University of Massachusetts Medical School

eScholarship@UMMS

GLOW Publications   Center for Outcomes Research

Impact of prevalent fractures on quality of life: baseline results from the global longitudinal study of osteoporosis in women

Jonathan D. Adachi
McMaster University

Et al.

Let us know how access to this document benefits you.

Follow this and additional works at: https://escholarship.umassmed.edu/cor_glow

Part of the Health Services Research Commons, Mental and Social Health Commons, Musculoskeletal Diseases Commons, Musculoskeletal System Commons, Nutritional and Metabolic Diseases Commons, and the Women's Health Commons

ORIGINAL ARTICLE

Impact of Prevalent Fractures on Quality of Life: Baseline Results From the Global Longitudinal Study of Osteoporosis in Women

Jonathan D. Adachi, MD; Silvano Adami, MD; Stephen Gehlbach, MD; Frederick A. Anderson Jr, PhD; Steven Boonen, MD; Roland D. Chapurlat, MD; Juliet E. Compston, MD; Cyrus Cooper, MD; Pierre Delmas, MD*; Adolfo Díez-Pérez, MD; Susan L. Greenspan, MD; Frederick H. Hooven, PhD; Andrea Z. LaCroix, MD; Robert Lindsay, MD; J. Coen Netelenbos, MD; Olivia Wu, PhD; Johannes Pfeilschifter, MD; Christian Roux, MD; Kenneth G. Saag, MD; Philip N. Sambrook, MD; Stuart Silverman, MD; Ethel S. Siris, MD; Grigor Nika, MS; and Nelson B. Watts, MD; for the GLOW Investigators

OBJECTIVE: To examine several dimensions of health-related quality of life (HRQL) in postmenopausal women who report previous fractures, and to provide perspective by comparing these findings with those in other chronic conditions (diabetes, arthritis, lung disease).

PATIENTS AND METHODS: Fractures are a major cause of morbidity among older women. Few studies have examined HRQL in women who have had prior fractures and the effect of prior fracture location on HRQL. In this observational study of 57,141 postmenopausal women aged 55 years and older (enrollment from December 2007 to March 2009) from 17 study sites in 10 countries, HRQL was measured using the European Quality of Life 5 Dimensions Index (EQ-5D) and the health status, physical function, and vitality questions of the Medical Outcomes Study 36-Item Short Form Health Survey (SF-36).

RESULTS: Reductions in EQ-5D health-utility scores and SF-36–measured health status, physical function, and vitality were seen in association with 9 of 10 fracture locations. Spine, hip, and upper leg fractures resulted in the greatest reductions in quality of life (EQ-5D scores, 0.62, 0.64, and 0.61, respectively, vs 0.79 without prior fracture). Women with fractures at any of these 3 locations, as well as women with a history of multiple fractures (EQ-5D scores, 0.74 for 1 prior fracture, 0.68 for 2, and 0.58 for ≥3), had reductions in HRQL that were similar to or worse than those in women with other chronic diseases (0.67 for diabetes, 0.69 for arthritis, and 0.71 for lung disease).

CONCLUSION: Previous fractures at a variety of bone locations, particularly spine, hip, and upper leg, or involving more than 1 location are associated with significant reductions in quality of life.

Mayo Clin Proc. 2010;85(9):806-813

EQ-5D = European Quality of Life 5 Dimensions Index; GLOW = Global Longitudinal Study of Osteoporosis in Women; HRQL = health-related quality of life; SF-36 = Medical Outcomes Study 36-Item Short Form Health Survey

Fractures are a major clinical concern in older women and men. The most commonly considered sites of fracture are the hip, spine, and wrist.[1-4] About 40% of white women aged 50 years and older will experience at least 1 clinically recognized fracture at one of these skeletal sites and be subjected to increased risks of morbidity and mortality.[5,6] However, other less recognized fractures, such as those of the pelvis, ribs, shoulder, distal femur, and proximal tibia, may also lead to reductions in quality of life.[7-10]

If their full health impact is to be appreciated, fractures at a range of sites need to be examined to determine their effects on health-related quality of life (HRQL).

From St. Joseph's Hospital, McMaster University, Hamilton, Ontario (J.D.A.); Department of Rheumatology, University of Verona, Ospedale, Verona, Valeggio, Italy (S.A.); Center for Outcomes Research, University of Massachusetts Medical School, Worcester (S.G., F.A.A., F.H.H., G.N.); Division of Geriatric Medicine, Leuven University Center for Metabolic Bone Diseases, Katholieke Universiteit Leuven, Leuven, Belgium (S.B.); Division of Rheumatology, IN-SERM U831, Université de Lyon, Hôpital E. Herriot, Lyon, France (R.D.C., P.D.); University of Cambridge School of Clinical Medicine, Addenbrooke's Hospital, Cambridge, UK (J.E.C.); MRC Epidemiology Resource Centre, University of Southampton, Southampton General Hospital and Norman Collisson Chair of Musculoskeletal Sciences, University of Oxford, Oxford, UK (C.C.); Hospital del Mar-IMIM-Autonomous University of Barcelona, Barcelona, Spain (A.D.-P.); University of Pittsburgh, Pittsburgh, PA (S.L.G.); Fred Hutchinson Cancer Research Center, Seattle, WA (A.Z.L.); Regional Bone Center, Helen Hayes Hospital, West Haverstraw, NY (R.L.); Department of Endocrinology, VU University Medical Center, Amsterdam, The Netherlands (J.C.N.); Division of Community Based Sciences, Faculty of Medicine, University of Glasgow, Scotland, UK (O.W.); Department of Internal Medicine III, Alfried Krupp Krankenhaus, Essen, Germany (J.P.); Paris Descartes University, Cochin Hospital, Paris, France (C.R.); Division of Clinical Immunology and Rheumatology, University of Alabama-Birmingham, Birmingham (K.G.S.); University of Sydney Royal North Shore Hospital, St. Leonards, Sydney, NSW, Australia (P.N.S.); Department of Rheumatology, David Geffen School of Medicine, Los Angeles, CA (S.S.); Columbia University Medical Center, New York, NY (E.S.S.); and Bone Health and Osteoporosis Center, University of Cincinnati, Cincinnati, OH (N.B.W.).

*Deceased.

© 2010 Mayo Foundation for Medical Education and Research

The European Quality of Life 5 Dimensions Index (EQ-5D) is a generic, preference-based instrument that provides a comprehensive framework within which to determine health status and measure HRQL.[11,12] The EQ-5D describes states of health in 5 dimensions: mobility, self-care, usual activities, pain or discomfort, and anxiety or depression. The Medical Outcomes Study 36-Item Short Form Health Survey (SF-36) is used widely to compare the HRQL of general and specific populations, to estimate the burden of disease, and to examine the benefits of treatment interventions; we used it in the current study to measure overall health status, physical function, and vitality.

The purpose of our study was to examine the impact of common fractures on quality of life. Using data from participants aged 55 years and older from the Global Longitudinal Study of Osteoporosis in Women (GLOW), we performed a cross-sectional analysis to determine whether a history of fracture after age 45 years is associated with reduced HRQL, as measured by the EQ-5D instrument and the physical function and vitality subscales of the SF-36.

PATIENTS AND METHODS

GLOW is an observational follow-up study designed to improve understanding of international patterns of susceptibility, recognition, management, and outcomes of care in women 55 years and older at risk of fragility fractures. The study methods have been described previously[13] and are outlined herein. Enrollment occurred between December 2007 and March 2009.

STUDY SITE SELECTION
GLOW was conducted at 723 physician practices in 17 study sites in 10 countries in Europe, North America, and Australia. A scientific advisory board consisting of investigators at each of the 17 sites was constituted to provide scientific oversight and study management. These individuals are independent, university-based investigators with content expertise in osteoporosis, who represent the disciplines of endocrinology, rheumatology, geriatric medicine, and epidemiology.

PHYSICIAN AND PATIENT SELECTION
Practices typical of each region were recruited through primary care networks organized for administrative, research, or educational purposes, or by identifying all physicians in a geographic area. Primary care physicians were defined as physicians who spent the majority of their time providing primary health care to patients. Each physician completed a standardized form that collected data on personal demographics and practice characteristics.

Practices provided lists of the names and addresses of women aged 55 years and older who had been seen by their physician in the past 24 months. These lists comprised the sampling frame. Sampling was stratified by age to ensure that two-thirds consisted of women aged 65 years and older. In each practice, all eligible women aged 65 years and older and a random sample of half that number younger than 65 years were recruited.

Patients were excluded if they were unable to complete the study survey because of cognitive impairment, language barriers, institutionalization, or illness.

INSTRUMENT DEVELOPMENT
Questionnaires were designed to be self-administered. When possible, items from published validated instruments were used, including the National Health and Nutrition Examination Survey,[14] the EQ-5D,[11,12] and the SF-36 (physical function and vitality components).[12,15] Questions that had not been used previously were tested cognitively in the context of the complete questionnaire in a sample of women in the study age group. To gauge participant comprehension and completion time, the complete baseline questionnaire was also pilot-tested before being finalized.

SURVEY ADMINISTRATION
Each study site obtained ethics committee approval to conduct the study in that location. Invitations to participate in the study signed by the local principal investigator together with baseline questionnaires were mailed to all potential participants. Nonrespondents were followed up with a series of postcard reminders, second questionnaires, and telephone interviews.

MEASURES ANALYZED
Our main outcome, HRQL, was measured by the EQ-5D scale and the SF-36 subscales. The EQ-5D is a 5-question, 3-response option scale. Each of the possible 243 health states was mapped to a country-specific preference-based value or utility, in which 1.00 represents full health and 0.00 represents a state equivalent to death. The minimum clinically important difference in individuals with osteoporosis is 0.03.[16] The SF-36 subscales for physical function (10 items rating degree of limitation in activities such as walking 100 yd to >1 mile, climbing stairs, or carrying groceries), vitality (4 items on perceived energy in the past 4 weeks), and self-reported general health status (dichotomized as "fair or poor" or "good, very good, or excellent") were used. In the SF-36 subscales, a higher score means better HRQL. The minimally important difference in these SF-36 subscales is about 5.[17]

Information on previous (since age 45 years) fractures of the hip, pelvis, spine, upper or lower leg, ankle, arm,

TABLE 1. **Health-Related Quality-of-Life Scores by Location of Prior Fracture Among 57,141 Women (Age-Standardized)[a]**

	No fracture (n=42,577)	Clavicle (n=761)	Arm (n=1755)	Wrist (n=4825)	Rib (n=2318)	Spine (n=1197)	Hip (n=1074)	Pelvis (n=604)	Upper leg (n=609)	Lower leg (n=1440)	Ankle (n=3574)
EQ-5D health-utility score,[b] mean ± SD	0.79±0.2	0.68±0.3	0.71±0.3	0.73±0.3	0.69±0.3	0.62±0.3	0.64±0.3	0.64±0.3	0.61±0.3	0.70±0.3	0.72±0.2
EQ-5D domains,[c] problems with:											
Mobility	10,953 (26)	341 (42)	752 (39)	1799 (33)	980 (40)	630 (50)	704 (59)	334 (52)	383 (64)	639 (44)	1485 (40)
Self-care	2147 (6)	143 (16)	298 (15)	537 (10)	317 (13)	247 (20)	307 (23)	141 (20)	165 (25)	198 (13)	416 (11)
Usual activities	10,367 (26)	336 (41)	770 (39)	1742 (33)	1035 (43)	695 (57)	624 (52)	339 (53)	347 (58)	603 (41)	1381 (37)
Pain	28,068 (67)	582 (77)	1324 (76)	3531 (73)	1853 (80)	1041 (87)	859 (80)	494 (85)	490 (82)	1114 (78)	2754 (78)
Anxiety or depression	16,629 (40)	351 (47)	804 (48)	2093 (45)	1160 (51)	599 (52)	515 (50)	307 (53)	289 (52)	656 (47)	1672 (48)
SF-36 subscales											
Health status fair/poor[d]	8300 (20)	265 (34)	590 (33)	1402 (28)	830 (35)	528 (45)	409 (39)	227 (39)	253 (43)	475 (33)	1110 (31)
Physical function,[e] mean ± SD	74±26	62±31	65±30	68±29	63±30	53±30	52±31	56±31	47±32	62±30	65±29
Vitality,[e] mean ± SD	61±20	55±22	55±22	58±21	54±22	50±22	53±22	52±22	51±22	55±22	55±21

[a] Values are No. (percentage), unless otherwise indicated. Dividing number of patients in a row by column total does not always give the age-standardized percentage in parentheses because age-standardized percentages reflect overall age distribution in the Global Longitudinal Study of Osteoporosis in Women, not age distribution for a particular fracture. EQ-5D = European Quality of Life 5 Dimensions Index; SF-36 = Medical Outcomes Study 36-Item Short Form Health Survey.

[b] EQ-5D: lower scores reflect poorer health.

[c] EQ-5D domain scores: higher scores reflect the percentage with greater difficulties.

[d] SF-36 health status: higher scores reflect the percentage with poorer health status.

[e] SF-36 physical function and vitality: lower scores reflect poorer function.

wrist, clavicle, or rib was collected by a list that allowed for more than 1 fracture location to be checked. Therefore, a multiple fracture designation included women who broke different bone types (for example, spine and hip) at the same or a different time. A woman who fractured the same bone more than once appeared on the list as a single fracture (fracture at a single site).

To provide additional perspective on the impact of fractures on HRQL, scores were computed for women who had no previous fracture but who reported having 1 of 3 comparison conditions: type 1 diabetes; osteoarthritis or rheumatoid arthritis (designated *arthritis*); or asthma or emphysema (designated *lung disease*).

STATISTICAL ANALYSES

Means and standard deviations are reported for continuous variables (HRQL health outcomes) and percentages for dichotomous variables. Mean unadjusted outcomes are reported for various fracture types and chronic diseases, with the "no fracture" group serving as a comparison. These categories are not mutually exclusive. Unadjusted means by fracture or disease type are age-standardized to reflect the age composition of the entire study population.

To estimate comparative effects of various types of fracture and chronic disease, we performed multiple linear regression analyses for models of the form HRQL outcome = fracture type + chronic disease, adjusting for age and study site. We considered selected 2-way interactions among the 10 fracture types: spine with rib, wrist, hip, humerus,

pelvis; wrist with hip, humerus, pelvis; hip with humerus, pelvis; and humerus with pelvis. Results are expressed as "reductions" in HRQL, which are mean adjusted differences in HRQL score for women with and without each condition.

RESULTS

Of the 137,151 eligible women who were mailed a questionnaire survey, 60,393 (44%) responded (56% nonresponse rate). The mean ± SD age of the nonresponders was 71±10 years vs 69±9 years for the responders (*P*<.001). Complete data were available for 57,141 (95%) of the 60,393 responders. The participants' mean ± SE age was 68.66±0.04 years. Most women (76%; n=42,577) reported no history of fracture, 18% (n=9815) reported a single fracture, and 6.1% (n=3391) reported multiple fractures. The location of single past fractures varied in prevalence from 8.5% at the wrist to 1.1% at the pelvis and upper leg (Table 1). Low HRQL was most notable for fractures of the upper leg, spine, pelvis, and hip, with the age-standardized mean EQ-5D health-utility scores ranging from 0.61 to 0.64 compared with 0.79 for women with no fracture. About twice the percentage of women with these 4 fracture types reported problems with mobility and performing usual activities, compared with women without a previous fracture, and more than 3 times as many experienced problems with self-care. In addition, about twice the percentage of women with these 4 fracture types said that

TABLE 2. **Health-Related Quality-of-Life Scores by Presence of Fractures and Medical Conditions Among 57,141 Women (Age-Standardized; Subgroups Not Mutually Exclusive)[a]**

| | No. of fracture locations | | | | | | |
	0 (n=42,577)	1 (n=9815)	2 (n=2425)	≥3 (n=966)	Diabetes (n=2284)	Arthritis (n=24,749)	Lung disease (n=9576)
EQ-5D health-utility score,[b] mean ± SD	0.79±0.2	0.74±0.2	0.68±0.3	0.58±0.3	0.67±0.3	0.69±0.2	0.71±0.2
EQ-5D domains,[c] problems with:							
Mobility	10,953 (26)	3525 (34)	1177 (46)	590 (62)	1188 (50)	10,359 (41)	3918 (41)
Self-care	2147 (6)	966 (9)	401 (15)	262 (26)	417 (17)	2738 (11)	1050 (11)
Usual activities	10,367 (26)	3374 (33)	1183 (46)	570 (60)	1133 (48)	10,186 (41)	3923 (41)
Pain	28,068 (67)	7167 (73)	1945 (81)	826 (88)	1798 (80)	21,524 (88)	7442 (79)
Anxiety or depression	16,629 (40)	4220 (44)	1202 (53)	502 (56)	1097 (50)	11,861 (49)	4704 (50)
SF-36 subscales							
Health status fair/poor[d]	8300 (20)	2656 (27)	884 (37)	452 (49)	1071 (47)	8155 (33)	3263 (34)
Physical function,[e] mean ± SD	74±26	68±29	60±30	49±22	54±31	63±28	61±29
Vitality,[e] mean ± SD	61±20	58±21	53±30	48±22	51±21	55±21	53±21

[a] Values are No. (percentage), unless otherwise indicated. Dividing number of patients in a row by column total does not always give the age-standardized percentage in parentheses because age-standardized percentages reflect overall age distribution in the Global Longitudinal Study of Osteoporosis in Women, not age distribution for a particular fracture or disease. EQ-5D = European Quality of Life 5 Dimensions Index; SF-36 = Medical Outcomes Study 36-Item Short Form Health Survey.
[b] EQ-5D: lower scores reflect poorer health.
[c] EQ-5D domain scores: higher scores reflect the percentage with greater difficulties.
[d] SF-36 health status: higher scores reflect the percentage with poorer health status.
[e] SF-36 physical function and vitality: lower scores reflect poorer function.

their health was "fair or poor" (Table 1). Differences in frequency of reported pain and anxiety or depression were less dramatic, as were lower (ie, poorer function) vitality subscale scores. Women with a history of wrist fracture, the most common of the reported prior fractures, had the least difference for all quality-of-life measures compared with women with no history of fracture.

The HRQL scores according to number of past fractures (none, single, or multiple) and comparison conditions (type 1 diabetes, arthritis, and lung disease) are summarized in Table 2 and in the Figure. The mean EQ-5D health-utility scores were lower in all groups with a fracture compared with women with no past fracture. Disability increased with multiple vs single fractures. Mean age-standardized EQ-5D health-utility scores declined from 0.79 to 0.74 and 0.65 for no fracture, single fracture, and multiple fractures,

respectively. This pattern was also seen for specific determinants of HRQL. About twice as many women with a history of multiple fractures vs those with no prior fractures reported fair or poor health and problems with mobility and usual activities, and 3 times the number had problems with self-care.

Arthritis was reported by 44% (n=24,749), lung disease by 17% (n=9576), and type 1 diabetes by 4.1% (n=2284) of participants. The mean EQ-5D health-utility scores for women with these conditions were 0.69, 0.71, and 0.67, respectively; 33%, 34%, and 47%, respectively, reported that their general health was fair or poor (Table 2). Women with a self-reported diagnosis of osteoporosis appeared to have reductions in HRQL even if they had not had a fracture; reductions are greater in women who have had a fracture.
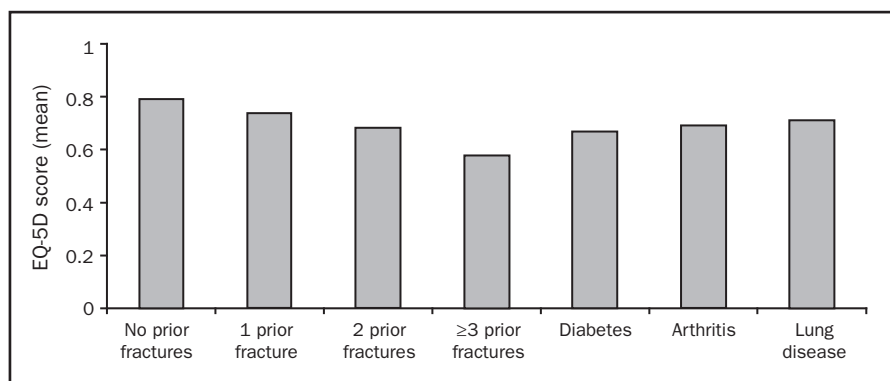

FIGURE. Health-related quality-of-life scores. EQ-5D = European Quality of Life 5 Dimensions Index.

TABLE 3. **Reductions in Health-Related Quality of Life (EQ-5D, Physical Function, and Vitality) for Women With Previous Fractures, Arthritis, Type 1 Diabetes, or Lung Disease Compared With Women Without Fracture History or Medical Condition, Adjusted for All Listed Conditions Plus Age and Study Site[a]**

	EQ-5D (n=51,165)			Physical function (n=52,109)			Vitality (n=51,962)		
	Reduction[b]	95% CI	P value	Reduction[b]	95% CI	P value	Reduction[b]	95% CI	P value
Comparison condition									
Arthritis (n=22,331)[c]	0.12	0.11-0.12	<.001	13.9	13.5-14.3	<.001	8.1	7.8-8.5	<.001
Type 1 diabetes (n=1950)	0.09	0.08-0.09	<.001	14.5	13.5-15.6	<.001	7.1	6.3-8.0	<.001
Lung disease (n=8659)	0.06	0.05-0.06	<.001	9.8	9.3-10.4	<.001	6.5	6.0-6.9	<.001
Previous fracture location									
Spine (n=1025)	0.09	0.07-0.10	<.001	10.5	9.1-11.9	<.001	5.9	4.7-7.1	<.001
Upper leg (n=505)	0.07	0.06-0.09	<.001	11.5	9.5-13.6	<.001	2.3	0.6-4.0	<.01
Hip (n=905)	0.07	0.06-0.08	<.001	11.2	9.7-12.8	<.001	4.0	2.7-5.3	<.001
Clavicle (n=661)	0.04	0.02-0.05	<.001	3.4	1.7-5.2	<.001	1.8	0.3-3.2	<.05
Pelvis (n=512)	0.04	0.02-0.05	<.001	4.5	2.4-6.5	<.001	3.0	1.3-4.7	<.001
Ankle (n=3123)	0.04	0.03-0.04	<.001	4.3	3.4-5.1	<.001	2.8	2.1-3.5	<.001
Arm (n=1505)	0.03	0.02-0.04	<.001	2.1	0.9-3.3	<.001	2.3	1.3-3.3	<.001
Rib (n=2018)	0.03	0.02-0.04	<.001	3.3	2.2-4.3	<.001	3.2	2.3-4.0	<.001
Lower leg (n=1254)	0.03	0.02-0.04	<.001	3.0	1.7-4.3	<.001	1.3	0.2-2.3	<.05
Wrist (n=4250)	0.01	0.001-0.01	<.05	0.1	−0.6-0.9	<.8	0.6	0.0-1.2	<.05

[a] EQ-5D = European Quality of Life 5 Dimensions Index; CI = confidence interval.
[b] Reduction in score between comparison groups (eg, with vs without diabetes).
[c] Numbers differ slightly for physical function and vitality because of missing data.

Table 3 depicts the HRQL reduction associated with each fracture location and comparison condition while controlling for age and study site. Among conditions studied, arthritis was associated with the largest reduction in HRQL, with reductions of 0.12, 13.9, and 8.1 points for the EQ-5D, physical function, and vitality scales, respectively, compared with women without arthritis. Type 1 diabetes; fractures of the spine, upper leg, and hip; and lung disease were also associated with decreased measures of HRQL, particularly for EQ-5D and physical function. Fractures of the wrist were associated with little disability. Table 3 results estimate the independent contribution of each variable while controlling for the others. Therefore, assuming no interactions exist (only 1 statistically significant interaction was found, for spine + rib fracture [P<.001], indicating a lesser combined reduction in HRQL for women who fractured both than would be expected from individual fracture estimates), we can in theory add individual factor reductions to estimate the effect of having multiple conditions. For example, women who fractured both an arm and the spine (n=121) would be expected to have an EQ-5D reduction of 0.12 (0.03+0.09), whereas those with both arthritis and spine fracture (n=690) would be expected to have a reduction of 0.21 (0.12+0.09). We attempted to confirm this additive property by grouping women into 1 of 4 groups: women with factor A alone, factor B alone, both, and neither. In the example of arm and spine fractures, this 4-group classification gave an adjusted reduction estimate for women with both conditions of 0.11 (0.01 less than expected from the additive model), whereas the estimate for women with both spine fracture and arthritis was 0.21 (0.01 more than expected from the model). These examples support our ability to add individual estimates to assess the effect of having more than 1 condition.

DISCUSSION

A cross-sectional view of data from this large international, observational study shows that women aged 55 years and older with a history of fracture at any of 9 different locations have a lower HRQL than women without such a history. Lower scores were most apparent for prior fractures of the hip and spine, but also for the upper leg. Dimensions of HRQL that were notably affected included mobility, self-care, and performance of usual activities. Lower fracture-associated quality-of-life values were similar to those experienced by women who reported having chronic health conditions such as arthritis, asthma or emphysema, or type 1 diabetes. Impaired HRQL was particularly evident for women with more than 1 prior fracture.

As is often seen in clinical practice, multiple clinical fractures can occur in an individual. These fractures have an additive effect, resulting in disability similar to a single hip (0.07) or vertebral (0.09) fracture. For example, the combination of a pelvic (0.04) and rib (0.03) or arm (0.03) fracture has the same effect as a hip fracture. In addition, fractures occur in women with other comorbidities. In a patient with arthritis (0.12), sustaining a hip (0.07) or vertebral (0.09) fracture is particularly devastating, with reductions ranging from 0.19 to 0.21. Moreover, reductions in EQ-5D resulting from most combinations of multiple fractures that include hip or spine (but exclude wrist) fractures match or exceed reductions due to type 1 diabetes or lung disease.

Our data are consistent with the findings of others who reported that HRQL is affected adversely by several types of fractures. After a hip fracture, mobility, ambulation, and self-care are significantly affected.[4,18-21] This reduction in quality of life has been shown to persist for several years.[20] Spine fractures result in severe pain and reductions in general health and vitality. In contrast to hip fractures, the negative impact of spine fractures occurs primarily in those who experienced fracture more recently.[20] Although some improvement in HRQL may occur over time, reductions in quality of life are long-term.[18,22]

In the current study, wrist fractures had a minimal long-term impact on HRQL, a finding that concurs with some other reports.[20,23] During the acute period after a wrist fracture, substantial pain may develop, and movement may be limited. However, individuals with wrist fractures may experience chronic loss of function.[24] In one study, older people with wrist fractures were reported to have trouble ascending and descending stairs, which may have been due to difficulty in holding onto the banister.[21]

Less well recognized is the long-term impact of previous fractures at other bone locations. Our survey did not ascertain when prior fractures occurred (other than after age 45 years); the fracture could have occurred in the preceding year or many years in the past. Still, as a group, those reporting fractures of 9 of the 10 bones evaluated had diminished HRQL compared with their nonfracture counterparts.[20] The importance of this finding is underscored by the fact that the impact on HRQL was similar to that of 2 medical conditions (lung disease and arthritis) that are more likely than past fractures to produce symptoms at the time of survey completion.

Few detailed data are available that establish the association between fractures and utility measures. As in the current study, these studies focused on hip, spine, and wrist fractures.[18,25] One study demonstrated that hip and vertebral fractures had a negative impact on quality-adjusted life years as estimated with time trade-off values using an automated computer-based instrument.[26] In another study using the EQ-5D, Colles fractures appeared to have a minimal impact on quality-adjusted life years.[27] The authors suggested that the loss associated with a Colles fracture was about 2%.

Assessments of HRQL are important for evaluating patients with osteoporosis.[18,28,29] These measurements provide data that are necessary to better describe osteoporosis and the functional outcomes of this condition. Our study examines a wide variety of fractures in a population-based international sample of postmenopausal women.

The major limitation of the current study was that fractures were self-reported and were not confirmed radiographically. Nonetheless, hip and wrist fractures are generally reported accurately, whereas spine fractures are reported less accurately.[30] We did not report on subclinical vertebral deformities because x-ray films were not a part of this study. It has been postulated that only severe vertebral deformities are associated with pain and pain-related dysfunction[31] and that subclinical deformities may tend to be less severe. Compared with a clinically recognized deformity, subclinical deformities have been shown to result in only a modest increase in morbidity.[18]

Because no specific date of fracture was recorded, we were unable to account for the effect of time on quality of life since the fracture occurred. If we had been able to distinguish fractures that occurred more recently from those that occurred several years earlier, and had adjusted results on that basis, the effect of fractures on quality of life would probably have been more pronounced.

We report quality of life associated with fractures and cannot infer causation or poorer health leading to fractures or fractures leading to poorer health. Because data on previous fractures since age 45 years were collected as a single checklist, we are unable to determine whether multiple fractures occurred on single or multiple occasions. Similarly, because some women may have experienced more than 1 fracture at a specific bone location (eg, multiple rib fractures in a single episode or multiple spine fractures over time), which would have been tallied as a single fracture, the rate of multiple fractures is probably underestimated. We compare women with or without fractures (single or multiple) with women with medical conditions, but we are unable to determine whether these medical conditions were accompanied by any fractures.

Misclassification of the comparison medical conditions is also possible and would likely result in an underestimation of their effect on quality of life. One reason for combining rheumatoid arthritis and osteoarthritis was concern that many respondents who report the former may have the latter. Some patients with type 2 diabetes may have reported type 1 diabetes. If this were the case, the effect of diabetes on HRQL would likely be underestimated. Because this study is cross-sectional, we cannot make inferences about the causality of these associations. Moreover, many comparisons were performed, and some results with little a priori evidence might have arisen by chance. Although several potential confounding variables were included in the analysis, not all risk factors may have been captured adequately in the GLOW data set.

CONCLUSION

The results of this large international, observational study demonstrate the significant effects that fractures of a variety of bones have on postmenopausal women's HRQL.

Particularly strong are associations for prior fractures of the hip, spine, and upper leg and multiple fractures of other bone types. Notwithstanding improvements in medical management of fractures, women with fractures continue to have lower HRQL, and these impairments need to be addressed.

INDIVIDUAL DISCLOSURES FOR AUTHORS

Dr Adachi: Consultant/speaker: Amgen, AstraZeneca, Lilly, GlaxoSmithKline, Merck, Novartis, Nycomed, Pfizer, Proctor & Gamble, Roche, Sanofi-Aventis, Servier, Wyeth, Bristol-Myers Squibb. Clinical trials: Amgen, Lilly, GlaxoSmithKline, Merck, Novartis, Pfizer, Proctor & Gamble, Roche, Sanofi-Aventis, Wyeth, Bristol-Myers Squibb. Clinical trials: Stock: nothing to declare.

Dr Adami: Speakers' bureau: Merck Sharp & Dohme, Lilly, Roche, Proctor & Gamble, Novartis. Honoraria: Merck Sharp & Dohme, Roche, Proctor & Gamble. Consultant/advisory board: Merck Sharp & Dohme, Amgen.

Dr Gehlbach: The Alliance for Better Bone Health (Sanofi-Aventis and Warner Chilcott).

Dr Anderson: Research grant: Sanofi-Aventis: GRACE, GLOW, ENDORSE; The Medicines Company; STAT. Scios: Orthopedic Registry. Consultant/advisory board: Sanofi-Aventis, Scios, GlaxoSmithKline, The Medicines Company, Millennium Pharmaceuticals.

Dr Boonen: Research grant: Amgen, Lilly, Novartis, Pfizer, Proctor & Gamble, Sanofi-Aventis, Roche, GlaxoSmithKline. Speakers' bureau: Amgen, Lilly, Merck, Novartis, Proctor & Gamble, Sanofi-Aventis, Servier. Honoraria: Amgen, Lilly, Merck, Novartis, Proctor & Gamble, Sanofi-Aventis, Servier. Consultant/advisory board: Amgen, Lilly, Merck, Novartis, Proctor & Gamble, Sanofi-Aventis, Servier.

Dr Chapurlat: Research grant: French Ministry of Health, Servier, Lilly, Proctor & Gamble. Speakers' bureau: none. Honoraria: Servier, Novartis, Lilly, Roche, Sanofi-Aventis, Maxence Pharma. Consultant/advisory board: Servier, Nycomed, Novartis, Maxence Pharma.

Dr Compston: Paid consultancy work: Servier, Shire, Nycomed, Novartis, Amgen, Proctor & Gamble, Wyeth, Pfizer, The Alliance for Better Bone Health (Sanofi-Aventis and Warner Chilcott), Roche, GlaxoSmithKline. Paid speaking engagements, reimbursement, and travel and accommodation: Servier, Proctor & Gamble, Lilly. Research grants: Servier R&D and Proctor & Gamble. No stocks or shares in relevant companies.

Dr Cooper: Received consulting fees and lectured for Amgen, The Alliance for Better Bone Health (Sanofi-Aventis and Warner Chilcott), Lilly, Merck Sharp & Dohme, Servier, Novartis, and Roche-GSK.

Dr Delmas: None

Dr Diez-Perez: Honoraria: Novartis, Lilly, Amgen, Proctor & Gamble, Roche. Expert witness: Merck. Consultant/advisory board: Novartis, Lilly, Amgen, Proctor & Gamble.

Dr Greenspan: Consultant/advisory board: Amgen, Lilly, Merck. Research grants: The Alliance for Better Bone Health (Sanofi-Aventis and Warner Chilcott), Lilly.

Dr Hooven: The Alliance for Better Bone Health (Sanofi-Aventis and Warner Chilcott).

Dr LaCroix: The Alliance for Better Bone Health (Sanofi-Aventis and Warner Chilcott).

Dr Lindsay: The Alliance for Better Bone Health (Sanofi-Aventis and Warner Chilcott).

Dr Netelenbos: Paid consultancy work: Roche Diagnostics, Daiichi-Sankyo, Proctor & Gamble, Nycomed. Paid speaking engagements, reimbursement, and travel and accommodation: Roche Diagnostics, Novartis, Daiichi-Sankyo, Proctor & Gamble. Research grants: The Alliance for Better Bone Health (Sanofi-Aventis and Warner Chilcott), Amgen.

Dr Wu: Research grant: Center for Outcomes Research (which in turn received funding from Sanofi-Aventis and The Medicines Company).

Dr Pfeilschifter: Research grant: Amgen, Kyphon, Novartis, Roche. Other research support: Equipment: GE Lunar. Speakers' bureau: Amgen, Sanofi-Aventis, GlaxoSmithKline, Roche, Lilly Deutschland, Orion Pharma, Merck Sharp & Dohme, Merckle, Nycomed, Proctor & Gamble. Advisory board: Novartis, Roche, Proctor & Gamble, Teva.

Dr Roux: Honoraria: The Alliance for Better Bone Health (Sanofi-Aventis and Warner Chilcott), Amgen, Lilly, Merck Sharp & Dohme, Novartis, Nycomed, Roche, GlaxoSmithKline, Servier, Wyeth. Consultant/advisory board: The Alliance for Better Bone Health (Sanofi-Aventis and Warner Chilcott), Amgen, Lilly, Merck Sharp & Dohme, Novartis, Nycomed, Roche, GlaxoSmithKline, Servier, Wyeth.

Dr Saag: Speakers' bureau: Novartis. Consulting fees or other remuneration: Lilly, Merck, Novartis, Amgen, Roche, Proctor & Gamble, Sanofi-Aventis. Paid research: Lilly, Merck, Novartis, Amgen, Proctor & Gamble, Sanofi-Aventis. Advisory committee or other paid committee: Lilly.

Dr Sambrook: Honoraria: Merck, Sanofi-Aventis, Roche, Servier. Consultant/advisory board: Merck, Sanofi-Aventis, Roche, Servier.

Dr Silverman: Research grants: Wyeth, Lilly, Novartis, The Alliance for Better Bone Health (Sanofi-Aventis and Warner Chilcott). Speakers' bureau: Lilly, Novartis, Pfizer, Proctor & Gamble. Honoraria: Proctor & Gamble. Consultant/advisory board: Lilly, Amgen, Wyeth, Merck, Roche, Novartis.

Dr Siris: Speakers' bureau: Lilly, Merck, Proctor & Gamble, Sanofi-Aventis, Novartis.

Dr Watts: Stock options/holdings, royalties, company owner, patent owner, official role: none. Honoraria for lectures in past year: Amgen, Novartis, Proctor & Gamble, Sanofi-Aventis. Consulting in past year: Amgen, Baxter, InteKrin, Johnson & Johnson, MannKind, Novo Nordisk, NPS, Pfizer, Proctor & Gamble, Sanofi-Aventis, Takeda Pharmaceuticals, Warner Chilcott. Research support (through University): Amgen, Lilly, Merck, NPS.

REFERENCES

1. Jones G, Nguyen T, Sambrook PN, Kelly PJ, Gilbert C, Eisman JA. Symptomatic fracture incidence in elderly men and women: the Dubbo Osteoporosis Epidemiology Study (DOES). *Osteoporos Int*. 1994;4(5):277-282.

2. Kannus P, Niemi S, Parkkari J, Palvanen M, Vuori I, Jarvinen M. Hip fractures in Finland between 1970 and 1997 and predictions for the future. *Lancet*. 1999;353(9155):802-805.

3. Melton LJ III, Thamer M, Ray NF, et al. Fractures attributable to osteoporosis: report from the National Osteoporosis Foundation. *J Bone Miner Res*. 1997;12(1):16-23.

4. Boonen S, Autier P, Barette M, Vanderschueren D, Lips P, Haentjens P. Functional outcome and quality of life following hip fracture in elderly women: a prospective controlled study. *Osteoporos Int*. 2004;15(2):87-94.

5. Lips P. Epidemiology and predictors fractures associated with osteoporosis. *Am J Med*. 1997;103(2A):3S-8S.

6. Melton LJ III, Chrischilles EA, Cooper C, Lane AW, Riggs BL. Perspective: how many women have osteoporosis? *J Bone Miner Res*. 1992;7(9):1005-1010.

7. Kanis JA, Oden A, Johnell O, Jonsson B, de Laet C, Dawson A. The burden of osteoporotic fractures: a method for setting intervention thresholds. *Osteoporos Int*. 2001;12(5):417-427.

8. Luthje P, Nurmi I, Kataja M, Heliovaara M, Santavirta S. Incidence of pelvic fractures in Finland in 1988. *Acta Orthop Scand*. 1995;66(3):245-248.

9. Rose SH, Melton LJ III, Morrey BF, Ilstrup DM, Riggs BL. Epidemiologic features of humeral fractures. *Clin Orthop Relat Res*. 1982;(168):24-30.

10. Nguyen TV, Center JR, Sambrook PN, Eisman JA. Risk factors for proximal humerus, forearm, and wrist fractures in elderly men and women: the Dubbo Osteoporosis Epidemiology Study. *Am J Epidemiol*. 2001;153(6):587-595.

11. Brooks R. EuroQol: the current state of play. *Health Policy*. 1996;37(1):53-72.

12. Brazier JE, Walters SJ, Nicholl JP, Kohler B. Using the SF-36 and Euroqol on an elderly population. *Qual Life Res*. 1996;5(2):195-204.

13. Hooven FH, Adachi JD, Adami S, et al. The Global Longitudinal Study of Osteoporosis in Women (GLOW): rationale and study design. *Osteoporos Int*. 2009;20(7):1107-1116.

14. Centers for Disease Control and Prevention (CDC). National Health and Nutrition Examination Survey. NHANES 2005-2006: National Center for Health Statistics; 2008. http://www.cdc.gov/nchs/nhanes.htm. Accessed June 9, 2010.

15. Brazier JE, Harper R, Jones NM, et al. Validating the SF-36 health survey questionnaire: new outcome measure for primary care. *BMJ*. 1992;305(6846):160-164.

16. Sullivan PW, Lawrence WF, Ghushchyan V. A national catalog of preference-based scores for chronic conditions in the United States. *Med Care*. 2005;43(7):736-749.

17. Walters SJ, Brazier JE. What is the relationship between the minimally important difference and health state utility values? The case of the SF-6D. *Health Qual Life Outcomes*. 2003;1:4.

18. Adachi JD, Ioannidis G, Pickard L, et al. The association between osteoporotic fractures and health-related quality of life as measured by the Health Utilities Index in the Canadian Multicentre Osteoporosis Study (CaMos). *Osteoporos Int*. 2003;14(11):895-904.

19. Adachi JD, Ioannidis G, Berger C, et al. The influence of osteoporotic fractures on health-related quality of life in community-dwelling men and women across Canada. *Osteoporos Int*. 2001;12(11):903-908.

20. Papaioannou A, Kennedy CC, Ioannidis G, et al. The impact of incident fractures on health-related quality of life: 5 years of data from the Canadian Multicentre Osteoporosis Study. *Osteoporos Int*. 2008.

21. Greendale GA, Barrett-Connor E, Ingles S, Haile R. Late physical and functional effects of osteoporotic fracture in women: the Rancho Bernardo Study. *J Am Geriatr Soc*. 1995;43(9):955-961.

22. Begerow B, Pfeifer M, Pospeschill M, et al. Time since vertebral fracture: an important variable concerning quality of life in patients with postmenopausal osteoporosis. *Osteoporos Int*. 1999;10(1):26-33.

23. Hallberg I, Rosenqvist AM, Kartous L, Lofman O, Wahlstrom O, Toss G. Health-related quality of life after osteoporotic fractures. *Osteoporos Int*. 2004;15(10):834-841.

24. Kaukonen JP, Karaharju EO, Porras M, Luthje P, Jakobsson A. Functional recovery after fractures of the distal forearm: analysis of radiographic and other factors affecting the outcome. *Ann Chir Gynaecol*. 1988;77(1):27-31.

25. Papaioannou A, Kennedy CC, Ioannidis G, et al. The impact of incident fractures on health-related quality of life: 5 years of data from the Canadian Multicentre Osteoporosis Study. *Osteoporos Int*. 2009;20(5):703-714.

26. Tosteson AN, Gabriel SE, Grove MR, Moncur MM, Kneeland TS, Melton LJ III. Impact of hip and vertebral fractures on quality-adjusted life years. *Osteoporos Int*. 2001;12(12):1042-1049.

27. Dolan P, Torgerson D, Kakarlapudi TK. Health-related quality of life of Colles' fracture patients. *Osteoporos Int*. 1999;9(3):196-199.

28. Oleksik AM, Ewing S, Shen W, van Schoor NM, Lips P. Impact of incident vertebral fractures on health related quality of life (HRQOL) in postmenopausal women with prevalent vertebral fractures. *Osteoporos Int*. 2005;16(8):861-870.

29. Silverman SL, Minshall ME, Shen W, Harper KD, Xie S. The relationship of health-related quality of life to prevalent and incident vertebral fractures in postmenopausal women with osteoporosis: results from the Multiple Outcomes of Raloxifene Evaluation Study. *Arthritis Rheum*. 2001;44(11):2611-2619.

30. Ivers RQ, Cumming RG, Mitchell P, Peduto AJ. The accuracy of self-reported fractures in older people. *J Clin Epidemiol*. 2002;55(5):452-457.

31. Ettinger B, Black DM, Nevitt MC, et al; Study of Osteoporotic Fractures Research Group. Contribution of vertebral deformities to chronic back pain and disability. *J Bone Miner Res*. 1992;7(4):449-456.