Is lower income associated with an increased likelihood of qualification for treatment for osteoporosis in Canadian women?

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ABSTRACT

Purpose: Lower income has been associated with increased fracture risk. We examined whether lower income in women was associated with an increased likelihood of treatment qualification determined by Canada FRAX[®].

Methods: We calculated 10-year FRAX probabilities in 51,327 Canadian women aged ≥ 50 years undergoing baseline bone mineral density (BMD) measured by dual energy x-ray absorptiometry 1996-2001. FRAX probabilities for hip fracture $\geq 3\%$ or major osteoporotic fracture (MOF) $\geq 20\%$ were used to define treatment qualification. Mean household income from Canada Census 2006 public use files was used to categorize the population into quintiles. Logistic regression analyses were used to model the association between income and treatment qualification.

Results: Percentages of women who qualified for treatment based upon high hip fracture probability increased linearly with declining income quintile (all p -trend < 0.001), but this was partially explained by older age among lower income quintiles (p -trend < 0.001). Compared to the highest income quintile, women in the lowest income quintile had a greater likelihood of treatment qualification based upon high hip fracture probability determined with BMD (age-adjusted odds ratio [OR] 1.34, 95%CI 1.23-1.47) or high MOF fracture probability determined with BMD (age-adjusted OR 1.31, 95%CI 1.18-1.46). Differences were non-significant when FRAX was determined without BMD, implying that BMD differences may be the primary explanatory factor.

Conclusions: FRAX determined with BMD identifies a larger proportion of lower income women as qualifying for treatment than higher income women.

MINI ABSTRACT

We examined whether low income was associated with an increased likelihood of treatment qualification for osteoporotic fracture probability determined by Canada FRAX in women aged ≥ 50 yr. A significant negative linear association was observed between income and treatment qualification **when FRAX included BMD**, which **may have** implications for clinical practice.

KEYWORDS: income, osteoporosis, treatment qualification, FRAX, disadvantage

INTRODUCTION

With few exceptions, adverse socioeconomic position is associated with most causes of morbidity and mortality (1), an association well-documented for lower income countries (1), but now increasingly observed in higher overall income countries (2). Osteoporosis, a systemic skeletal disease characterized by micro-architectural deterioration of bone tissue and an increased susceptibility to fracture, appears to be no exception to this. Increased fracture risk has been associated with social disadvantage in many (3-10), but not all (11-13) studies. While disentanglement of the underlying mechanisms for these associations continues, it is clear that associations regarding fracture burden have important public health implications.

Clinical risk factors associated with 10-year fracture probability estimated from the World Health Organization fracture risk assessment (FRAX®) calculator (14) are age, body mass index (BMI), smoking, alcohol consumption, and several co-morbidities, many of which are associated with social disadvantage (15, 16). The gradient of 10-year fracture probability determined from FRAX® with or without bone mineral density (BMD) supports clinical decision making by identifying individuals at high risk of fracture (17).

It is not known whether income is associated with a greater likelihood of qualifying for treatment based upon FRAX-derived hip or major osteoporotic fracture (MOF) probability. We have previously shown that income has a strong dose-response with the likelihood of having an osteoporotic BMD T-score, independent of clinical risk factors included in the FRAX model (18). Given those data, and also the association shown between social disadvantage and fracture, it is plausible that those of greater social disadvantage are more likely to be in need of treatment. However, there are no data that examine whether those with lower income are more likely to qualify for treatment according to FRAX, the most widely used clinical tool for fracture risk assessment. It is imperative to better understand this association in order to examine whether those of lower income are being identified as at greater need for treatment by FRAX. Taken in

context, it is important to identify whether income is associated with an increased likelihood of treatment qualification identified by FRAX tools. We examined, in a country with universal access to BMD testing when referred by a clinician, whether income was associated with an increased likelihood of qualifying for treatment based upon elevated hip probability ($\geq 3\%$) or MOF probability ($\geq 20\%$) (19-21) as determined by FRAX.

METHODS

Data sources

We performed a cross-sectional study to examine the association between income and treatment qualification based upon hip fracture or MOF probability in women aged ≥ 50 years ($n=51,327$). Records of patients who were referred to the Manitoba Bone Density Program, Canada, 1996-2001 for a baseline BMD test that assessed the femoral neck were linked to anonymized population-based administrative health records extracted from the data repository housed at the Manitoba Centre for Health Policy (MCHP), University of Manitoba, Canada (22, 23). This study was reviewed and approved by the Health Research Ethics Board for the University of Manitoba, and the Health Information Privacy Committee (HIPC) of Manitoba Health (HIPC File Number 2012/2013-15).

Adverse socioeconomic position

Mean household income for dissemination areas (DAs) was extracted from the public use files of the Statistics Canada Census for 2006, and ranked from the lowest to highest. As of 2001 Census, DAs replace enumeration areas as the basic unit for dissemination, and are the smallest geographic unit for which Census data are released to the public. DAs are composed of one or more neighbouring blocks, and are uniform in population size, ranging from 400 to 700 persons. Income was categorized into quintiles, with each quintile containing $\sim 20\%$ of the population, as previously described (18). Quintile 1 had the lowest income and quintile 5 had the highest income; quintile 5 was held as the referent category for model-based analyses.

Bone mineral density

Residents of the Province of Manitoba (1.25 million) have universal access to BMD testing when requested by a health care professional (24). The Manitoba Bone Density Program is a unique integrated program that has managed all clinical dual energy x-ray absorptiometry (DXA) testing for the province since 1994 (24). DXA testing rates for the Manitoba Bone Density Program have been published, and the program's database has been shown to be over 99% complete and accurate (24). Prior to 2000, BMD was measured by DXA using a pencil-beam instrument (Lunar DPX, GE Lunar, Madison, WI, USA), and post-2000, DXA was performed using a fan-beam instrument (Lunar Prodigy, GE Lunar). All instruments were cross-calibrated using anthropomorphic phantoms and volunteers.

Clinical risk factors in FRAX calculations

Age, weight and height were recorded at the time of DXA. Prior to 2000 weight and height was by self-report, however, post-2000 weight was assessed without shoes using a standard floor scale, and height was assessed with a wall-mounted stadiometer. BMI was calculated as weight divided by height-squared in kg/m^2 . Medically diagnosed conditions prior to BMD testing (rheumatoid arthritis, and prior fracture of the hip, spine, wrist or humerus since 1987) were ascertained through a combination of hospital discharge abstracts (coded using the International Classification of Diseases, 9th Revision, Clinical Modification [ICD-9-CM] prior to 2004 and the 10th revision, Canadian version [ICD-10-CA] thereafter) and physician billing claims (coded using ICD-9-CM) (22). A 6 month wash-out period where fracture affected the same site was applied. A diagnosis of chronic obstructive pulmonary disease (COPD) was used as a proxy for smoking status, and a diagnosis of alcohol or substance abuse was used as a proxy for high alcohol intake. Prolonged corticosteroid use (>90 days dispensed in the year prior to DXA testing) was obtained from a province-wide retail pharmacy system (22). Self-reported parental hip fracture data at the time of DXA was available from 2005 onwards (44% of the cohort); therefore adjustments were made for incomplete history of parental hip fracture using age- and sex-specific adjustment factors based on 2005-7 parental hip

fracture responses. As previously published (25, 26), this averaged effect incorporated the prevalence of a positive response and the relative change in risk: the risk adjustment factor ranged from 1.00 to 1.25 for hip fractures and 1.06 to 1.11 for MOF. These ratios were used to adjust the FRAX risk estimate for those years of data where parental fracture information was incomplete.

Statistical analyses

Ten year probability of hip fracture and MOF was calculated for each subject using the Canada FRAX tool with and without femoral neck BMD. The frequencies and percentages of women qualifying for treatment based on probability of hip fracture ($\geq 3\%$) and MOF ($\geq 20\%$), and clinical risk factors, were examined across income quintiles. The Cochran-Armitage statistic, which follows a χ^2 distribution, was used to test for a linear trend across the income quintiles on clinical risk factors and BMD measurements. Univariable associations between the predictor variable of income quintile and the likelihood of treatment qualification for hip or MOF were examined with and without the inclusion of BMD in the FRAX calculation, and presented as odds ratios (OR) and 95% confidence intervals (95%CI). Age-adjusted logistic regression analyses (using age as a continuous variable), were used to model the association between income quintile and treatment qualification. Models were unaffected by including a quadratic age term, confirming that the effect of age was approximately linear. Significance was set at $p \leq 0.05$, and statistical analyses were performed using MINITAB (Version 16.0; Minitab, State College, PA) software.

RESULTS

Table 1 presents characteristics of the study population ($n=51,327$) across income quintiles. A statistically significant negative linear trend was observed across income quintiles for the clinical risk factors of age, BMI, prior fracture, COPD, glucocorticoid use, and also for BMD measurements, osteoporotic T-score at the femoral neck, and FRAX probabilities measured with and without BMD (all $p < 0.001$). A positive linear

trend was seen across income quintiles for parental hip fracture ($p<0.001$), rheumatoid arthritis ($p=0.045$) and alcohol abuse ($p<0.001$).

Table 2 presents the frequency and percentages of women in income quintiles qualifying for treatment based upon hip fracture probability ($\geq 3\%$) and MOF probability ($\geq 20\%$), defined with and without BMD. Percentages in income quintiles 1 (lowest income) through 5 (highest income) that qualified for treatment based upon hip fracture probability (calculated with BMD) were 34.6%, 28.2%, 24.9%, 19.9% and 17.3%, respectively. For MOF, similar negative associations were observed between treatment qualification and income quintiles; percentages in quintiles 1 (lowest income) through 5 (highest income) were, respectively, 13.5%, 9.7%, 8.3%, 6.5%, and 5.8% (calculated with BMD). Similar trends were seen when treatment qualification was based upon probabilities determined without BMD. Slightly greater percentages were observed when treatment qualification for MOF was defined without BMD. Regardless of whether treatment qualification was determined with or without BMD, a statistically significant negative linear trend was observed across the income quintiles in women who qualified for treatment based upon hip or MOF probability ($p<0.001$).

Age-adjusted logistic regression models showed a negative linear association between income and the odds of qualifying for treatment based upon high hip fracture probability (p for linear trend <0.001 with BMD, p for linear trend $=0.005$ without BMD). Compared to the highest income quintile, and after age adjustment, women in the lowest income quintile were significantly more likely to qualify for treatment (OR 1.34, 95%CI 1.23-1.47,) when FRAX was determined with BMD, however this association was non-significant when FRAX was determined without BMD in the model (OR 1.08, 95%CI 0.97-1.22) (Figure 1).

Significant age-adjusted associations were also observed between income and treatment qualification based upon high MOF probability with BMD (p for linear trend <0.001) but not without BMD (p for linear trend $=0.24$). Compared to the highest income quintile, women in the lowest income quintile had a greater likelihood of qualifying for treatment

for MOF (OR 1.31, 95%CI 1.18-1.46) when FRAX was determined with BMD, but not when BMD was excluded (OR 1.12, 95%CI 1.00-1.26) (Figure 2).

DISCUSSION

To the best of our knowledge, no previous study has reported the association between income and likelihood of treatment qualification under FRAX. We report in this large study population of women that as income increases, the likelihood of qualifying for treatment for fracture risk decreases **when FRAX is determined with BMD, an association that was only partially explained by age.**

Individuals who are more likely to experience financial barriers to attending health services, including undergoing tests such as DXA (27-29), are the socially disadvantaged; the same group that is more likely to have lower health literacy (30) and thus limited capacity or ability to seek out, assess, comprehend and utilize health services and health-related information (31). Indeed, recent estimates suggest that up to 50% of US and UK citizens have suboptimal health literacy (32, 33), with a similar level of 60% observed in Canada (34). Given that osteoporosis is asymptomatic prior to fracture, many individuals will be unaware of their bone status. Combined with lower health literacy, poorer lifestyle behaviours and reduced likelihood of treatment adherence for asymptomatic diseases (35), osteoporosis will have a relatively low priority in the awareness of socially disadvantaged individuals. Given this, there are important clinical implications if targeted attention is not directed toward socially disadvantaged individuals.

Our data show that, when FRAX is calculated without BMD, women with lower income remain at greater risk of fracture and thus qualify for treatment; **effect sizes that are consistent with those we have previously reported regarding the association between income and BMD (18).** However we also showed that differences in treatment qualification were non-significant when FRAX was determined without BMD, implying that **BMD differences may be the primary explanatory factor.** We suggest that in the clinical setting, women **of lower income** who are more likely to qualify for osteoporosis

treatment should be identified from histories or healthcare records. An immediate application of FRAX for disadvantaged women is to ensure they do not remain untreated if identified as at high risk, given the disproportionate rates of fracture experienced by those that are socially disadvantaged. Furthermore, these groups may be worthy of extra clinical attention to ensure adherence with osteoporosis medications, given that the overall low treatment adherence of between 40-70% (36).

The development of country-specific FRAX models has enhanced the ability of clinicians to make informed treatment decisions by accounting for readily available clinical risk factors (14). However social determinants are not considered as a risk factor when calculating 10-year fracture risk probability with the FRAX tool. Whilst it is likely that different individuals may respond similarly to the same risk factor, for instance smoking or alcohol, with potentially similar outcomes on fracture probability, other social determinants such as occupation and lifestyle should not be disregarded as playing a role in bone health. Our data shows that treatment qualification differs by income, and thus suggests that an increased risk of fracture is associated with easily identifiable social parameters such as income.

This study has various strengths. First, and to the best of our knowledge, we present the first data examining this question. Second, we examined fracture probability and income within a large study sample of over 50,000 women. That this group was a clinical referral population could be considered a strength of the study, as it suggests that even among those referred to DXA there is still a dose-response association between income and qualification for treatment when FRAX is determined with BMD. Third, these data complement the large body of work examining osteoporosis in this region, and add to the sparse but emerging literature base examining social determinants and osteoporosis. Our study also has some limitations. We do not suggest that a direct pathway of association exists between income and qualification for treatment for fracture, rather that there may be other underlying mechanisms at play along the pathway, one of which may be lower BMD. Furthermore, we acknowledge that social parameters such as income do not exist in isolation from factors such as education, occupation, or accumulated wealth, amongst

other parameters. Due to the self-reported nature of our data exposure to some diseases may be unknown. We acknowledge that the use of surrogate disease variables to indicate lifestyle factors for the FRAX tools may tend to underestimate the frequency of these factors. However, we have previously employed the Johns Hopkins Adjusted Clinical Groups Case-Mix System (version 10) to undertake sensitivity analyses in this population, whereby clusters of diagnosis codes were determined by use of Aggregated Diagnoses Groups (ADGs). We used the number of ADGs to replace COPD, alcohol abuse and rheumatoid arthritis in models that examined associations between income quintiles and BMD. Those analyses showed that the ORs were of the same magnitude when the number of ADGs was used in the models (18). Our results pertain to females and therefore cannot be generalized to males, or to other geographical regions. It is important to acknowledge that qualification for treatment is different to treatment initiation. Given the cross-sectional nature of our study design, we are unable to comment on cause and effect. Our sample showed a bias toward greater numbers in the higher income quintiles compared to the lowest income quintile, which may influence our results. This study did not examine whether there were any disparities in the receipt of treatment for those who qualify, however identify this as an important area for further enquiry. Given that we did not have income quintile assignment at the individual level, the ORs (95%CI) from our logistic regression models may not correspond with marginal effects averaged across individuals. However, a study from the MCHP has compared income measured at the household and area-level and shown that risk estimates from area-level income measures are not attenuated relative to estimates obtained from household income (37). Furthermore, if there was bias in the quintile measurement at the individual level (by using an area-level proxy), this would have the effect of biasing the ORs downward, so our estimates are, if anything, conservative. Finally, as mentioned, our study was performed using a clinical referral population. In absolute terms the percentage difference between the lowest income quintile and the highest income quintile was 17% vs. 20%; suggesting that the effects of a referral bias may be apparent in our population. However, disadvantaged individuals may be less aware of, or concerned about, osteoporosis, and thus plausibly less likely to follow through with a referral appointment compared with less disadvantaged individuals. Our use of observational data

limits our ability to ascertain whether the difference in the proportions between lower and higher income quintiles is due to the referral practices of physicians or patient uptake.

In conclusion, this study showed that percentages of women who qualified for treatment based upon high hip fracture probability increased linearly with declining income quintile, but this was partially explained by older age among lower income quintiles. Age-adjusted differences were only significant when FRAX was determined with BMD, implying that BMD differences may be the primary explanatory factor. These findings may have implications for public health and preventive awareness. Given the worldwide gap in osteoporosis care, further work should examine whether income is associated with treatment initiation in those who qualify for treatment.

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Disclosures/Competing Interests

Sharon L Brennan has no disclosures.

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Table 1: Characteristics of the study population (n=51,327) across quintiles of household income, presented as mean ($\pm$ SD), median (IQR range), or frequency (%).

	Quintile 1 (n=8,699, 17%)	Quintile 2 (n=10,370, 20%)	Quintile 3 (n=11,219, 22%)	Quintile 4 (n=10,679, 21%)	Quintile 5 (n=10,360, 20%)	Test for linear trend (<i>p</i> value)
<i>Clinical Risk Factors</i>						
Age (yr)	68.6 (60.0-76.7)	66.7 (59.0-74.5)	65.8 (58.3-73.3)	64.0 (57.2-71.2)	61.9 (55.7-69.8)	<0.001
BMI (kg/m ²)	27.3 ($\pm$ 5.8)	27.3 ($\pm$ 5.5)	27.0 ($\pm$ 5.4)	27.0 ($\pm$ 5.3)	26.5 ($\pm$ 5.1)	<0.001
Prior fracture	913 (10.5%)	879 (8.5%)	889 (7.9%)	778 (7.3%)	683 (6.6%)	<0.001
Parental hip fracture ^ψ	430 (4.9%)	513 (4.9%)	619 (5.5%)	665 (6.2%)	621 (6.0%)	<0.001
COPD	1,014 (11.7%)	990 (9.5%)	890 (7.9%)	744 (7.0%)	594 (5.7%)	<0.001
Glucocorticoid use	446 (5.1%)	442 (4.3%)	456 (4.1%)	370 (3.5%)	342 (3.3%)	<0.001
Rheumatoid arthritis	332 (3.8%)	377 (3.6%)	347 (3.1%)	352 (3.3%)	351 (3.4%)	0.045
Alcohol abuse	227 (2.6%)	210 (2.0%)	202 (1.8%)	150 (1.4%)	162 (1.6%)	<0.001
<i>BMD measurements</i>						
Femoral Neck	-1.63 ($\pm$ 0.98)	-1.52 ($\pm$ 0.98)	-1.47 ($\pm$ 0.96)	-1.39 ($\pm$ 0.94)	-1.33 ($\pm$ 0.96)	<0.001
<i>Osteoporosis T-score[†]</i>						
Femoral neck	1,612 (18.5%)	1,575 (15.2%)	1,507 (13.4%)	1,194 (11.2%)	1,048 (10.1%)	<0.001
<i>FRAX probabilities</i>						
MOF without BMD	10.9 (6.9-18.4)	9.7 (6.3-16)	9.2 (6-15)	8.4 (5.6-13.1)	7.7 (5.1-12.4)	<0.001
MOF with BMD	10.6 (6.9-16.4)	9.4 (6.4-14.7)	9 (6.1-13.9)	8.1 (5.8-12.5)	7.5 (5.3-11.8)	<0.001
Hip fracture without BMD	2.2 (0.7-6.8)	1.7 (0.6-5.2)	1.4 (0.5-4.6)	1.1 (0.4-3.4)	0.9 (0.4-2.9)	<0.001
Hip fracture with BMD	1.8 (0.6-4.9)	1.3 (0.4-3.9)	1.1 (0.4-3.3)	0.9 (0.3-2.6)	0.7 (0.3-2.2)	<0.001

Mean household income (\$CDN) Quintile1 \$34,355; Quintile 2 \$47,109; Quintile 3 \$57,068; Quintile 4 \$70,354; Quintile 5 \$101,076

[†] ≥ 2.5 SD below young adult mean

^ψ Parental hip fracture data limited to 2005-2011.

COPD=chronic obstructive pulmonary disease, MOF=major osteoporotic fracture

Note: Frequencies are weighted to the population in each quintile

Table 2: Frequency (%) of women in income quintiles qualifying for treatment based upon FRAX hip fracture and major osteoporotic fracture (MOF) probability, defined with and without bone mineral density (BMD).

Income quintile	Hip fracture probability $\geq 3\%$		MOF probability $\geq 20\%$	
	<i>With BMD</i>	<i>Without BMD</i>	<i>With BMD</i>	<i>Without BMD</i>
Quintile 1* (n=8,699)	3,009 (34.6%)	3,578 (41.1%)	1,176 (13.5%)	1,591 (18.3%)
Quintile 2 (n=10,370)	2,927 (28.2%)	3,524 (34.0%)	1,010 (9.7%)	1,341 (12.9%)
Quintile 3 (n=11,219)	2,791 (24.9%)	3,454 (30.8%)	928 (8.3%)	1,267 (11.3%)
Quintile 4 (n=10,679)	2,128 (19.9%)	2,634 (24.7%)	700 (6.5%)	924 (8.6%)
Quintile 5 (n=10,360)	1,791 (17.3%)	2,282 (22.0%)	600 (5.8%)	816 (7.9%)
Test for linear trend (<i>p</i> value)	<0.001	<0.001	<0.001	<0.001
Total (n=51,327)	12,646 (24.6%)	15,472 (30.1%)	4,414 (8.6%)	5,939 (11.6%)

* lowest income quintile

Figure 1: Logistic regression analysis results for the association between income quintile and treatment qualification based upon high 10-year probability of hip fracture ($\geq 3\%$) defined with and without BMD, after adjustment for age. Results are presented as odds ratios (ORs) with error bars indicating 95% confidence intervals (95% CI). Quintile 5 (highest income) is the referent.

Figure 2: Logistic regression analysis results for the association between income quintile and treatment qualification based upon high 10-year probability of major osteoporotic fracture ($\geq 20\%$) defined with and without BMD, after adjustment for age. Results are presented as odds ratios (ORs) with error bars indicating 95% confidence intervals (95% CI). Quintile 5 (highest income) is the referent.

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