25-50	251	23.7 (1.3)	9.7 (0.8)	114	15.3 (1.3)	14.0 (4.6)
51-70	1232	35.2 (0.8)	13.1 (0.7)	301	21.9 (1.1)	9.9 (0.6)
71+	635	32.4 (1.1)	15.3 (1.2)	152	20.4 (1.5)	11.8 (1.2)
Youth Year 2						
18	7	14.3 (5.1)	7.8 (1.3)	5	11.9 (4.6)	8.0 (1.5)
19-26	57	16.4 (2.0)	8.8 (1.0)	46	15.1 (2.1)	9.0 (0.6)
Adult Year 10						
35-50	99	36.0 (2.9)	11.0 (0.8)	57	28.2 (3.2)	10.7 (1.2)
51-70	1036	63.8 (1.2)	17.4 (0.7)	277	39.1 (1.8)	16.2 (1.4)
71+	1401	66.7 (1.0)	23.7 (1.5)	314	47.6 (1.9)	16.5 (1.2)

¹ Data are percent (SEM)

² Data are mean (SEM)

Table 4. Prevalence of use and daily contribution for users of vitamin D supplements by sex and age group in the Canadian Multicentre Osteoporosis Study.

Estimate and 95% CI (g/cm ²)			Women (n=515)			Men (n=463)		
			Lumbar spine	Total hip	Femoral neck	Lumbar spine	Total hip	Femoral neck
Calcium model	Low intake	<600 mg/day	0.003 (-0.023; 0.029)	0.001 (-0.025; 0.027)	0.005 (-0.019; 0.029)	0.018 (-0.016; 0.052)	0.040 (0.004; 0.076)	0.029 (-0.008; 0.065)
	Moderate intake	≥600-<1100 mg/day	Reference category			Reference category		
	High intake	1100-<1500 mg/day	-0.013 (-0.040; 0.013)	-0.011 (-0.038; 0.017)	-0.010 (-0.035; 0.014)	0.012 (-0.021; 0.044)	0.027 (-0.008; 0.062)	0.022 (-0.013; 0.057)
	Very high intake	≥1500 mg/day	-0.003 (-0.030; 0.023)	0.009 (-0.018; 0.035)	0.015 (-0.009; 0.040)	0.026 (-0.002; 0.053)	0.047 (0.018; 0.077)	0.033 (0.004; 0.063)
Vitamin D model	No use		-	-	-	-	-	-
	Low intake	<5 µg/day	Reference category			Reference category		
	Moderate intake	≥5-<10 µg/day	0.001 (-0.021; 0.023)	0.009 (-0.013; 0.032)	0.016 (-0.004; 0.036)	0.011 (-0.014; 0.037)	0.009 (-0.019; 0.036)	0.012 (-0.015; 0.040)
	High intake	≥10 µg/day	0.001 (-0.033; 0.035)	0.030 (-0.005; 0.066)	0.033 (0.001; 0.065)	0.026 (-0.001; 0.053)	0.049 (0.020; 0.079)	0.036 (0.006; 0.065)

Table 5. The association between baseline total calcium or total oral vitamin D intake and BMD in the youth cohort (aged 16-24 y) by sex, age group, adjusted for confounders: age, height, body mass index, centre, cigarette use (yes/no), alcohol intake, cola intake, regular activity (yes/no), sedentary hours per day, personal history of fracture, family history of osteoporosis and fracture in the Canadian Multicentre Osteoporosis Study. Results in bold exclude zero in their confidence interval.

above UL was 0.5% (95% CI: 0.3%, 0.6%) at baseline and increased to 1.3% (95% CI: 1.0%, 1.6%) at Year 10 (data not shown).

BMD

Adjusted regression estimates between baseline calcium or vitamin D intake with baseline BMD (lumbar spine, total hip, and

femoral neck) for the youth cohort are shown in Table 5. In young men, very high calcium intake (≥1500 mg daily) and high vitamin D intake [≥10 µg (400IU) daily] were both associated with higher BMD in total hip and femoral neck when compared to the reference intake category, while low calcium intake (<600 mg) was associated with higher total hip BMD. In young women,

Estimate and 95% CI (g/cm ²)			Women (n=3260)			Men (n=1354)		
			Lumbar spine	Total hip	Femoral neck	Lumbar spine	Total hip	Femoral neck
Calcium model	Low intake	<600 mg/day	0.004 (-0.006; 0.013)	-0.004 (-0.011; 0.003)	-0.005 (-0.014; 0.005)	0.001 (-0.010; 0.011)	0.004 (-0.004; 0.012)	0.005 (-0.002; 0.012)
	Moderate intake	≥600-<1100 mg/day	Reference category			Reference category		
	High intake	1100-<1500 mg/day	0.003 (-0.005; 0.010)	0.002 (-0.004; 0.007)	0.002 (-0.003; 0.007)	0.015 (0.004; 0.025)	0.008 (-0.001; 0.016)	0.004 (-0.004; 0.011)
	Very high intake	≥1500 mg/day	0.014 (0.006; 0.022)	0.006 (0.001; 0.012)	0.007 (0.002; 0.012)	-0.002 (-0.014; 0.010)	-0.002 (-0.012; 0.008)	0.002 (-0.007; 0.011)
Vitamin D model	No use		-0.006 (-0.039; 0.026)	0.006 (0.001; 0.012)	-0.001 (-0.023; 0.021)	0.015 (-0.016; 0.046)	0.003 (-0.020; 0.026)	0.004 (-0.018; 0.026)
	Low intake	<5 µg/day	Reference category			Reference category		
	Moderate intake	≥5-<10 µg/day	0.000 (-0.007; 0.008)	-0.003 (-0.002; 0.009)	0.004 (-0.001; 0.009)	0.000 (-0.010; 0.011)	0.000 (-0.009; 0.008)	-0.001 (-0.008; 0.007)
	High intake	≥10 µg/day	0.007 (0.000; 0.014)	0.008 (0.003; 0.013)	0.006 (0.002; 0.011)	0.001 (-0.011; 0.012)	0.006 (-0.003; 0.015)	0.000 (-0.008; 0.009)

Table 6. The association between mean 10-year total calcium or total vitamin D intake and 10-year BMD change in the adult cohort, adjusted for confounders: age, height, body mass index, centre, cigarette use (yes/no), alcohol intake, cola intake, regular activity (yes/no), sedentary hours per day, personal history of fracture, family history of osteoporosis and fracture, inflammatory bowel disease, and antiresorptive use in the Canadian Multicentre Osteoporosis Study. Results in bold exclude zero in their confidence interval.

high vitamin D intake [≥10 µg (400 IU) daily] was associated with higher BMD in femoral neck. No association was found between the average 2-year total calcium intake and the 2-year change in BMD except for young men with an average 2-year total calcium intake >1500 mg/day for which a 2-year change femoral neck decrease of 0.018 g/cm² (0.002; 0.034) was seen.

In the adult cohort, baseline calcium intake of 1100-1500 mg/day, compared to an intake of 600-1100 mg/day, was associated with higher baseline total hip BMD by 0.010 g/cm² (0.000; 0.020) in women but with lower total hip BMD in men by 0.023 g/cm² (0.004; 0.042). No intake of vitamin D at baseline was associated with lower baseline L1-L4 and femoral neck BMDs in men by 0.038 g/cm² (0.010; 0.066) and 0.018 g/cm² (0.002; 0.034), respectively. We also assessed the associations between average 10-year total intake of calcium and vitamin D and longitudinal 10-year BMD change at lumbar spine, total hip and femoral neck (Table 6), adjusting for baseline BMD and other covariates noted in the methods section. In adult women, very high average calcium intakes (≥1500 mg/day) and high average vitamin D intakes (≥10 µg/day) were both associated with better BMD maintenance at all three skeletal sites when compared to the reference intake category. In adult men, overall associations between intake and BMD change over 10 years were inconclusive.

Discussion

This is the first longitudinal assessment of total calcium and vitamin D intakes among Canadians and the potential impact of

cumulative intake on an important bone health parameter, BMD. We found that calcium and vitamin D intakes increased over time in CaMos adults, but decreased in young women adolescents. The increased intakes in adults were largely attributable to the increased use of calcium and/or vitamin D supplements. Overall the percentage of supplement users increased over time in both youth and adults cohorts, as well as the average dose among adult users. The net result of these changes was a decrease in the estimated percentage of Canadians with inadequate calcium and vitamin D intake, while some groups, particularly young women remain at high risk of inadequacy.

To put the more recent CaMos results in context we can compare the CaMos adult Year 10 data (2005-2006) and youth Year 2 data (2004-2006) with the national survey data from CCHS 2.2 (Canada 2004 with a 24-hour recall) and NHANES (US 2003-2006 24-hour recall) found in Appendix H of the 2011 IOM report¹ and Bailey et al (US only)²⁷. Dietary calcium intakes of CaMos women were higher compared to both CCHS and NHANES. In men, dietary calcium intakes in CaMos were also higher compared to CCHS and lower compared to NHANES. It is possible that a significant change in consumption had occurred over the 2 year time difference between the CaMos and CCHS data accrual. A 24-hour recall was used to assess nutrient intake in CCHS and NHANES while a semi-quantitative FFQ, which covered only calcium-rich food, was employed in CaMos. Consequently, it is probable that CaMos participants overestimated their frequency of consumption or portion size in the FFQ. An additional possibility is that because of the focus on bone health, those agree-

ing to participate in the CaMos cohort may have had higher calcium intakes than the Canadian population as a whole.

In view of the fact that there is controversy about whether supplemental calcium (rather than food source calcium) may be associated with adverse cardiovascular outcomes²⁸⁻³¹, and until the issue has been resolved, recommendations to increase oral calcium intake in those who are deficient should probably emphasize optimizing food sources first, and using supplemental sources only as needed to achieve recommended intakes.

Comparing dietary vitamin D intake of CaMos data at the last follow-up (2005-2006) to those of NHANES 2005-2006 (using a 24-hour recall)²⁷, mean dietary vitamin D intake was lower in CaMos women and men age 35 years or older. Thus, the 24-hour recall used by NHANES would have included other vitamin D sources, such as fish, not accounted for in the CaMos FFQ. However, mean total oral vitamin D intakes in CaMos women and men were higher in those aged 51 years or older. This appears due to the higher prevalence of supplemental vitamin D use and higher dose used in those ≥ 51 years of age in CaMos participants compared to NHANES. CaMos dietary vitamin D intake is also lower in all adults 35 or older compared to the CCHS. However, a high prevalence of vitamin D intakes below the EAR was observed in all these studies. We recognize that the vitamin D intake in CaMos is underestimated because it does not include, for instance, fatty fish and margarine. However, using data from the 2004 CCHS 2.2, Vatanparast et al. reported that meat and meat alternatives (including fish) represented only 31.1% of the dietary vitamin D intake³². However, Table 3 shows that at baseline, an increase of 31% of the dietary intake is not enough to increase the total intake to a level close to the EAR. At year 10 follow-up, because of the increase in vitamin D supplement intake, the dietary intake represents only a small portion of the total intake and therefore an increase of 31% in dietary intake is not enough to change our conclusion.

In contrast to the vitamin D intake analyses, when serum 25(OH)D levels are considered relative to the IOM's EAR threshold (less than 40 nmol/L), both CaMos¹⁷ and Canadian Health Measures Survey (CHMS)³³ have shown low percentages of individuals failing to reach that target. Thus, the data appear discordant, with many individuals failing to reach the EAR for vitamin D intake, while most reach the EAR for 25(OH)D. It should be recognized, however, that the EAR and RDA for vitamin D intake developed by the IOM refer to total oral intake assuming the absence of sunlight exposure. Thus, the discordance may be largely due to the contribution of sunlight exposure to vitamin D status. It should also be noted that in addition to reflecting vitamin D intake and synthesis, serum 25(OH)D is also influenced by factors affecting vitamin D catabolism, such as parathyroid hormone and age-related decline in renal function. These results suggest that average yearly vitamin D intake alone may not be an appropriate measure to assess vitamin D sufficiency. In both CaMos and the CHMS studies, supplement use did appear to be particularly important as modifiers of 25(OH)D levels in winter when the highest prevalence of 25(OH)D less than 40 or 50 nmol/L was ob-

served. Despite the importance of supplements in winter, however, there is an apparent non-linearity between the oral intake of vitamin D (and particularly of vitamin D supplements) and increases in serum 25(OH)D levels. The variability in serum 25(OH)D achieved with a given dose of vitamin D may reflect such determinants as the baseline 25(OH)D level at which the vitamin D supplement is given³⁴⁻³⁶, and the body mass index³⁷. Consequently it seems doubtful that total oral vitamin D intake calculations provide the best index of vitamin D needs year-round, both because of its tendency to underestimate 25(OH)D levels, especially in summer, and because of the difficulty in accurately predicting increases in 25(OH)D with defined augmentation in oral vitamin D intake. Despite these shortcomings as indices of adequacy, increases in total oral vitamin D intake should be recommended in fall and winter months for those living in the Northern hemisphere, and year-round for those chronically receiving little sunlight exposure. At present, serum 25(OH)D is the best available measure for assessing vitamin D adequacy because it reflects the summative effects of oral (food and supplement) intakes and sunlight exposure, and its half-life of 14-21 days provides a relatively stable measurement.

We also examined BMD change as a potential biological outcome of calcium and vitamin D intake. In adult women, there were small but statistically significant relationships showing that those in the highest 10-year mean intake categories of calcium and vitamin D had better maintenance of BMD (i.e. lost less BMD over time) than those in the reference categories. Findings related to bone outcomes of calcium and vitamin D intake have been mixed. For example, a subgroup analysis of the Women's Health Initiative (WHI) found that in women age 50 to 70, increasing calcium and vitamin D intake with large dose supplementation achieved a modest improvement in BMD in postmenopausal women³⁸, but the Kuopio Osteoporosis Study reported that low dose supplementation of vitamin D and calcium did not prevent bone loss in early postmenopausal women³⁹. Conversely, meta-analyses have indicated that supplementation with appropriate amounts of calcium and vitamin D may reduce hip fracture⁴⁰⁻⁴². Our results in women 25 years and older, showed that maintaining cumulatively high levels of calcium and vitamin D intakes over time (with high or low dose of supplementation) contributed to improve BMD at lumbar spine as well as hip sites. Furthermore, a more recent subset analysis of the WHI found that long-term use of calcium and vitamin D appeared to confer a reduction in the risk of hip fracture among postmenopausal women and that other health benefits and risks of supplementation at the doses considered, including an elevation in urinary tract stone formation, appear to be approximately balanced⁴³. Certainly it seems wise to advise caution in terms of sustaining intakes of calcium and vitamin D that exceed recommendations by a considerable margin, and intervention/education is needed about avoiding unnecessary high calcium intakes, especially in the population who reported intakes exceeding UL.

The strengths of this study are that CaMos is a large population-based longitudinal cohort of Canadian men and women (representative of 40% of the Canadian population) with

prospective data on an array of biological, behavioural, and environmental correlates. The wide age range in CaMos enabled the study of bone loss change over the life-course. Study limitations include the limited scope and specified portion sizes of the semi-quantitative FFQ which may yield biased estimates of dietary calcium and vitamin D intake. A CaMos study on osteoporosis status stated that there was a negligible nonresponse bias, except in the very elderly, where the nonresponse affected only slightly the prevalence of osteoporosis. The authors therefore concluded that those who accepted to participate in CaMos did so for reasons unrelated to their osteoporosis status or that their differences in major osteoporosis risk factors with those who refused did not vary enough to change the osteoporosis estimates⁴⁴. A further potential limitation of this study is the loss to follow up of 21% of adults and 26% of youth. Among youth, those lost to follow-up were similar at baseline in terms of age, menarche age, BMD, body mass index (BMI), history of fracture, regular activity, and race to those who remained in the study. Adults who discontinued the study indicated they were too sick to continue, and were older than those who continued to participate. Furthermore, women who left the study had lower BMD compared to those who remained in the study. Although there is no obvious source or direction of bias in other measured variables, as in all longitudinal observational cohort studies, limitations include possible selection bias due to incomplete follow-up.

In summary, we observed that a higher cumulative calcium and vitamin D intake among adult women was associated a better maintenance of bone health as measured by BMD at multiple sites. We also observed that total calcium and vitamin D intakes increased over time in Canadian adults, but not among adolescents; and that the increases were mainly attributable to increased supplement use. Nevertheless, total intakes, particularly of vitamin D, frequently fell below IOM recommendations.

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