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ORIGINAL ARTICLE

# Variation in bone mineral density and fractures over 20 years among Canadians: a comparison of the Canadian Multicenter Osteoporosis Study and the Canadian Longitudinal Study on Aging

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## Abstract

**Summary** International variations in osteoporosis and fracture rates have been reported, with temporal trends differing between populations. We observed higher BMD and lower fracture prevalence in a recently recruited cohort compared to that of a cohort recruited 20 years ago, even after adjusting for multiple covariates.

**Purpose** We explored sex-specific differences in femoral neck bone mineral density (FN-BMD) and in prevalent major osteoporotic fractures (MOF) using two Canadian cohorts recruited 20 years apart.

**Methods** We included men and women aged 50–85 years from the Canadian Multicentre Osteoporosis Study (CaMos, $N=6{,}479$; 1995–1997) and the Canadian Longitudinal Study on Aging (CLSA, $N=19{,}534$; 2012–2015). We created regression models to compare FN-BMD and fracture risk between cohorts, adjusting for important covariates. Among participants with prevalent MOF, we compared anti-osteoporosis medication use.

**Results** Mean (SD) age in CaMos (65.4 years [8.6]) was higher than in CLSA (63.8 years [9.1]). CaMos participants had lower mean body mass index and higher prevalence of smoking ($p<0.001$). Adjusted linear regression models (estimates [95%CI]) demonstrated lower FN-BMD in CaMos women ($-0.017$ g/cm$^2$ [$-0.021$; $-0.014$]) and men ($-0.006$ g/cm$^2$ [$-0.011$; 0.000]), while adjusted odds ratios (95%CI) for prevalent MOF were higher in CaMos women (1.99 [1.71; 2.30]) and men (2.33 [1.82; 3.00]) compared to CLSA. In women with prevalent MOF, menopausal hormone therapy use was similar in both cohorts (43.3% vs 37.9%, $p=0.076$), but supplements (32.0% vs 48.3%, $p<0.001$) and bisphosphonate use (5.8% vs 17.3%, $p<0.001$) were lower in CaMos. The proportion of men with MOF who received bisphosphonates was below 10% in both cohorts.

**Conclusion** Higher BMD and lower fracture prevalence were noted in the more recently recruited CLSA cohort compared to CaMos, even after adjusting for multiple covariates. We noted an increase in bisphosphonate use in the recent cohort, but it remained very low in men.

**Keywords** Bone mineral density · Canadian longitudinal study on aging · Canadian multicenter osteoporosis study · Care gap · CLSA · Fracture · Secular trends

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## Introduction

Osteoporosis, a chronic age-associated disease [1, 2], is characterized by an increased propensity to fracture caused by loss of bone strength [3, 4]. Osteoporosis-related fractures increase the likelihood of subsequent fractures and place a substantial burden on the healthcare system [5, 6]. As the population is aging, it is projected that by 2031, at least one in every four Canadians will be 65 years or older [7], and as a result, the prevalence of age-associated diseases like osteoporosis is expected to increase.

During the past decades, variations in osteoporosis and fracture rates have been reported internationally [8–10]. In the USA, analysis of National Health and Nutrition Examination Survey (NHANES) data demonstrated that the prevalence of osteoporosis (T-score $\leq -2.5$) among people aged 50 years and older declined between 1988–1994 and 2005–2006, stabilized from 2005–2006 to 2009–2010, and then increased in 2014 [11–13]. There was some evidence that the mean bone mineral density (BMD) at the femoral neck among US men and women was stable for the first three NHANES cycles from 2005 to 2010, but significantly decreased until 2013–2014 [12]. In Canada, femoral neck BMD in women has increased 0.52% per year from 1996 to 2006 [14].

Hip fracture rates plateaued or decreased in the last two decades in many developed countries and have increased mostly in the developing world [9, 15]. Decreasing trends in hip fracture rates were observed in USA, Europe, Oceania, and some Asian countries including Japan, Taiwan, and Hong Kong, while increasing rates were detected in China and Korea [15]. In Canada, age-standardized rates of hip fracture declined during the period 1985 through 2005 [16]. Recent data from the Public Health Agency of Canada support this trend up to 2016 [2].

Improved identification of those at high fracture risk and widespread availability of effective pharmacological therapies have led to improvement in osteoporosis management over the last decades [17, 18]. Country-specific clinical guidelines provide recommendations to reduce fracture risk [19–21]. However, treatment rates have been shown to be suboptimal in up to 80% of men and women at high risk of fractures [2, 22]. The lack of awareness of the clinical impact of fractures by patients and physicians, concerns regarding medication adverse effects, and variations in policies in osteoporosis assessment have contributed to this wide caregap [22]. Introduction of fracture risk assessment tools and post-fracture management programs have the potential to improve the treatment of osteoporosis [23].

More information about the magnitude of change in BMD, fracture rates, and anti-osteoporosis medication use among the general population in Canada in recent years is required to address this critical caregap [24]. The Canadian Multicentre Osteoporosis Study (CaMos) (baseline 1995–1997) and the Canadian Longitudinal Study on Aging (CLSA, baseline 2012–2015) are two large population-based longitudinal cohorts in Canada that provide valuable information about the skeletal health determinants of Canadians. Using baseline data from the CLSA and CaMos cohorts, separated by a 20-year period, we aimed to (a) compare age- and sex-specific BMD, and prevalent fracture patterns between the two cohorts, and (b) compare the use of vitamin D and calcium supplements and anti-osteoporosis medications between cohorts to determine how the treatment gap has evolved in individuals at high risk for fracture.

## Methods

### Data source and study population

This study was performed using the baseline data from the CaMos [25] and CLSA cohorts [26]. CaMos is a longitudinal population-based prospective cohort study of 6,539 women and 2,884 men who were recruited between 1995 and 1997 to examine osteoporosis and fracture risk in community-dwelling Canadians [25]. Participants aged 25 years and older were recruited through a random telephone-based sampling frame from within 50 km of one of nine study centers (Vancouver in British Columbia; Calgary in Alberta; Saskatoon in Saskatchewan; Toronto, Hamilton, and Kingston in Ontario; Quebec City in Quebec; Halifax in Nova Scotia; and St John's in Newfoundland and Labrador). Data collection included an in-person interviewer-administered questionnaire and physical measurements. Exclusion criteria were being unable to communicate in English, French, or Chinese and being institutionalized.

CLSA is an ongoing longitudinal study in Canada initiated in 2012 to recognize determinants of healthy ageing in Canadian 45–85 years. CLSA includes two separate cohorts: a tracking cohort and a comprehensive cohort; the latter constituting the study subjects of this analysis [26]. In the CLSA comprehensive cohort, 14,777 men and 15,320 women were recruited using provincial health registries and random digit dialing sampling frames from 25 to 50 km radius of 11 centers (Data Collection Site: Victoria, Vancouver, and Surrey in British Columbia; Calgary in Alberta; Winnipeg in Manitoba; Hamilton and Ottawa in Ontario; Montreal and Sherbrooke in Quebec; Halifax in Nova Scotia; St. John's in Newfoundland and Labrador). Data were collected through a 90-min face-to-face in-home interview and in-person visit for physical assessments at one of the CLSA data centers. The exclusion

criteria were being a resident of Northwest Territories, Nunavut, Yukon or federal First Nations reserves, being a full-time member of the Canadian Armed Forces, living in an institution, inability to respond in English or French, or having cognitive impairment. Potential participants were evaluated for cognitive impairment through telephone screening tools designed specifically for the CLSA.

This study was conducted using baseline data of men and women aged 50 to 85 years from CaMos and CLSA (Supplemental Fig. 1). We used the data of participants who had no missing data on BMD measurements or key variables (age, body mass index, smoking, calcium and vitamin D supplement, corticosteroid and anti-osteoporosis medication use).

## Bone mineral density

We used BMD measured at the femoral neck for this analysis (CLSA did not measure lumbar spine BMD). In CaMos, BMD was measured at baseline using dual-energy X-ray absorptiometry (DXA) from Hologic (7 centers) or Lunar manufacturers (2 centers). Machine calibration was done daily using the manufacturer-specific spine phantom as per standard procedure. Daily and weekly quality assurance tests were performed. Lunar data were converted into equivalent Hologic values by standard methods [27]. Cross-calibration was performed yearly across centers using a Bona Fide Spine Phantom (Bio-Imaging Technologies, Newtown PA).

In CLSA, BMD measurements were completed using Hologic densitometers at all centers [28]. Appropriate quality control and cross-calibration of DXA machines were performed within and between centers using standard operating procedures. Local quality control was done daily using a spine phantom and weekly using a whole-body phantom. Once a year, cross-calibrations across all densitometers were done with the gold-standard traveling phantom.

In order to assess cross-calibration between CLSA and CaMos densitometers, we followed the International Society for Clinical Densitometry (ISCD) recommendation for quality assurance between the scanners used in both cohorts [29]. In the CaMos cohort, measurements on the Hologic densitometers used at the Quebec City center had been observed to be stable over the course of the study, and no longitudinal corrections were ever required. Therefore, we used the CaMos Bona Fide Spine Phantom for cross-calibration purposes between the CaMos and CLSA densitometers. We scanned the CaMos phantom 30 times on each of two Hologic densitometers: the CaMos densitometer still in use in Quebec City and a CLSA densitometer located in Hamilton. As the differences between densitometers were within the threshold limit of 1.5% [30] in CaMos (0.971 g/cm$^2$) and CLSA (0.970 g/cm$^2$), no adjustment was required.

## Osteoporosis, fractures, and anti-osteoporosis treatment

Osteoporosis was defined as the presence of a femoral neck T-score equal to − 2.5 or less. We generated femoral neck BMD T-scores using the young normal values from the NHANES III BMD of white women 20–29 years old [31].

Fractures were defined as prevalent self-reported major osteoporotic fractures (MOF; hip, clinical spine, forearm and humerus) that occurred with low trauma (standing height or less) during adult life. In CaMos, we selected fractures that occurred after the age of 18 years, while in CLSA, the fracture variable was derived from the Osteoporosis (OST) module asking specifically for fractures occurring in adult life. We generated 10-year fracture risk probabilities for MOF and hip fracture from femoral neck T-score and clinical risk factors using the Canadian FRAX® tool [31].

Pharmacotherapy is recommended for those at high risk for fracture, including men and women with a prevalent MOF, a FRAX probability for MOF of ≥ 20% over the next 10 years, or those with osteoporosis with a BMD T-score ≤ − 2.5 [19, 32, 33]. We defined participants with any of these characteristics at cohort entry as being at high risk for fracture and documented the proportion that was receiving supplemental calcium, vitamin D, or anti-osteoporosis medication.

## Anthropometric measurements

In CaMos, weight (kg) and height (cm) were measured using portable scale and carpenter's ruler, respectively, during the DXA measurement visit or at the time of the interview if no DXA scans were scheduled. In CLSA, weight (kg) and height (cm) were measured twice using a 140–10 Healthweigh digital physician scale and Seca 213 stadiometer, respectively [34, 35], and the average of both measures was used. For both cohorts, body mass index (BMI) was calculated by dividing the weight in kilogram by height (in meter) squared.

## Other variables

Other explanatory variables were selected based on literature review and their availability in both CaMos and CLSA datasets. The variables considered were race/ethnicity (White or other), level of education (holding or not at least a high school diploma), smoking (current smoker or non-smoker), and alcohol consumption in the past 12 months divided (less than 3 drinks /day or 3 or more drinks/day). Vitamin D and calcium supplement intake on a regular basis, as well as any use of glucocorticoids, bisphosphonates, and menopausal hormone therapy (women only), were derived from the Drugs and Medication questionnaire in CaMos and In-Home

Questionnaire (Version 4.0) in CLSA. Of note, etidronate and alendronate were approved for the treatment of osteoporosis in 1995 (CaMos baseline) and risedronate in 2000 in Canada. Raloxifene use was very low in both cohorts and therefore was not considered in the analyses.

### Statistical methods

All analyses were stratified by sex. Descriptive statistics were generated using means and standard deviations (SD) or medians and interquartile ranges (IQR), and frequency and percentages as appropriate. Standard tests (Chi-squared, student's *t* test, and analysis of variance) were used to compare categorical and continuous variables between cohorts.

The prevalence of osteoporosis and MOF was further stratified by age groups. Furthermore, since participants in CLSA are known to have a higher education level than the average Canadian population [26], we additionally examined the effect of education on the prevalence of osteoporosis in both cohorts. To do so, we used logistic regression, stratified by sex and age, including cohort membership, post-secondary education (yes/no), and the interaction of cohort membership with education level.

Differences between cohorts were assessed by including cohort membership (CaMos vs. CLSA) as an independent variable in regression models. Unadjusted and multivariable adjusted linear regression models were created to estimate the differences in femoral neck BMD between cohorts using CLSA as the reference. We first created unadjusted linear models looking at the association of femoral neck BMD with cohort membership and each covariable. Multiple linear regression models were then generated; age, BMI, and height were forced in these models. Other covariables meeting statistical significance ($p < 0.05$) in the univariate models were included in the fully adjusted models. Logistic regressions were used to examine the associations of cohort membership with MOF. Similar strategy for variable selection as above was applied. We further adjusted the final model for femoral neck BMD.

Finally, sensitivity analyses were done in participants who self-reported White race/ethnicity.

All statistical analyses were performed using statistical R software (Version 1.2.5033© 2009–2019 RStudio, Inc). A 2-sided *p*-value of < 0.05 was considered significant.

## Results

### Baseline characteristics

The total number of eligible participants from both cohorts was 26,013 (CaMos: 4608 women and 1871 men; CLSA: 9583 women and 9951 men) (Supplemental Fig. 1); their baseline characteristics are shown in Table 1. In general, participants from CaMos were older than participants from CLSA (mean [SD] of 65.4 years [8.6] vs 63.8 years [9.1]). They also had lower mean height, weight, and BMI than those from CLSA. The prevalence of current smokers in CaMos was significantly higher in both women (13.5% vs 7.0%, $p < 0.001$) and men (15.8% vs 8.5%, $p < 0.001$). The percentage of women and men with post-secondary education was lower in CaMos than CLSA (women 44.2% vs 76.6%, $p < 0.001$; men 51.6% vs 80.2%, $p < 0.001$). Individuals who self-identified as White constituted over 92% of both cohorts.

### Prevalence of osteoporosis and bone mineral density

Prevalence of osteoporosis is presented by sex and age group in Fig. 1. In women, in all age groups, the prevalence of osteoporosis was significantly higher in CaMos compared to CLSA. In logistic regression analysis, the interactions between education level and cohort membership were not significant in women nor in men; therefore, we do not show data stratified by level of education.

Participants from CaMos had significantly lower mean (SD) femoral neck T-score (women: − 1.4 [1.0], men: − 0.6 [1.0]) than CLSA (women: − 1.1 [1.0], men: − 0.4 [1.0]) ($p < 0.001$). Compared to CLSA, unadjusted estimates (95% CI) for femoral neck BMD were lower in CaMos women by − 0.032 g/cm$^2$ (95% CI − 0.036; − 0.028) and in CaMos men by − 0.024 g/cm$^2$ (95% CI − 0.030; − 0.018) (Fig. 2). Adjusting for age, BMI, height, and other important covariates decreased the differences between the cohorts. However, estimates remained significantly lower in CaMos women (− 0.017 g/cm$^2$ [95% CI − 0.021; − 0.014]) and men (− 0.006 g/cm$^2$ [95% CI − 0.011; 0.000]) (both, $p < 0.05$), compared to CLSA.

### Major osteoporosis fractures

The prevalence of MOF by sex and age group is presented in Fig. 1. In all categories, the prevalence of MOF was higher among CaMos participants compared to CLSA except for men aged 75–85 years where the difference was not statistically significant.

Unadjusted odds ratios (OR, 95% CI) for prevalent MOF were significantly higher in women and men from CaMos compared to CLSA (Fig. 3). After adjusting for covariates, prevalence of MOF remained significantly higher in CaMos than CLSA in both women (OR 1.99 [95% CI 1.71, 2.30]) and in men (OR 2.33 [95% CI 1.82, 3.00]) (both, $p < 0.05$).

**Table 1** Baseline characteristics by cohort membership

| | Women | | | Men | | |
|---|---|---|---|---|---|---|
| | CaMos ($n=4608$) | CLSA ($n=9583$) | P-value | CaMos ($n=1871$) | CLSA ($n=9951$) | *p*-value |
| Age (years) — mean (SD) | 65.5 (8.5) | 63.3 (9.0) | < 0.001 | 65.1 (8.7) | 64.2 (9.1) | < 0.001 |
| Height (cm) — mean (SD) | 159.4 (6.3) | 161.6 (6.5) | < 0.001 | 173.0 (6.9) | 175.3 (7.0) | < 0.001 |
| Weight (kg) — mean (SD) | 69.0 (13.4) | 72.5 (15.7) | < 0.001 | 81.8 (13.2) | 86.9 (15.4) | < 0.001 |
| Body mass index (kg/m$^2$) — mean (SD) | 27.1 (5.0) | 27.8 (5.8) | < 0.001 | 27.3 (3.8) | 28.2 (4.5) | < 0.001 |
| Smoking (current) — *N* (%) | 620 (13.5) | 674 (7.0) | < 0.001 | 296 (15.8) | 848 (8.5) | < 0.001 |
| Alcohol (≥ 3 drink/day) — *N* (%) | 42 (0.9) | 305 (3.2) | < 0.001 | 131 (7.0) | 898 (9.0) | 0.005 |
| Race/ethnicity (White) — *N* (%) | 4433 (96.2) | 8889 (92.8) | < 0.001 | 1757 (93.9) | 9241 (92.9) | 0.115 |
| Postsecondary degree — *N* (%) | 2038 (44.2) | 7343 (76.6) | < 0.001 | 965 (51.6) | 7978 (80.2) | < 0.001 |
| Calcium supplement use (past month) — *N* (%) | 2216 (48.1) | 4203 (43.9) | < 0.001 | 486 (26.0) | 1513 (15.2) | < 0.001 |
| Vitamin D supplement use (past month) — *N* (%) | 1614 (35.0) | 5982 (62.4) | < 0.001 | 419 (22.4) | 3811 (38.3) | < 0.001 |
| Bisphosphonate use — *N* (%) | 110 (2.4) | 582 (6.1) | < 0.001 | 3 (0.2) | 103 (1.0) | < 0.001 |
| Menopausal hormone therapy use (ever) — *N* (%) | 2231 (48.4) | 3212 (33.5) | < 0.001 | – | – | – |
| FRAX probability for MOF (%)[a] — mean (SD) | 10.6 (7.5) | 9.7 (6.6) | < 0.001 | 5.4 (3.1) | 5.5 (3.1) | 0.023 |
| FRAX probability for hip fracture (%)[a] — mean (SD) | 2.6 (4.7) | 1.8 (3.6) | < 0.001 | 1.2 (2.0) | 1.1 (1.8) | < 0.001 |
| Femoral neck BMD (g/cm$^2$) — mean (SD) | 0.691(0.119) | 0.723(0.114) | < 0.001 | 0.791(0.125) | 0.816(0.125) | < 0.001 |
| Prevalent MOF — *N* (%) | 503 (10.9) | 594 (6.2) | < 0.001 | 103 (5.5) | 266 (2.7) | < 0.001 |
| Prevalent any fracture — *N* (%) | 1158 (25.1) | 1855 (19.4) | < 0.001 | 355 (19.0) | 1113 (11.2) | < 0.001 |
| Osteoporosis (T-score ≤ − 2.5 at femoral neck[b]) — *N* (%) | 562 (12.2) | 478 (5.0) | < 0.001 | 38 (2.0) | 87 (0.9) | < 0.001 |

Non-weighted results

*SD* standard deviation, *MOF* major osteoporosis fracture (low trauma fractures of the hip, clinical spine, wrist and humerus), *FRAX* 10-year fracture risk probabilities

[a]Calculated with BMD

[b]Calculated using NHANESIII data for women

In sensitivity analyses, the regression models for BMD and fracture prevalence were limited to participants of White race/ethnicity. Results were similar to the findings in the entire cohorts.

### Anti-osteoporosis treatment use in participants at high risk for fracture

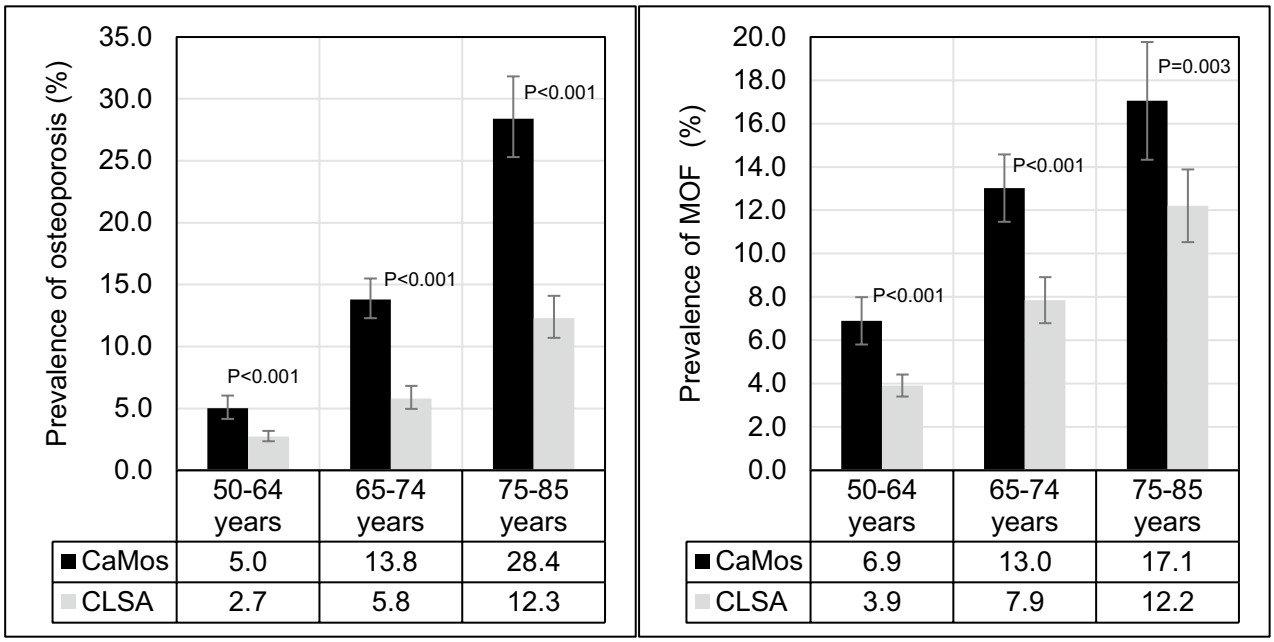
The proportion of participants at high risk for fractures was higher in CaMos than in CLSA in women and men, overall, and for each criterion except in men when defined as a high FRAX probability (Table 2). As seen in Fig. 4, in women, use of supplements (calcium and vitamin D) and bisphosphonates was significantly lower in CaMos for every category of high-risk definition. Overall, the use of menopausal hormone therapy did not differ between CaMos women at high risk for fractures (35.6%) compared to those from CLSA (37.4%). In men, the comparisons of supplements and anti-osteoporosis treatment use were inconclusive, mainly due to the small number of men at high risk for fracture.

## Discussion

We documented higher BMD and lower risk of fractures in the CLSA participants compared to the participants of CaMos, recruited 20 years apart, even after adjusting for important covariates. This is in agreement with reports from other countries where BMD has increased and fracture rates have decreased over the last decades [9]. We also noted improvement in anti-osteoporosis treatment over time in participants with high risk for fractures; nevertheless, the treatment gap remains elevated, specifically in men.

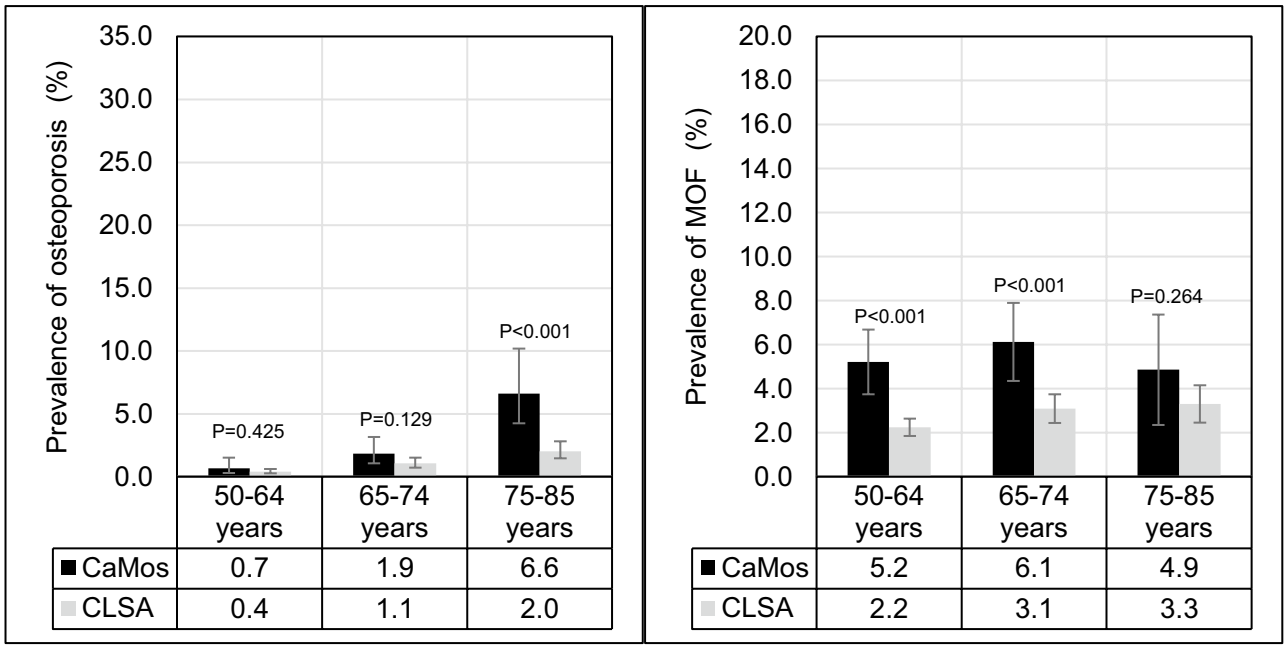
Changes over time in BMD measurements are documented in many countries. In a study examining BMD in older US adults between 2005 and 2014 from the National Health and Nutrition Examination Survey, there was some evidence of a decline in femur neck BMD between 2005–2006 and 2013–2014, but not in lumbar spine BMD. Changes in the risk factors that could be examined, such as BMI, smoking, and milk intake, did not explain the femoral neck BMD trends [12]. In Canada, a significant annual linear increase of 0.52% in BMD at the femoral neck and 0.32% at the lumbar spine BMD was documented using the large

**A Women**




Osteoporosis: defined as femoral neck T-score ≤ -2.5
MOF=Major Osteoporosis Fracture (low trauma fractures of the hip, clinical spine, forearm and humerus); FRAX=10-year fracture risk probabilities

**B Men**




Osteoporosis: defined as femoral neck T-score ≤ -2.5
MOF=Major Osteoporosis Fracture (low trauma fractures of the hip, clinical spine, forearm and humerus); FRAX=10-year fracture risk probabilities

**Fig. 1** Prevalence of osteoporosis and major osteoporotic fractures (%, 95%CI) by sex and age group

Manitoba BMD registry data of women aged 50 years and older from 1996 to 2006 [14]. Temporal increases in BMI, obesity, and osteoporosis treatment also did not explain these changes. We found that femoral neck BMD was higher in the CLSA participants as compared to the CaMos cohort, supporting an improvement in bone mass in Canadians over

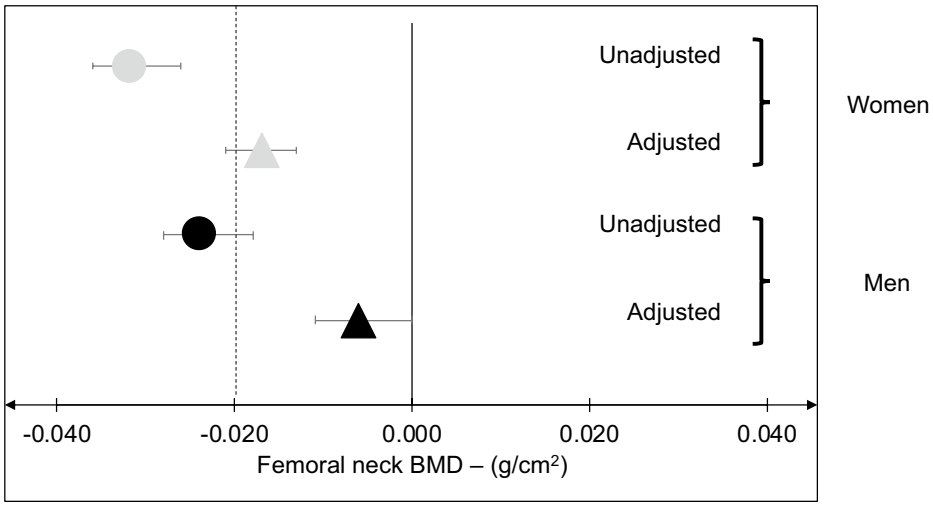



**Fig. 2** Unadjusted and adjusted femoral neck bone mineral density (BMD) estimates (95% CI) for cohort membership — CaMos vs. CLSA (reference)

Grey triangle (adjusted model in women): adjusted for age, BMI, height, smoking, calcium and vitamin D supplement, corticosteroid, bisphosphonates, menopausal hormone therapy
Solid triangle (adjusted model in men): adjusted for age, BMI, height, smoking, calcium supplement, corticosteroid, bisphosphonates
All associations were statistically significant (P<0.05)
Non-weighted results

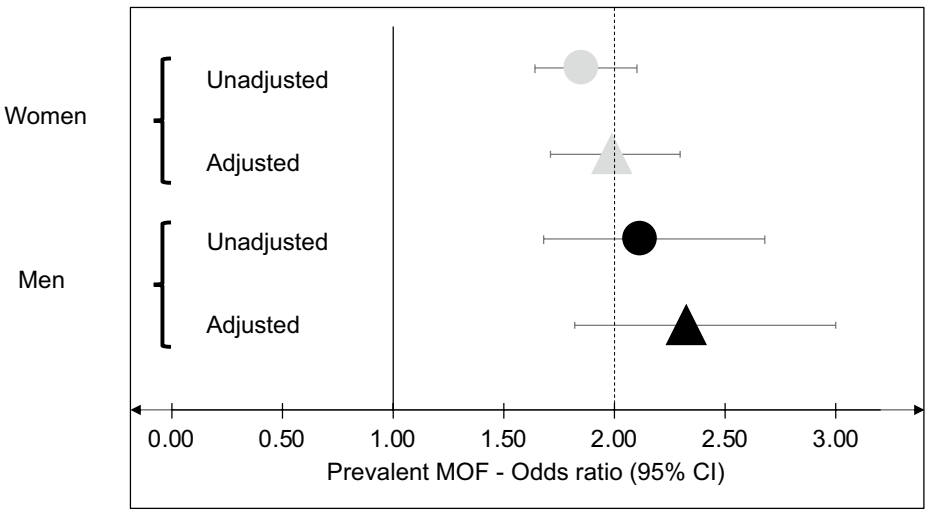



**Fig. 3** Unadjusted and adjusted odds ratios (95% CI) for major osteoporotic fractures (MOF) according to cohort membership — CaMos vs. CLSA (reference)

Grey triangle (adjusted model in women): adjusted for age, BMI, height, calcium and vitamin D supplement, corticosteroid, bisphosphonates, BMD at femoral neck, education, alcohol, ethnicity
Solid triangle (adjusted model in men): adjusted for age, BMI, height, calcium supplement, bisphosphonates, BMD at femoral neck, education
All associations were statistically significant (P<0.05)
Non-weighted results

a 20-year period. Although we also documented that BMI, smoking, alcohol consumption, level of education, supplement, and anti-osteoporosis medication use were different between the cohorts, adjusting for these variables did not explain the differences.

Secular changes in MOF have been documented in many countries. The overall incident rate of fragility fractures has been predicted to increase in many countries [17, 36], mainly due to the age trajectory [8]. However, trends in osteoporotic fracture rates differ depending on the skeletal site. In Denmark, data from 1995 to 2010 demonstrated a general decline in the incidence of MOF in both men and women [8]. In Finland, the decline in the incidence of hip fracture which started in 1997 has continued through 2016 among adults 50 years of age or older [37]. Similarly, the trend in Italy from 2007 to 2014 revealed an overall decline in the incidence rate of hip fractures in older women [36]. In the USA, Medicare and the National Inpatient Survey data

**Table 2** CaMos and CLSA participants with baseline characteristics that meet the definition of high-risk for fracture

| | Women | | | Men | | |
|---|---|---|---|---|---|---|
| | CaMos ($n=4608$) | CLSA ($n=9583$) | $P$-value | CaMos ($n=1871$) | CLSA ($n=9951$) | $p$-value |
| FRAX probability for MOF ≥ 20% — $N$ (%) | 430 (9.3) | 684 (7.1) | < 0.001 | 12 (0.6) | 44 (0.4) | 0.333 |
| With prevalent MOF — $N$ (%) | 503 (10.9) | 594 (6.2) | < 0.001 | 103 (5.5) | 266 (2.7) | < 0.001 |
| Osteoporosis (femoral neck T-score ≤ − 2.5) — $N$ (%) | 562 (12.2) | 478 (5.0) | < 0.001 | 38 (2.0) | 87 (0.9) | < 0.001 |
| High-risk for fracture — either of the following:<br>FRAX probability for MOF ≥ 20%<br>With prevalent MOF<br>Osteoporosis (femoral neck T-score ≤ − 2.5) | 562 (12.2) | 478 (5.0) | < 0.001 | 38 (2.0) | 87 (0.9) | < 0.001 |

Non-weighted results

*MOF* major osteoporosis fracture (low trauma fractures of the hip, clinical spine, forearm and humerus), *FRAX* 10-year fracture risk probabilities

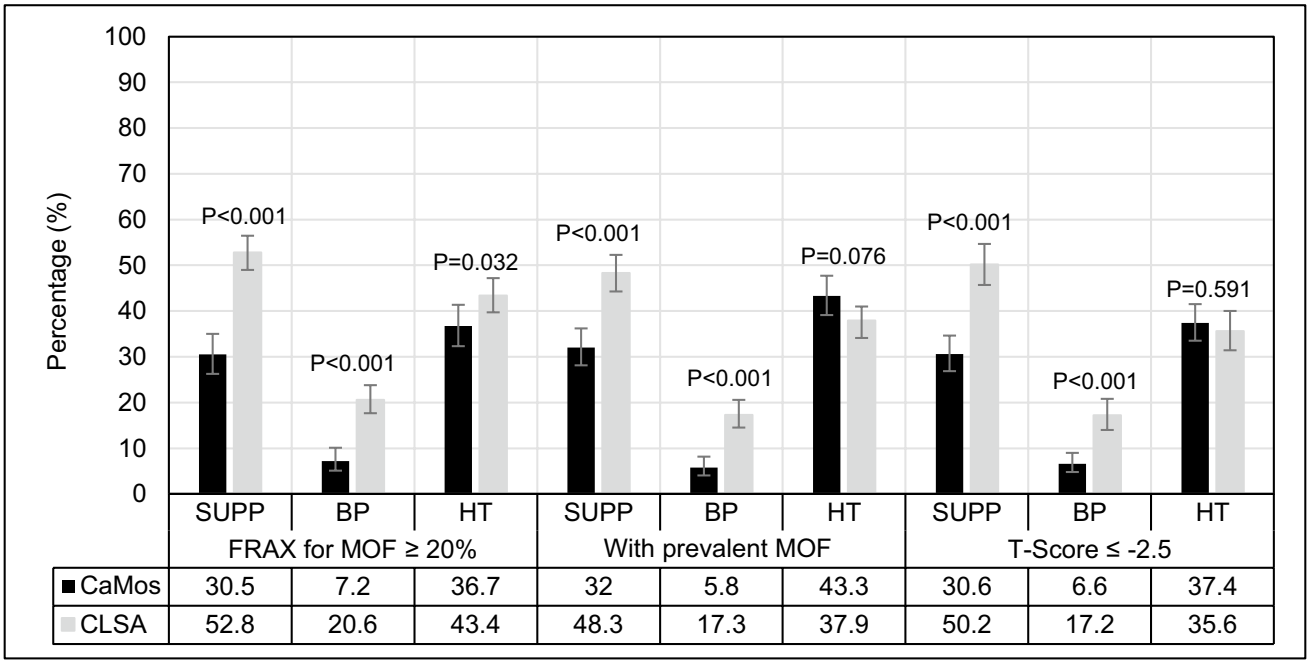
indicated a decline in hip fracture incidence between 1985 and 2012 [12]. A recent study using the UK Clinical Practice Research Datalink with a 20-year follow-up revealed stable overall sex-specific fracture incidence, with radius-ulna fractures decreasing in women and hip fractures rising in men [38]. Recent data revealed an increase in hip fracture rates in Singapore (2000–2017) [39] and Lebanon (2006–2017) [40].

We found that the prevalence of MOF in both women and men, except in men aged 75–85 years, were lower in CLSA compared to CaMos. These results are consistent with the data from the Manitoba BMD registry, which documented a decline in major osteoporotic fractures from 1996 to 2006, attributed to a secular increase in BMD, rather than changes in anti-osteoporosis treatment or in BMI [14]. In a Canada-wide study over the fiscal years 2000 to 2015, the age-standardized annual hip and forearm fracture rates decreased, humeral fracture rates were relatively stable, and spine fracture rates increased over the study period [2]. The basis for the stabilization and often reduction in fracture rates in industrialized countries remains uncertain. Although an improvement in BMD has been considered as the major factor contributing to reductions in osteoporotic fracture rates [14], other factors, such as greater rates of osteoporosis treatment, change in lifestyle, introduction of new anti-osteoporosis medication (bisphosphonates), increasing prevalence of obesity, and alterations in tobacco consumption, likely also contribute [6, 17]. Over the past half-century, there have been rapid and marked advancements in pharmacological interventions for osteoporosis [41]. However, evidence suggests that only a minority of patients at high-risk for fractures receive screening or treatment known to reduce fracture risk [24]. A study by Jean S and coll. demonstrated that both period and birth cohort effects possibly explained the linear decrease in hip fracture rates in Canadian men and women between 1985 and 2005. Indeed, period effect reflects a change occurring at a specific time (regardless of age) such as an increase in BMD testing, whereas birth cohort effect reflects changes applicable to individuals born at a specific time such as a change in smoking or BMI [42].

We documented improvements in vitamin D supplementation and in anti-osteoporosis pharmacotherapy in women in the last 2 decades. Calcium supplementation decreased in women and in men, possibly secondary due to perceived adverse cardiovascular events. The introduction of bisphosphonates and clinical practice guidelines after the CaMos baseline (1995–1997) possibly explains this improvement. However, the care gap is still remarkably high. Regardless of the definition of the high-risk category, only about 20% of CLSA women at high risk for fracture were being treated with bisphosphonates. This result is similar to that of other studies where less than 20% of Canadians with a recent MOF received an osteoporosis diagnosis, underwent a BMD test, or received a prescription for an osteoporosis-related medication [2]. Our small sample size in men at high risk for fracture prevented us from comparing both cohorts. Nevertheless, our results support the previous evidence that there is a larger care gap in men than in women.

The main strengths of this study include the large sample size and comprehensiveness of CaMos and CLSA, the quality control of densitometers within and between cohorts, and similar ascertainment of bone health outcomes. As with other observational studies, there are some limitations. CLSA was designed to study healthy aging, while CaMos was designed to study bone health, osteoporosis, and fractures. The difference in the design and objectives of these two studies would have affected participants' characteristics and be subject to selection and healthy participant biases. Individuals with prevalent fractures or

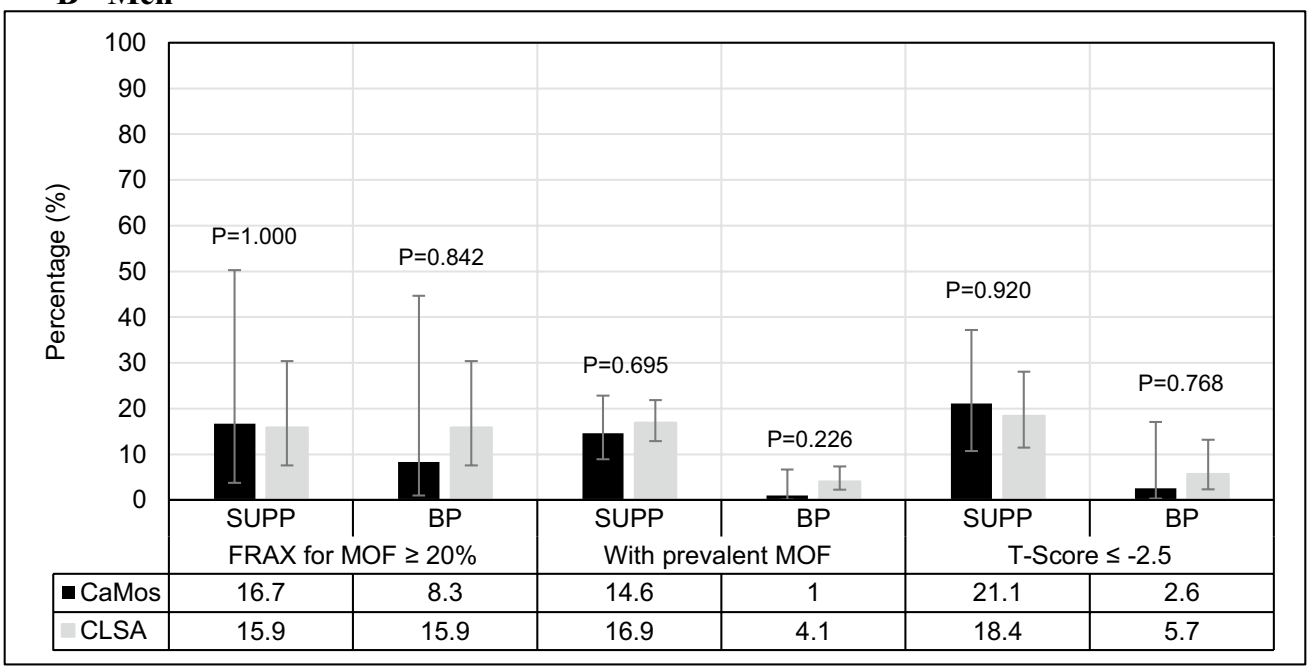
**A Women**




| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| CaMos | 30.5 | 7.2 | 36.7 | 32 | 5.8 | 43.3 | 30.6 | 6.6 | 37.4 |
| CLSA | 52.8 | 20.6 | 43.4 | 48.3 | 17.3 | 37.9 | 50.2 | 17.2 | 35.6 |

SUPP: supplement (calcium and vitamin D); BP (bisphosphonates); HT (menopausal hormone therapy)
T-score at femoral neck, Non-weighted results

**B Men**




| | | | | | | |
|---|---|---|---|---|---|---|
| CaMos | 16.7 | 8.3 | 14.6 | 1 | 21.1 | 2.6 |
| CLSA | 15.9 | 15.9 | 16.9 | 4.1 | 18.4 | 5.7 |

SUPP: supplement (calcium and vitamin D); BP (bisphosphonates);
T-score at femoral neck, Non-weighted results

**Fig. 4** Anti-osteoporosis treatment use (%, CI) in participants at high-risk for fracture stratified by cohort

osteoporosis might have been more likely to participate in CaMos than healthy adults, while the CLSA may have been more attractive to healthy adults. Even though we adjusted for multiple factors, selection bias remains a concern, and our results should be interpreted with this limitation in mind. This analysis was performed on CaMos and CLSA participants, regardless of the participant's race/ethnicity, a complex construct known to affect bone health outcomes. Although less than 10% of participants reported race/ethnicity other than White (CLSA: White 92.8%; South East Asian 1.09%; East Asian 0.87% Black 0.57%, other 4.45% and CaMos: White 95.5%; South East Asian: 0.97%; East Asian 2.39%; Black: 0.49% and other 0.45%), a sensitivity analysis in White participants only was performed, and results were similar. Finally, as similar sampling weights did not exist for both cohorts, the sampling weights could not be applied. To compensate for the difference in sampling strategy between both cohorts, we presented the prevalence by sex and age group.

## Conclusion

In conclusion, higher BMD values and lower risk of fracture were noted in the CLSA participants 50 years and older as compared to the participants of CaMos. An improvement in anti-osteoporosis treatment was noted over a 20-year period in women at high risk for fracture; the care gap, however, remains high, particularly in men.

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**Data availability** Data are available from the Canadian Longitudinal Study on Aging (www.clsa-elcv.ca) for researchers who meet the criteria for access to de-identified CLSA data.

## Declarations

**Conflict of interest** N Hassanabadi, SN Morin, C Berger, E Rahme, WD Leslie and D Goltzman declare they have no conflict of interests. A Papaioannou has received grants and honoraria from Amgen. AM Cheung has received honoraria from Amgen and Paladin.



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