The impact of incident fractures on health-related quality of life: 5 years of data from the Canadian Multicentre Osteoporosis Study

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Abstract
Summary Using prospective data from the Canadian Multicentre Osteoporosis Study (CaMos), we compared health utilities index (HUI) scores after 5 years of follow-up among participants (50 years and older) with and without incident clinical fractures. Incident fractures had a negative impact on HUI scores over time.

Introduction This study examined change in health-related quality of life (HRQL) in those with and without incident clinical fractures as measured by the HUI.

Methods The study cohort was 4,820 women and 1,783 men (50 years and older) from the CaMos. The HUI was administered at baseline and year 5. Participants were subdivided into incident fracture groups (hip, rib, spine, forearm, pelvis, other) and were compared with those without these fractures. The effects of both time and fracture type on HUI scores were examined in multivariable regression analyses.

Results Men and women with hip fractures, compared to those without, had lower HUI measures that ranged from −0.05 to −0.25. Both women and men with spine fractures had significant deficits on the pain attributes (−0.07 to −0.12). In women, self-care (−0.06), mobility and ambulation (−0.05) were also negatively impacted. Women with rib fractures had deficits similar to women with spine fractures.
fractures, and these effects persisted over time. In men, rib fractures did not significantly affect HUI scores. Pelvic and forearm fractures did not substantially influence HUI scores.

Conclusion The HUI was a sensitive measure of HRQL change over time. These results will inform economic analyses evaluating osteoporosis therapies.

Keywords Cost–utility · Epidemiology · Fractures · Health utilities index · Osteoporosis · Quality of life

Introduction

Osteoporosis is a major public health concern for men and women aged 50 years and older. Fractures are the most serious consequence of osteoporosis, a disease in which the bones become weak and more susceptible to fracture. Osteoporosis can affect any bone in the body; however, the most typical sites of fracture are at the hip, spine, wrist and ribs. Fractures of the hip and spine are associated with increased morbidity, mortality, institutionalisation and length of hospital stay [1–6]. Approximately 40% of Caucasian women and 13% of men 50 years and older will experience at least one clinically recognised osteoporotic fracture at the hip, wrist or spine in their lifetimes [7, 8]. It is estimated that 23.5% of Canadian women and 21.5% of men 50 years and older have a prevalent spine fracture [9].

Quality of life is an important marker of the disease experience for individuals with osteoporosis and fractures [10–13]. The Canadian Multicentre Osteoporosis Study (CaMos) [14], a prospective, 10-year study of osteoporosis in the Canadian population has used the health utilities index (HUI) since its inception. The HUI is a generic, preference-scored system that measures an individual’s health status and health-related quality of life (HRQL) [15–17]. HUI scores can be used to calculate quality-adjusted life years, a common measure in economic and health outcomes research. The HUI has been validated and commonly used in clinical settings to measure HRQL for a variety of disease states [18–21]. It is also a valid measure of health status in the general population [22, 23].

Using baseline CaMos data, we have previously demonstrated that HUI scores were negatively related to prevalent hip, rib and sub-clinical spine fractures [13]. Few studies have longitudinally examined the impact of osteoporotic fractures on HRQL and whether individuals with fracture regain previous levels of HRQL over time. HRQL differences among fracture types are also not well-documented. Cranney et al. [24] reported that the HUI was a sensitive measure of change over time (9-month follow-up) in women with recent hip fractures.

Using 5 years of prospective data from CaMos, we examined the impact of incident clinical fractures on HRQL as measured by the HUI instrument at year 5. Our secondary objective was to examine data according to the year of fracture to determine how time influenced year 5 HRQL scores.

Materials and methods

Participants

CaMos is a 10-year study that was initiated in 1996 and is a randomly selected, prospective cohort study of non-institutionalised Canadians [14]. The study population represents an age-stratified, sex- and region-specific sample consisting of 9,423 individuals (n=6,539 women and n=2,884 men) aged 25 to 80+ from nine study centres across Canada. Participants were randomly recruited from a list of residential telephone numbers within a 50-km radius of each of the nine study centers and were recruited regardless of any known diagnosis of osteoporosis. Informed consent was obtained from each individual and the study received approval by the institutional review boards at each participating centre.

Eligibility

For this analysis, CaMos participants aged 50 years and older at baseline with valid HUI scores at two points in time (baseline and a second evaluation 5 years later) were included. Baseline assessments took place between February 1996 and September 1997, and the 5-year assessments took place between February 2001 and September 2002.

CaMos data collection

Study assessments at baseline and year 5 included lateral lumbar and thoracic spine X-rays, bone mineral density testing, an interviewer-administered CaMos questionnaire (demographic, anthropometric, medical history, medication use, dietary intake and lifestyle data) and quality of life tools (SF-36, HUI2 and HUI3). Annually, in the intervening years, participants were mailed a two-page questionnaire regarding fractures, hospitalisations and the use of prescription medications for bone that occurred during the previous calendar year. Participants who did not return their questionnaires were contacted and interviewed by telephone.

Fracture assessment

Only clinically recognised incident fractures that occurred as a result of minimal trauma (i.e. ‘fragility’ or osteoporotic
fracture) were included in this analysis. The World Health Organization (WHO) defines fragility fracture as “a fracture caused by injury that would be insufficient to fracture normal bone” [25] (e.g. a fall from standing height or less or no identifiable trauma [26]). ‘Clinical’ incident fractures were based on self-reports as documented in the annually mailed questionnaires (years 1, 2, 3 and 4) and at the 5-year interview. Participants who reported fractures were asked for consent to contact their physician or hospital, and fractures were confirmed by medical and/or X-ray reports.

For the primary analysis, participants were sub-divided into the following incident clinical fracture groups: (1) hip, (2) rib, (3) spine, (4) forearm, (5) pelvis, (6) other and were compared with patients without these fracture types. Clinical spine fractures were considered incident if they occurred on a new vertebra (i.e. were not present at baseline).

HUI2 and HUI3

HUI2 and HUI3 were administered by a CaMos interviewer at baseline and year 5 (and asked the participant to recall for a period of 1 week). The HUII systems are a comprehensive framework and “are deliberately focused on the fundamental core attributes of health status, and on the capacity of individuals to function with respect to these attributes” [15]. HUI questionnaires use a preference-based system and are available in several languages, self- and proxy-assessment versions, and self- and interviewer-administered formats [27].

Health states on the HUII are measured using several ‘attributes’ (domains) of health. On the HUI2, there are seven attributes: sensation (vision, hearing and speech), mobility, emotion, cognition, self-care, pain and fertility (for the current analysis, the fertility attribute is assumed to be level 1 for all participants). The HUI3 has eight attributes: vision, hearing, speech, ambulation, dexterity, emotion, cognition and pain. The two systems may be viewed as independent and complementary to each other; attributes of the same name have different underlying constructs [16]. ‘Emotion’ on HUI2 is concerned with distress and anxiety whilst ‘emotion’ on HUI3 focuses on happiness versus depression. ‘Cognition’ on HUI2 is centred on learning whilst on the HUI3 ‘cognition’ focuses on the ability to solve day-to-day problems. ‘Pain’ on HUI2 measures frequency and type of control, whilst on HUI3 ‘pain’ is focused on the severity [16].

Within each attribute, there are three to six descriptive levels of functioning ranging from severely impaired to normal [15, 27]. For example, the ‘mobility’ attribute (HUI2) has five levels: level 1—able to walk, bend, lift, jump and run normally for age; level 2—walks, bends, lifts, jumps or runs with some limitations but does not require help; level 3—requires mechanical equipment (such as canes, crutches, braces or wheelchair) to walk or get around independently; level 4—requires the help of another person to walk or get around and requires mechanical equipment as well; level 5—unable to control or use arms and legs.

Coding algorithms are used to derive attribute levels from responses to the questionnaires. In the multi-attribute approach, each unique combination of one level from each attribute represents a unique health state [28]. For example, on HUI2, there are 24,000 health states. HUI questionnaires are scored using single- and multi-attribute utility functions [16]. Utility functions are based on preference data from random samples of the general population. The utility functions translate the attribute level data (categorical) into interval-scale, single-attribute and multi-attribute (i.e. summary HRQL scores) utility scores. Single-attribute utility scores vary from 0 to 1. Multi-attribute utility scores may have negative scores: −0.36 on the HUI3 and −0.03 on the HUI2 (i.e. all attributes at the lowest functional level, representing states worse than death). A multi-attribute score of 1.00 represents ‘perfect health’. From clinical studies, differences of 0.03 or greater in mean multi-attribute scores are considered clinically important [16]. Among the HUII single attributes, the smallest difference between levels is 0.05; thus, 0.05 is considered meaningful and likely smaller differences are as well [16].

Statistical analysis

All analyses were conducted separately for men and women. Means and standard deviations (SD) for baseline demographics, clinical variables and HUI2 and HUI3 scores were calculated.

Separate analyses were performed for each of the HUI2 and HUI3 single attributes and for the overall multi-attribute scores; in each of these analyses, the dependent variable was year 5 scores. Multivariable linear regression analyses were used to examine the association between various incident clinical fracture types and year 5 HUII scores, adjusting for baseline HUII scores and potential confounding factors. Participants with more than one fracture type were included in each fracture group that applied to them; coefficient estimates represented participants with versus without that particular fracture type. Our analysis included only CaMos participants that survived a fracture since participants must have completed the follow-up (year 5) HUII to be included in the analysis cohort. Regression coefficient estimates and 95% confidence intervals (95% CI) were calculated for all parameters.

In all analyses, the following variables were adjusted for: baseline HUI scores, incident fractures, age (years), height (centimeters), weight (kilograms), self-reported prevalent fragility fractures after age 50 (yes/no), number of comorbid conditions, smoking (current versus former/
never), alcohol intake (beverages per week consumed during the previous year), exercise (kilocalories spent per week for strenuous, vigorous and moderate activities e.g., jogging and brisk walking), number of surgeries, use of bisphosphonates (yes/no) and use of ovarian hormone therapy (women only; yes/no).

As a secondary objective, we examined how time after incident fracture influenced HRQL. For each fracture type, multivariable linear regression models were performed to examine the association between when the incident fracture occurred (year 1, 2, 3 or 4/5) and year 5 HUI scores. For this analysis, incident clinical fracture groups examined were hip, rib, spine and other and were compared with patients without these fracture types. The above covariates were adjusted for in these analyses.

Statistical significance was defined as \( p < 0.05 \). All statistical analyses were using the SAS/STAT (version 9.1.3; SAS Institute, Cary, NC, USA) software package.

**Results**

A total of 6,603 CaMos participants (4,820 women and 1,783 men) aged 50 years and older were included in this analysis. Baseline participant characteristics and mean scores on the HUI2 and HUI3 (single- and multi-attributes) are presented in Table 1.

Tables 2 and 3 present the adjusted regression coefficient estimates that predict the year 5 HUI2 and HUI3 single-/multi-attribute scores for subjects with each fracture type. Coefficients represent the difference in year 5 HUI scores between patients with and without that fracture type (adjusted for confounders). Figure 1 displays the attributes with statistically \( p < 0.05 \) and clinically \( \pm 0.03 \) significant deficits in scores for the fracture versus non-fracture participants.

**Women**

On the HUI2, women with hip, spine, rib and other fractures had significant deficits for the multi-attribute, mobility (ability to move independently), pain (frequency and use of analgesics) and self-care (eating, bathing, dressing, toileting) attributes compared with participants without those fractures (Fig. 1, Table 2). Deficits ranged in magnitude from \(-0.02\) to \(-0.18\). Pelvic and forearm fractures in women did not produce significant HUI2 deficits.

On the HUI3, women with spine, hip and rib fractures had significant deficits for the multi-attribute, ambulation (ability to walk around/distance) and pain (severity and frequency of interruption) attributes compared with participants without those fractures (Fig. 1, Table 2). Deficits ranged from \(-0.05\) to \(-0.25\). In addition, women with hip fractures experienced a \(-0.05\) deficit on the emotion (happiness and interest in life) attribute. Pelvic, forearm and other fractures in women did not produce significant HUI3 deficits except for the dexterity (ability to use hands and fingers; pelvic and forearm fractures) and ambulation (other fractures) attributes.

In general, hip fractures had the most severe deficits, except on the HUI3 pain attribute (where it was surpassed by spine). Women with spine and rib fractures had deficits on the HUI that were similar in magnitude with the exception of ambulation (where rib fractures had greater impact) and pain attributes (where spine fractures had greater impact). Significant deficits for women with fractures were not observed for the sensation, emotion, cognition, vision, hearing, speech and cognition attributes.

**Men**

Some similarities existed between men and women (Fig. 1, Table 3): like women, men with hip fracture experienced substantial deficits in self-care \((-0.09\)\), mobility \((-0.20\)\) and ambulation \((-0.22\)\). However, men with spine fractures experienced a substantial deficit only for HUI3 pain \((-0.12\)\) and actually had higher scores than non-fracture participants for the mobility and ambulation attributes (in comparison, women with spine fractures experienced deficits for several attributes). Furthermore, men with rib fractures were not significantly impaired (compared to men without rib fractures) for any of the attributes, whereas women with rib fractures experienced several deficits. Only one man had a pelvic fracture, thus it is difficult to examine utility values for this fracture type. Men with forearm fractures had no clinically significant impairments for any of the attributes.

**Time effects**

Figures 2 and 3 examine year of fracture in relation to year 5 multi-attribute HUI scores (i.e. global HRQL). In Figs. 2a and b, the negative impact on global HRQL for women with hip fractures remained for several years (with the exception of the hip fracture group from year 1 who had a non-significant increase in scores compared to non-hip fracture participants). A lasting negative impact was also true of the mobility, self-care, ambulation and pain attributes. In contrast, the negative impact for spine fractures occurred primarily for women who fractured more recently (i.e. closer to 5-year follow-up), as evidenced by global HRQL (Fig. 2), and for mobility, self-care, ambulation and pain attributes. Women with rib fractures experienced lesser deficits, but they appeared to remain over time for HUI2 multi-attribute (Fig. 2), and for mobility, self-care, ambulation and pain attributes. A time trend was not observed for ‘other’ fractures types, except on the self-care attribute where a deficit occurred for more recent fractures (year 4/5).
The time effects were less clear for men than in women. Similar to women, the negative impact of hip fracture on mobility and ambulation attributes remained for several years after the fracture. This lasting effect was not seen for multi-attribute scores (Fig. 3); on the HUI2, it was only men with recent fractures (year 4/5) who experienced a substantial deficit. Due to the small number of clinical spine fractures reported in men, it was difficult to examine time trends. On the HUI2 multi-attribute (Fig. 3), clinically significant deficits are seen for men with spine fractures in years 2 and 4/5. For rib and ‘other’ fractures, there was no consistent trend with respect to time on multi-attribute functions (Fig. 3). Though not all years were significant, it appears that men who fractured a rib in earlier years had persistent deficits in pain.

**Table 1**  
Patient characteristics and mean HUI scores at baseline

|                      | Women (n=4,820)* | Men (n=1,783)* |
|----------------------|------------------|----------------|
| Age (years)          | 65.9 (8.8)       | 65.2 (8.9)     |
| Height (cm)          | 159.4 (6.3)      | 173.2 (7.0)    |
| Weight (kg)          | 68.8 (13.4)      | 81.9 (13.3)    |
| Alcohol beverages per year | 106.5 (215.0)  | 278.3 (435.7)  |
| Exercise (kcal/week) | 4,275.7 (3,160.6)| 5,192.8 (4,703.0) |
| Number of comorbid conditions | 1.5 (1.3)    | 1.1 (1.10)     |
| Self-reported fragility fracture after age 50 (%) | 28.9 | 27.9 |
| Current smoker (%)   | 12.8             | 16.8           |
| Bisphosphonate use (%) | 28.4             | 0.2            |
| Ovarian hormone therapy use (%) | 26.2 |                |
| HUI2, multi-attribute| 0.858 (0.13)     | 0.881 (0.12)   |
| Sensation            | 0.866 (0.09)     | 0.868 (0.10)   |
| Mobility             | 0.973 (0.09)     | 0.981 (0.08)   |
| Emotion              | 0.954 (0.10)     | 0.969 (0.09)   |
| Cognition            | 0.977 (0.05)     | 0.976 (0.06)   |
| Self-care            | 0.993 (0.07)     | 0.996 (0.06)   |
| Pain                 | 0.917 (0.16)     | 0.940 (0.13)   |
| HUI3, multi-attribute| 0.823 (0.19)     | 0.839 (0.18)   |
| Vision               | 0.946 (0.08)     | 0.954 (0.06)   |
| Hearing              | 0.960 (0.13)     | 0.943 (0.16)   |
| Speech               | 0.999 (0.01)     | 0.999 (0.01)   |
| Ambulation           | 0.963 (0.12)     | 0.975 (0.09)   |
| Dexterity            | 0.991 (0.06)     | 0.993 (0.04)   |
| Emotion              | 0.966 (0.09)     | 0.970 (0.08)   |
| Cognition            | 0.978 (0.08)     | 0.976 (0.09)   |
| Pain                 | 0.881 (0.19)     | 0.906 (0.18)   |

*Total sample size; data missing for some variables

The time effects were less clear for men than in women. Similar to women, the negative impact of hip fracture on mobility and ambulation attributes remained for several years after the fracture. This lasting effect was not seen for multi-attribute scores (Fig. 3); on the HUI2, it was only men with recent fractures (year 4/5) who experienced a substantial deficit. Due to the small number of clinical spine fractures reported in men, it was difficult to examine time trends. On the HUI2 multi-attribute (Fig. 3), clinically significant deficits are seen for men with spine fractures in years 2 and 4/5. For rib and ‘other’ fractures, there was no consistent trend with respect to time on multi-attribute functions (Fig. 3). Though not all years were significant, it appears that men who fractured a rib in earlier years had persistent deficits in pain.

**Discussion**

Prior to this study, the longitudinal impact of osteoporotic fractures on HRQL has not been documented. In this population-based study, we tracked incident fractures over 5 years and compared how both the time after fracture and type of fracture impacted on HUI scores at year 5.

Our study confirms that hip fractures have a profound effect on HRQL, particularly for the mobility, ambulation and self-care attributes in both men and women and additionally pain for women. These attributes measure such items as the ability to ambulate, frequency of pain and the extent to which it interferes with life and ability to perform basic self-care. Furthermore, time did not ‘heal all wounds’; on some attributes (particularly mobility and ambulation), participants who fractured several years before the follow-up HRQL assessment experienced lasting deficits in comparison to their non-fracture counterparts. This is consistent with reports that suggest hip fracture patients never regain previous levels of functioning [4, 29, 30].

Similar to the hip, spine fractures in women also exerted a negative influence on HRQL, particularly on pain attributes. Self-care, mobility and ambulation were also negatively impacted. In women, in most cases, it was the recent spine fractures that exerted the greatest negative influence on HUI scores. In men, spine fractures produced deficits primarily on the HUI3 pain attribute—a measure of the extent to which pain interferes with life activities. Due to the small number of clinical spine fractures reported in men, it was difficult to examine time trends. In years 4/5, men with spine and hip fractures had identical deficits (−0.12) on the HUI2 multi-attribute.

Rib fractures in women exerted a deficit on HRQL that was similar to that of spine fractures for most attributes and
| HU12 (multi) | Sensation | Mobility | Emotion | Cognition | Self-care | Pain | HU13 (multi) | Vision | Hearing | Speech | Ambulation | Dexterity | Emotion | Cognition | Pain |
|--------------|-----------|----------|---------|-----------|-----------|------|-------------|--------|---------|--------|-----------|-----------|---------|-----------|-------|
| -0.05* (-0.09, -0.02) | -0.02 (-0.05, 0.01) | -0.05* (-0.08, -0.03) | 0.00 (0.03, 0.05) | 0.00 (0.00, 0.00) | -0.06* (-0.09, -0.04) | -0.12* (-0.16, -0.08) | 0.00 (-0.02, 0.06) | 0.00 (-0.03, 0.02) | 0.00 (-0.00, 0.00) | 0.00 (-0.00, 0.00) | -0.05* (-0.12, -0.08) | 0.01 (0.01, 0.03) | 0.02 (0.01, 0.04) | 0.00 (-0.01, 0.02) | -0.12* (-0.16, -0.07) |

Coefficients represent the difference between patients with and without that fracture type. The variables adjusted for in the analysis include: baseline HUI scores, incident fractures, age, height, weight, prevalent fragility fracture after age 50, number of comorbid conditions, smoking (current versus former/never), alcohol intake, exercise, number of surgeries and use of bisphosphonates and ovarian hormone therapy.

*p<0.05, significant

Table 3 Adjusted regression coefficients and 95%CIs for the single/multi-attribute HUI2 and HUI3 scores at year 5, by incident clinical fracture type, men

| Spine (n=70) | Hip (n=47) | Rib (n=83) | Pelvic (n=14) | Forearm (n=23) | Other (n=218) |
|-------------|-----------|-----------|--------------|----------------|---------------|
| HU12 (multi) | 0.04 (-0.05, 0.13) | -0.09* (-0.17, -0.02) | -0.00 (-0.06, 0.03) | -0.25* (-0.48, -0.02) | -0.01 (-0.07, 0.04) | -0.02 (-0.06, 0.01) |
| Sensation | 0.01 (-0.09, 0.11) | -0.06 (-0.14, 0.02) | -0.02 (-0.07, 0.03) | 0.07* (-0.19, 0.32) | -0.02 (-0.08, 0.04) | -0.04 (-0.08, 0.00) |
| Mobility | 0.08* (0.01, 0.16) | -0.20* (-0.26, -0.13) | 0.01 (-0.02, 0.05) | -0.09* (-0.28, 0.10) | -0.01 (-0.05, 0.04) | -0.01 (-0.04, 0.02) |
| Emotion | -0.05* (-0.11, -0.02) | -0.01 (-0.07, 0.04) | 0.01 (-0.02, 0.04) | -0.29* (-0.47, -0.12) | -0.01 (-0.04, 0.03) | 0.01 (-0.02, 0.04) |
| Cognition | 0.02 (-0.04, 0.07) | -0.00 (-0.04, 0.05) | 0.00 (-0.03, 0.02) | 0.09* (-0.06, 0.23) | -0.00 (-0.03, 0.03) | -0.00 (-0.02, 0.02) |
| Self-care | 0.03 (-0.05, 0.10) | -0.09* (-0.15, -0.03) | 0.01 (-0.02, 0.05) | 0.04* (-0.16, 0.24) | -0.03 (-0.08, 0.01) | -0.01 (-0.04, 0.02) |
| Pain | 0.02 (-0.08, 0.12) | 0.04 (-0.05, 0.12) | -0.03 (-0.08, 0.02) | -0.37* (-0.63, -0.11) | 0.00 (-0.06, 0.06) | -0.03 (-0.07, 0.00) |
| HU13 (multi) | 0.00 (-0.13, 0.14) | -0.09 (-0.21, 0.03) | -0.01 (-0.08, 0.05) | 0.01* (-0.35, 0.37) | -0.02 (-0.10, 0.07) | -0.03 (-0.09, 0.02) |
| Vision | 0.03 (-0.04, 0.09) | -0.07* (-0.12, -0.01) | -0.00 (-0.05, 0.03) | 0.02* (-0.15, 0.19) | 0.01 (-0.03, 0.05) | -0.02 (-0.05, 0.00) |
| Hearing | -0.00 (-0.14, 0.14) | 0.01 (-0.11, 0.13) | -0.02 (-0.09, 0.05) | 0.11* (-0.26, 0.48) | -0.02 (-0.10, 0.07) | -0.02 (-0.07, 0.03) |
| Speech | 0.00 (-0.01, 0.02) | 0.00 (-0.01, 0.01) | 0.00 (-0.01, 0.00) | 0.00* (-0.04, 0.04) | -0.02 (-0.03, -0.01) | -0.00 (-0.01, 0.00) |
| Ambulation | 0.08* (0.00, 0.17) | -0.22* (-0.30, -0.15) | 0.01 (-0.03, 0.05) | 0.19* (-0.04, 0.41) | -0.02 (-0.07, 0.03) | -0.01 (-0.04, 0.02) |
| Dexterity | 0.01 (-0.04, 0.06) | -0.00 (-0.04, 0.04) | 0.01 (-0.02, 0.03) | 0.03* (-0.10, 0.15) | 0.01 (-0.02, 0.03) | -0.02 (-0.03, 0.00) |
| Emotion | 0.03 (-0.02, 0.09) | -0.02 (-0.07, 0.02) | 0.01 (-0.01, 0.04) | -0.04* (-0.19, 0.11) | 0.00 (-0.03, 0.04) | -0.00 (-0.02, 0.02) |
| Cognition | -0.02 (-0.11, 0.07) | 0.05 (-0.03, 0.12) | -0.01 (-0.06, 0.03) | 0.07* (-0.17, 0.30) | -0.02 (-0.07, 0.03) | -0.02 (-0.06, 0.01) |
| Pain | -0.12* (-0.22, -0.01) | 0.03 (-0.06, 0.13) | -0.02 (-0.07, 0.03) | -0.21* (-0.49, 0.07) | 0.02 (-0.05, 0.08) | -0.01 (-0.05, 0.03) |

Coefficients represent the difference between patients with and without that fracture type. The variables adjusted for in the analysis include: baseline HUI scores, incident fractures, age, height, weight, prevalent fragility fracture after age 50, number of comorbid conditions, smoking (current versus former/never), alcohol intake, exercise, number of surgeries and use of bisphosphonates and ovarian hormone therapy.

*p<0.05, significant

a Only one male participant had a pelvic fracture.
Fig. 1 HUI attributes with significant deficits, by fracture type. Only estimates that were significant ($p<0.05$) and with increase/decrease of $\geq 0.03$ are displayed. All estimates were adjusted for confounders (variables listed in the “Materials and methods” section); estimates represent the difference between patients with and without that fracture type.
Fig. 2  Effect of year of fracture on HUI2 and HUI3 scores, women. The reference group is participants without that fracture type. ‘Other’ includes pelvis, forearm and other fractures. All estimates are adjusted (variables listed in the “Materials and methods” section). Error bars represent the 95%CI.
Fig. 3 Effect of year of fracture on HUI2 and HUI3 scores, men. The reference group is participants without that fracture type. ‘Other’ includes pelvis, forearm and other fractures. All estimates are adjusted for confounders (variables listed in the “Materials and methods” section). Error bars represent the 95% CI.
an even greater deficit on the ambulation and mobility attributes. This effect appeared fairly consistent irrespective of when the fracture occurred. Overall, rib fractures did not exert a significant effect on HUI scores in men. In the time analysis, men who fractured a rib earlier on demonstrated some persistent deficits for pain.

In women, pelvic and forearm fractures did not significantly impact any of the HUI2 and HUI3 attributes with the exception of dexterity. However, since there were only 14 pelvic fractures in women, our inferences are limited regarding this fracture type. In men, only one participant had a pelvic fracture (thus, it was not valid to examine utility values), and forearm fractures did not significantly impact HUI scores. For forearm fractures, we may not have seen any differences in HRQL measured up to 5 years after a fracture since forearm fracture likely impacts quality of life most in the months following this fracture. Hallberg et al. [31] have demonstrated that women with forearm fractures had normalised HRQL values (on the SF-36) in all domains at the 2-year follow-up.

In recent years, it has been recognised that measuring HRQL is an important outcome to assess in osteoporosis [11], particularly for patients who have had a fracture. Given the wide array of potential consequences associated with a fracture, such as chronic pain, reduced mobility, disability, loss of height, increased dependence, depression and loss of self-esteem, there are many reasons fractures can impact on quality of life. Indeed, we demonstrated in this study that the HUI was a sensitive measure for detecting impairments in quality of life, particularly for pain and functional parameters (i.e. self-care, mobility and ambulation). Given the nature of a fracture injury, this is consistent with what we would expect. It was also sensitive to differences amongst fracture types.

Whilst this prospective study focused on incident fractures, we have previously demonstrated that, at baseline, a negative association existed between prevalent osteoporotic fractures and HRQL in both men and women (aged 50 years and older) for several HUI attributes [13]. Compared to patients without a prevalent fracture, lower HRQL scores occurred for patients with clinical hip, rib, lower body and sub-clinical spine fractures. Sawka et al. [32] have also demonstrated in a cross-sectional CaMos cohort (aged 65 years and older) that HUI deficits related to osteoporosis are similar to other chronic medical conditions such as arthritis, diabetes mellitus and heart disease.

Few other studies have longitudinally examined the impact of fractures on HUI scores. In a prospective study of hip fracture patients, Cranney et al. [24] demonstrated that the HUI was a sensitive measure of change post-hip fracture. HRQL was measured at baseline, 3 months, and 9 months; scores improved significantly between baseline and 9 months with the majority of the change occurring in the first 3 months. It is interesting to note that, in our study, deficits for fracture versus non-fracture participants persisted in some cases for several years (i.e., hip for men and women, rib for women).

These data are important for future health economic analyses evaluating osteoporosis therapies, in particular cost–utility analysis. A cost–utility analysis utilises quality-adjusted life years (QALYs) as the measure of effectiveness. A QALY takes into account both the quantity and quality of life generated by a health care intervention. By incorporating quality of life, it moves beyond a purely biological view of health, for example, incorporating functional capacity and general well-being [33]. QALYs are standardised and allow for comparisons across interventions and diseases.

Gabriel et al. [34] demonstrated that the HUI is valid for measuring quality of life related to osteoporotic fracture states. Since the HUI uses the preferences of a representative community sample who have not directly experienced the health state, this is an important consideration. In their study, preference scores obtained directly from the fracture subjects (time tradeoffs) versus those obtained using the HUI preference classification systems were not significantly different. The authors suggest that using the HUI system in economic evaluations offers a valid approach that is less time-consuming and costly than the direct measurement of utilities.

The strengths of this study are many. This study benefits from both a longitudinal design and the ability to control for several factors which may influence HRQL including age, comorbid diseases and surgeries. The results of this study are relevant for use in future health economic analyses for several reasons: since our estimates are based on a large, unselected, population sample, our findings are likely to be generalisable. Furthermore, with 5 years of prospective data, we were able to accurately examine the time variable. Previous baseline examinations have implied that HRQL impairment persists in the long-term [10, 13]. In this prospective examination, we also demonstrated that long-term impairment persists, but in some cases such as for spine fracture, important gains in HRQL occur over time.

There are several limitations worth noting. Fractures were self-reported and captured via the annual CaMos questionnaire and year 5 interview. Although we sought radiographic confirmation for the reported fractures, it is possible we missed fractures for some participants either due to recall issues or because they had fractures that did not come to clinical attention. However, this would result in a misclassification that would likely underestimate the effect of any deficits we observed (for example, sub-clinical spine fractures may result in back pain and functional limitations [35]). Although several potential confounding variables were included in the analysis, it is possible that we did not capture all potential risk factors which may have an influence on
Although our analysis comprehensively assessed both time and fracture sub-types, many comparisons were performed and some results might have arisen by chance. For men, we did not find many significant associations for rib and spine fractures, as opposed to women who had several. Whilst this may have been a true effect, it may also be attributable to the smaller sample size for men. Results should be confirmed. A meta-analysis combining multiple population-based cohorts may be warranted.

**Conclusion**

This study demonstrates that men and women who have hip and clinical spine fractures and women with rib fractures show adverse changes in quality of life using the HUI instruments. Forearm and pelvic fractures appeared not to substantially influence HUI scores; however, sample size was limited for the latter. The HUI was a sensitive measure of change with the ability to discriminate between different fracture types and to capture the effects of time after a fracture. In addition to its use in health economic analyses, the HUI may prove to be a useful measure for health care providers to track the effects of a fracture in individual patients.

**Conflicts of interest**

Alexandra Papaioannou, MD, FRCPC, MSc

Consulting and Advisory Role: Amgen, Eli Lilly, Merck Frosst, Novartis, Proctor and Gamble, sanofi-aventis, Servier

Clinical Trials: Amgen, Eli Lilly, Merck, Novartis, Proctor and Gamble, sanofi-aventis

Jacques P. Brown, MD, FRCPC has received honoraria for lecturing, consultancies, grants and research support for clinical trials: Abbott, Alpharx, Amgen, Arthrobol, sanofi-aventis Canada, Boehringer Ingelheim/Roche, Bristol-Myers Squibb, Celltech, Eli Lilly Canada, Genizon, Glaxosmithkline, Merck Frosst, Niox, Novartis, NPS Pharma, Pfizer, Proctor and Gamble, Quintiles, Rhône-Poulenc Rorer, Servier, Wyeth, Zelos

Robert G. Josse, MB, FRCPC

Advisory boards, honoraria, research grants: Lilly, Proctor and Gamble/sanofi-aventis, Merck, Novartis, Servier, GlaxoSmithKline, Amgen, Wyeth

Emmanuel Papadimitriou, PhD is an employee of Eli Lilly and Company in the Research and Development division.

Stephanie M Kaiser, MD, FRCPC

Advisory Boards: Amgen, Eli Lilly, Novartis, Wyeth-Ayerst, Servier

Speaker for: Amgen, Eli Lilly, Novartis, Merck, Proctor and Gamble/sanofi-aventis, AstraZeneca, Servier

David Goltzman, MD, FRCPC

Consulting Role: Lilly, Novartis, sanofi-aventis, Proctor and Gamble, Servier

Wojciech P. Olszynski, MD, FRCPC

Consulting Role: Abbott Laboratories, Limited; Merck Frosst Canada Ltd.; Amgen Canada Inc.; Novartis Pharmaceutical Canada Inc.; Aventis Pharma Inc.; Pfizer Canada Inc.; Boehringer Ingelheim (Canada) Ltd.; Proctor and Gamble Pharmaceutical Canada, Inc.; Eli Lilly Canada Inc.; sanofi-aventis Canada Inc.; Genzyme Canada Inc.; Schering Canada Inc.; GlaxoSmithKline Inc.; Servier Canada Inc.; Hoffmann-LaRoche Limited; Solvay Pharma Inc.; Janssen-Ortho Inc./Ortho-Biotech; Wyeth Canada

Jonathan D. Adachi, MD, FRCPC

Consulting Role: Amgen; Astra Zeneca, Eli Lilly; GlaxoSmithKline; Merck Frosst; Novartis; Proctor and Gamble; Roche; sanofi-aventis; Servier

Clinical Trials: Eli Lilly; GlaxoSmithKline; Merck; Novartis; Pfizer; Proctor and Gamble; sanofi-aventis; Servier; Wyeth-Ayerst

Courtney C. Kennedy, MSc; George Ioannidis, MSc; Anna M. Sawka MD, FRCPC, PhD; Wilma M. Hopman, MSc; Laura Pickard MSc; Tassos Anastasiades, MD; Alan Tenenhouse, MD; Jerilynn C. Prior MD: No competing interests to declare.

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