Declining Rates of Osteoporosis Management Following Fragility Fractures in the U.S., 2000 Through 2009

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Background: Clinical practice recommendations state that patients with fragility fractures should be evaluated for osteoporosis and treated for the disease if it is present. The purpose of this study was to assess osteoporosis evaluation and treatment patterns for patients with fragility fractures and assess whether anti-osteoporosis pharmacotherapy initiated immediately following a fragility fracture is associated with improved adherence to the treatment protocol.

Methods: This retrospective cohort study involved data from a large commercially insured population seen in the period from 2001 through 2009. Patients were community-dwelling individuals aged fifty years or older who had a new low-energy fracture at the hip, vertebra, wrist, or humerus with no evidence of a fragility fracture, osteoporosis treatment, malignant disease, or Paget disease for twelve months preceding the fracture. Rates of diagnostic testing and pharmacotherapy for osteoporosis within twelve months post-fracture were evaluated. Patients treated with oral bisphosphonates were evaluated to determine whether twelve-month adherence to the treatment protocol differed between those who had initiated therapy sooner (at zero to ninety days) and those who initiated it later (at ninety-one to 365 days) following the fracture.

Results: The 88,571 women and 41,984 men had an average age of 72.3 years and 70.5 years, respectively. Nineteen percent (16,464) of the women and 10% (4014) of the men initiated osteoporosis pharmacotherapy, and 30% (26,481) of the women and 15% (6427) of the men underwent diagnostic testing and/or pharmacotherapy following fracture. Treatment rates were highest following vertebral fracture and lowest following wrist or humeral fracture. Treatment rates significantly decreased over time (from 2001 through 2009). The average twelve-month adherence (medication possession ratio) was 56% and 61% among women and men, respectively. Adherence was similar between patients who had initiated treatment sooner after the fracture and those who had initiated it later after the fracture.

Conclusions: Clinical guidelines for evaluation and treatment following fragility fracture were met for less than one-third of women and less than one-sixth of men. While primary fracture prevention remains the ideal, secondary prevention is critical and there is a need to reverse the downward trend in adherence to post-fracture guidelines.

Level of Evidence: Prognostic Level III. See Instructions for Authors for a complete description of levels of evidence.

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Fragility fractures are associated with prolonged disability and increased risk of death. Mortality risk increases not only following hip fracture, but also following other fragility fractures[1-3]. Furthermore, a history of any fragility fracture is among the strongest risk factors for subsequent fracture[4-7]. Despite the availability of several anti-osteoporosis medications that effectively reduce fracture risk, most patients with fragility fracture are not treated[8,9]. In addition, patients who use anti-osteoporosis

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TABLE I Baseline Characteristics of Study Participants

	Women				
	Total* (N = 88,571)	Hip Fracture (N = 24,061)	Vertebral Fracture (N = 22,276)	Wrist Fracture (N = 26,093)	Humeral Fracture (N = 16,141)
Mean age (SD) *(yr)*	72.3 (12.4)	79.3 (10.2)	73.1 (12.0)	66.9 (11.7)	69.7 (11.8)
Age group *(%)*					
50-54 yr	9.1	2.3	8.5	15.2	10.3
55-64 yr	23.9	9.4	20.6	36.1	30.1
65-74 yr	17.7	13.7	18.5	18.8	20.9
75-84 yr	30.6	40.3	33.9	21.1	27.0
≥85 yr	18.7	34.4	18.5	8.7	11.8
Charlson-Deyo comorbidity index *(%)*					
0	70.5	65.8	66.8	79.2	68.7
≥1	29.5	34.2	33.2	20.8	31.3
Median no. of concomitant medications (IQR)	7 (8)	7 (8)	8 (9)	6 (8)	7 (9)
Hospitalization during 12 mo preceding fracture *(%)*	21.8	27.6	27.8	13.1	18.6
DXA test during 12 mo preceding fracture *(%)*	9.6	6.0	13.0	10.3	9.3

*Total = hip, vertebral, wrist, or humeral.

medications exhibit suboptimal adherence with the therapy[10,11], which compromises treatment effectiveness[12,13].

Numerous efforts have been made to focus on improving post-fracture care. The 2004 U.S. Surgeon General's report indicated the need to recognize fracture as a sentinel event requiring action[14]. The Healthcare Effectiveness Data and Information Set (HEDIS), a set of measures designed to be used to evaluate the performance of health-care plans, defines quality of care for older women with a fracture as either obtaining a bone mineral density test or providing a prescription for an anti-osteoporosis medication within six months following the fracture[15]. Recent clinical guidelines emphasize both bone mineral density testing and treatment with anti-osteoporosis medication following fragility fracture[16-19]. Bone mineral density testing is recommended following any fragility fracture, and it is used to help guide treatment decisions for patients with a non-hip non-vertebral fragility fracture. Treatment is recommended following any hip or vertebral fracture. These guidelines also incorporate the recommendations of the Fracture Risk Assessment Tool (FRAX) developed by the World Health Organization (WHO)[20] and include fracture history as a key determinant of subsequent fracture risk. There has also been a call to action within the orthopaedic community to address post-fracture patient management through initiatives such as the Own the Bone[21] program and the establishment of multidisciplinary fracture liaison services in health-care systems[22].

Given the emphasis in the last decade on post-fracture care, we aimed to determine trends over a ten-year period in evaluation of osteoporosis and treatment with anti-osteoporosis pharmacotherapy following fragility fracture in a large population cohort. Additionally, we evaluated whether anti-osteoporosis pharmacotherapy initiated in the time period immediately following a fragility fracture was associated with improved adherence to treatment compared with adherence following later initiation of pharmacotherapy.

Materials and Methods

Study Design and Data Source

We conducted this retrospective cohort study using the MarketScan commercial health insurance database (Truven Health Analytics, Ann Arbor, Michigan). MarketScan represents individuals receiving health insurance coverage from large employers across the U.S. Individuals aged sixty-five years and older in this database have supplemental employer-sponsored insurance in addition to Medicare. Data from Medicare and supplemental insurance claims were available for these individuals.

Study Subjects

Patients included men and women fifty years of age or older who had experienced a new low-energy fracture at the hip, vertebra, distal parts of the radius or ulna (will be referred to as "wrist"), or humerus from January 1, 2001, through December 31, 2009. We selected these four anatomical sites because they represent the four most common locations of fragility fractures in older individuals in the U.S. and are the most strongly associated with increasing age[6]. We focused on incident fractures by identifying the first occurrence of such a fracture within the study period ("index" fracture) and excluding individuals with evidence of any other fragility fracture in the twelve months before the index fracture. We excluded individuals with evidence of multiple index fractures as these fractures would likely indicate high-energy trauma. The study focused on treatment initiation post-fracture; thus, we excluded patients with claims for anti-osteoporosis pharmacotherapy (oral or injectable bisphosphonates, teriparatide, calcitonin, or

TABLE I (*continued*)

Men				
Total* Fracture (N = 41,984)	Hip Fracture (N = 12,435)	Vertebral Fracture (N = 15,857)	Wrist Fracture (N = 8277)	Humeral Fracture (N = 5415)
70.5 (12.2)	76.6 (10.6)	69.8 (12.0)	64.3 (10.7)	68.2 (11.7)
11.5	3.6	12.5	20.4	13.2
26.5	13.5	27.7	39.9	32.5
18.8	17.6	19.1	19.1	19.7
29.1	40.8	28.4	15.6	25.0
14.2	24.4	12.4	5.1	9.7
64.6	58.7	64.1	75.5	62.9
35.4	41.3	35.9	24.5	37.1
7 (8)	7 (7)	7 (7)	5 (7)	6 (8)
25.4	30.4	28.2	14.4	22.4
2.8	1.3	5.2	1.3	1.3

raloxifene) within twelve months before the index fracture. Additionally, we excluded patients with a diagnosis of malignant or Paget disease within twelve months before the index fracture and those who were institutionalized at the time of index fracture. Finally, we required that patients had been continuously enrolled in the database for at least twelve months preceding and twelve months following their index fracture.

Measurement of Exposures and Outcomes

We identified fractures using algorithms based on identification of appropriate diagnosis and procedure codes in the claims data. The major outcomes of interest were (1) receipt of a central dual x-ray absorptiometry (DXA) test for bone mineral density; (2) treatment with any of the following anti-osteoporosis medications: oral alendronate, risedronate, or ibandronate or injectable ibandronate, zoledronic acid, raloxifene, teriparatide, or calcitonin (referred hereafter as "treatment"); and (3) adherence to treatment. We used standard drug and procedure codes to identify these outcomes. These codes, along with our fracture identification algorithms, are available upon request.

We measured patient characteristics, including burden of comorbidities, concomitant medications, and hospitalizations, during the twelve-month period before the index fracture. We also estimated the Charlson-Deyo comorbidity index[23].

We identified the patients who had initiated oral bisphosphonate treatment within twelve months post-fracture, and we measured their adherence to treatment by estimating the medication possession ratio, which provides an indication of refill compliance in claims databases. We calculated the twelve-month medication possession ratio by dividing the number of days of supply (over a twelve-month period) of any oral bisphosphonate by 365 days of follow-up. We limited this analysis to patients who had had twelve months of continuous enrollment in the database following therapy initiation. We restricted it to those treated with oral bisphosphonates since calculating the medication possession ratio is less meaningful for longer-acting medications such as injectable bisphosphonates. We measured the medication possession ratio as a continuous variable and as a binary variable (≤80% or >80%). The cut-point of 80% is typically used in osteoporosis studies as oral bisphosphonates have been shown to substantially lose effectiveness at adherence levels of <80%[12].

The patient data used in this analysis were de-identified in compliance with Health Insurance Portability and Accountability Act (HIPAA) regulations and, therefore, the study was exempt from institutional review board approval. The MarketScan databases are considered statistically de-identified under Section 164.514 (b)(1)(i-ii) of the HIPAA privacy rule.

Statistical Analysis

We assessed the mean (and standard deviation [SD]) and median (and interquartile range [IQR]) for continuous variables and the frequency distributions for categorical variables. We used the Pearson chi-square test to assess differences between categorical variables and the Cochran-Armitage test to assess significance of trends seen in categorical data.

We compared adherence to treatment (medication possession ratio) between subjects who had initiated therapy sooner (at zero to ninety days) and those who had initiated it later (at ninety-one to 365 days) following the index fracture. We repeated analyses using quartiles of time from fracture to therapy initiation to evaluate sooner and later treatment initiation.

Source of Funding

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Results

We identified 88,571 women and 41,984 men who had a study-defined fracture and met the study selection criteria. The mean age was 72.3 years for women and 70.5 years

TABLE II Percentages of Study Participants Who Initiated Treatment with Anti-Osteoporosis Pharmacotherapy or Underwent DXA Screening within Twelve Months Following Fracture Assessed by Fracture Type

	Women (%)				
	Total* (N = 88,571)	Hip Fracture (N = 24,061)	Vertebral Fracture (N = 22,276)	Wrist Fracture (N = 26,093)	Humeral Fracture (N = 16,141)
Treatment†	18.6	19.5	32.3	11.0	10.7
DXA screening†	19.0	13.7	24.6	20.6	16.8
Treatment and DXA screening	7.7	6.7	12.1	6.4	5.3
Treatment or DXA screening	29.9	26.5	44.8	25.2	22.1

*Total = hip, vertebral, wrist, or humeral. †The reported percentages of treatment and of DXA screening are independent of each other—i.e., the reported percentages in these rows refer to anti-osteoporosis treatment in the twelve months following fracture regardless of DXA screening or DXA screening in the twelve months following fracture regardless of anti-osteoporosis treatment. Thus, the patients represented in these rows are not mutually exclusive, and the values do not sum to the values in the ''Treatment or DXA screening'' row.

for men (Table I). Patients with a hip fracture tended to be older and those with a wrist fracture tended to be younger than patients with a vertebral or humeral fracture. Patients with a wrist fracture had a relatively lower burden of illness compared with the others. During the twelve-month period before the index fracture, 9.6% of the women and 2.8% of the men had undergone DXA testing.

During the twelve months following the fracture, 19.0% (16,864) of the women and 10.2% (4284) of the men underwent DXA testing, 18.6% (16,464) of the women and 9.6% (4014) of the men initiated treatment, and 29.9% (26,481) of the women and 15.3% (6427) of the men underwent DXA and/or treatment (Table II). Treatment rates were highest following vertebral fracture, intermediate following hip fracture, and lowest following wrist or humeral fracture ($p < 0.001$). Patients with a vertebral fracture initiated treatment sooner than other patients. In the group that initiated treatment within twelve months following fracture, the median times to treatment initiation were forty-five, eighty-eight, 110, and 112 days following vertebral, hip, wrist, and humeral fractures, respectively. DXA testing rates followed a similar trend across fracture sites for men, but the rates for women were higher following wrist or humeral fracture than they were following hip fracture (Table II).

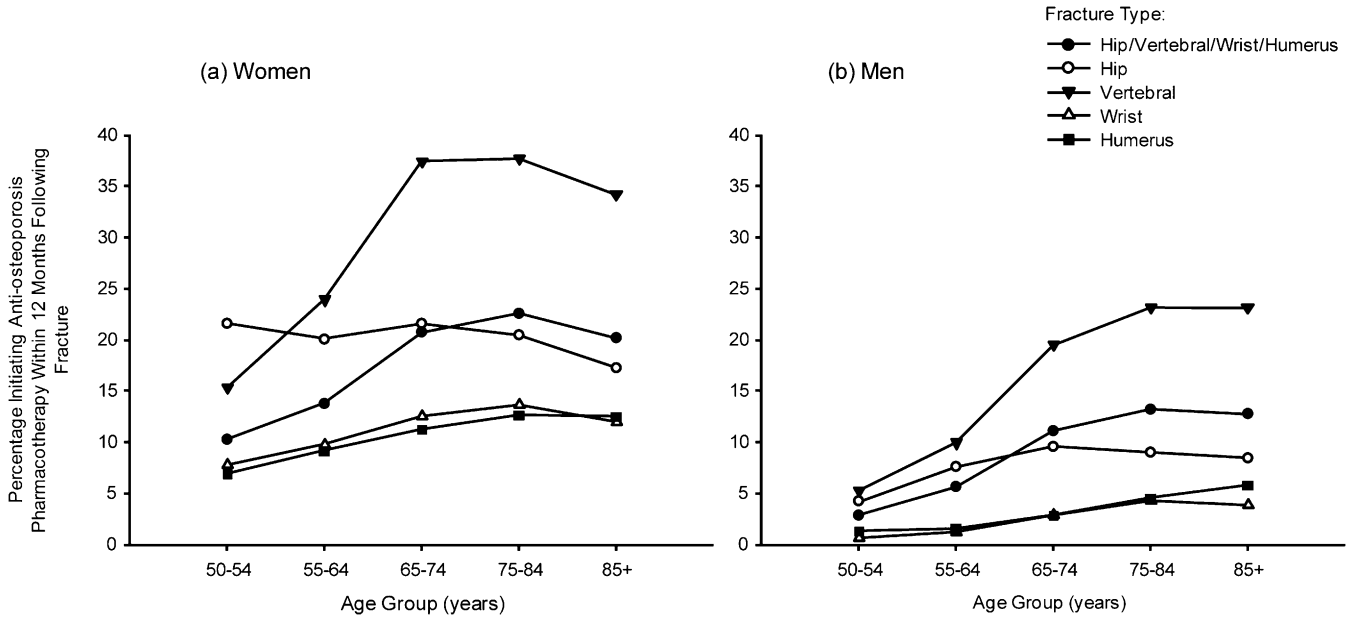

Fig. 1

Age-group-specific rates of treatment with anti-osteoporosis pharmacotherapy during the twelve months following fracture among women and men, by fracture site.

TABLE II (*continued*)

Men *(%)*				
Total* (N = 41,984)	Hip Fracture (N = 12,435)	Vertebral Fracture (N = 15,857)	Wrist Fracture (N = 8277)	Humeral Fracture (N = 5415)
9.6	8.6	16.6	2.0	2.9
10.2	8.1	16.7	4.3	4.8
4.5	3.7	7.7	1.3	1.6
15.3	13.0	25.6	5.0	6.1

Regardless of DXA testing, post-fracture treatment rates increased significantly with increasing age from fifty to eighty-four years ($p < 0.001$, Fig. 1). This pattern was observed among both men and women and was consistent across fracture sites; it differed only among women with a hip fracture, in whom treatment rates were consistently 20% to 22% across these age groups. Treatment rates for women declined in the "oldest old" age group of eighty-five years or more for all fracture sites except the humerus.

Overall, treatment rates decreased significantly over time, decreasing steadily from 23.8% during 2001-2002 to 15.9% during 2007-2009 ($p < 0.001$) among women and from 10.6% during 2001-2002 to 8.5% during 2007-2009 ($p < 0.001$) among men (Fig. 2). This trend was significant for women of all age groups and for men less than sixty-five years old (data not shown). When fracture sites were assessed individually, this trend was significant for all four fracture sites in women. In men, treatment rates tended to decrease over time, but this trend was inconsistent across fracture sites. Treatment rates following vertebral and humeral fractures in men showed a significant decreasing trend over time, from 21.2% and 4.0%, respectively, during 2001-2002 to 13.7% and 2.2%, respectively, during 2007-2009. Following hip and wrist fractures, the decreasing rates of treatment were either not consistent throughout the time period or not significant.

Adherence to Therapy Following Fracture

Oral bisphosphonates were the most common therapy (75.8%), followed by calcitonin (14.6%), teriparatide (4.0%), raloxifene (3.7%), and injectable bisphosphonates (2.0%). Among patients treated with oral bisphosphonates, the mean and median twelve-month medication possession ratios were 56.1% and 62.6%, respectively, for women and 61.4% and 73.8%, respectively, for men. A high twelve-month medication possession ratio (>80%) was found for 36.7% of women and 44.6% of men. There was no meaningful difference in the medication possession ratio

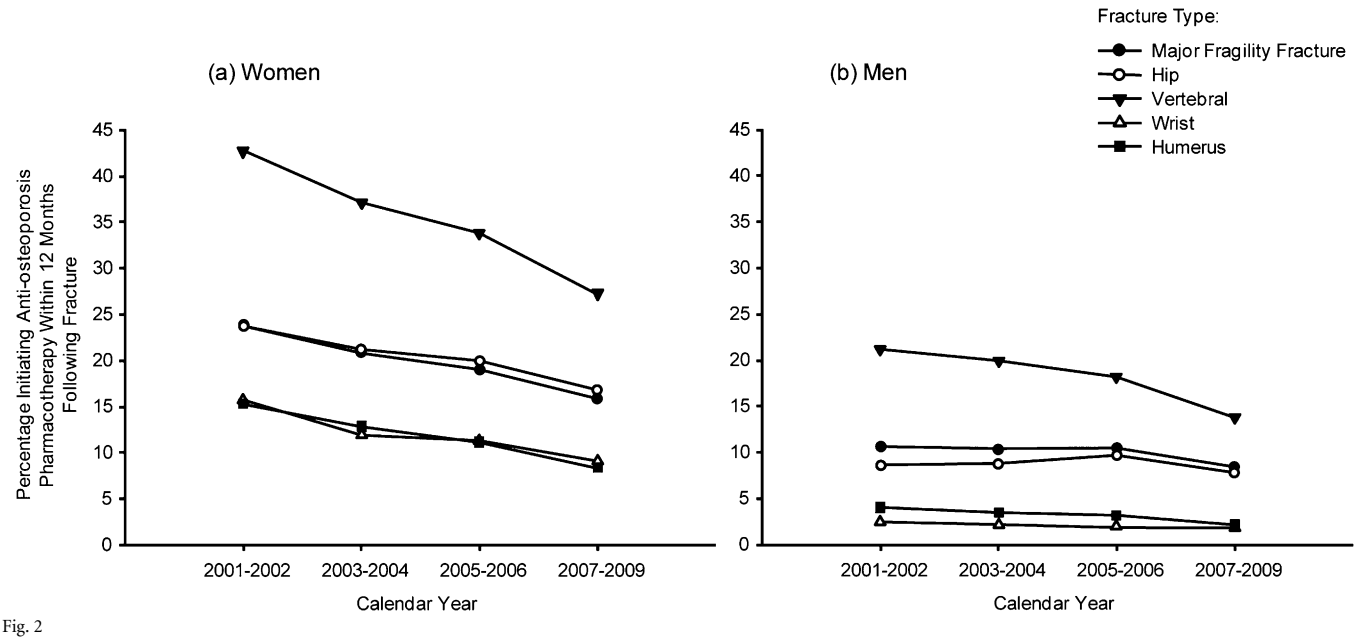

Fig. 2

Time trends in rates of treatment with anti-osteoporosis pharmacotherapy during the twelve months following fracture among women and men, by fracture site.

TABLE III Adherence to Oral Bisphosphonate Therapy During the Twelve Months Following Fracture Among Patients Initiating Treatment Sooner (Zero to Ninety Days) Versus Later (Ninety-one to 365 Days) Following Fracture

	Women (%)				Men (%)			
	0-365 Days (N = 11,055)	0-90 Days (N = 6214)	91-365 Days (N = 4841)	P Value*	0-365 Days (N = 2785)	0-90 Days (N = 1722)	91-365 Days (N = 1063)	P Value*
Median 12-mo medication possession ratio (IQR)†	62.6 (65.5)	60.5 (65.6)	65.3 (65.3)		73.8 (65.6)	74.3 (66.9)	71.3 (63.7)	
Patients with 12-mo medication possession ratio >80%	36.7	35.9	37.8	0.043	44.6	45.7	42.9	0.148

*Difference in medication possession ratio between patients initiating oral bisphosphonate treatment at zero to ninety days and those initiating it at ninety-one to 365 days following fracture. †As the medication possession ratio is not normally distributed, medians and interquartile ranges are provided. The mean medication possession ratio (standard deviation) was 56.1 (33.1) among women and 61.4 (33.3) among men.

between patients who had initiated treatment within zero to ninety days following fracture compared with those who had initiated it between ninety-one and 365 days following fracture (Table III). Results were similar when we evaluated the medication possession ratio by the specific fracture site and by using quartiles of time to therapy initiation to evaluate sooner and later treatment (data not shown).

Discussion

In this large population-based study of commercially insured individuals, the majority of patients with a new low-energy fracture at the hip, vertebra, wrist, or humerus did not undergo evaluation for osteoporosis or treatment with anti-osteoporosis pharmacotherapy within twelve months following the fracture, and the rates of treatment declined over the last decade. Approximately one-fifth of women and one-tenth of men underwent treatment in the year following the fracture. The treatment rates were even lower for patients with a wrist or humeral fracture. Approximately 20% of women and <5% of men with a wrist or humeral fracture underwent DXA evaluation in the year following the fracture. Thus, current clinical guidelines for evaluation and treatment following a fragility fracture were met for only a minority of patients in this study. To our knowledge, recently published data on osteoporosis diagnosis and treatment rates in this high-risk group of fracture patients in the U.S. are very limited. Given the aging of the population and the increased emphasis on bone health, particularly following fragility fracture, our study contributes important current population-level information in the context of trends over the last decade.

We also observed trends in specific subgroups. Post-fracture treatment rates were highest following vertebral fracture and lowest following wrist or humeral fracture. Patients with vertebral fracture also initiated therapy sooner than others. While the reasons for these trends are unknown, it may be that orthopaedists are less likely to address osteoporosis than are primary care practitioners, who would be more likely to manage vertebral fractures[24]. These differences may also reflect the perceived association of fractures with osteoporosis. Wrist and humeral fractures tend to be less commonly perceived to be osteoporotic despite epidemiologic evidence to the contrary[7,25] and despite the emphasis in clinical guidelines to evaluate and treat *any* fragility fracture[16-19]. The need for pharmacotherapy for these patients should not be overlooked, particularly as having experienced one fracture places them at increased risk of future fractures, including more debilitating ones such as those at the hip[4,5,7]. The low rates of DXA testing in this group are also troubling because DXA is important in guiding treatment of patients with a non-hip, non-vertebral fracture. Our observation of declining treatment rates in the "oldest old" group of women (eighty-five years of age or older) is a cause of concern given that the risk of fragility fracture increases substantially with increasing age[26].

Our finding that approximately 20% of women sixty-five years or older initiated treatment following fracture is similar to the 20.7% rate for female Medicare patients cited in the State of Health Care Quality 2011 Report[15]. Similarly, U.S. studies using data from the 1990s and early 2000s showed that <5% of female patients who sustained a fracture underwent DXA testing and 20% to 45% started or initiated osteoporosis treatment following the fracture[27-30]. A recent multinational study demonstrated that 17% of 1075 postmenopausal women initiated treatment following an incident fracture[31]. A recent study of men revealed treatment rates of 7% to 9% following any fracture and 7% following hip fracture[32], with older studies showing lower rates[33]. Consistent with our findings, previous investigators observed higher treatment rates among women than among men[30,33] and among those with a vertebral fracture than among those with another type of fracture[31,33]. Similar to our study, systematic reviews of adherence to bisphosphonate therapy have shown that the average twelve-month medication possession ratio is typically 60% to 70%, and ≥43% of patients achieve a "high" twelve-month

adherence of >80%[10,11,13]. One Belgian study showed a mean twelve-month medication possession ratio of 67% for women who had sustained a hip fracture[34]. We found that the twelve-month adherence was similar between patients who had initiated therapy sooner and those who had initiated it later following the fracture event. Delaying treatment for a few months, which a clinician may do to delay treatment until fracture-healing has occurred, does not appear to adversely affect adherence rates.

Our use of administrative claims data provided several strengths, including access to a large, real-world population and recent treatment data, which allowed us to examine trends over the last decade. A key limitation of administrative data is that claims lack the detail of a medical record. To address this, we used algorithms for identifying fragility fractures that were similar to those previously published for claims data[35], and we excluded fractures associated with trauma codes. Administrative claims data are frequently used to estimate medication adherence, as they can be used with large study samples without the biases of self-report. Using filled prescription claims as a proxy for medication possession results in reliable estimates of adherence[36], but we are aware that refilling prescriptions may not correlate perfectly with actual medication use and it does not capture medication samples. We were also not able to make inferences about physicians initiating DXA testing or treatment as the database is limited with regard to reliably linking procedures and prescriptions to the provider. Finally, our study was conducted in a population covered by Medicare supplemental or commercial insurance plans, and as such our results may not be generalizable to those insured by closed systems or to an uninsured population. However, this large database represents a broad spectrum of the U.S. insured population.

The medical community is increasingly recognizing the urgent need for fracture prevention among our elderly population. While primary fracture prevention remains the ideal, secondary prevention is critical. As the "oldest old" are the fastest growing segment of the U.S. population, there is a genuine need to reverse the current downward trend in adherence to post-fracture guidelines. ■

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References

1. Bliuc D, Nguyen ND, Milch VE, Nguyen TV, Eisman JA, Center JR. Mortality risk associated with low-trauma osteoporotic fracture and subsequent fracture in men and women. JAMA. 2009 Feb 4;301(5):513-21.

2. Colón-Emeric C, Kuchibhatla M, Pieper C, Hawkes W, Fredman L, Magaziner J, Zimmerman S, Lyles KW. The contribution of hip fracture to risk of subsequent fractures: data from two longitudinal studies. Osteoporos Int. 2003 Nov;14(11):879-83. Epub 2003 Oct 03.

3. Teng GG, Curtis JR, Saag KG. Mortality and osteoporotic fractures: is the link causal, and is it modifiable? Clin Exp Rheumatol. 2008 Sep-Oct;26(5)(Suppl 51):S125-37.

4. Center JR, Bliuc D, Nguyen TV, Eisman JA. Risk of subsequent fracture after low-trauma fracture in men and women. JAMA. 2007 Jan 24;297(4):387-94.

5. Klotzbuecher CM, Ross PD, Landsman PB, Abbott TA 3rd, Berger M. Patients with prior fractures have an increased risk of future fractures: a summary of the literature and statistical synthesis. J Bone Miner Res. 2000 Apr;15(4):721-39.

6. Taylor AJ, Gary LC, Arora T, Becker DJ, Curtis JR, Kilgore ML, Morrisey MA, Saag KG, Matthews R, Yun H, Smith W, Delzell E. Clinical and demographic factors associated with fractures among older Americans. Osteoporos Int. 2011 Apr;22(4):1263-74. Epub 2010 Jun 18.

7. Warriner AH, Patkar NM, Yun H, Delzell E. Minor, major, low-trauma, and high-trauma fractures: what are the subsequent fracture risks and how do they vary? Curr Osteoporos Rep. 2011 Sep;9(3):122-8.

8. Elliot-Gibson V, Bogoch ER, Jamal SA, Beaton DE. Practice patterns in the diagnosis and treatment of osteoporosis after a fragility fracture: a systematic review. Osteoporos Int. 2004 Oct;15(10):767-78. Epub 2004 Jul 16.

9. Teng GG, Warriner A, Curtis JR, Saag KG. Improving quality of care in osteoporosis: opportunities and challenges. Curr Rheumatol Rep. 2008 Apr;10(2):123-30.

10. Cramer JA, Gold DT, Silverman SL, Lewiecki EM. A systematic review of persistence and compliance with bisphosphonates for osteoporosis. Osteoporos Int. 2007 Aug;18(8):1023-31. Epub 2007 Feb 17.

11. Kothawala P, Badamgarav E, Ryu S, Miller RM, Halbert RJ. Systematic review and meta-analysis of real-world adherence to drug therapy for osteoporosis. Mayo Clin Proc. 2007 Dec;82(12):1493-501.

12. Siris ES, Harris ST, Rosen CJ, Barr CE, Arvesen JN, Abbott TA, Silverman S. Adherence to bisphosphonate therapy and fracture rates in osteoporotic women: relationship to vertebral and nonvertebral fractures from 2 US claims databases. Mayo Clin Proc. 2006 Aug;81(8):1013-22.

13. Siris ES, Selby PL, Saag KG, Borgström F, Herings RM, Silverman SL. Impact of osteoporosis treatment adherence on fracture rates in North America and Europe. Am J Med. 2009 Feb;122(2)(Suppl):S3-13.

14. U.S. Department of Health and Human Services, Office of the Surgeon General. Bone health and osteoporosis: A report of the surgeon general. 2004. http://www.surgeongeneral.gov/library/bonehealth/content.html. Accessed 2012 May 27.

15. National Committee for Quality Assurance. The state of health care quality 2011. Continuous improvement and the expansion of quality measurement. 2011. http://www.ncqa.org/LinkClick.aspx?fileticket=J8kEuhuPqxk%3d&tabid=836. Accessed 2012 May 27.

16. National Osteoporosis Foundation. Clinician's guide to prevention and treatment of osteoporosis. 2013. http://nof.org/files/nof/public/content/resource/913/files/580.pdf. Accessed 2013 Jul 19.

17. The International Society for Clinical Densitometry. 2007 Official positions of the International Society for Clinical Densitometry. 2007. http://www.iscd.org/wp-content/themes/iscd/pdfs/official-positions/ISCD2007OfficialPositions-Adult.pdf. Accessed 2013 July 19.

18. Watts NB, Bilezikian JP, Camacho PM, Greenspan SL, Harris ST, Hodgson SF, Kleerekoper M, Luckey MM, McClung MR, Pollack RP, Petak SM; 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 Nov-Dec;16(Suppl 3):1-37.

19. Management of osteoporosis in postmenopausal women: 2010 position statement of The North American Menopause Society. Menopause. 2010 Jan-Feb;17(1):25-54; quiz 55-6.

20. FRAX WHO fracture risk assessment tool. http://www.shef.ac.uk/FRAX/. Accessed 2013 Sep 11.

21. 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 Jan;90(1):163-73.

22. Dell R. Fracture prevention in Kaiser Permanente Southern California. Osteoporos Int. 2011 Aug;22(Suppl 3):457-60. Epub 2011 Aug 17.

23. Deyo RA, Cherkin DC, Ciol MA. Adapting a clinical comorbidity index for use with ICD-9-CM administrative databases. J Clin Epidemiol. 1992 Jun;45(6):613-9.

24. Simonelli C, Killeen K, Mehle S, Swanson L. Barriers to osteoporosis identification and treatment among primary care physicians and orthopedic surgeons. Mayo Clin Proc. 2002 Apr;77(4):334-8.

25. Warriner AH, Patkar NM, Curtis JR, Delzell E, Gary L, Kilgore M, Saag K. Which fractures are most attributable to osteoporosis? J Clin Epidemiol. 2011 Jan;64(1):46-53.

26. Ettinger B, Black DM, Dawson-Hughes B, Pressman AR, Melton L J 3rd. Updated fracture incidence rates for the US version of FRAX. Osteoporos Int. 2010 Jan;21(1):25-33. Epub 2009 Aug 25.

27. 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 Dec;85(12):2294-302.

28. Freedman KB, Kaplan FS, Bilker WB, Strom BL, Lowe RA. Treatment of osteoporosis: are physicians missing an opportunity? J Bone Joint Surg Am. 2000 Aug;82(8):1063-70.

29. Solomon DH, Finkelstein JS, Katz JN, Mogun H, Avorn J. Underuse of osteoporosis medications in elderly patients with fractures. Am J Med. 2003 Oct 1;115(5):398-400.

30. Solomon DH, Morris C, Cheng H, Cabral D, Katz JN, Finkelstein JS, Avorn J. Medication use patterns for osteoporosis: an assessment of guidelines, treatment rates, and quality improvement interventions. Mayo Clin Proc. 2005 Feb;80(2):194-202.

31. Greenspan SL, Wyman A, Hooven FH, Adami S, Gehlbach S, Anderson FA Jr, Boone S, Lacroix AZ, Lindsay R, Netelenbos JC, Pfeilschifter J, Silverman S, Siris ES, Watts NB. Predictors of treatment with osteoporosis medications after recent fragility fractures in a multinational cohort of postmenopausal women. J Am Geriatr Soc. 2012 Mar;60(3):455-61. Epub 2012 Feb 08.

32. Shepherd AJ, Cass AR, Ray LA, Tan A, Wilkinson GS. Treatment for older men with fractures. Osteoporos Int. 2012 Mar;23(3):1041-51. Epub 2011 Aug 03.

33. 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 Oct;163(18):2165-72.

34. Rabenda V, Vanoverloop J, Fabri V, Mertens R, Sumkay F, Vannecke C, Deswaef A, Verpooten GA, Reginster JY. Low incidence of anti-osteoporosis treatment after hip fracture. J Bone Joint Surg Am. 2008 Oct;90(10):2142-8.

35. Curtis JR, Mudano AS, Solomon DH, Xi J, Melton ME, Saag KG. Identification and validation of vertebral compression fractures using administrative claims data. Med Care. 2009 Jan;47(1):69-72.

36. Steiner JF, Koepsell TD, Fihn SD, Inui TS. A general method of compliance assessment using centralized pharmacy records. Description and validation. Med Care. 1988 Aug;26(8):814-23.