Osteoporos Int (2010) 21:399–408
DOI 10.1007/s00198-009-0962-6

ORIGINAL ARTICLE

Fragility fractures of the hip and femur: incidence and patient characteristics

J. W. Nieves · J. P. Bilezikian · J. M. Lane · T. A. Einhorn · Y. Wang · M. Steinbuch · F. Cosman

Received: 3 February 2009 / Accepted: 4 May 2009 / Published online: 30 May 2009

Abstract

Summary Using national discharge and medical claims data, we studied the epidemiology of femoral fractures from 1996 to 2006. The annual hip fracture incidence declined from 600/100,000 to 400/100,000, without decline in the more rare femur fractures. Incidence rates for subtrochanteric and femoral shaft fractures were each below 20 per 100,000.

Introduction This study's purpose is to describe the site-specific epidemiology of femur fractures among people aged 50 and older.

Methods Using the National Hospital Discharge Survey from 1996 to 2006 and a large medical claims database (MarketScan®), we studied epidemiology of all femur fractures. Hip fractures were grouped together; subtrochanteric, shaft, and distal femur fractures were kept separate.

Results In females, the overall hospital discharge rates of hip fracture decreased from about 600/100,00 to 400/100,000 person-years from 1996 to 2006. Subtrochanteric, femoral shaft, and lower femur rates remained stable, each approximately 20 per 100,000 person-years. Similar trends but lower rates existed in males. No significant trends were found in any of these fractures during the more recent years of 2002–2006 (MarketScan data). Using MarketScan, the overall incidence of hip fracture was <300/100,000 person-years; incidence of subtrochanteric and femoral shaft fractures combined was <25/100,000 person-years and distal femur fracture incidence was <18/100,000 person-years in females; rates were lower in males. The incidence of hip and other femur fractures increased exponentially with age.

Conclusions We found no evidence of an increasing incidence of any femoral fracture. Hip fracture incidence is declining but the incidence of each of the more rare femur fractures (distal to the lesser trochanter) is stable over time.

Keywords Bisphosphonates · Femoral fractures · Femoral shaft · Subtrochanteric

Introduction

The femur, the longest human bone, consists of a body (shaft or diaphysis) as well as the proximal and distal ends (Fig. 1). Most epidemiologic studies of fragility fractures of the femur have only considered the proximal aspects,

J. W. Nieves (✉) · J. P. Bilezikian · F. Cosman
Departments of Epidemiology and Medicine,
Columbia University,
New York, NY, USA
e-mail: jwn5@columbia.edu

J. W. Nieves · F. Cosman
Clinical Research Center, Helen Hayes Hospital,
Route 9W,
West Haverstraw, NY 10994, USA

J. M. Lane
Department of Orthopaedic Surgery, Hospital for Special Surgery,
535 East 70th Street,
New York, NY 10021, USA

T. A. Einhorn
Boston University Orthopaedic Surgical Associates,
720 Harrison Avenue, Suite 805,
Boston, MA 02118, USA

Y. Wang · M. Steinbuch
Epidemiology and Health Outcomes,
Procter & Gamble Pharmaceuticals,
Mason, OH 45040, USA

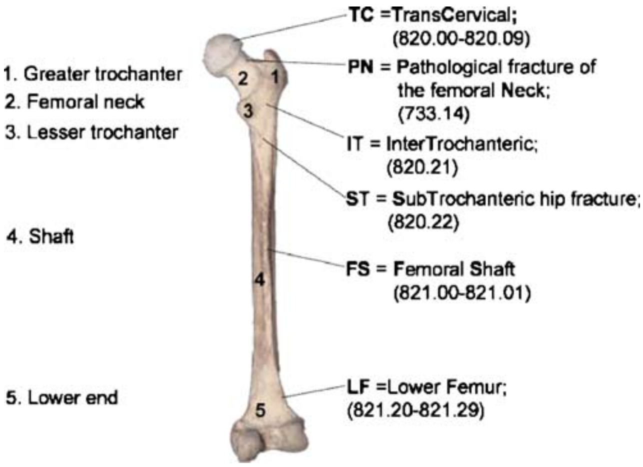

Fig. 1 Anatomy of the femur and fracture sites with ICD-9 codes

described collectively as hip fractures, including transcervical, intertrochanteric, trochanteric, and rarely subtrochanteric fractures (not well defined in terms of location). There are many epidemiologic studies of hip fractures but few site-specific studies [1–4]. It is estimated that proximal fractures (i.e., hip fractures) are ten times more common than femur fractures below the lesser trochanter [5].

Relatively few epidemiological studies have considered the subtrochanteric femur (recently suggested to be a femur fracture within 5 cm distal to the lesser trochanter [6]), femoral shaft, and the lower femur. A Finnish study reported that the incidence of femoral shaft fractures (including open and closed) was 9.9 per 100,000 person-years between 1985 and 1994 [7]. It is commonly thought that these femoral shaft fractures are exclusively the result of high-energy trauma and that they occur almost solely in younger populations. However, in the Finnish study, 25% of these fractures occurred in the context of low-energy trauma (such as those resulting from a simple fall from standing position) and 74% of the low-energy fracture cases were in people aged 60 or older. The pathogenesis of low-energy fractures of the femoral shaft among the elderly is poorly understood [8]. Earlier epidemiologic studies suggested that some diaphyseal femoral fractures share similar age-related features with hip fractures, suggesting a relationship to osteoporosis. For example, a study of Minnesota residents in the US during 1965–1984 [9] found that the incidence of diaphyseal, subtrochanteric, and distal femoral fractures all increased exponentially with age among women, and 80% of the patients with fractures associated with modest trauma had prior evidence of osteoporosis or a predisposing condition. Studies in Sweden [10, 11] and Singapore [12] have also reported that the incidence of femoral shaft fractures increased with age. In addition, Bengner and colleagues [10] observed a significant increase in the age-specific incidence of femoral shaft fractures from the early 1950s to early 1980s among women over age 50. Our review has not discovered more current studies of the epidemiology of femoral shaft fractures.

Further information about femur fractures (especially below the hip) is needed at this time to evaluate recent publications of individual case reports and several small case series [1, 13–16]. These publications have suggested a possible relationship between long-term bisphosphonate use and subtrochanteric or femoral shaft fractures. The concern was raised because subtrochanteric and femoral shaft fractures are a relatively rare osteoporosis-related fracture, and some of the clinical and radiographic features seemed particularly striking, including prodromal pain and a transverse or short oblique radiographic pattern. Many cases were associated with long-term bisphosphonate use. However, these reports cannot establish a causal relationship because there are no control groups and no denominators of the number of at-risk patients and clinical information on patients prior to initiation of osteoporosis therapy is often scarce. Background data are needed in order to better understand the expected incidence of these fractures, which will serve as a foundation for future research on the putative relationship between long-term bisphosphonate use and some of these fractures.

Using two large databases, we performed an epidemiologic study of fractures of the entire hip and femur by eight specific subgroups: transcervical, pathological fractures of the femoral neck, intertrochanteric, trochanteric unspecified, hip unspecified, subtrochanteric, femoral shaft, and lower femur. For clarity, we have chosen to present results for four exclusive categories of fracture: hip, subtrochanteric, femoral shaft, and lower femur. Complete information for all eight fracture groups is presented in "Appendix 1," "Appendix 2," and "Appendix 3." Secular trends of fracture discharge rates for each fracture group were evaluated using the National Center for Health Statistics' National Hospital Discharge Survey (NHDS) data between 1996 and 2006. We also calculated the annual incidence of these fractures between 2002 and 2006 among subjects aged 50 and older and tested for linear trends over these years in a large medical claims database, along with a description of medical and prescription drug history in the previous year.

Methods

We assessed the secular trends of femoral fractures in the entire US population between 1996 and 2006 using public data from the NHDS. Data were downloaded from the National Center for Health Statistics website [17], where detailed documentation of the survey design and analysis was available. Annual hospital discharge rates of femoral fractures were calculated as the number of discharges divided by the US civilian population for each of the 11 years. The International Classification of Diseases (ICD-9-CM) codes were used and femoral fracture cases of each calendar year were identified. The ICD-9 codes used for the eight subgroups of hip and femoral fractures were as follows (Fig. 1): (1) transcervical (including 820.00, intracapsular section, unspecified; 820.01, epiphysis; 820.02, midcervical section; 820.03, base of neck; and 820.09, other), (2) pathological fracture of neck of femur (733.14), (3) intertrochanteric (820.21), (4) trochanteric, unspecified (820.20), (5) hip fracture, unspecified part of neck of femur (820.8), (6) subtrochanteric (820.22), (7) femoral shaft (including 821.00, unspecified part of femur; 821.01, shaft), and (8) lower femur (including 821.20, lower end, unspecified; 821.21, condyle; 821.22, epiphysis, lower; 821.23, supracondylar; and 821.29, other). All of the ICD-9 codes above indicate closed femoral fractures since open fractures are usually related to major trauma and therefore excluded (as identified by inpatient or outpatient ICD-9 codes 821, "820.3x," "820.9," "821.1x," "821.3x," "822.1," and ICD-9 procedural codes v54.13-v54.15; aftercare for healing traumatic fracture of leg or hip). Furthermore, we excluded those with Paget's disease (ICD-9 731.0) or malignancy (ICD-9 140-208). Because patients with malignancy and Paget's disease diagnosis codes were excluded, the meaning of the diagnosis of "pathological fracture of neck of femur" was uncertain but likely included patients with osteoporosis and therefore this subgroup was retained. Analyses were based on four categories: (1) hip (excluding subtrochanteric), which included five subgroups: transcervical, pathological fracture of neck of femur, intertrochanteric, trochanteric, unspecified, and hip fracture, unspecified part of neck of femur, (2) subtrochanteric, (3) femoral shaft, and (4) distal femur.

The units for the NHDS discharge rates were the number of hospital discharges instead of the number of patients; this is because the same patient may have had multiple hospitalizations with the same provider within the same year. When using the NHDS data, we were unable to exclude prevalent fractures; therefore, the discharge rates may reflect not only how fast first fractures occur (i.e., incidence) but also the incidence of recurrent fractures. We did not obtain confidence intervals for the standardized NHDS discharge rates, which were considered to be population benchmarks. Linear trends of the standardized incidence and NHDS discharge rates were analyzed by simple linear regression of the rates (on the natural log scale) on the calendar years.

Data in the present study were also derived from the 2002–2006 MarketScan® Commercial Claims and Encounters and Medicare Supplemental and Coordination of Benefits databases, which obtained administrative data from approximately 45 large employers, health plans, and government and public organizations. As of December 2006, the MarketScan data represented the medical claims experience of 37 million people of which 15 million were currently eligible for a medical claim. MarketScan data were representative of the age and geographical distribution of the whole US population, with members residing primarily in the South (40%), as well as in the West (26%), Midwest (24%), and Northeast (10%). All enrollment records and inpatient, outpatient, and drug claims were collected. Diagnosis codes in the MarketScan databases use the ICD-9-CM, and procedure codes mainly use the Current Procedural Terminology, fourth edition system. Each inpatient admission records one principal ICD-9 diagnosis code and up to 15 secondary diagnosis codes.

We evaluated fracture incidence among the MarketScan enrollees aged 50 and older that had a minimum of 1 year's enrollment history for each of the 5 years between 2002 and 2006. Fracture incidence in each calendar year was calculated as the number of fracture cases divided by the total person-years of follow-up during that year. The person-year contribution from each individual enrollee was considered from January 1st of each year until the date of the first femoral fracture, date of disenrollment, or December 31st of that year, whichever came first.

Femoral fracture cases of each calendar year were identified from inpatient admission records, using the ICD-9 codes for the eight subgroups of hip and femoral fractures as described above. To focus on incident or new fractures of the femur, we also excluded femoral fracture cases that had a femoral fracture during the prior 12 months (ICD-9 codes 820, 821, 733.14, 733.15) since these were recurrent fractures. Fracture incidence rates were calculated by subgroups for each year between 2002 and 2006. To account for any differences in the age structure between the study subjects in the MarketScan and the US population over different years, we used the US year 2000 age distribution as the standard and calculated directly standardized rates. The following age groups were used: 50–54, 55–59, 60–64, 65–69, 70–74, 75–79, 80–84, 85–89, and≥ 90. Confidence intervals for the standardized incidence rates were computed using Dobson's methods [18].

To begin to understand patient characteristics associated with different femur fractures, we randomly selected five noncases for each fracture case in the MarketScan database, matching on gender and age in the same year. For each fracture case, the date of fracture hospitalization was designated as the index date, and the five matched noncases were assigned the same index date. We then pooled fracture cases of the same subgroups from all 5 years to compare the cases and their matched noncases with respect to their medical and prescription drug history during the 1 year before the index date. Less than 0.1% of fracture cases had repeat femoral fractures more than 1 year apart; in those instances, only the earliest fracture was considered so that the case pool included unique patients. We presented a total of 12 medical conditions and nine prescription drug categories. We compared the percentages of patients having these conditions during the previous year, where the percentages were directly weighted by the age structure of all fracture cases combined. Similar data were not available from the NHDS.

Results

Table 1 shows the annual age-standardized hospital discharge rates using the NHDS data for the four major femur fracture subgroups. Specific rates for the other subgroups are found in "Appendix 1." In women, the overall hospital discharge rates of hip fracture decreased from about 600 to 400 per 100,000 woman-years between 1996 and 2006. During the same 11 years, subtrochanteric, femoral shaft, and lower femur fracture discharge rates remained stable at approximately 20 per 100,000 women. The corresponding fracture groups in men showed similar trends, with lower rates compared to women at each femur site. The decreases in hip fracture rates occurred primarily during the late 1990s. During more recent years, 2002–2006, using MarketScan data, there were no significant trends in any of these fracture groups.

The study subjects from the MarketScan database contributed between 1.6 and 3.9 million person-years for each of the 5 years. There was a substantial overlap of the study cohorts by calendar year, especially between adjacent years, where up to 89% of the cohort could overlap. However, the overlap of fracture cases was negligible (<0.1%). The overall distribution of age and sex in these cohorts was also very similar; the mean age was about 63, and just over half (~56%) of the study subjects were women. Similar to the NHDS data, the fracture incidence rate in women was higher than in men for each fracture type. Overall, about 75% of femoral fracture cases were women and the average age was 80 years old. The femoral shaft and lower femur fracture cases were generally about 5 years younger than the other fracture subgroups; however, the subtrochanteric fracture cases had an average age similar to those in the hip region. The percentages of fracture subgroups among cases from each of the 5 years were similar; hip fractures collectively accounted for 87% of all femoral fractures. Subtrochanteric cases made up of about 3% of all femoral fractures, and femoral shaft and lower femur fracture cases each accounted for about 5% of all femoral fractures.

Table 2 shows the directly standardized annual incidence rates for the four groups of femoral fractures in the MarketScan database. Results for the other separate groups are shown in "Appendix 2." There was no suggestion that any of the hip fracture subcategories were different from each other; therefore, analyses presented are for pooled groups. There were no statistically significant trends in either overall femur or hip fracture rates (or incidence rates for any of the eight subgroups) over the 5 years. The standardized incidence rates of all subgroups remained stable over the 5 years among men and women combined (data not shown) or separately. The overall ranking of the

Table 1 Hospital discharge rates of closed femoral fractures, NHDS 1996–2006

	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	P^a
Women												
Hip, excluding subtrochanteric	598	522	489	507	497	490	449	400	445	400	428	<0.001
Subtrochanteric	17	21	21	19	16	8	12	14	15	13	16	0.19
Femoral shaft	16	26	18	16	13	17	22	22	21	16	19	0.77
Lower femur	23	32	29	33	34	26	31	27	29	22	18	0.13
Men												
Hip, excluding subtrochanteric	274	294	327	257	265	261	252	274	261	234	248	0.03
Subtrochanteric	16	5	10	5	4	12	10	10	11	14	11	0.37
Femoral shaft	13	11	6	15	14	10	8	14	12	8	10	0.74
Lower femur	7	6	11	9	9	7	9	10	5	9	11	0.68

Hospital discharge rates per 100,000 persons, directly standardized to the age structure of the 2000 US civilian population, using the following age groups: 50–54, 55–59, 60–64, 65–69, 70–74, 75–79, 80–84, 85–89, and ≥90

NHDS National Hospital Discharge Survey

[a] *P* values for linear trend of the discharge rates over the 11 years, not adjusted for multiple comparisons

Table 2 Incidence rates of fragility fractures, MarketScan 2002–2006

	Incidence rates (95% confidence interval)					P^a
	2002	2003	2004	2005	2006	
Women						
Hip, excluding subtrochanteric	260 (257–272)	261 (258–271)	296 (293–303)	281 (278–288)	266 (263–275)	0.58
Subtrochanter	10 (9–12)	10 (9–12)	12 (11–14)	12 (12–14)	9(8–11)	0.96
Femoral shaft	13 (13–16)	13 (12–15)	14 (13–15)	13 (12–15)	13 (12–15)	0.50
Lower femur	16 (15–19)	17 (17–20)	18 (18–20)	17 (17–19)	18 (17–20)	0.33
Men						
Hip, excluding subtrochanteric	163 (158–176)	174 (170–186)	182 (179–191)	181 (178–190)	159 (155–169)	0.97
Subtrochanteric	7 (6–10)	5 (5–7)	7 (6–9)	7 (6–8)	7 (6–9)	0.59
Femoral shaft	7 (7–10)	11(10–14)	7 (7–9)	7(6–8)	6 (6–8)	0.30
Lower femur	5 (4–7)	6 (6–9)	5 (4–6)	5 (5–7)	5 (4–7)	0.98

Incidence rates per 100,000 person-years, directly standardized to the age and sex distribution of the 2000 US civilian population, using the following age groups: 50–54, 55–59, 60–64, 65–69, 70–74, 75–79, 80–84, 85–89, and ≥90

[a] *P* values for linear trend of the incidence rates over 5 years, not adjusted for multiple comparisons

incidence rates of the eight subgroups of fractures is similar to the ranking of the discharge rates in the NHDS, but the absolute magnitude of the discharge rates was in general about 30% higher in the NHDS than the MarketScan incidence rates. The fracture rates for the eight fracture subgroups varied by up to 50-fold with intertrochanteric fracture being the most common type and pathological fracture of the femoral neck the least common type (see "Appendix 1" and "Appendix 2" and "Discussion" below) in both men and women. Incidence rates of femoral shaft and lower femur fractures were greater in women than in men, although this was not always the case for subtrochanteric fractures. The annual incidence for hip fractures in women was less than 296 per 100,000 and less than 182 per 100,000 in men between 2002 and 2006. The annual incidence for subtrochanteric, shaft, and lower femur fractures, respectively, was lower than 12, 14, and 18 per 100,000 in women and lower than 7, 11, and six per 100,000 in men throughout the period 2002 to 2006.

Figure 2 shows that the incidence rates of the four fracture groups increased exponentially with age (shown as nine age categories) in women and men, respectively. Assuming that fracture incidence follows Poisson distribution with a rate parameter λ, the fitted models for λ as a function of age in all eight fracture subgroups can be found in "Appendix 3."

Finally, we compared the fracture cases with their matched noncases from the MarketScan databases, focusing particularly on four categories of fracture cases: hip, subtrochanteric,

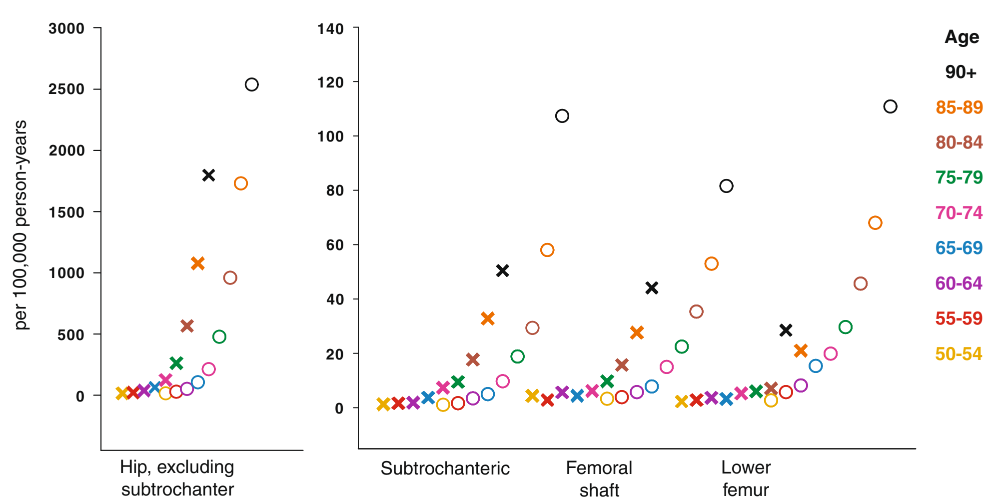

Fig. 2 Age-specific incidence rates in men (**X**) and women (**O**) for the four fracture groups (MarketScan)

femoral shaft, and lower femur. Table 3 shows the age-adjusted percentages for each of the medical conditions and prescription drug use during the 1 year before the index date. Overall, the fracture subgroups appeared similar in comorbidities and prescription drug use in the year before fracture. Conditions known to predispose to fracture (such as previous fractures, osteoporosis, rheumatoid arthritis, other musculoskeletal diseases, diabetes, chronic obstructive pulmonary disease, renal disease, Alzheimer's and other mental illness, cardiovascular disease, and use of glucocorticoids, antidepressants, and proton pump inhibitors) were quite common for all cases and appeared to be more common than their matched noncases in both women and men. The percentage of bone density tests (approximately 10% in women and 4% in men) were similar between cases and noncases (data not shown).

Discussion

In females, hospital discharge rates for hip fracture decreased from 1996 to 2006, from about 600 to 400 per 100,000 person-years, whereas subtrochanteric, femoral shaft, and lower femur discharge rates remained stable during this time, each at about 20 per 100,000 person-years. Similar trends existed in males, but, as expected, the corresponding rates were lower as compared to females. In the more recent years of 2002 to 2006, using the medical

Table 3 Medical and prescription drug history (percentage) during the 1 year before index date

	Women					Men				
	Noncases	Hip	Subtrochanter	Femoral shaft	Lower femur	Noncases	Hip	Subtrochanter	Femoral shaft	Lower femur
Medical history										
Prior fractures	5.6	12.7	15.5	13.8	14.9	2.8	9.1	6.9	8.2	9
Osteoporosis	7.4	9.9	10.5	9.7	10.9	1.1	2.4	2.8	6.5	2.7
Rheumatoid arthritis	1.4	2.7	2.9	3.9	3.8	0.7	1.3	0.3	1.3	0.7
Other musculoskeletal diseases	43	54.8	56.6	62.8	61.7	32.4	47.7	47.8	58	62.3
Diabetes	12.4	15.7	15.9	15.2	21	15.7	20.7	22	26.1	21.4
Chronic obstructive pulmonary disease	11.7	16.7	13.9	12.9	14.1	12.1	18	15.6	17.7	20.4
Thyroid disorder	7.8	8.9	10.7	7.7	8.2	3.2	4.8	4	1.8	3.6
Vision or eye problems	19.3	18.9	18.8	16.6	15.6	16.3	17.6	17.6	16.7	15.9
Cardiovascular diseases	25	30	29.3	28.1	32.2	30.7	40	34.5	47.3	44.2
Alzheimer's, Parkinson's disease	5	10.4	8.5	5.8	6.4	4.6	12.7	6.7	8.7	7.6
Other mental/nervous system	15.6	25.8	23.8	20.2	21	12.9	24.6	12.7	18.1	24.8
Renal failure or dialysis	2.3	3.9	2	4.9	5.8	3.3	7.1	6.2	6.7	8.6
Prescription drugs										
Oral glucocorticoids	8.9	12.2	13.4	11.5	11.5	7.6	10.4	8.5	12.2	11.2
Antidepressants	20.1	33.6	35.5	30.1	33.7	12.1	25.9	20.8	25.3	27
Proton pump inhibitors	17.8	22	23.4	22.6	25.6	14.9	20.4	16.9	22	24.1
Oral bisphosphonates	13.6	16	19.1	22.2	14.3	1.6	3.3	5.2	5.2	6.9
Estrogens	10.6	8.6	10.2	8.3	5.7	–	–	–	–	–
Raloxifene	3.2	3.3	2.7	2.2	2.9	–	–	–	–	–
Calcitonin	2.8	4.9	4.4	3.7	4.8	0.3	1.1	0	0.9	2.1
Thyroid or antithyroid drugs	20.9	22.5	26.1	22.2	23.6	7.7	11.1	13.9	11.4	9.2
Diuretics	38.1	39.2	43.8	44.9	43.7	28	36	37.1	43.8	41.7

Percentages were adjusted for age according to the age distribution of all eight groups of cases combined, using the following age groups: 50–54, 55–59, 60–64, 65–69, 70–74, 75–79, 80–84, 85–89, ≥90. The date of fracture hospitalization for fracture cases was assigned as the index date for fracture cases and their matched noncases. Other musculoskeletal diseases included osteoarthritis (ICD-9 codes 715), arthopathies, dorsopathies, and rheumatism (ICD-9 codes 710–729), and acquired musculoskeletal deformities (ICD-9 codes 733.2–739), major bone/joint surgeries, hip/knee replacement. Other mental/nervous system diseases also included ICD-9 codes 290–319, 320–330, and 333-359 claims database, there were no trends in the incidence rates of fragility fractures for any of the femur fracture categories. The incidence of all femur fracture types increased exponentially with age in both men and women. Medical conditions and use of medications that predispose to fracture were seen more commonly in fracture cases as compared to controls.

The strengths of the present study include the large sample size that enabled us to calculate incidence rates for specific fracture subgroups. To the best of our knowledge, our study is the first to directly compare the incidence rates of all major subgroups of femur fractures. The decreases seen in overall hospital discharge rates of hip and femur fractures in the US over the 11 years from 1996 to 2006 is similar to the findings of Gehlbach and colleagues [19] who reported a decreasing secular trend in the age-adjusted rates of hip fracture hospitalizations in the US during 1993–2003. In contrast, we found that, during the most recent 5 years (2002–2006), the overall age-standardized incidence rates of these fractures remained stable among patients aged 50 and older in a large claims database. The relative frequency across subgroups was also stable over these years. Our study did not find any increasing trend, either in the incidence or hospital discharge rates for any of the subgroups of femoral fractures, in particular shaft or subtrochanteric fractures. Recent case studies raised the question of whether there had been an increase of subtrochanteric or femoral shaft fractures, particularly those with a transverse or short oblique pattern [5, 13–16]. Although transverse or short oblique type femoral shaft fractures may account for about 50% of all femoral shaft fractures (oblique 37% and spiral 23%) among skeletally mature patients [7], we could not evaluate the number with this specific radiographic pattern in this study. If we assume that the transverse pattern had increased consistently over the time periods we evaluated and that all other patterns had either remained stable or increased consistently, we could have detected a significant trend of 8% increase overall (20% increase in transverse or short oblique type) in this database. Our data provided evidence that the overall fracture rates at these sites did not increase from the time of the introduction of bisphosphonate drugs in the mid-1990s until most recently. However, without specific radiologic or clinical information about the fractures in either MarketScan or NHDS databases, we were not able to infer pattern-specific (e.g., transverse versus spiral radiologic pattern) trends within the same fracture subgroups. For example, if the incidence of the transverse fracture pattern had increased while the spiral fracture pattern had decreased, these opposing trends of different patterns may have been masked leading to an overall stable rate in subtrochanteric and shaft fractures. In addition, the potential inconsistencies in coding for the different nonhip sites (subtrochanteric versus femoral shaft versus lower femur) can also lead to a difficulty in finding any trends.

On the other hand, each of the four subgroups of femoral fractures increased exponentially with age, despite the variable incidence among subgroups. Therefore, these femoral fractures may overall share common etiology with osteoporosis. Diseases that increase with age exponentially may also involve more complicated etiologies, such as general frailty and other comorbidities [20]. It was apparent from Table 3 that the fracture cases overall shared medical and prescription drug history compared with noncases.

Although we found that intertrochanteric fractures were the most common of all femoral fractures, if we combined hip fracture, unspecified (ICD-9 820.8), with transcervical fractures, then these would be the most common ("Appendix 2"). One previous study found that most hip fractures, unspecified (>80%), were in fact of the transcervical type [2, 21]. We did not combine these subgroups together because we could not verify the actual location of the unspecified fractures. Besides ICD-9, other classification systems have also been used to classify femoral fractures; the AO system in particular has been recommended for planning treatment and predicting outcome [22]. However, radiologic data were not available in order to use these alternative classification systems. Although misclassification of the fracture subgroups is possible, the overall relative frequency of the subgroups was similar to these previous studies [2, 21, 22].

The incidence rates from the MarketScan data were lower than the US NHDS for the same calendar years. The reasons for this are unknown. One possible reason may be that the MarketScan population with private insurance may be healthier than the general US population. Another reason may be that we excluded prevalent fracture cases and applied additional exclusion criteria (malignancy, Paget's disease, and <1-year enrollment history) in the MarketScan database. Therefore, the MarketScan incidence rates could only measure how many new femoral fractures occurred among subjects free of previous or recent femoral fractures during a specified time, while the NHDS counted the total hospitalizations of femoral fractures among all subjects, including new and repeat fractures, as well as multiple hospitalizations for the same fracture. In the MarketScan data, we may have underestimated the incidence of (new) contralateral fractures that occurred in the same patients within 1 year; we did not have detailed data as to which leg (i.e., left or right) was fractured. Early studies reported that up to 83% of noncontemporary bilateral fractures of the hip were of the same type as the initial fracture [23]. About 7% of patients admitted for a hip fracture have in the past sustained a fracture of the contralateral hip [24]. Furthermore, refracture rates may differ between fracture subgroups. Dretakis and colleagues [24] found among patients with bilateral fractures that 92% of the trochanteric and 68% of the cervical fractures were followed by a second hip fracture of the same type. However, the impact should be small because the average time between the bilateral hip fractures in different studies ranged from 3 years to up to 7 years [24].

Although we described fracture cases in the particular subgroups of interest with respect to a list of recent (within 1 year) medical and prescription drug history (Table 3), the comparisons across subgroups were descriptive and exploratory, and we did not conduct statistical tests for any particular etiological hypothesis. For example, although bisphosphonate use in the past year appeared more common among cases of any of the fracture subgroups compared with the noncases, it cannot be presumed that these drugs were causing fractures, based on the descriptive nature of the data. In addition, we did not examine the duration or type of bisphosphonate used for the cases or noncases. A more prolonged enrollment history that allows a more complete analysis would be required to evaluate any association. The likely explanation may be that fracture cases had been more prone to fractures in the first place and initiated bisphosphonate therapy to reduce the risk of future fractures. A formal analysis of these subgroups of fracture cases in terms of long-term medical and drug history is beyond the scope and intent of the present study.

However, our findings provide useful information for the planning of future studies of the possibly unique clinical and radiographic femur fractures reported in recent case studies. The overall incidence of subtrochanteric and shaft fractures combined was less than 30 per 100,000 person-years. Given the fact that femoral shaft and subtrochanteric fractures are related to age and possibly osteoporosis, many potential confounders need to be considered. Confounding by indication is a particular challenge.

Previous studies have suggested that the specific site of femoral fractures may be related to patient-level variables, such as nutrition [25] and morphology of the femur [26, 27], including hip axis length and cortical thickness. A review article by Mautalen and colleagues [26] showed that women with trochanteric hip fractures may be older, thinner, and shorter, have lower bone mass at the proximal femur and spine, and have a more severe alteration of trabecular bone properties than women with femoral neck hip fractures [26]. In addition, in that cohort, previous vertebral fractures were up to twice as common in women with trochanteric fractures compared to those with femoral neck fractures. Subtrochanteric/diaphyseal femur fractures were found to share the epidemiology and treatment response of classical hip fractures and the authors concluded that they are best classified as osteoporosis-related fractures [28]. More research is needed to identify distinctive characteristics of different femur fracture subgroups.

To our knowledge, this is the first study to estimate the incidence and secular trends of all specific femoral fracture sites, as well as describe some of the patient characteristics. This information should be useful for future etiologic research. In summary, our study did not find any increasing trend in the incidence and hospital discharge rates in any individual or subcategory of femoral fractures. Hospital discharge rates either remained stable (subtrochanteric, femoral shaft, or lower femur) or decreased (overall hip fractures) in recent years. As expected, fracture cases had a greater rate of known conditions predisposing to osteoporosis than noncases. Although some conditions appeared more common in specific subgroups, all fracture subgroups displayed an exponentially increased rate with age, and predominance in women suggesting a possible common osteoporosis-related etiology. Furthermore, the incidence of subtrochanteric and shaft femur fractures is very low, accounting for less than 10% of all femur fractures. No real conclusions can be drawn about additional predisposing factors at this time.

Acknowledgement We thank the following people for their help in preparing this manuscript: David Cahall from Sanofi-aventis, Karen Driver, Didier Huber, Andrea Klemes, Jeff L. Lange, Darrel Russell, Richard Sheer, J. Mike Sprafka, and Diane Vonderheide from Procter and Gamble, and Barbara McCarty Garcia.

Conflicts of interest and financial disclosures Dr. Nieves has attended advisory meetings for Merck and Bayer and is a member of the Speakers Bureau for Sciele Pharma, Inc.

Dr. Bilezikian is a consultant to the Alliance for Better Bone Health (a Procter & Gamble and Sanofi-aventis partnership), Merck, Lilly, Novartis, and Johnson & Johnson, has received research grants from the Alliance for Better Bone Health and Radius, and is on the Speakers Bureau for the Alliance for Better Bone Health, Novartis, and Lilly.

Dr. Lane is a consultant to BioMimetics, DFine, Innovative Clinical Solutions, Orthovita, Osteotech, Soteira, Zelos, and Zimmer, has received research grants from The Charles Cohn Foundation, and is on the Speakers Bureau for Lilly, Novartis, Procter & Gamble, and Sanofi-aventis.

Dr. Einhorn is a consultant to Eli Lilly, Novartis, Zelos, Amgen, and Pfizer and has received grants from Zelos.

Dr. Wang is an employee of Procter and Gamble.

Dr. Steinbuch is an employee of Procter and Gamble and holds company stock.

Dr. Cosman is a consultant or on an advisory board for Novartis, Eli Lilly, Merck, Amgen, Procter and Gamble, Pfizer, and Zosano and on the Speakers Bureau for Novartis and Eli Lilly.

Appendix 1

Table 4 Hospital discharge rates of closed femoral fractures, NHDS 1996-2006

	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	P^a
Women												
Femur, overall	654	601	557	575	559	541	514	464	509	451	481	<0.001
Hip, excluding subtrochanteric	598	522	489	507	497	490	449	400	445	400	428	<0.001
Subtrochanter and shaft combined	33	47	39	35	29	25	34	36	36	29	35	0.37
Transcervical	193	161	170	138	151	164	141	125	104	121	123	<0.001
Neck, pathologic	25	21	20	17	20	16	10	7	11	8	6	<0.001
Intertrochanteric	235	200	194	222	195	197	186	166	213	180	189	0.06
Trochanteric, unspecified	14	11	9	12	16	13	19	12	10	12	13	0.95
Hip, unspecified	131	129	95	118	114	101	94	91	106	80	97	<0.008
Men												
Femur, overall	311	316	354	286	291	290	279	309	289	265	279	0.02
Hip, excluding subtrochanteric	274	294	327	257	265	261	252	274	261	234	248	0.03
Subtrochanter and shaft combined	29	16	16	20	18	22	18	24	23	22	21	0.58
Transcervical	94	86	110	64	60	65	67	73	75	74	73	0.17
Neck, pathologic	9	1	8	8	11	12	5	9	5	5	6	0.91
Intertrochanteric	113	117	142	107	129	107	106	124	116	86	101	0.10
Trochanteric, unspecified	6	11	7	6	8	13	4	9	9	13	12	0.26
Hip, unspecified	53	78	60	72	57	64	70	60	57	57	57	0.36

Hospital discharge rates per 100,000 persons, directly standardized to the age structure of the 2000 US civilian population, using the following age groups: 50–54, 55–59, 60–64, 65–69, 70–74, 75–79, 80–84, 85–89, and ≥90

NHDS National Hospital Discharge Survey

[a] *P* values for linear trend of the discharge rates over the 11 years, not adjusted for multiple comparisons

Appendix 2

Table 5 Incidence rates of fragility fractures, MarketScan 2002–2006

	Incidence rates (95% confidence interval) [a]					P^b
	2002	2003	2004	2005	2006	
Women						
Femur, overall	300 (296–312)	301 (298–312)	340 (337–348)	323 (320–331)	305 (301–315)	0.62
Subtrochanter and shaft combined	23 (22–27)	23 (22–26)	25 (25–28)	25 (24–27)	21 (20–24)	0.73
Transcervical	89 (86–96)	80 (78–86)	89 (88–94)	81 (79–85)	75(74–80)	0.20
Neck, pathologic	4 (4–6)	3 (3–5)	4 (4–5)	3 (3–4)	3 (3–4)	0.34
Intertrochanter	94 (92–101)	101(99–107)	114 (112–118)	111(110–116)	109 (107–115)	0.10
Trochanter, unspecified	8 (7–10)	7 (6–9)	8 (8–9)	9 (9–11)	8 (8–10)	0.15
Hip, unspecified	66 (64–72)	70 (68–76)	80 (79–85)	76 (75–80)	70 (68–75)	0.50
Men						
Femur, overall	181 (177–196)	197 (193–209)	201 (198–210)	200 (197–209)	177 (173–187)	0.87
Subtrochanter and shaft combined	14 (13–18)	17 (15–20)	14 (13–17)	13 (13–16)	13 (12–16)	0.29
Transcervical	50 (48–58)	52 (50–58)	51 (50–56)	48(47–53)	45 (43–51)	0.10
Neck, pathologic	1 (1–3)	2 (2–4)	1 (1–2)	1 (1–2)	1(1–2)	0.15
Intertrochanteric	63 (61–72)	63 (61–71)	73 (71–79)	72(70–78)	62 (60–69)	0.77
Trochanter, unspecified	7(6–10)	5(5–7)	6 (5–7)	6 (6–8)	5(5–7)	0.41
Hip, unspecified	41 (39–48)	51(49–58)	51 (50–56)	53 (52–58)	46 (44–51)	0.52

[a] Incidence rates per 100,000 person-years, directly standardized to the age and sex distribution of the 2000 US civilian population, using the following age groups: 50–54, 55–59, 60–64, 65–69, 70–74, 75–79, 80–84, 85–89, and ≥90

[b] *P* values for linear trend of the incidence rates over 5 years, not adjusted for multiple comparisons

Appendix 3:

Table 6 Fitted model parameters for Poisson rate parameters [a]

Fracture groups	Women		Men	
	Intercept	Slope	Intercept	Slope
Hip, excluding subtrochanteric				
Intertrochanteric	−17.37	0.15	−17.11	0.14
Transcervical	−16.12	0.13	−17.27	0.13
Hip, unspecified	−15.58	0.12	−15.82	0.12
Subtrochanteric	−17.40	0.12	−16.43	0.10
Trochanteric, unspecified	−18.27	0.12	−17.32	0.11
Neck, pathologic	−17.89	0.11	−17.75	0.09
Femoral shaft	−14.82	0.09	−13.21	0.06
Lower femur	−14.57	0.09	−13.61	0.06

Assuming that fracture incidence follows a Poisson distribution with a rate parameter λ, the fitted models for λ as a function of age may be written as $\ln(\lambda) = \text{intercept} + \text{slope} \times \text{age}$

References

1. Fisher AA, Davis MW, Rubenach SE, Le Couteur DG et al (2007) The site-specific epidemiology of hip fracture in the Australian Capital Territory with projections for the first half of the 21st century: implications for clinical management and health services planning. Australas J Ageing 26:45–51
2. Hinton RY, Lennox DW, Ebert FR, Jacobsen SJ et al (1995) Relative rates of fracture of the hip in the United States. Geographic, sex, and age variations. J Bone Joint Surg Am 77:695–702
3. Karagas MR, Lu-Yao GL, Barrett JA, Beach ML et al (1996) Heterogeneity of hip fracture: age, race, sex, and geographic patterns of femoral neck and trochanteric fractures among the US elderly. Am J Epidemiol 143:677–682
4. Levy AR, Mayo NE, Grimard G (1995) Rates of transcervical and pertrochanteric hip fractures in the province of Quebec, Canada, 1981–1992. Am J Epidemiol 142:428–436
5. Martinet O, Cordey J, Harder Y, Maier A et al (2000) The epidemiology of fractures of the distal femur. Injury 31(Suppl 3): C62–C63
6. Kwek EB, Goh SK, Koh JS, Png MA et al (2008) An emerging pattern of subtrochanteric stress fractures: a long-term complication of alendronate therapy? Injury 39:224–231
7. Salminen ST, Pihlajamäki HK, Avikainen VJ, Böstman OM (2000) Population based epidemiologic and morphologic study of femoral shaft fractures. Clin Orthop Relat Res 372:241–249
8. Moran CG, Gibson MJ, Cross AT (1990) Intramedullary locking nails for femoral shaft fractures in elderly patients. J Bone Joint Surg Br 72(1):19–22
9. Arneson TJ, Melton LJ 3rd, Lewallen DG, O'Fallon WM (1988) Epidemiology of diaphyseal and distal femoral fractures in Rochester, Minnesota, 1965–1984. Clin Orthop Relat Res 234:188–194
10. Bengnér U, Ekbom T, Johnell O, Nilsson BE (1990) Incidence of femoral and tibial shaft fractures. Epidemiology 1950–1983 in Malmö, Sweden. Acta Orthop Scand 61:251–254
11. Hedlund R, Lindgren U (1986) Epidemiology of diaphyseal femoral fracture. Acta Orthop Scand 57:423–427
12. Wong PC (1966) Fracture epidemiology in a mixed southeastern Asian community (Singapore). Clin Orthop Relat Res 45:55–61
13. Lenart BA, Lorich DG, Lane JM (2008) Atypical fractures of the femoral diaphysis in postmenopausal women taking alendronate. N Engl J Med 358:1304–1306
14. Neviaser AS, Lane JM, Lenart BA, Edobor-Osula F et al (2008) Low-energy femoral shaft fractures associated with alendronate use. J Orthop Trauma 22:346–350
15. Lee P, van der Wall H, Seibel MJ (2007) Looking beyond low bone mineral density: multiple insufficiency fractures in a woman with post-menopausal osteoporosis on alendronate therapy. J Endocrinol Invest 30:590–597
16. Odvina CV, Zerwekh JE, Rao DS, Maalouf N et al (2005) Severely suppressed bone turnover: a potential complication of alendronate therapy. J Clin Endocrinol Metab 90:1294–1301
17. National Center for Health Statistics (2008) National Hospital Discharge Survey datasets. ftp://ftp.cdc.gov/pub/Health_Statistics/NCHS/Datasets/NHDS/ Accessed 5 December 2008
18. Dobson AJ, Kuulasmaa K, Eberle E, Scherer J (1991) Confidence intervals for weighted sums of Poisson parameters. Stat Med 10:457–462
19. Gehlbach SH, Avrunin JS, Puleo E (2007) Trends in hospital care for hip fractures. Osteoporos Int 18:585–591
20. Melton LJ 3rd (1996) Epidemiology of hip fractures: implications of the exponential increase with age. Bone 18(3 Suppl):121S–125S
21. Levy AR, Mayo NE, Grimard G (1996) Re: "Heterogeneity of hip fracture: age, race, sex, and geographic patterns of femoral neck and trochanteric fractures among the US elderly". Am J Epidemiol 144:801–803
22. Pervez H, Parker MJ, Pryor GA, Lutchman L et al (2002) Classification of trochanteric fracture of the proximal femur: a study of the reliability of current systems. Injury 33:713–715
23. Boston DA (1982) Bilateral fractures of the femoral neck. Injury 14:207–210
24. Dretakis KE, Dretakis EK, Papakitsou EF, Psarakis S et al (1998) Possible predisposing factors for the second hip fracture. Calcif Tissue Int 62:366–369
25. Maffulli N, Dougall TW, Brown MT, Golden MH (1999) Nutritional differences in patients with proximal femoral fractures. Age Ageing 28(5):458–462
26. Mautalen CA, Vega EM, Einhorn TA (1996) Are the etiologies of cervical and trochanteric hip fractures different? Bone 18(3 Suppl):133S–137S
27. Ferris BD, Kennedy C, Bhamra M, Muirhead-Allwood W (1989) Morphology of the femur in proximal femoral fractures. J Bone Joint Surg Br 71:475–477
28. Abrahamsen B, Eiken P, Eastell R (2009) Subtrochanteric and diaphyseal femur fractures in patients treated with alendronate: a register-based National Cohort Study. J Bone Miner Res 24:1095–1102