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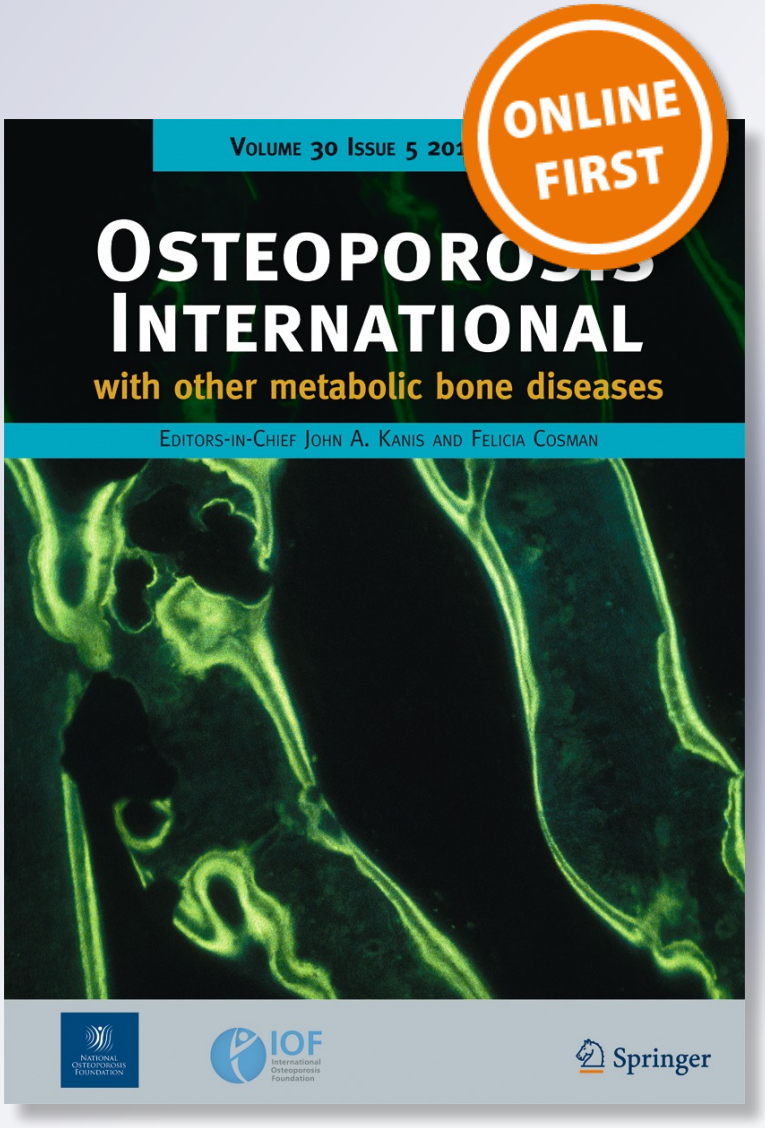

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ORIGINAL ARTICLE

Longitudinal assessment of health-related quality of life in osteoporosis: data from the population-based Canadian Multicentre Osteoporosis Study

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Abstract

Summary Little is known about the association between health-related quality of life (HRQOL) and osteoporosis in the absence of fracture, and how HRQOL may change over time. This study provides evidence of substantially reduced HRQOL in women and men with self-reported and/or BMD-confirmed osteoporosis, even in the absence of fragility fracture.

Introduction Fragility fractures have a detrimental effect on the health-related quality of life (HRQOL) of those with osteoporosis. Less is known about the association between HRQOL and osteoporosis in the absence of fracture.

Methods Canadian Multicentre Osteoporosis Study participants completed the SF-36, a detailed health questionnaire and measures of bone mineral density (BMD) at baseline and follow-up. We report the results of participants ≥ 50 years with 10-year follow-up. Self-reported osteoporosis at baseline and BMD-based osteoporosis at follow-up were ascertained. Multivariable linear regression models were developed for baseline SF-36 domains, component summaries, and change over time, adjusting for relevant baseline information.

Results Baseline data were available for 5266 women and 2112 men. Women in the osteoporosis group had substantially lower SF-36 baseline scores, particularly in the physically oriented domains, than those without osteoporosis. A similar but attenuated pattern was evident for the men. After 10-year follow-up (2797 women and 1023 men), most domain scores dropped for women and men regardless of osteoporosis status, with the exception of mentally-oriented ones. In general, a fragility fracture was associated with lower SF-36 scores and larger declines over time.

Conclusions This study provides evidence of substantially reduced HRQOL in women and men with self-reported and/or BMD-confirmed osteoporosis, even in the absence of fragility fracture. HRQOL should be thoroughly investigated even prior to fracture, to develop appropriate interventions for all stages of the disease.

Keywords CaMos · Fracture · Longitudinal · Osteoporosis · Population-based · Quality of life · SF-36

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s00198-019-05000-y) contains supplementary material, which is available to authorized users.

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Introduction

A sizeable body of literature has documented the detrimental effect of fragility fractures on the health-related quality of life (HRQOL) of those with osteoporosis [1–10]. This effect was consistent regardless of whether HRQOL was measured using the Medical Outcomes Trust 36-item health survey (SF-36) [1, 5, 8], the Health Utilities Index [3, 7], the Osteoporosis Assessment Questionnaire [2, 4], the Euro-QOL (EQ-5D) [6, 8, 9], or the Qualeffo-41 [10]. HRQOL was substantially more adversely affected when the fractures were of the hip and vertebrae than sites such as wrist [3, 6], and quality of life deteriorated with increasing numbers of fractures [8, 10]. One study combining 3011 EU and 4886 US osteoporotic women demonstrated poorer HRQOL in those with previous fracture, as well as a highly significant fear of falling [9]. Two longitudinal studies demonstrated that the negative effects of fractures were sustained 1 year [6] and 5 years [7] after the event.

However, much less is known about the effect of osteoporosis on HRQOL in the absence of the primary manifestation of the disease, a fragility fracture. This is in part because it is often not until a person falls and experiences a fracture that they and their physicians become aware of the loss of bone mass and density [11]. Studies of people with low bone mineral density (BMD) alone, who completed a quality of life assessment prior to an osteoporosis diagnosis, have had mixed results. One study of women attending an orthopedic clinic pre-diagnosis, another of undiagnosed community-based women who were only aware that they were at increased risk for osteoporosis, and a third who completed HRQOL screening prior to diagnosis found little association between low BMD and HRQOL [10, 12, 13]. Other studies have, however, noted differences in HRQOL prior to diagnosis including prior to BMD testing [14–18].

A number of factors may be contributing to the reduced HRQOL in those with osteoporosis, but who have not sustained a fragility fracture. Increased frailty associated with aging can predispose individuals to a higher risk of fracture in the future [19]. Moreover, osteoporosis is perceived as a disease that can lead to severe discomfort and disability, chronic pain, reduced physical ability, reduced social activity, poor well-being, depression, and loss of autonomy [18, 20, 21]. In a multivariable analysis of 222 women with osteoporosis, 101 with low BMD and 142 without documented osteoporosis, fears related to osteoporosis explained a small but relevant proportion of the variation in quality of life for both mentally and physically oriented domains of the SF-36 [21]. Uncertainty associated with a chronic illness is sometimes described as a cognitive stressor, resulting in a sense of loss of control, which can be associated with poorer coping, psychological distress, and reduced quality of life over time [22, 23]. Although the initiation and maintenance of therapy can have a positive effect on HRQOL [10, 24], this is not enough to eliminate the negative impact of the disease on perceived HRQOL [18]. This is all the more relevant given that there is also evidence that those who worry about their chronic disease, those who believe that their disease can have serious consequences and those with a long timeline perspective had substantially higher health-care utilization in the 2 years following diagnosis [23].

The Canadian Multicentre Osteoporosis Study (CaMos) is a prospective cohort study which has collected repeated assessments of HRQOL, and BMD using dual-energy X-ray absorptiometry DXA. Using the first 10 years of follow-up data, we aim to study the association of HRQOL with osteoporosis. The objectives include the following: (1) At baseline, to compare the HRQOL of those with and without self-reported osteoporosis, in men and women separately, and to further examine those with and without frailty fractures in the subset reporting osteoporosis and (2) To examine the changes in HRQOL over 10 years, stratified by those who were never diagnosed with osteoporosis, those diagnosed at baseline (or believed they had the disease) and those diagnosed during the 10-year follow-up; and within the subset of those diagnosed with osteoporosis, to examine differences in those who did and did not sustain a fragility fracture in those 10 years.

Methods

Participants

CaMos is a prospective cohort study of 9423 non-institutionalized, randomly selected men and women aged 25 years and older at baseline, drawn from a 50-km radius of nine Canadian cities (St John's, Halifax, Quebec City, Toronto, Hamilton, Kingston, Saskatoon, Calgary, and Vancouver). Baseline interviews took place between September 1995 and September 1997, with 10-year follow-ups taking place between September 2005 and September 2007. The interviews were conducted in person at both time points. Participants provided written consent, and ethics approval was obtained through the Review Boards of each participating centre.

A detailed description of the objectives, methodology and sampling framework for CaMos is available elsewhere [24, 25]. Briefly, households within each region were selected by random draws of listed telephone numbers, and one randomly selected household member 25 years of age or older was asked to participate. Of 22,173 eligible households, 27.5% declined to participate, 30.0% completed a short questionnaire that provided information about the age, gender, and fracture history of the residents, and 9423 (42.5%) went on to participate fully in the study. CaMos was designed to collect epidemiological data related to the incidence and prevalence of osteoporosis, so although the sampling framework was random, it was

designed to include more women than men, and a higher number of older than younger Canadian residents.

Questionnaires

Data collection included psychosocial information, medical and family history, lifestyle (e.g., alcohol, caffeine, tobacco), dietary intake, physical activity, reproductive history, and medication use, in addition to measured height, weight [24, 25] and DXA assessment of the spine (L1-L4), femoral neck, and total hip [26]. Comorbidities were collected by means of a modified version of the Charleson Comorbidity Index [27] and included self-reported diseases such as several forms of cancer; kidney, liver, and lung diseases; neuromuscular diseases; heart disease; diabetes; osteoporosis; rheumatoid arthritis; osteoarthritis; thyroid disease; and dementia. Comorbidities were based on the participants' responses to the question "Have you ever been told by a doctor that you have any of the following conditions" in an attempt to ensure that the presence of these diseases was confirmed by a physician rather than being based on self-diagnosis [28]. The SF-36 [29, 30] was self-completed during the same visit. The same questionnaire and clinical assessments were repeated at 3-year (for those 40–60 only), 5-year (2000–2002), and 10-year follow-up (2005–2007). This study includes 5266 women and 2112 men aged ≥ 50 years with at least one SF-36 domain score and non-missing BMI and self-reported diagnosis of osteoporosis at baseline.

Definition of osteoporosis

The definition of those with osteoporosis in the context of this study requires some explanation, for clarity. At baseline, participants were asked if they had been told by a health-care professional that they had osteoporosis. This self-reported diagnosis was used as our definition for the baseline cross-sectional analyses, as there is evidence that it is the perception of osteoporosis that may have a negative impact on HRQOL, even in the absence of actual testing. Following completion of the baseline questionnaire, CaMos participants had DXA scans to assess BMD. As per our protocol, the results of the initial evaluation were variously shared with the participant, the family physician, or both [31]. As a result, the proportion of BMD-based cases of osteoporosis increased over time. However, those without BMD-based osteoporosis but who continued to believe that they had the disease were retained in the cohort in their original classification. For the longitudinal analyses, we therefore grouped the baseline to year 10 follow-up data on the basis of those who never had osteoporosis, those who believed they already had it at baseline, and those who developed it over the first 10 years of follow-up.

Fractures

Self-reported prevalent fragility fractures were identified at the baseline interview. We excluded fractures of the head, hands, and feet. Fragility (low-trauma) fractures are those occurring with less than or equivalent force as a fall from standing height. Self-reported incident clinical fragility fractures were identified by annual postal questionnaire up to Year 10 follow-up or by interviewer-administered questionnaires at the scheduled interviews (in the 3rd, 5th, and 10th years after study entry). Where possible, and with participant consent, fractures were confirmed by radiology or physician report. However, an incident fragility fracture did not imply a diagnosis of osteoporosis in this analysis.

SF-36

The SF-36 measure has 8 domain scores including physical functioning (PF), role physical (RP), role emotional (RE), bodily pain (BP), general health perceptions (GH), vitality (VT), social function (SF), and mental health (MH) [29]. These eight domains are scored from 0 to 100, with a score of 100 representing excellent HRQOL and no pain [29]. In addition, a Physical Component Summary (PCS) and a Mental Component Summary (MCS) can also be derived. The PCS and MCS are standardized to a mean of 50, with scores above and below 50 representing better than average and poorer than average scores respectively [30]. A 5-point change and 2-to-3-point change are considered clinically relevant for domain or summary scores, respectively [29, 30]. This survey is widely used to assess the HRQOL of general and specific adult populations, estimate the relative burden of different diseases, and examine the impact of a wide range of treatment interventions on HRQOL [25, 29, 30, 32–35], and is considered valid for use in osteoporosis [8]. These data can therefore be used to compare the HRQOL of women and men with self-reported osteoporosis to those who do not believe they have the disease, in those over 50 years of age, when osteoporosis is more likely to manifest itself.

Statistical analysis

Graphs of age and body mass index (BMI) by SF-36 scores (baseline and 10-year changes) were assessed for non-linearity. Polynomials of age and BMI, up to 3 degrees, were selected on the basis of the best fit for each SF-36 domain or component summary. Linear regression models were then developed for baseline SF-36 and 10-year changes with the non-linear terms of age and BMI, and with prevalent fragility fractures. The residuals were used to assess the association of osteoporosis status with SF-36 adjusted for baseline height, education, regional centre, baseline regular physical activity and a number of comorbidities at baseline. The baseline

regressions were further adjusted for baseline self-reported diagnosis of comorbidities, while longitudinal regressions were further adjusted for self-reported diagnosis of comorbidities (diagnosed at baseline, never diagnosed, diagnosed during the 10-year follow-up), baseline SF-36 score and 10-year BMI change.

Results

At baseline, CaMos included 7753 women and men ≥ 50 years old. Of that number, 375 (4.8%) were excluded because of missing BMI ($n = 222$), missing self-reported osteoporosis information ($n = 147$), and missing SF-36 scores in all domains ($n = 6$). Complete baseline data for those ≥ 50 years old were therefore available for 5266 women and 2112 men. Within the women, 699 (13.3%) self-reported a diagnosis of osteoporosis and of the 699, 251 (35.9%) indicated that they had sustained a fragility fracture in the past. Also within the 699, 46% actually had a T-score ≤ − 2.5, suggesting true osteoporosis, while of those who did not indicate that they had osteoporosis, 24% actually did have a T-score ≤ − 2.5. Within the men, 39 (1.8%) indicated that they had osteoporosis and within that group of 39, 11 (28.4%) indicated that they had sustained a fragility fracture. Of the 39, 30% actually had a T-score of ≤ − 2.5 while of those who did not indicate that they had osteoporosis, 6% did have a T-score of ≤ − 2.5. Baseline characteristics of the sample are provided in Table 1, stratified by sex and by presence of osteoporosis.

Table 2 provides the unadjusted baseline mean SF-36 domain and component summary scores for the women and men with and without self-reported osteoporosis; Online Resource 1 provides the same for the subset of women and men with self- reported osteoporosis, stratified by history of fragility fracture. Within the sample of women, those with self-reported osteoporosis had substantially and clinically lower SF-36 baseline scores than those without osteoporosis, except for the differences in mental health and mental component summary scores which were inconclusive. A similar but attenuated pattern was evident for the men. Within the osteoporosis sample, in women, having a history of fragility fracture appeared to result in even lower SF-36 scores for most domains and the PCS; in men, the results were mixed and inconclusive due to the small sample size.

Online Resource 2 provides the unadjusted baseline mean SF-36 scores for the subset of women and men with self-reported osteoporosis stratified by DXA T-scores of ≤ − 2.5 vs. > − 2.5. Within women with self-reported osteoporosis, we saw a clinical difference in the BP domain in those with T-scores ≤ − 2.5 compared to those with T-score > − 2.5. Inconclusive results were seen for PF, RP, and RE while other domains did not show any clinical differences. In men, the results were inconclusive due to the small sample size.

Figure 1 provides the adjusted baseline differences for those with and without self-reported osteoporosis, for men and women. Once adjusted for polynomials of age and BMI, as well as prevalent fragility fracture, comorbidities and several demographic variables (see complete list in footnote of figure), all but the MH domain and the MCS demonstrated clinically relevant differences, with differences ranging from − 5.1 (both SF and RE) to − 11.0 (RP). For men, none of the differences in the eight domains or the two component summaries were clinically relevant; however, the 95% confidence intervals (CIs) were wide due to the small number of men reporting a diagnosis of osteoporosis, leading to inconclusive results. Online Resource 3 depicts the adjusted baseline estimates for SF-36 scores in women with self-reported osteoporosis, comparing those with a T-score ≤ − 2.5 to those with a T-score > − 2.5. None of the estimates were clinically different, although PF, RP, BP, SF, and RE showed inconclusive results with one or both of their confidence limits being greater than the 5-point clinical difference. This analysis could not be done for men due to small sample size.

Complete follow-up data at 10 years were available for 2797 women and 1023 men. For the women, 1907 (68.2%) did not develop osteoporosis, 300 (10.7) believed they had it at baseline and an additional 590 (21.1) developed osteoporosis over the 10-year period. Within the sample of 590 who developed osteoporosis, 134 (22.7%) sustained a fragility fracture. For men, 910 (89.0%) did not develop osteoporosis, 20 (2.0%) believed that they already had it at baseline and 93 (9.1%) developed it over the 10 years. For the 93 who developed it, 15 (16.1%) sustained a fragility fracture.

Table 3 provides the unadjusted differences between baseline and year 10 (with loss represented by negative values) for women and men separately, stratified by whether they had no osteoporosis, had it already, or developed it over the 10 years of follow-up. With the exception of the MH domain and MCS, the scores dropped for women and men regardless of the osteoporosis status. Online Resource 4 provides the same information for the subset of women and men who developed osteoporosis over the 10 years of follow-up, stratified by incident fragility fracture. For those who developed osteoporosis, the declines were not that different for the women with and without a fragility fracture. However, for the men, the declines appeared much larger in the presence of a fragility fracture, although since the sample is small the results are inconclusive.

Figure 2 provides the sex-stratified estimates, adjusted for the same covariates as Fig. 1 as well as change in BMI, change in comorbidities, and the relevant baseline SF-36 score. It compares 10-year changes of those who had reported osteoporosis at baseline and those who developed osteoporosis, to those who never reported a diagnosis. The adjusted differences for women who believed that they had osteoporosis at baseline as compared with those never

Table 1 Characteristics of adult Canadian Multicentre Osteoporosis Study participants aged ≥ 50 years at baseline by sex

		Women ($n = 5266$)		Men ($n = 2112$)	
		No self-reported OP 4567	Self-reported OP 699	No self-reported OP 2073	Self-reported OP 39
Categorical variables presented as *n* (%)					
Age	50–59	1222 (26.8)	89 (12.7)	579 (27.9)	12 (30.8)
	60–69	1691 (37.0)	252 (36.1	726 (35.0)	10 (25.6)
	70–79	1279 (28.0)	264 (37.8)	587 (28.3)	15 (38.5)
	80+	375 (8.2)	94 (13.5)	181 (8.7)	2 (5.1)
Centre	Vancouver	517 (11.3)	78 (11.2)	237 (11.4)	6 (15.4)
	Calgary	523 (11.5)	88 (12.6)	231 (11.1)	3 (7.7)
	Saskatoon	512 (11.2)	98 (14.0)	234 (11.3)	1 (2.6)
	Hamilton	522 (11.4)	92 (13.2)	242 (11.7)	6 (15.4)
	Toronto	409 (9.0)	79 (11.3)	218 (10.5)	4 (10.3)
	Kingston	476 (12.6)	68 (9.7)	231 (11.1)	2 (5.1)
	Quebec City	576 (12.6)	59 (8.4)	243 (11.7)	4 (10.3)
	Halifax	535 (11.7)	81 (11.6)	239 (11.5)	6 (15.4)
	St-John's	497 (10.9)	56 (8.0)	198 (9.6)	7 (18.0)
Postmenopausal		4312 (94.4)	688 (98.4)	–	–
Caucasian		4391 (96.2)	677 (96.9)	1935 (93.3)	37 (94.9)
Education	< gr 13 w/o diploma	1923 (42.1)	335 (47.9)	792 (38.2)	17 (43.6)
	High school/trades	1964 (43.0)	262 (37.5)	742 (35.8)	16 (41.0)
	University	680 (14.9)	102 (14.6)	538 (26.0)	6 (15.4)
Participation in regular physical activity		2587 (56.7)	357 (51.1)	1160 (56.0)	18 (46.2)
Paid work	Usually sitting	1236 (27.1)	186 (26.7)	653 (31.5)	7 (18.0)
	Stand/walk a lot	2492 (54.7)	403 (57.7)	872 (42.1)	23 (59.0)
	Lift/climb	652 (14.3)	85 (12.2)	270 (13.0)	3 (7.7)
	Heavy work	176 (3.9)	24 (3.4)	278 (13.4)	6 (15.4)
# of comorbidities	None	2007 (44.0)	229 (32.8)	883 (42.6)	16 (41.0)
	1 or 2	2250 (49.3)	401 (57.4)	1023 (49.4)	20 (51.3)
	3+	310 (6.8)	69 (9.9)	167 (8.1)	3 (7.7)
Postmenopausal hormone use		1117 (24.5)	203 (29.0)		
Bisphosphonate use		9 (0.22)	129 (18.5)	0 (0.0)	3 (7.7)
Prevalent fragility fracture*		875 (19.2)	251 (35.9)	344 (16.6)	11 (28.2)
T-score (L1-L4, femoral neck or total hip) ≤ -2.5 **		972 (24.0)	273 (46.8)	107 (5.8)	11 (29.7)
Continuous variables presented as mean (SD)					
BMI (kg/m^2)		27.2 (5.1)	26.0 (4.8)	27.2 (4.0)	26.7 (4.3)
Total calcium intake (mg/day)		1014 (605)	1340 (672)	909 (579)	1192 (796)

*women No OP $n = 4559$; men No OP $n = 2068$; **women no OP $n = 4048$; women OP $n = 583$; men no OP $n = 1856$; men OP = 37

diagnosed were clinically relevant in only two domains (RP and RE) but the overall pattern is consistent with greater decline in HRQOL for those with osteoporosis. In women with osteoporosis at baseline, however, those who sustained an incident fragility fracture, compared with those who did not, showed a greater clinical decline in three of the four physical domains (PF, RP, BP), the physical component summary score and one of the mental domains (SF) (Online Resource 5). The trend was similar for those who developed osteoporosis over the 10 years although the differences were not clinically important.

In women who developed osteoporosis over the 10 years, those who sustained a fragility fracture showed a greater decline in PF and PCS (data not shown). The

Table 2 Mean SF-36 baseline scores for women and men without or with self-reported osteoporosis in the population-based CaMos data

	Without osteoporosis				With self-reported osteoporosis				Differences (with-without)	
	N	Mean	STD	95% C.I.	N	Mean	STD	95% C.I.	Mean	95% C.I.
Women										
PF	4565	74.2	23.7	(73.5; 74.9)	698	58.9	27.6	(56.9; 61.0)	− 15.3	(− 17.4; − 13.1)
RP	4565	76.4	36.7	(75.3; 77.4)	696	57.5	43.1	(54.3; 60.7)	− 18.9	(− 22.2; − 15.5)
BP	4567	72.8	23.7	(72.1; 73.5)	699	58.2	25.6	(56.3; 60.1)	− 14.6	(− 16.5; − 12.5)
GH	4557	75.0	17.8	(74.5; 75.5)	695	64.1	21.2	(62.5; 65.6)	− 10.9	(− 12.6; − 9.3)
VT	4561	64.6	19.1	(64.0; 65.1)	698	54.6	21.3	(53.0; 56.2)	− 10.0	(− 11.7; − 8.3)
SF	4565	87.1	20.1	(86.5; 87.6)	697	78.8	25.9	(76.9; 80.7)	− 8.3	(− 10.3; − 6.3)
RE	4564	84.8	30.8	(83.9; 85.7)	698	76.4	38.2	(73.6; 79.3)	− 8.4	(− 11.4; − 5.4)
MH	4561	78.7	15.1	(78.2; 79.1)	698	74.8	17.1	(73.5; 76.0)	− 3.9	(− 5.2; − 2.6)
PCS	4543	46.9	10.0	(46.6; 47.2)	692	39.7	11.2	(38.9; 40.5)	− 7.2	(− 8.1; − 6.3)
MCS	4543	53.6	8.6	(53.3; 53.8)	692	52.2	10.0	(51.5; 53.0)	− 1.4	(− 2.1; − 0.6)
Men										
PF	2072	78.2	22.8	(77.2; 79.2)	39	73.8	24.5	(65.9; 81.8)	− 4.3	(− 11.6; 2.9)
RP	2070	78.8	35.1	(77.2; 80.3)	39	75.6	35.6	(64.1; 87.2)	− 3.1	(− 14.2; 8.0)
BP	2073	76.1	22.9	(75.1; 77.1)	39	69.2	23.9	(61.4; 76.9)	− 6.9	(− 14.2; 0.4)
GH	2071	73.8	18.2	(73.0; 74.6)	39	67.2	19.8	(60.8; 73.7)	− 6.6	(− 12.3; − 0.8)
VT	2071	67.8	18.3	(67.0; 68.6)	39	65.5	19.4	(59.2; 71.8)	− 2.3	(− 8.1; 3.5)
SF	2073	88.5	19.3	(87.7; 89.3)	39	88.8	18.8	(82.7; 94.9)	0.3	(− 5.8; 6.4)
RE	2071	87.9	27.8	(86.7; 89.1)	39	86.3	28.3	(77.1; 95.5)	− 1.6	(− 10.4; 7.2)
MH	2070	81.8	13.9	(81.2; 82.4)	39	79.6	13.6	(75.2; 84.0)	− 2.2	(− 6.6; 2.2)
PCS	2065	47.7	9.6	(47.3; 48.1)	39	45.1	9.3	(42.1; 48.2)	− 2.5	(− 5.6; 0.5)
MCS	2065	54.8	7.7	(54.4; 55.1)	39	54.6	7.2	(52.3; 57.0)	− 0.1	(− 2.6; 2.3)

STD, standard deviation; CI, confidence interval; OP, osteoporosis; PF, physical function; RP, role physical; BP, bodily pain; GH, general health perceptions; VT, vitality; SF, social function; RE, role emotional; MH, mental health; PCS, physical component summary; MCS, mental component summary

sample size for men who already had osteoporosis was very small ($n = 20$) and thus change could not be reliably assessed. For the 93 who developed it over the 10-year follow-up, the trends in general do support a greater decline in RP, BP, and SF, as compared to those who never developed it. All other domains also showed the same pattern, with consistently larger declines in HRQOL but with wide confidence intervals.

Discussion

In this 10-year prospective population-based Canada-wide study of HRQOL in adult women, the presence of a self-reported osteoporosis, even in the absence of any clinical manifestation such as a fracture, can have a substantial, negative association with HRQOL, as demonstrated by the sizeable differences in baseline scores between those with and without the disease even after adjusting for known covariates. Findings were similar but weaker for men, and limited by a relatively small sample size.

These findings are consistent with a growing body of work [10, 14, 17, 18], as well as a systematic review [20], that suggests that even the diagnosis of osteoporosis is associated with lower HRQOL. However, a history of a fragility fracture appears to be associated with even lower HRQOL scores, particularly in the physically oriented domains, than for those self-reporting osteoporosis without fracture. This was more pronounced in women than in men, but the sample of men was very small, with only 11 in the group that had osteoporosis with a fragility fracture at baseline. The finding that the physically oriented domains tended to be more affected than the mentally oriented ones is consistent with the findings of one large Spanish study of postmenopausal women ($n = 804$) assessing HRQOL prior to diagnosis from densitometry [14], as well as the findings in other chronic diseases [34, 35].

The longitudinal data also suggest that having or developing osteoporosis may be associated with greater decline in HRQOL over 10 years relative to those without osteoporosis. While all three groups saw substantial declines in most HRQOL domains that are likely associated with simply being 10 years older [36], the largest declines tended to be in the

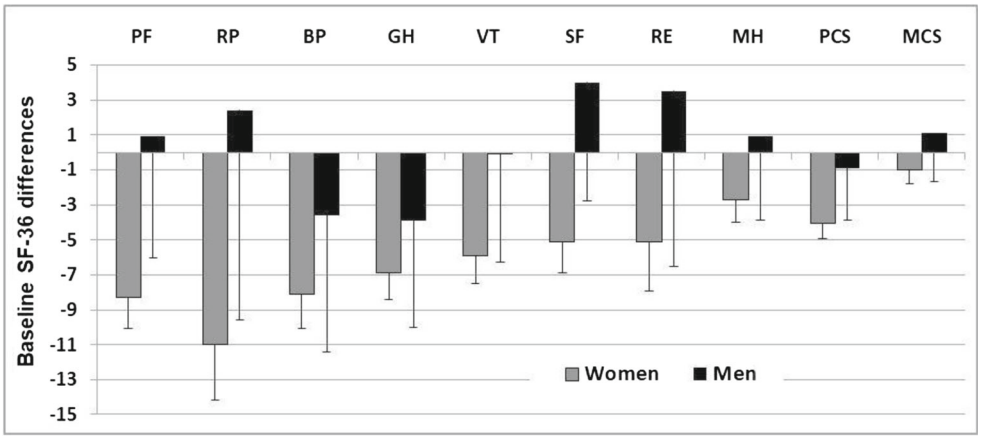

Fig. 1 Adjusted baseline differences comparing sf-36 scores of participants with self-reported osteoporosis to those who did not report it, for men and women in CaMos

First adjusted by polynomials of age and BMI, prevalent fracture and then by scoliosis, bowel disease, neurological disease, hypertension, heart disease, stroke, cancer (breast, uterus, prostate, myeloma, other), diabetes, rheumatoid or osteoarthritis, lung disease (asthma, emphysema, chronic bronchitis), height, education, regional center, regular physical activity and number of comorbidities.

sample that became osteoporotic over the 10 years of follow-up. An analysis of the subset that became osteoporotic showed that the women tended to have similar declines regardless of whether they sustained a fracture, but for the men, a fracture

Table 3 Mean differences for SF-36 at year 10 and baseline (Y10–baseline), for women and men, without (No OP) and with (OP) self-reported osteoporosis at baseline, and those who developed osteoporosis (became OP) over 10 years in CaMos

	No OP				OP				Became OP			
	N	Mean	STD	95% C.I.	N	Mean	STD	95% C.I.	N	Mean	STD	95% C.I.
Women												
PF	1907	− 9.9	20.8	− 10.9; − 9.0	300	− 7.6	24.4	− 10.4; − 4.8	590	− 12.1	21.4	− 13.8; − 10.4
RP	1907	− 6.9	42.2	− 8.8; − 5.0	299	− 5.2	48.0	− 10.6; 0.3	590	− 10.1	43.9	− 13.7; − 6.6
BP	1907	− 5.5	24.5	− 6.6; − 4.4	300	0.0	26.7	− 3.1; 3.0	590	− 5.1	24.3	− 7.1; − 3.1
GH	1903	− 3.0	16.2	− 3.8; − 2.3	296	− 1.7	17.9	− 3.7; 0.4	588	− 3.4	17.7	− 4.8; − 2.0
VT	1902	− 2.9	17.6	− 3.7; − 2.1	299	− 1.2	20.0	− 3.5; 1.0	590	− 4.1	17.8	− 5.5; − 2.6
SF	1907	0.1	22.7	− 0.9; 1.1	300	0.3	27.3	− 2.8; 3.3	590	− 1.8	22.6	− 3.6; 0.0
RE	1907	− 1.0	37.4	− 2.7; 0.7	300	− 2.6	45.8	− 7.8; 2.6	590	− 4.4	39.6	− 7.6; − 1.1
MH	1902	1.2	14.5	0.6; 1.9	298	2.1	15.8	0.3; 3.9	590	− 0.8	15.1	− 2.0; 0.5
PCS	1894	− 3.8	9.4	− 4.2; − 3.4	294	− 2.3	10.5	− 3.5; − 1.1	588	− 4.1	9.5	− 4.9; − 3.4
MCS	1894	1.4	9.1	1.0; 1.8	294	1.0	10.3	− 0.2; 2.2	588	0.4	9.4	− 0.4; 1.2
Men												
PF	910	− 9.0	21.1	− 10.4; − 7.7	20	− 11.0	25.9	− 23.1; 1.1	93	− 8.9	20.1	− 13.0; − 4.7
RP	910	− 7.3	39.8	− 9.9; − 4.7	20	− 5.0	38.6	− 23.0; 13.0	93	− 15.1	45.6	− 24.4; − 5.7
BP	910	− 4.1	23.6	− 5.6; − 2.5	20	− 2.3	25.4	− 14.2; 9.5	92	− 8.8	23.5	− 13.7; − 3.9
GH	910	− 4.7	16.0	− 5.7; − 3.7	20	− 3.2	21.1	− 13.1; 6.7	93	− 3.3	15.0	− 6.4; − 0.2
VT	910	− 4.4	17.3	− 5.5; − 3.3	20	− 5.0	15.5	− 12.2; 2.2	92	− 3.7	15.3	− 6.9; − 0.5
SF	910	− 1.6	20.7	− 2.9; − 0.2	20	− 5.0	21.6	− 15.1; 5.1	92	− 4.2	20.3	− 8.4; 0.0
RE	909	− 2.4	30.8	− 4.4; − 0.4	20	− 11.7	37.9	− 29.4; 6.1	92	− 2.2	36.9	− 9.8; 5.5
MH	909	0.4	14.3	− 0.6; 1.3	20	0.4	13.9	− 6.1; 6.9	92	− 0.5	14.5	− 3.5; 2.5
PCS	908	− 3.5	9.1	− 4.1; − 2.9	20	− 2.7	10.8	− 7.8; 2.4	92	− 4.6	9.8	− 6.6; − 2.5
MCS	908	0.5	8.2	− 0.1; 1.0	20	− 1.2	8.1	− 5.0; 2.6	92	0.5	8.3	− 1.2; 2.2

STD, standard deviation; CI, confidence interval; OP, osteoporosis; Fx, fracture; PF, physical function; RP, role physical; BP, bodily pain; GH, general health perceptions; VT, vitality; SF, social function; RE, role emotional; MH, mental health; PCS, physical component summary; MCS, mental component summary

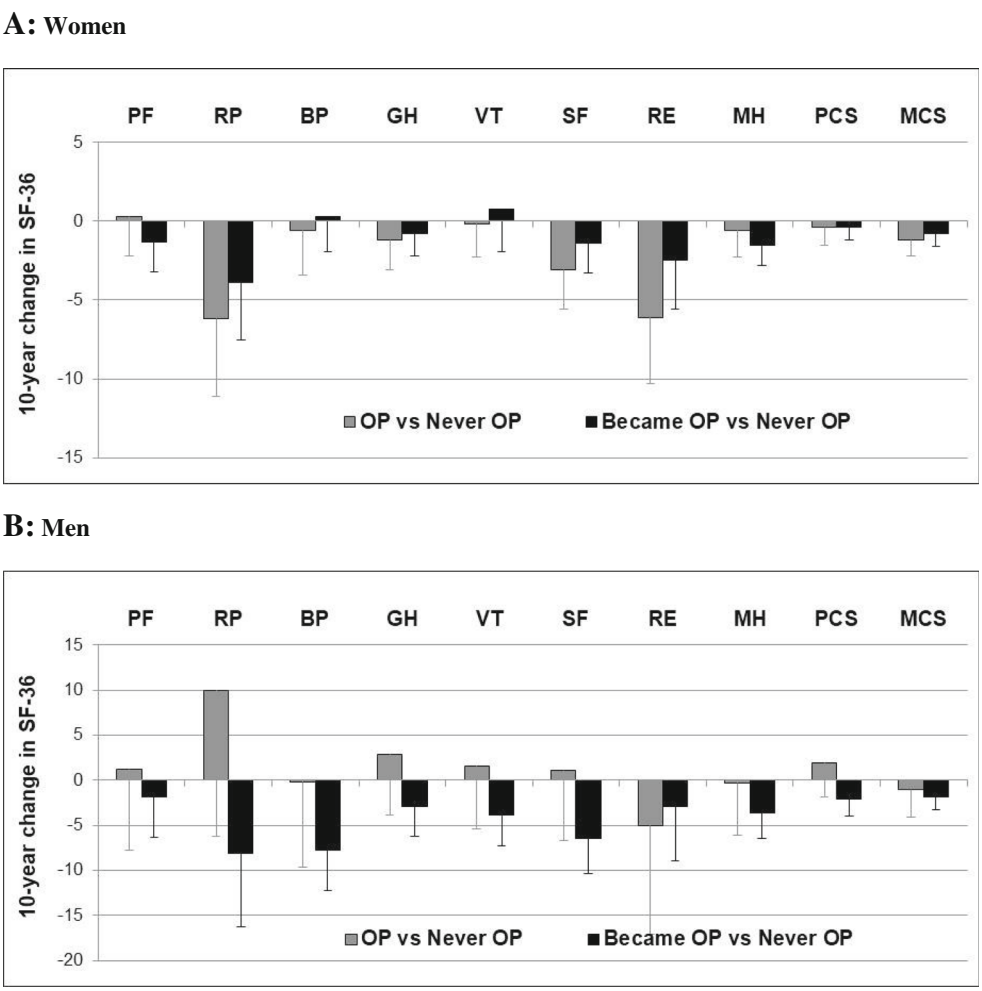

Fig. 2 Adjusted estimates comparing 10-year change in sf-36 scores of women **a** and men **b** with those who had osteoporosis at baseline, and those who developed it during the 10 years of follow-up in CaMos

First adjusted by polynomials of age and BMI, prevalent fracture and secondly by baseline height, education, regional center, baseline regular physical activity, number of comorbidities at baseline, change in BMI over 10 years, baseline SF-36 score, as well as self-reported diagnosis (diagnosed at baseline, never diagnosed, diagnosed during the 10-year follow-up) of scoliosis, bowel disease, neurological disease, hypertension, heart disease, stroke, cancer (breast, uterus, prostate, myeloma, other), diabetes, rheumatoid or osteoarthritis and lung disease (asthma, emphysema, chronic bronchitis).

was associated with larger declines than those who did not sustain a fracture, although with $n = 15$, it is difficult to draw any real conclusions from these data.

It is of concern that, when combining the findings of poorer baseline HRQOL with greater decline over time, women and men with osteoporosis may develop substantially impaired quality of life over time. A prevalent fragility fracture at baseline was associated with even poorer scores, as already documented by a large body of literature documenting the negative impact of fracture [1–10]. But the finding that a health-care provider diagnosis, or the belief that one already has osteoporosis can result in substantially lower HRQOL values, should be of substantial concern to health-care professionals and policy makers; it suggests that interventions such as counseling and support for all osteoporosis stages are needed [10]. It is of considerable interest that when looking at the subset of 699 women who believe they have osteoporosis, there were few differences in the baseline HRQOL of those who actually did or did not have osteoporosis as defined by DXA T-scores split at −2.5 (Online Resource 3).

There are a number of limitations to this work. First, while the sampling framework was random, it was designed to include a larger number of older women than men and as a result, the sample for men was generally too small to draw conclusions. However, the results for the men are presented despite this limitation, as there are very little data available regarding the association of osteoporosis and HRQOL in men, either cross-sectionally or longitudinally. A second limitation was the loss to follow-up for the longitudinal

component. Only 61.1% of women and 54.5% of men in the original cohort completed the SF-36 at year 10 [36], and selection of those over 50 years of age further reduced the sample size. Finally, while the use of the generic SF-36 has advantages in that it is widely used and allows comparisons to other populations using the same measure, it does not collect osteoporosis-specific aspects of HRQOL such as the effects on activities of daily living, fear of falling, self-image and fear of the future [37].

However, this work also has a number of strengths. First, CaMos is a population-based longitudinal cohort comprising a large sample of adults with and without osteoporosis; to our knowledge, only one study had a larger sample of 7897 but included only women [9]. In addition, CaMos collected data on an array of behavioral and environmental corelates, which enabled us to adjust our analyses for baseline variables as well as new diagnoses of a number of comorbidities over the 10-year period.

A change in health state can result in a change in the internal standards, values or conceptualization known as a "response shift" [38]. This can affect HRQOL outcome measures, particularly in longitudinal settings. However, a meta-analysis of the effect size of response shifts in studies that assessed quality of life found that the magnitude was small, and positive and negative values canceled each other out [38]. The authors concluded that a definite conclusion regarding the clinical significance of response shifts cannot currently be drawn based on existing studies. An assessment of measurement equivalence of the SF-36 within CaM*os* concluded that sex and race did not affect the conceptualization of HRQOL within this sample [36]. Moreover, an assessment of differential item functioning in the context of the CaM*os* physical and mental subscales noted that although there were differences across population subgroups, the effect was not large for most items [39, 40]. Therefore no adjustment for response shift was made in the current analysis.

In conclusion, this study provides additional evidence of substantially lower HRQOL in women and men with self-reported osteoporosis, even in the absence of fragility fracture, which may worsen over time. Whether this is due to frailty [19], the perceptions about the disease itself [10, 21], fear of falling [9], cognitive stress due to uncertainty [22, 23], or a combination of these, the belief that osteoporosis can have serious consequences could result in considerably higher health-care utilization following diagnosis [23]. HRQOL in men and women with osteoporosis should therefore be thoroughly investigated even prior to the occurrence of fracture, to develop appropriate interventions that would empower patients to effectively manage all stages of the disease.

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Compliance with ethical standards

Conflicts of interest Wilma M. Hopman, Claudie Berger, Lawrence Joseph, Tanveer Towheed, Tassos Anastassiades, David A. Hanley, Jerilynn Prior, and David Goltzman declare that they have no conflict of interest.

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Jonathan D. Adachi declares that he has conflicts of interest but he does not believe that they pertain to the current paper. He is on the Amgen speaker's bureau, conducts clinical trials with them and is a scientific advisor. In addition he is a past president of Osteoporosis Canada and sits on the board of directors, and is a scientific advisor for the International Osteoporosis Foundation.

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