



Burden of Illness for Osteoporotic Fractures Compared With Other Serious Diseases Among Postmenopausal Women in the United States

Andrea Singer, MD; Alex Exuzides, PhD; Leslie Spangler, PhD; Cynthia O'Malley, PhD; Chris Colby, PhD; Karissa Johnston, PhD; Irene Agodoa, MD; Jessica Baker, BSc; and Risa Kagan, MD

Abstract

Objectives: To provide a national estimate of the incidence of hospitalizations due to osteoporotic fractures (OFs) in women; compare this with the incidence of myocardial infarction (MI), stroke, and breast cancer; and assess temporal trends in the incidence and length of hospitalizations.

Patients and Methods: The study included all women 55 years and older at the time of admission, admitted to a hospital participating in the US Nationwide Inpatient Sample for an outcome of interest. We performed a retrospective analysis of hospitalizations for OFs (hip, forearm, spine, pelvis, distal femur, wrist, and humerus), MI, stroke, or breast cancer, using the US Nationwide Inpatient Sample, 2000-2011. **Results:** From 2000 to 2011, there were 4.9 million hospitalizations for OF, 2.9 million for MI, 3.0 million for stroke, and 0.7 million for breast cancer. Osteoporotic fractures accounted for more than 40% of the hospitalizations in these 4 outcomes, with an age-adjusted rate of 1124 admissions per 100,000 person-years. In comparison, MI, stroke, and breast cancer had age-adjusted incidence rates of 668, 687, and 151 admissions per 100,000 person-years, respectively. The annual total population facility-related hospital cost was highest for hospitalizations due to OFs (\$5.1 billion), followed by MI (\$4.3 billion), stroke (\$3.0 billion), and breast cancer (\$0.5 billion).

Conclusion: These data provide evidence that in US women 55 years and older, the hospitalization burden of OFs and population facility-related hospital cost is greater than that of MI, stroke, or breast cancer. Prioritization of bone health and supporting programs such as fracture liaison services is needed to reduce this substantial burden.

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Mayo Clin Proc. 2015;90(1):53-62

steoporosis is a silent disease but its impact is not: in the United States, an estimated 2 million osteoporotic fractures occur each year, resulting in more than half a million hospitalizations, more than 800,000 emergency room encounters, more than 2,600,000 physician office visits, and the placement of nearly 180,000 individuals into nursing homes, a situation that most of the participants in a study compared unfavorably to death.^{1,2} Despite the staggering clinical and societal impact of fragility fractures, osteoporosis continues to be underdiagnosed and undertreated.¹ Moreover, osteoporotic fractures are associated with a decreased quality of life.^{3,4} It is estimated that 50% of women older than 50 years will sustain an osteoporotic fracture,^{5,6} whereas an estimated 13%

will be diagnosed with breast cancer in their lifetime.⁷

Although the burden of osteoporotic fractures is substantial in terms of morbidity, mortality, and incidence, it is not perceived as an important health risk by many women, particularly in comparison to other health concerns including cardiovascular disease and breast cancer. Previous studies conducted in the United States, Canada, and Europe have consistently found that women tend to underestimate the risk of osteoporosis, with respect to frequency relative to other diseases,^{8,9} seriousness of health outcomes,¹⁰⁻¹² and risk factors, contributing to increased susceptibility to osteoporotic fractures.^{13,14}

Characterizing the burden of an illness with respect to health care resource utilization

From Georgetown University Hospital, Washington, DC (A.S.); ICON plc., San Francisco, CA (A.E., C.C., K.J., J.B.); Amgen, Thousand Oaks, CA (L.S., C.M., I.A.); and Sutter East Bay Medical Foundation, Berkeley, CA (R.K.). and associated costs plays an important role in optimal management of constrained resources. This is particularly true in elderly populations for which limited health care resources must be allocated across a number of diseases. The motivation for this observational study was to provide an updated description of the US hospitalization burden associated with osteoporotic fractures and other serious diseases in postmenopausal women. We used a nationally representative data set to characterize the incidence and temporal trends of US hospitalizations due to osteoporotic fractures during the period 2000 to 2011 and compare this with corresponding results for myocardial infarction (MI), stroke, and breast cancer. In addition, we report the resource utilization burden of hospital lengths of stay and associated costs for these outcomes.

METHODS

Nationwide Inpatient Sample Data

We used the Nationwide Inpatient Sample (NIS), produced by the US Agency for Healthcare Research and Quality. The NIS contains data from all payers describing approximately 8 million inpatient hospitalizations (defined as an admission to a short-term acute care facility; emergency room-only visits and sameday surgery center visits are not included) per year in more than 1000 participating hospitals in the United States. Included hospitals were sampled to approximate a 20% stratified sample of US acute care hospitals. These hospitals included specialty centers, public hospitals, and academic medical centers. The hospitals included in the NIS were drawn from the 46 states participating in the US Agency for Healthcare Research and Quality Healthcare Cost and Utilization Project, which comprise more than 97% of the US population.

Study Population

The initial study population included all US women aged 55 years and older in the NIS data from January 1, 2000, to December 31, 2011. Age 55 years was selected as a surrogate marker for postmenopausal status.¹⁵ We then restricted the population to those with hospitalizations for osteoporotic fracture, MI, stroke, or breast cancer.

Outcomes

Outcomes of interest included clinical and demographic patient characteristics, incidence, length of hospital stay, and cost per hospitalization for osteoporotic fractures (defined as hip, forearm, spine, pelvis, distal femur [including shaft], wrist, and humerus), MI, stroke, and breast cancer. The International Classification of Disease, Ninth Revision codes used to define disease conditions of interest are listed in the Appendix at the end of this article. Only principal diagnosis codes were used to identify these outcomes. Institutional charges for each hospitalization (which include all charges except professional fees from providers not directly employed by the facilities) were collected from the reporting hospitals. To estimate actual inpatient costs, we used cost-to-charge ratios provided by the NIS. Cost-to-charge ratios are commonly used to convert charges from individual hospitalizations to a cost of care that includes a share of the hospitals' fixed costs. These cost-to-charge ratios were obtained from hospital accounting reports collected by the Centers for Medicare & Medicaid Services. For 2000 and 2011, these hospital-specific cost-tocharge ratios were not available. However, most of these hospitals were included in the 2001 or 2010 survey, and we substituted these ratios for the conversion. Otherwise, we used the US mean for the 2001 or 2010 ratio. Not every hospital reported a cost-to-charge ratio, so some imputations for missing ratios were necessary. These imputations were based on the hospital's urban/rural location, ownership type, and bed size. The Consumer Price Index produced by the US Bureau of Labor Statistics was used to inflate costs throughout the study period to a common price-year of 2011.¹⁶

Statistical Analyses

The period from January 1, 2000, to December 31, 2011, was stratified into the following time periods: 2000-2003, 2004-2007, and 2008-2011. Hospitalization incidence during each time period was calculated and standardized to the age distribution in the US population of women 55 years and older. The NIS-provided sampling weights were used to transform the observed hospitalizations into projected national estimates (Figure 1). Confidence intervals for age-standardized incidences were based on the normal approximation to the Poisson



distribution. Confidence intervals for costs and length of stay were calculated assuming a normal distribution for the mean, according to the central limit theorem.

To characterize the relative temporal changes in osteoporotic fractures hospitalization incidence with the other 3 conditions, time trends were estimated with a generalized linear model using PROC GENMOD in SAS 9.2. Time was the only independent variable, the Poisson distribution was specified, and the log of the population size was used as an offset variable to incorporate the population size as a denominator so that any fluctuations in population size over time would be appropriately accounted for when assessing trends in outcome rates. The time trends were estimated separately for each type of admission, and for each of the year groupings (2000-2003, 2004-2007, and 2008-2011). Time trends were also estimated for length of hospitalization, using the same methodology.

RESULTS

Patient and Hospital Characteristics

The osteoporotic fracture population was relatively older, with a mean age of 80.5 years, and 60.4% of the admissions for osteoporotic fractures were in women 80 years and older, compared with a mean age of 75.9 years and 41.0% of admissions in women 80 years and older for MI, 77.3 years and 46.9% for stroke, and 70.0 years and 19.3% for breast cancer (Table 1).

Across all diseases, in hospitalizations with race recorded, most of the women were white, ranging from 76.1% of stroke admissions to 90.1% of osteoporotic fracture admissions. Black women comprised 8.3% of hospitalizations for all diseases, ranging from 3.4% of osteoporotic fracture admissions to 14.3% of stroke admissions. The percentage of Hispanic women and those in the combined category of Asian/Pacific Islander/Native American were smaller, at 5.7% and 2.4% of hospitalizations for all 4 diseases, respectively.

Hospital Admissions

During the 12-year study period, there were 4.9 million hospitalizations for osteoporotic fractures (2.6 million for hip fractures, 70,025 for forearm fractures, 888,845 for spinal fractures, 407,544 for pelvic fractures, 295,565 for distal femur fractures, 173,925 for wrist fractures, and 421,164 for humerus fractures), 2.9 million for MI, 3.0

TABLE 1. Patient Characteristics Observed During 2000-2011 for Osteoporotic Fractures and Other Diseases of Interest in Women 55 y and Older ^a							
	OF ^b	MI	Stroke	Breast cancer	Overall		
	(N _{obs} =992,021)	(N _{obs} =588,937)	(N _{obs} =606,763)	(N _{obs} =133,017)	(N _{obs} =2,320,738)		
Characteristic	(N _{proj} =4,863,977)	(N _{proj} =2,889,580)	(N _{proj} =2,973,431)	(N _{proj} =652,052)	(N _{proj} =11,379,040)		
Age (y), mean \pm SD	80.5±21.3	75.9±23.6	77.3±23.1	70.0±21.7	77.9±23.2		
Age (y), N _{proj} (%)							
55-64	399,091 (8.2)	523,524 (18.1)	440,413 (14.8)	226,090 (34.7)	1,589,119 (14.0)		
65-69	305,820 (6.3)	328,512 (11.4)	287,154 (9.7)	106,516 (16.3)	1,028,002 (9.0)		
70-74	462,312 (9.5)	388,811 (13.5)	363,453 (12.2)	98,832 (15.2)	1,313,407 (11.5)		
75-79	757,299 (15.6)	463,398 (16.0)	487,970 (16.4)	94,570 (14.5)	1,803,238 (15.9)		
80+	2,939,455 (60.4)	1,185,334 (41.0)	1,394,441 (46.9)	126,044 (19.3)	5,645,274 (49.6)		
Race, ^c N _{proj} (%)							
White	3,347,192 (90.1)	1,763,642 (81.4)	1,719,947 (76.1)	399,827 (80.4)	7,230,608 (83.7)		
Black	126,477 (3.4)	209,507 (9.7)	323,730 (14.3)	53,807 (10.8)	713,520 (8.3)		
Hispanic	172,346 (4.6)	143,023 (6.6)	146,476 (6.5)	30,058 (6.1)	491,904 (5.7)		
Asian or Pacific Islander or Native American	70,907 (1.9)	50,615 (2.3)	68,736 (3.0)	13,521 (2.7)	203,779 (2.4)		
Other/Unknown/Missing ^d	288,368 (7.2)	192,089 (8.1)	186,063 (7.6)	39,872 (7.4)	706,392 (7.6)		
Urban hospital, N _{proj} (%)	4,019,471 (82.9)	2,467,037 (85.7)	2,486,913 (84.0)	556,610 (85.7)	9,530,030 (84.1)		
Teaching hospital, N _{proj} (%)	1,718,793 (35.5)	1,199,944 (41.7)	1,182,890 (39.9)	284,413 (43.8)	4,386,040 (38.7)		
Geographic region, N _{proj} (%)							
Northeast	950,712 (19.6)	636,597 (22.0)	556,113 (18.7)	142,662 (21.9)	2,286,083 (20.1)		
Midwest	1,216,657 (25.0)	681,170 (23.6)	695,193 (23.4)	153,243 (23.5)	2,746,262 (24.1)		
South	1,831,535 (37.7)	1,113,474 (38.5)	1,185,145 (39.9)	228,874 (35.1)	4,359,028 (38.3)		
West	865,074 (17.8)	458,339 (15.9)	536,981 (18.1)	127,273 (19.5)	1,987,667 (17.5)		
Bed size, ^e N _{proj} (%)							
Small	620,273 (12.8)	320,940 (11.1)	355,715 (12.0)	83,461 (12.9)	1,380,389 (12.2)		
Medium	1,256,626 (25.9)	710,511 (24.7)	738,225 (24.9)	158,976 (24.5)	2,864,337 (25.3)		
Large	2,969,119 (61.3)	1,848,545 (64.2)	1,867,511 (63.1)	407,264 (62.7)	7,092,439 (62.6)		

^aN_{obs} = observed number in the NIS; N_{proj} = total projected number in the United States based on the Nationwide Inpatient Sample weights; OF, osteoporotic fracture. ^bOF count does not include patients with major trauma diagnosis or patients receiving a revision or removal of orthopedic hardware.

^cPercentage of nonmissing responses, all categories are mutually exclusive.

^dPercentage of cases with Other/Unknown/Missing race.

^eSmall, medium, and large bed size definitions vary by geographic region, urban/rural, and teaching status.

million for stroke, and 0.7 million for breast cancer. Osteoporotic fractures accounted for more than 40% of the hospitalizations in these 4 outcomes combined. When we restricted the analysis to women 75 years and older, osteoporotic fractures accounted for nearly 50% of the hospitalizations. The total number of hospitalizations for osteoporotic fractures increased over the 12-year study period, whereas these decreased for MI, stroke, and breast cancer (Table 2). The increase in the number of hospitalizations was seen for fractures occurring at all anatomic locations except the hip.

Hospitalization Rates and Time Trends

The unadjusted rates of osteoporotic fractures, MI, stroke, and breast cancer hospitalizations are shown in Figure 1, whereas the age-adjusted rates are detailed in Table 3. Osteoporotic fractures had the highest rate of hospitalization, ranging from 1046 to 1211 admissions per

100,000 person-years from 2000 to 2011 (Table 3). Among the fracture categories, hip fractures had the highest incidence for hospitalization, with rates ranging from 538 to 691 admissions per 100,000 person-years. Hospitalization rates for MI and stroke were lower than those for osteoporotic fractures, with rates from 2000 to 2011 ranging from 534 to 853 admissions per 100,000 person-years for MI and 612 to 820 admissions per 100,000 person-years for stroke. Incidence rates for hospitalization were the lowest for breast cancer, ranging from 120 to 201 admissions per 100,000 person-years.

The rate of hospitalizations for all diseases in this analysis, except nonhip osteoporotic fractures, decreased from 2000 to 2011 (Table 3 and Figure 1). Interestingly, nonhip osteoporotic fractures increased 1.0% in the 2000-2003 period and 0.2% in the 2004-2007 period (both statistically significant at the P<.001 level). Time trends for other diseases of interest were

Fracture outcomes of interest in women 35 y and otder								
		N _{proj} (%) ^c						
Condition	2000-2003	2004-2007	2008-2011	2000-2011				
Total OF	1,565,911 (39.4)	1,628,944 (43.9)	1,669,122 (45.3)	4,863,977 (42.7)				
Hip, closed	892,812 (22.4)	856,027 (23.1)	858,070 (23.3)	2,606,909 (22.9)				
Nonhip								
Forearm	23,193 (0.6)	23,247 (0.6)	23,585 (0.6)	70,025 (0.6)				
Spine	255,315 (6.4)	322,625 (8.7)	310,905 (8.4)	888,845 (7.8)				
Pelvis	125,484 (3.2)	34,530 (3.6)	147,530 (4)	407,544 (3.6)				
Distal femur	94,317 (2.4)	93,883 (2.5)	107,365 (2.9)	295,565 (2.6)				
Wrist	51,463 (1.3)	57,856 (1.6)	64,606 (1.8)	173,925 (1.5)				
Humerus	123,327 (3.1)	140,776 (3.8)	157,061 (4.3)	421,164 (3.7)				
Non-OF								
MI	1,103,274 (27.7)	933,544 (25.2)	852,762 (23.1)	2,889,580 (25.4)				
Stroke	1,059,861 (26.6)	937,469 (25.3)	976,102 (26.5)	2,973,432 (26.1)				
Breast cancer	260,441 (6.5)	200,264 (5.4)	191,347 (5.2)	652052 (5.73)				

TABLE 2. Total Hospital Admissions During 2000-2011 for Osteoporotic Fractures and Non-Osteoporotic Fracture Outcomes of Interest in Women 55 y and Older^{a,b}

 ${}^{a}MI =$ myocardial infarction; N_{proj} = projected total number in the United States based on Nationwide Inpatient Sample weights; OF = osteoporotic fracture.

^bOnly the primary diagnosis was used to determine inclusion, patients with a trauma diagnosis, and patients receiving revisions or removal of orthopedic devices were excluded.

^cDenominator for this percentage equals the total osteoporotic fracture, MI, stroke, and breast cancer hospital admissions for women older than 55 years for each year.

also statistically significant and showed annual declines of 2.7% or more.

Resource Utilization

The mean length of hospitalization and the mean total cost of hospitalization, by time

period and outcome type, are shown in Figure 2. Length of hospitalization decreased over time for hip, nonhip, and other diseases during all 3 time periods (P<.001). Across all time periods, the longest hospitalizations were associated with distal femur fractures, hip

TABLE 3. Age-Standardized Incidence Rates per 100,000 Person-Years with 95% CIs During 2000-2011 for Osteoporotic Fracture and Non-Osteoporotic Fracture Outcomes of Interest in Women 55 y and Older^{a,b}

	2000)-2003	2004	1-2007	2008-2011		2000-2011	
Condition	Age- standardized incidence	95% CI	Age- standardized incidence	95% CI	Age- standardized incidence	95% CI	Age- standardized incidence	95% CI
Total OF	1211.2	1207.4-1215.0	1131.5	28.0- 35.0	1045.9	1042.7-1049.1	1123.7	25.8- 2 .7
Hip, closed	690.6	687.8-693.3	594.6	592.2-597.1	537.7	535.5-539.9	602.3	603.7-600.9
Nonhip								
Forearm	17.9	17.4-18.4	16.2	15.7-16.6	14.8	14.4-15.2	16.2	16.4-15.9
Spine	197.5	195.9-199.0	224.1	222.5-225.7	194.8	193.4-196.2	205.5	206.2-204.5
Pelvis	97.1	96.0-98.1	93.5	92.5-94.4	92.4	91.5-93.4	94.2	94.7-93.6
Distal femur	73.0	72.0-73.9	65.2	64.3-66.1	67.3	66.4-68.1	68.3	68.8-67.8
Wrist	39.8	39.1-40.6	40.2	39.5-40.9	40.5	39.8-41.2	40.2	40.6-39.8
Humerus	95.4	94.3-96.5	97.8	96.7-98.9	98.4	97.4-99.5	97.3	97.9-96.7
Non-OF								
MI	853.4	849.9-856.8	648.5	645.6-651.3	534.4	531.9-536.8	667.6	669.3-665.9
Stroke	819.8	816.4-823.1	651.2	648.4-654.0	611.6	609.1-614.2	687.0	688.6-685.3
Breast cancer	201.4	199.7-203.2	139.1	137.8-140.5	119.9	8.7- 2 .	150.6	151.5-149.8

 $^{a}OF =$ osteoporotic fracture.

^bOnly the primary diagnosis was used to determine inclusion, patients with a trauma diagnosis, and patients receiving revisions or removal of orthopedic devices were excluded.





fractures, stroke, MI, spinal fractures, and pelvic fractures, all ranging from a mean of 4.4 to 7.0 days per admission. For most conditions including hip fracture, MI, and stroke, the mean length of stay decreased over time. Breast cancer was associated with the shortest hospitalization, ranging from 2.6 to 2.8 days across time periods.

After adjusting to a common price-year, the costs associated with hospitalizations increased

over time, despite a decreasing trend in length of stay. Hospitalizations for MI tended to be the most costly, with a mean total of \$18,896 per admission during 2008-2011. Distal femur fractures and hip fractures were also associated with relatively high costs per admission, \$18,371 and \$15,845, respectively, during 2008-2011. The total population cost for hospitalization per year for the 2000-2011 time period was \$5.1 billion for osteoporotic fractures, \$4.3 billion for MI, \$3.0 billion for stroke, and \$0.5 billion for breast cancer.

DISCUSSION

In this large US study, we report updated national estimates of hospitalization rates, length of stay, and cost of inpatient hospitalizations associated with osteoporotic fractures, MI, stroke, and breast cancer in women 55 years and older. We found that hospitalization rates were highest for osteoporosis fractures followed by stroke and MI.

There is limited information in the literature to compare our hospitalization rates with those obtained from other US data sources. Our 2004-2007 hospitalization rates of hip fracture (595 per 100,000) were lower than the 2006 rate (917 per 100,000) reported using data from the National Hospital Discharge Survey (NHDS).¹⁷ This was expected because hip fracture incidence increases dramatically with age¹⁸ and our postmenopausal population was younger (55 years and older women) than the population in the NHDS study, which included women 65 years and older. Our ageadjusted 2004-2007 hospitalization rates of MI (648 per 100,000) and stroke (651 per 100,000) in women 55 years or older are higher than the age-adjusted hospitalization rates reported in younger populations using the NHDS data. These studies report approximately 180 hospitalizations for MI per 100,000 in women older than 25 years in 2003-2005¹⁹ and 223 hospitalizations for stroke per 100,000 women of any age in 2004.²⁰

Similar to our study, a study assessing the comparative burden of hospitalization in a Swiss health care system from 2000 to 2008 reported the age-adjusted incidence of hospitalizations associated with osteoporotic fracture to be greater than that for breast cancer, chronic obstructive pulmonary disease, MI, or stroke.²¹ Of note, a similar pattern was observed in the incidence of disease in the United States. The 2010 American Association of Clinical Endocrinologists Postmenopausal Osteoporosis Guidelines, using data from different sources, reported that US women had more osteoporotic fractures than new strokes, heart attacks, or invasive breast cancer combined during the 2004-2006 period.²² In addition, the annualized age-adjusted rates of

total fractures were higher than those of invasive breast cancer, stroke, and cardiovascular disease in white, Hispanic, American Indian, and Asian/Pacific Islander 50- to 79-year-old women enrolled from 1993 to 1998 in the Women's Health Initiative Observational Study.²³ In black women, however, the rate of cardiovascular disease was higher than that of total fracture.²³

Across most of the conditions considered in this study, hospitalization rates were generally found to be decreasing over time, consistent with documented trends in the United States of a shift in health care utilization from inpatient to ambulatory care and a general decrease in both hospitalization rates and length of stay.²⁴⁻²⁷ Even though the hospitalization incidence rate for major osteoporotic fractures decreased during the study period, the absolute number of hospital admissions increased from 2000 to 2011, mostly because of an increase in nonhip fractures. The Swiss study also reported an increase in the absolute numbers of hospitalizations for nonhip fractures and a decrease in both the number of hip fractures and breast cancer hospitalizations.²¹ However, we did not see the increase in absolute numbers of cardiovascular events that was reported in Switzerland; this may be due to their broader definition of cardiovascular events than ours. The decreased number of hospitalizations for MI and stroke we describe is supported by reports of decreased hospitalizations for MI in Medicare fee-for-service population the $(2002-2007)^{25}$ and for stroke in the NHDS sample population (1997-2004).²⁰

Throughout the study period, the longest and most expensive hospitalizations were associated with hip fracture, distal femur fracture, MI, and stroke. Although the total cost per hospital admission was highest for MI, total projected cost across all hospitalizations in the US population is more than 40% greater for osteoporotic fractures than for MI, attributable to the higher hospitalization rate for osteoporotic fractures. It should be emphasized that the intent of this analysis was not to quantify or compare the overall cost of disease. This study focused on hospitalization, the largest contributor to health resource utilization, to compare the relative burden across severe diseases experienced by older women. The full cost

burden of illness for osteoporotic fracture is higher than that reported here because we evaluated only inpatient hospital costs. For example, although our analysis found the mean total inpatient cost of hip fracture per admission to be \$15,845, other studies have shown the mean health care costs (including inpatient, outpatient, and pharmacy) associated with fracture during the first year to be between \$25,332 and \$38,662.28,29 Concurrently, the annual total fracture costs across all fracture types for US women are projected to be more than 18 billion in 2025.² These numbers are significant and further highlight the need for increased focus on prevention of fractures and their associated resource utilization. We acknowledge that the full cost burden of illness for the comparator diseases considered in this analysis might also be higher than that reported here; however, most of these diseases tend to be treated more frequently in the inpatient setting.

A few limitations of this study should be considered. The number of hospitalizations reported is accurate; however, NIS data do not include a patient identifier and multiple hospitalizations in the same individual could not be identified. This could result in overestimation of the number of unique individuals experiencing hospitalizations. To minimize this in our osteoporotic fracture population, we excluded fracture admissions associated with fracture complication codes (see the Appendix). It is also possible that we undercounted events occurring simultaneously by using only the principal diagnostic code. In addition, breast cancer and nonhip osteoporotic fractures are more likely than MI or stroke to be treated in outpatient and emergency room settings. The multinational Global Longitudinal Study of Osteoporosis in Women³⁰ as well as US-only studies^{31,32} have reported hospitalizations in the range of more than 90% of hip, 60% of spine to 40% of nonhip, nonspine fractures. Mortality data after hospital discharge are not available in the NIS data. Therefore, we report the hospitalization burden, not the overall disease burden, for these conditions. Wrist and forearm fractures were included as separate subcategories of nonhip osteoporotic fractures, as defined in the Appendix. A limitation of the subcategory-specific reported results is the potential for misclassification across wrist vs forearm fractures. Throughout the followup period, we found a higher ratio of wrist fractures per forearm fracture, a finding that has also been reported in other US studies.^{33,34}

This study has significant strengths, particularly its use of a nationally representative sample of the US population of women 55 years and older. Data were available through 2011, providing a contemporary characterization of burden of hospitalization for the population of older women in the United States.

This study provides evidence that in US women 55 years and older, the hospitalization burden of osteoporotic fractures, as estimated by the number of hospitalizations and corresponding facility-related hospital cost, is greater than that of other serious diseases (MI. stroke, and breast cancer). These results highlight the substantial benefit that could be realized by improving both primary and secondary prevention of fractures in high-risk individuals. The goal of primary prevention is to prevent an initial fracture in individuals at high risk for osteoporotic fracture. Individuals at high risk can be identified by virtue of risk factors, bone mineral density testing, and absolute fracture risk assessment tools. Approximately 50% of hip fractures are preceded by an osteoporotic fracture at another skeletal site,³⁵ and by responding to the first fracture with secondary prevention strategies, such as fracture liaison service programs, the likelihood of a second fracture can be substantially reduced.36-38 Given the evidence-based success of primary and secondary prevention, the need for greater emphasis on preventive care to reduce the burden of fractures is critical.³⁹⁻⁴⁶ The substantial burden of fractures described in this study underscore the magnitude of humanistic and economic benefits that could be realized through prioritizing both primary and secondary prevention of osteoporotic fractures.

Abbreviations and Acronyms: MI = myocardial infarction; NIS = Nationwide Inpatient Sample; NHDS = National Hospital Discharge Survey

Grant Support: Funding for this study was provided by Amgen, Inc.

Correspondence: Address to Alex Exuzides, PhD, ICON plc., 456 Montgomery St, Ste 2200, San Francisco, CA 94104 (Alex.Exuzides@ICONplc.com).

APPENDIX: CODES FOR PATIENT SELECTION—*ICD-9* CODES AND E-CODES USED BY DISEASE

Osteoporotic Fractures: One of the Following ICD-9 Codes as the First (principal) Diagnosis ^a							
Category	Description			ICD-9 ^b			
Hip	Hip, closed	820.0	820.2	820.8	733.14		
Nonhip	Radius/ulna-other (forearm)	813.0		813.2		813.8	
	Spine, closed or pathologic	805.0	805.2	805.4	805.8	733.13	
	Pelvis, closed	808.0	808.2	808.4	808.8		
	Distal femur shaft or distal femur (closed)	821.0	821.2	/33.15			
	Distal radius/ulna (wrist)	813.4	813.5	/33.12	72211		
NA (%)		812.0	81Z.Z	812.4	/33.11		
With none	of the following E-codes (in any position)						
Description						E-Code ^c	
Auto and o	ther transportation accidents					E800-E848	
Accidental falls, other than falls on stairs and slips and falls on same level						E881-E884	
Accidents c	lue to cataclysmic storms and earth surface mov	/ements				E908-E909	
Other accidents (including falling objects, machinery, explosions, and unspecified)							
With none of these codes (indicating readmission) in any position							
Description							
Revision of hip replacement, acetabular component							
Revision of hip replacement, not otherwise specified						81.53	
Removal of implanted devices from bone							
Malunion of fracture						733.81	
Nonunion of fracture						733.82	
Other serious diseases: One of the following ICD-9 codes as the first (principal) diagnosis							
Description	ICD-9 ^d						
MI	410						
Stroke	430 431	43	3.×1	434.	хI	436	
Breast canc	er 174						
a ICD-9 = International Classification of Diseases Ninth Revision							

 $^{\circ}$ ICD-9 = International Classification of Diseases, Ninth Revision.

^bFor ICD-9 codes with 4 digits, any principal diagnosis starting with the 4 digits listed is considered a match.

^cAny E-code starting with the 3 digits listed will cause the admission to be excluded.

^dFor *ICD-9* codes with 3 digits, any principal diagnosis starting with the 3 digits listed is considered a match. For 433.x1 and 434.x1, a principal diagnosis starting with 433 or 434 and ending with 1 as the fifth digit is considered a match.

REFERENCES

- US Department of Health and Human Services. Bone Health and Osteoporosis: A Report of the Surgeon General. Rockville, MD: Office of the Surgeon General; 2004.
- Burge R, Dawson-Hughes B, Solomon DH, Wong JB, King A, Tosteson A. Incidence and economic burden of osteoporosisrelated fractures in the United States, 2005-2025. J Bone Miner Res. 2007;22(3):465-475.
- 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.
- Brenneman SK, Barrett-Connor E, Sajjan S, Markson LE, Siris ES. Impact of recent fracture on health-related quality of life in postmenopausal women. J Bone Miner Res. 2006;21(6): 809-816.
- Chrischilles EA, Butler CD, Davis CS, Wallace RB. A model of lifetime osteoporosis impact. Arch Intern Med. 1991;151(10): 2026-2032. Erratum in: Arch Intern Med. 1922;152(3):655.

- van Staa TP, Dennison EM, Leufkens HG, Cooper C. Epidemiology of fractures in England and Wales. Bone. 2001;29(6): 517-522.
- NCI. Breast cancer risk in American women. 2012. http://www. cancer.gov/cancertopics/factsheet/detection/probability-breastcancer. Accessed August 4, 2013.
- Gerend MA, Aiken LS, West SG, Erchull MJ. Beyond medical risk: investigating the psychological factors underlying women's perceptions of susceptibility to breast cancer, heart disease, and osteoporosis. *Health Psychol.* 2004; 23(3):247-258.
- Siris ES, Gehlbach S, Adachi JD, et al. Failure to perceive increased risk of fracture in women 55 years and older: the Global Longitudinal Study of Osteoporosis in Women (GLOW). Osteoporos Int. 2011;22(1):27-35.
- Kasper MJ, Peterson MG, Allegrante JP, Galsworthy TD, Gutin B. Knowledge, beliefs, and behaviors among college women concerning the prevention of osteoporosis. Arch Fam Med. 1994;3(8):696-702.

- Rozenberg S, Twagirayezu P, Paesmans M, Ham H. Perception of osteoporosis by Belgian women who work in a university hospital. Osteoporos Int. 1999;10(4):312-315.
- Sale JE, Beaton DE, Bogoch ER, Elliot-Gibson V, Frankel L. The BMD muddle: the disconnect between bone densitometry results and perception of bone health. J Clin Densitom. 2010;13(4): 370-378.
- Giangregorio L, Papaioannou A, Thabane L, et al. Do patients perceive a link between a fragility fracture and osteoporosis? BMC Musculoskelet Discord. 2008;9:38.
- Gregson CL, Dennison EM, Compston JE, et al. Disease-specific perception of fracture risk and incident fracture rates: GLOW cohort study. Osteoporos Int. 2014;25(1):85-95.
- Gold EB, Crawford SL, Avis NE, et al. Factors related to age at natural menopause: longitudinal analyses from SWAN. Am J Epidemiol. 2013;178(1):70-83.
- US Census Bureau. Current population survey. 2012. http:// www.census.gov/cps/. Accessed November 4, 2013.
- 17. Stevens JA, Anne Rudd R. Declining hip fracture rates in the United States. Age Ageing. 2010;39(4):500-503.
- Ettinger B, Black DM, Dawson-Hughes B, Pressman AR, Melton LJ III. Updated fracture incidence rates for the US version of FRAX. Osteoporos Int. 2010;21(1):25-33.
- Fang J, Alderman MH, Keenan NL, Ayala C. Acute myocardial infarction hospitalization in the United States, 1979 to 2005. *Am J Med.* 2010;123(3):259-266.
- Fang J, Alderman MH, Keenan NL, Croft JB. Declining US stroke hospitalization since 1997: National Hospital Discharge Survey, 1988-2004. Neuroepidemiology. 2007;29(3-4):243-249.
- Lippuner K, Grifone S, Schwenkglenks M, et al. Comparative trends in hospitalizations for osteoporotic fractures and other frequent diseases between 2000 and 2008. Osteoporos Int. 2012;23(3):829-839.
- 22. Watts NB, Bilezikian JP, Camacho PM, et al; AACE Osteoporosis Task Force. American Association of Clinical Endocrinologists Medical Guidelines for Clinical Practice for the diagnosis and treatment of postmenopausal osteoporosis. *Endocr Pract.* 2010;16(Suppl. 3):1-37.
- 23. Cauley JA, Wampler NS, Barnhart JM, et al; Women's Health Initiative Observational Study. Incidence of fractures compared to cardiovascular disease and breast cancer: the Women's Health Initiative Observational Study. Osteoporos Int. 2008; 19(12):1717-1723.
- Avalere Health AHA. Trendwatch Chartbook 2013: Trends Affecting Hospitals and Health Systems. American Hospital Association; 2013.
- Chen J, Normand SL, Wang Y, Drye EE, Schreiner GC, Krumholz HM. Recent declines in hospitalizations for acute myocardial infarction for Medicare fee-for-service beneficiaries: progress and continuing challenges. *Circulation*. 2010;121(11): 1322-1328.
- 26. Downing A, Lansdown M, West RM, Thomas JD, Lawrence G, Forman D. Changes in and predictors of length of stay in hospital after surgery for breast cancer between 1997/98 and 2004/05 in two regions of England: a population-based study. *BMC Health Serv Res.* 2009;9:202.
- Wang OJ, Wang Y, Chen J, Krumholz HM. Recent trends in hospitalization for acute myocardial infarction. Am J Cardiol. 2012;109(11):1589-1593.
- Christensen L, Iqbal S, Macarios D, Badamgarav E, Harley C. Cost of fractures commonly associated with osteoporosis in a managed-care population. J Med Econ. 2010;13(2): 302-313.

- Shi N, Foley K, Lenhart G, Badamgarav E. Direct healthcare costs of hip, vertebral, and non-hip, non-vertebral fractures. *Bone*. 2009;45(6):1084-1090.
- Ioannidis G, Flahive J, Pickard L, et al; GLOW Investigators. Non-hip, non-spine fractures drive healthcare utilization following a fracture: the Global Longitudinal Study of Osteoporosis in Women (GLOW). Osteoporos Int. 2013;24(1):59-67.
- Ray WA, Griffin MR, Fought RL, Adams ML. Identification of fractures from computerized Medicare files. J Clin Epidemiol. 1992;45(7):703-714.
- Dimai HP, Svedbom A, Fahrleitner-Pammer A, et al. Epidemiology of proximal humeral fractures in Austria between 1989 and 2008. Osteoporos Int. 2013;24(9):2413-2421.
- Baron JA, Karagas M, Barrett J, et al. Basic epidemiology of fractures of the upper and lower limb among Americans over 65 years of age. *Epidemiology*. 1996;7(6):612-618.
- US Centers for Disease Control and Prevention. Incidence and costs to Medicare of fractures among Medicare beneficiaries aged 65 years – United States, July 1991-June 1992. Morb Mortal Wkly Rep. 1996;(41):877-883.
- Port L, Center J, Briffa NK, Nguyen T, Cumming R, Eisman J. Osteoporotic fracture: missed opportunity for intervention. Osteoporos Int. 2003;14(9):780-784.
- 36. Eisman JA, Bogoch ER, Dell R, et al; ASBMR Task Force on Secondary Fracture Prevention. Making the first fracture the last fracture: ASBMR task force report on secondary fracture prevention. J Bone Miner Res. 2012;27(10):2039-2046.
- Lih A, Nandapalan H, Kim M, et al. Targeted intervention reduces refracture rates in patients with incident non-vertebral osteoporotic fractures: a 4-year prospective controlled study. Osteoporos Int. 2011;22(3):849-858.
- Majumdar SR, Beaupre LA, Harley CH, et al. Use of a case manager to improve osteoporosis treatment after hip fracture: results of a randomized controlled trial. Arch Intern Med. 2007; 167(19):2110-2115.
- Jennings LA, Auerbach AD, Maselli J, Pekow PS, Lindenauer PK, Lee SJ. Missed opportunities for osteoporosis treatment in patients hospitalized for hip fracture. J Am Geriatr Soc. 2010;58(4): 650-657.
- Tosi LL, Gliklich R, Kannan K, Koval KJ. The American Orthopaedic Association's "own the bone" initiative to prevent secondary fractures. J Bone Joint Surg Am. 2008;90(1):163-173.
- Feldstein AC, Nichols GA, Elmer PJ, Smith DH, Aickin M, Herson M. Older women with fractures: patients falling through the cracks of guideline-recommended osteoporosis screening and treatment. J Bone Joint Surg Am. 2003;85-A(12):2294-2302.
- 42. Feldstein A, Elmer PJ, Orwoll E, Herson M, Hillier T. Bone mineral density measurement and treatment for osteoporosis in older individuals with fractures: a gap in evidence-based practice guideline implementation. *Arch Intern Med.* 2003;163(18): 2165-2172.
- Solomon DH, Finkelstein JS, Katz JN, Mogun H, Avom J. Underuse of osteoporosis medications in elderly patients with fractures. Am J Med. 2003;115(5):398-400.
- Gallagher TC, Geling O, Comite F. Missed opportunities for prevention of osteoporotic fracture. Arch Intern Med. 2002; 162(4):450-456.
- Cuddihy MT, Gabriel SE, Crowson CS, et al. Osteoporosis intervention following distal forearm fractures: a missed opportunity? Arch Intern Med. 2002;162(4):421-426.
- Bahl S, Coates PS, Greenspan SL. The management of osteoporosis following hip fracture: have we improved our care? Osteoporos Int. 2003;14(11):884-888.