Sex and age specific associations between income and incident major osteoporotic fractures in Canadian men and women: A population-based analysis

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MINI ABSTRACT (49 words)

We investigated sex- and age-specific associations between income and fractures at the hip, humerus, spine and forearm in adults aged ≥ 50 years. Compared to men with the highest income, men with the lowest income had an increased fracture risk at all skeletal sites. These associations were attenuated in women.

Abstract

Purpose/Introduction: Associations between income and hip fractures are contested; even less is known about other fracture sites. We investigated sex- and age-specific associations between income and major osteoporotic fractures (MOF) at the hip, humerus, spine and forearm.

Methods: Incident fractures were identified from administrative health data for adults aged ≥ 50 years in Manitoba, Canada, 2000-2007. Mean neighborhood (postal-code area) annual household incomes were extracted from 2006 census files and categorized into quintiles. We calculated age-adjusted and age-specific sex-stratified fracture incidence across income quintiles. We estimated relative risks (RR) and 95%CI for income quintile 1 (Q1, lowest income) vs. income quintile 5 (Q5) and tested the linear trend across quintiles.

Results: We identified 15,094 incident fractures (4,736 hip; 3,012 humerus; 1,979 spine; 5,367 forearm) in 2,718 men and 6,786 women. For males, the RR of fracture for the lowest vs. highest income quintile was 1.63 (95%CI 1.42-1.87) and the negative trend was statistically significant ($p < 0.0001$); individual skeletal sites showed similar associations. For females, the RR of fracture for the lowest vs. highest income quintile was 1.14 (95%CI 1.01-1.28), with a statistically significant negative trend ($p = 0.0291$); however, the only skeletal site associated with income in women was the forearm (Q1 vs. Q5 RR 1.09, 95%CI 1.01-1.28).

Conclusions: Compared to men with the highest income, men with the lowest income had an increased fracture risk at all skeletal sites. These associations were attenuated in women. For men, these effect sizes seem large enough to warrant public health concern.

Introduction

Osteoporotic fractures have significant attributable morbidity and mortality (1). More than a 10-fold variation for hip fracture risk has been shown to exist between countries worldwide (2). This large geographic variation may, in part, be explained by social determinants of fracture incidence, **such as lower income or education**, as suggested in an earlier review (3). For instance, compared to their more advantaged counterparts, socially disadvantaged individuals are more likely to have lower quality lifestyles including physical inactivity, smoking and poorer nutritional intake (4-8). These same factors are some of the key predictors of an increased fracture risk. **Furthermore, social disadvantage is strongly associated with lower health literacy, and therefore will influence the ability of individuals to gain access to, understand and use health-related information (9).** The social gradient of risk factors may partly explain the inverse association observed between social disadvantage and risk of hip fracture in the US (10), Sweden (11), Germany (12), Denmark (13) and Australia (14).

Furthermore, it is plausible that a social gradient of fractures at skeletal sites other than hip exists; however, few studies have addressed this question. Three recent exceptions are: (i) Court-Brown et al (15) who examined fractures at all skeletal sites, and reported that, over a one year period and using a composite index of deprivation, the most socially deprived 10% of the population have an increased likelihood of fracture at most sites, (ii) Crandall et al (16) who investigated fractures in women at a number of sites over nine years and reported that, in non-Caucasian women and independent of household income, those who completed at least some postgraduate education compared to women with high school education alone had 87% lower rates of incident non-traumatic fracture, and (iii) Taylor et al (17) who showed an inverse association between fracture at six skeletal sites and income measured at the area-level for men and women. The small number of studies that have examined relationships between fracture incidence and income present conflicting findings, whereby positive associations are observed in some (11, 13, 18, 19) but not all studies (10, 16).

If we are to effectively identify predisposing risk factors and target populations for intervention, it is imperative to understand the associations between income and incident fracture; these investigations should assess both sexes, span the older adult age range and include skeletal sites

other than just the hip. We hypothesized that individuals with lower income would have a greater fracture incidence than individuals with greater income. Therefore, we investigated sex-specific associations between income levels and incident fractures of the hip, humerus, spine and forearm in men and women aged 50 years and above.

Methods

Study population

We examined population-based data from Manitoba, Canada. Data on all fractures were obtained from the Manitoba Population Health Research Data Repository, which contains demographic data, healthcare utilization and diagnoses information, on nearly all residents of Manitoba, Canada (population ~1.2 million, 2006 Statistics Canada Census) (20); importantly, residents of all Canadian provinces receive universal health care coverage. Diagnoses in hospital data up to and including the 2003/04 fiscal year are recorded using the International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM), whilst for subsequent fiscal years the International Classification of Diseases, 10th Revision, Canadian version (ICD-10-CA) was used. Physicians' claims submitted to the provincial health ministry capture most outpatient services, including services provided in outpatient and hospital emergency departments. All person-specific health records are protected by encryption of personal identifiers; this encryption allows for anonymous linkage across data sets and the creation of longitudinal records of health service utilization (21). We identified residents of Manitoba aged ≥ 50 years with one or more diagnoses of fracture at the hip, humerus, spine or forearm between 2000 and 2007. Individuals who lived in personal care homes at the time of fracture were excluded. 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 2008/2009-16).

Incident fractures

An incident hip fracture was determined where the individual had at least one hospitalization with a hip fracture diagnosis (coded using the ICD-9-CM (22) code 820-821 or the ICD-10-CA

code S72.0-2) with a hip fracture fixation procedure. An incident fracture of the distal forearm was identified from an ICD-9-CM code 813 or ICD-10-CA code S52 where an individual had at least one hospitalization (most responsible diagnosis) or two physician visits (with one site-specific orthopedic procedure for immobilization or fixation). Incident fractures of the spine (ICD-9-CM code 805 or ICD-10-CA codes S22.0, S22.1, S32.0) and of the humerus (ICD-9-CM code 812 or ICD-10-CA code S42.2) were identified where an individual had at least one hospitalization (most responsible diagnosis) or two physician visits (within three months). We employed a 6 month fracture-free “wash out” period to differentiate an incident fracture from a prevalent fracture event. We excluded fractures with codes indicating high trauma.

Household income

We used an ecological measure of income, whereby mean neighborhood (postal code area) annual household income was determined from area of residence in the year of the fracture, and dissemination areas (DAs) extracted from the public use files of the Statistics Canada Census for 2006. DAs are composed of one or more neighboring blocks and are uniform in population size, ranging from 400 to 700 persons; in 2006, the Province of Manitoba comprised 2,235 DAs (23). Income was categorized into quintiles, with each quintile containing approximately 20% of the population, as previously described (8). Mean intra-quintile income (2006 Canadian dollars) were: quintile 1 (most disadvantaged) \$34,355, quintile 2 \$47,109, quintile 3 \$57,068, quintile 4 \$70,354, quintile 5 (least disadvantaged) \$101,076. Mean household income was ranked from the lowest to highest, where quintile 1 had the lowest income, and quintile 5 had the highest income. Where income data was missing, these fracture patients were excluded from analyses (n=2,483; 81% female).

Statistical analyses

For each fracture definition we calculated crude fracture incidence rates per 100,000 person-years, by dividing the number of fractures by the at-risk observation time (person-years) population according to sex, age subgroup (10-year age groups) and income quintile. We estimated age-adjusted fracture incidence (with standard error [SE]) in males and females at major osteoporotic sites combined and at individual fracture sites from a generalized linear

model using a negative binomial distribution; age (in 5-year age groups) was included as a covariate. In the age-specific model, analyses were stratified by 10-year age groups; age was not included as a covariate in the model. Model fit was confirmed by examining the ratio of deviance to degrees of freedom and the likelihood ratio statistic. From this model, we tested the relative risk (RR) for fractures in the lowest income quintile (quintile 1) vs. the highest income quintile. Treating income quintile as a categorical variable, we tested the linear trend across the income quintiles using a linear contrast in the generalized linear model; the contrast was tested using a likelihood ratio statistic, which follows a chi-square distribution. We examined individual years of data (from fiscal years 2000/01 to 2006/07) and saw no evidence of a change in RRs over time (data not shown), and therefore combined all years of data. Significance was set at $p \leq 0.05$, and statistical analyses were performed using SAS (Version 9.3, SAS Institute Inc, Cary, NC).

Results

During eight years of follow-up, 15,094 fractures were observed (4,736 hip, 3,012 humerus, 1,979 spine, and 5,367 forearm) in 2,718 men and 6,786 women (with some individuals experiencing more than one type of fracture). Table 1 presents the sex-specific and age-adjusted fracture incidence rates per 100,000 person-years for each income quintile, and the RR of fracture for income quintile 1 (lowest income) vs. income quintile 5 (highest income). For men, the RR of fracture for the lowest vs. highest income quintile was 1.63 (95%CI 1.42-1.87) and the negative trend was statistically significant ($p < 0.0001$). Similar negative linear associations were observed for men when stratified by skeletal site; compared to the highest income quintile, men in the lowest income quintile had a significantly greater age-adjusted RR of fracture at the hip (1.62, 95%CI 1.30-2.02), humerus (1.97, 95%CI 1.59-2.43), spine (1.65, 95%CI 1.28-2.13), and forearm (1.41, 95%CI 1.23-1.62). For females, the RR of fracture at any site for the lowest vs. highest income quintile was 1.14 (95%CI 1.01-1.28) and the negative trend was statistically significant ($p = 0.029$). The only individual site to show a significant association with income for women was the forearm (RR lowest vs. highest income quintile 1.09, 95%CI 1.01-1.28).

Table 2 presents the sex-specific fracture incidence rates ($\pm$ SE) per 100,000 person-years for each income quintile in 10-year age groups, and the RR of fracture for income quintile 1 (lowest income) vs. income quintile 5. For males, we observed a clear income gradient for fracture incidence (all sites combined) that diminished linearly with age (men aged < 90 years all p -linear

trend<0.05, men aged 90+ years p -linear trend=0.114). Furthermore, compared to the highest income quintile, men in the lowest income quintile were significantly more likely to fracture in the age groups of 50-59 years (RR 1.82, 95%CI 1.49-2.22), 60-69 years (RR 2.20, 95%CI 1.76-2.75) and 70-79 years (RR 1.91, 95%CI 1.52-2.39), whilst a trend was observed for the two oldest age groups. For women, although we observed substantial variability in fracture incidence across income quintiles in the different age groups (p -linear trend not significant), nevertheless, compared to the highest income quintile, women in the lowest income quintile were significantly more likely to fracture in the age groups of 50-59 years (RR 1.44, 95%CI 1.24-1.67), 60-69 years (RR 1.37, 95%CI 1.19-1.59) and 70-79 years (RR 1.33, 95%CI 1.18-1.50), with a non-significant but linearly decreasing RR for women in the two oldest age groups.

Figure 1 presents the sex- and age-specific fracture incidence rates ($\pm$ SE) per 100,000 person years by income quintiles for the hip, humerus, spine and forearm. Without exception, and compared to all other income quintiles, men and women in income quintile 1 (lowest income) had the greatest fracture incidence at each skeletal site.

Discussion

To our knowledge, this is the largest study to date to examine associations between income and incident fracture at the major osteoporotic sites (hip, humerus, spine and forearm) in men and women. In this Canadian population, we observed a consistent linear association between decreasing income and higher fracture incidence in men, and a similar but weaker association in women. The strength of association between fracture incidence and income diminished with advancing age for both sexes, although the magnitude (and statistical significance) of this finding was more robust in men.

Geographic variation in hip fracture has been reported worldwide (2); our data support the suggestion of Kanis et al that the large heterogeneity in the probability of hip fracture between countries may in part relate to social determinants. Associations between higher income levels and reduced hip fracture incidence have been reported in some studies (11, 13, 17, 19, 24, 25), but not all (10, 26). Literature regarding associations between income and fracture at skeletal sites other than the hip is even sparser. Recent data from the UK (15), however, reported that the

most socially deprived 10% of their study population (measured using the Carstairs deprivation index (27)) had an increased odds of fractures at most skeletal sites over a one year period. Previous data from the UK have shown similar associations between social disadvantage and fractures of the hand and tibia (28, 29). Our findings enhance those of previous studies by confirming associations between income and all-cause fracture at a number of skeletal sites in a larger sample size, over a longer time period, across the entire adult age range and in both sexes.

Age has strong associations with bone strength. Indeed, we observed that the greatest difference in fracture risk between income quintiles 1 and 5 occurred in midlife, with the associations decreasing in strength with advancing age; findings that are consistent with the suggestion of others (16, 17). Social determinants of risk factors associated with fracture are complex and vary across the life course. In addition, it may be plausible that women are at greater risk of variation in risk factors for fracture than men. For instance, associations between income and fracture risk may be mediated for older women regardless of income levels, due to the significant reduction in BMD experienced post-menopause (30). Furthermore, we did not account for the possibility that individuals may be on anti-resorptive therapy which could affect their fracture risk; given that we have previously shown Canadian women to be four times more likely than men to be prescribed drug treatment associated with osteoporosis (31), this may provide an explanation for weaker associations between income and fracture for women compared to men. Indeed, we have previously shown in 51,327 Canadian women that many of the clinical risk factors included within FRAX (32) are more likely associated with individuals in lower income groups than other groups, for instance older age and higher BMI, chronic obstructive pulmonary disease (as a proxy of smoking), an increased prevalence of prior fracture, and glucocorticoid use (8). Taken in context, the sex-specific social patterning of risk factors may play a stronger role in fracture risk than has previously been considered.

This study has several strengths. We performed a population-based analysis of incident fractures over an eight year period encompassing the entire Province of **Manitoba**, thus our comprehensive dataset provided a large sample size for analysis. Due to the nature of the data, our results are not influenced by referral or self-selection biases. Given that osteoporotic fracture rates in the Province of Manitoba are known to be representative of the rest of Canada (21), our findings have the potential to be generalisable to other Canadian Provinces. Our study also has several

limitations that should be considered when interpreting these findings. First, our income quintiles were based on the Statistics Canada Census for 2006, and were thus an ecological measure. We were unable to verify household income data, however, a comparison of income measured at the household and area level showed that risk estimates for thirteen health status measures from area-level income measures were not attenuated relative to estimates obtained from household income (33). However, it is possible that some DAs may straddle health region boundaries, and thus the physical-legal boundaries of provinces may result in split dissemination blocks. Second, we acknowledge that SES, as reflected by income, is a proxy for other mediating variables that affect fracture risk. Our objective was to examine the importance of income as an indicator of fracture risk that straddles multiple pathways. Therefore, we did not examine other clinical risk factors for fracture, BMD, or osteoporosis treatment: any of these measures, which could include multiple co-morbidities, are explanatory variables associated with household income. Untangling these complex causal pathways is an important question that should be the focus of future analyses. Third, our analysis excluded data from postal code areas which could not be ranked to an income quintile, leading to the exclusion of 2,483 subjects. Individuals included in the "Income Unknown" group commonly include residents of long-term care facilities, some personal care homes, psychiatric facilities, federal and long-term prisoners, wards of the state, and Aboriginal communities that did not report income in the census (34). As these groups tend to be lower income but at higher risk for fracture, our results are likely to be conservative (biased towards the null). Finally, we were unable to account for ethnicity in these analyses or define the causal pathway between lower household income and fracture.

In conclusion, this study showed that the risk of fracture for men increased linearly with every decrease in income quintile, with effect sizes large enough to warrant public health concern. In contrast, much smaller differences in fracture risk across income quintiles were observed for women. These data add to the mounting evidence-base regarding the social gradient of fracture, and thus have important implications in the public health setting. These data provide evidence that men with lower income may be an important target population for intervention to reduce the burden of fracture, whilst for women further investigation is needed to account for the weaker association observed between income and fracture.

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Conflicts of interest

Suzanne N Morin: Consultant to: Amgen, Eli Lilly, Merck. Speaker bureau: Amgen, Eli Lilly. Research grant: Amgen, Merck.

William D Leslie: Speaker bureau: Amgen, Eli Lilly, Novartis. Research grants: Amgen, Genzyme.

Sharon L Brennan, Lin Yan, Lisa M Lix and Sumit Majumdar have no conflicts to declare.

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Figure 1: Sex- and age-specific fracture incidence rates ($\pm$ SE) per 100,000 person years by income quintiles for individual skeletal sites.

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Table 1: Age-adjusted fracture incidence per 100,000 person years ($\pm$ SE) and RR (95%CI) by income quintile (significant results in boldface), stratified by skeletal site.

	<i>Number of fractures</i>	<i>Quintile 1*</i>	<i>Quintile 2</i>	<i>Quintile 3</i>	<i>Quintile 4</i>	<i>Quintile 5</i>	<i>p-value for linear trend</i>	<i>RR Q1 vs. Q5 (95%CI)</i>
Males								
Hip	1,268	190.3 (16.8)	137.2 (5.1)	122.0 (6.4)	118.1 (8.9)	117.6 (8.5)	<0.0001	1.62 (1.30, 2.02)
Humerus	734	135.3 (11.0)	84.4 (7.9)	71.7 (5.6)	73.6 (4.8)	68.7 (5.6)	0.0001	1.65 (1.28, 2.13)
Spine	766	115.1 (6.7)	103.9 (8.1)	90.5 (5.5)	92.1 (8.7)	69.7 (8.1)	<0.0001	1.97 (1.59, 2.43)
Forearm	1,098	144.9 (8.9)	120.4 (7.9)	115.2 (6.9)	111.9 (7.2)	102.7 (5.1)	<0.0001	1.41 (1.23, 1.62)
<i>All sites</i>	3,866	646.6 (33.1)	491.3 (11.6)	440.7 (16.9)	437.8 (16.8)	397.3 (19.2)	<0.0001	1.63 (1.42, 1.87)
Females								
Hip	3,468	236.9 (18.4)	194.2 (9.2)	200.5 (10.4)	198.1 (10.9)	206.7 (17.5)	0.154	1.15 (0.93, 1.41)
Humerus	2,278	264.4 (10.3)	193.5 (9.9)	206.9 (10.2)	198.5 (11.4)	200.3 (19.9)	0.085	1.10 (0.98, 1.24)
Spine	1,213	104.0 (3.6)	105.9 (2.5)	104.4 (4.3)	98.5 (5.6)	94.4 (4.8)	0.063	1.23 (0.99, 1.53)
Forearm	4,269	423.3 (12.2)	389.6 (9.0)	376.2 (9.3)	368.7 (13.4)	389.6 (10.5)	0.016	1.09 (1.01, 1.17)
<i>All sites</i>	11,228	1,149.2 (44.3)	995.3 (18.3)	1,005.4 (25.9)	978.9 (23.3)	1,011.5 (47.2)	0.029	1.14 (1.01, 1.28)

* Lowest income quintile.

Table 2: Age-specific major osteoporotic fracture incidence and all skeletal sites combined) per 100,000 person years ($\pm$ SE) and RR (95%CI) according to income quintile (significant results in boldface)

Age group	<i>Number of fractures</i>	<i>Quintile 1*</i>	<i>Quintile 2</i>	<i>Quintile 3</i>	<i>Quintile 4</i>	<i>Quintile 5</i>	<i>p- value for linear trend</i>	<i>RR Q1 vs. Q5 (95%CI)</i>
Males								
50-59	915	255.1 (15.8)	193.7 (7.9)	173.3 (8.4)	171.3 (9.4)	155.4 (9.2)	<0.0001	1.82 (1.49, 2.22)
60-69	769	343.1 (32.2)	260.4 (14.5)	233.1 (15.5)	230.4 (14.4)	209.0 (15.9)	<0.0001	2.20 (1.76, 2.75)
70-79	960	607.5 (33.1)	461.1 (17.6)	412.7 (16.8)	407.9 (24.5)	370.1 (26.9)	0.0002	1.91 (1.52, 2.39)
80-89	960	1,402.7 (114.9)	1,064.7 (57.5)	952.8 (50.6)	941.9 (55.3)	854.5 (78.8)	0.045	1.12 (0.91, 1.38)
90+	262	3,167.1 (284.4)	2,403.8 (174.3)	2,151.2 (170.2)	2,126.6 (174.1)	1,929.3 (184.3)	0.114	1.09 (0.72, 1.64)
Females								
50-59	1,610	311.4 (40.6)	255.2 (33.5)	250.7 (34.8)	238.6 (34.3)	241.1 (38.2)	0.119	1.44 (1.24, 1.67)
60-69	1,982	528.9 (82.2)	433.5 (73.5)	425.7 (72.8)	405.2 (73.6)	409.5 (76.5)	0.236	1.37 (1.19, 1.59)
70-79	2,987	945.5 (153.6)	775.0 (131.1)	761.1 (131.8)	724.4 (123.5)	732.1 (138.9)	0.403	1.33 (1.18, 1.50)
80-89	3,582	2,116.2 (313.3)	1,734.5 (259.5)	1,703.5 (281.7)	1,621.4 (279.9)	1,638.6 (311.7)	0.945	0.90 (0.80, 1.00)
90+	1,067	4,254.3 (576.6)	3,486.9 (473.8)	3,424.7 (547.0)	3,259.6 (517.8)	3,294.1 (580.5)	0.771	0.89 (0.72, 1.10)

* Lowest income quintile.