

Trends in Drug Prescribing for Osteoporosis After Hip Fracture, 1995-2004

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ABSTRACT. *Objective.* To examine trends in osteoporosis drug prescribing after hip fracture from 1995 to 2004.

Methods. We conducted a population-based study of enrollees in the Pennsylvania Pharmaceutical Assistance Contract for the Elderly. Hip fractures were identified using Medicare hospital claims between January 1, 1995, and June 30, 2004. Osteoporosis treatment comprised oral bisphosphonates, calcitonin, hormone therapy, raloxifene, and/or teriparatide. Kaplan-Meier methods were used to estimate the probability of treatment within 6 months of fracture, censoring patients on their date of death or 6 months postfracture.

Results. Treatment within 6 months after hip fracture improved from 7% in 1995 to 31% in 2002, and then remained stable through 2004. Similar patterns were observed among new users, with treatment increasing from 4% in 1995 to 17% in 2002, with no subsequent increase through 2004. Bisphosphonates led other treatments in the frequency of prescribing, except during 1997-99, when calcitonin was the most common. Among women, hormone therapy prescribing decreased from 22% of those treated in 1995 to 4% in 2004, and raloxifene prescribing remained relatively constant (4%-10%) since its introduction (p for trend = 0.15). Of patients treated before and after hip fracture, 18% changed therapy postfracture. Significantly more patients changed therapy following fracture if a different physician prescribed treatment (26%) compared to those treated by the same physician pre- and postfracture (13%; $p < 0.0001$).

Conclusion. Prescribing practices changed substantially over the 10 years of study. The proportion of hip fracture patients treated with osteoporosis drugs has increased, but remains low, with fewer than one-third receiving pharmacotherapy. (First Release Dec 1 2007; J Rheumatol 2008;35:319-26)

Key Indexing Terms:

HIP FRACTURES

OSTEOPOROSIS

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Significant advances in the treatment of osteoporosis have occurred since 1995 with the availability of oral pharmaceutical treatments other than hormone therapy (HT). Prior to 1995, HT (among women) and calcitonin injections were the only approved treatments for osteoporosis in the United States. However, etidronate (approved for Paget's disease) was also prescribed off-label¹. In 1995, alendronate and nasal calcitonin received approval for osteoporosis treatment in the United States. Raloxifene (1997), risedronate (2000), and

teriparatide (2002) followed, providing clinicians and their patients greater choice with respect to osteoporosis management. Efficacy of these treatments in reducing fracture risk is best evident among those with established osteoporosis²⁻⁴. Despite effective pharmacotherapy, postfracture treatment remains suboptimal⁵⁻⁷. It is well established that postfracture treatment is poor, with fewer than half receiving pharmacotherapy. However, little information is available regarding treatment patterns postfracture, particularly with respect to

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calcitonin, raloxifene, teriparatide, or combination therapy, or how postfracture treatment relates to prefracture prescribing. To date, evidence supports only the use of alendronate, risendronate, teriparatide, and HT to prevent hip fractures^{4,8,9}. Although data suggest that combination therapy provides modest increases in bone mineral density (BMD) compared to monotherapy, there is no evidence showing that combination therapy is superior to monotherapy for fracture prevention^{2,4}. Guidelines also provide no recommendations for managing future fracture risk among those who fracture on therapy^{1,10}.

Prescribing trends can be used to examine the uptake of new evidence and treatment preferences over time. We completed a population-based study of hip fracture patients to examine osteoporosis drug prescribing from 1995 to 2004. The specific study objectives were to determine the proportion of hip fractures treated with osteoporosis drugs, describe prescribing patterns, and examine changes in therapy postfracture among those previously treated.

MATERIALS AND METHODS

Study cohort. The study population was identified from Medicare claims for enrollees in the Pennsylvania Pharmaceutical Assistance Contract for the Elderly (PACE). This state-run program provides drug coverage without restriction for residents aged 65 years or more with annual household income too high for Medicaid, yet below \$20,000. Our cohort consisted of PACE enrollees who had a hip fracture (hospital discharge diagnosis of ICD-9-CM 820.xx or 733.14) between January 1, 1995, and June 30, 2004. To ensure complete plan coverage, study eligibility was limited to patients with one or more claims in both Medicare and PACE in each of the two 6-month intervals preceding the hip fracture, and one or more prescriptions filled through PACE in the 6 months following hip fracture. Patients with a Medicare claim for Paget's disease (ICD-9-CM 731.0) were excluded.

Osteoporosis treatment. Osteoporosis treatment comprised oral bisphosphonate (alendronate, etidronate, risedronate), calcitonin, HT, raloxifene, or teriparatide within 6 months after hip fracture. The generic name, dose, strength, and prescriber (medical license number) were identified for each drug using PACE pharmacy claims. It is estimated that the medical license number in PACE correctly identifies the prescribing physician in 96% of cases¹¹. We also identified physician specialty by linking prescriber license number to the American Medical Association Masterfile¹². Patients were categorized according to the first osteoporosis drug(s) dispensed postfracture. Treatment was classified as combination therapy if 2 or more osteoporosis drugs were dispensed on the same day. Similarly, osteoporosis treatment prior to hip fracture was identified by drugs dispensed within 6 months before the fracture, and was defined by the most recent osteoporosis medication(s) dispensed before hip fracture.

The Partners HealthCare Institutional Review Board approved this project. Data Use Agreements are in place from the Centers for Medicare and Medicaid Services and PACE.

Statistical analysis. We used the Kaplan-Meier method to estimate the probability of treatment within 6 months of fracture and 95% confidence intervals (CI), censoring patients on their date of death or 6 months postfracture. The probability of treatment was examined by year of fracture, sex, and drug class. We also examined treatment trends over time among new users (treatment-naïve), defined as those with no prescriptions filled for osteoporosis medications within 6 months prior to their hip fracture. Postfracture treatment by drug class and prescriber specialty were summarized overall and among the subgroup of new users. Among those with prior osteoporosis treatment, we examined change in therapy postfracture by year of fracture, drug class, and whether or not the same physician prescribed the drug(s) pre- and post-

fracture. The Pearson chi-square statistic or Fisher's exact test was used to compare proportions, and the Mantel-Haenszel chi-square statistic to test trends over time. Analyses were completed using SAS 9.1 (SAS, Cary, NC, USA).

RESULTS

Of 20,893 hip fractures identified, 25% were excluded (5070 with no prescriptions for any indication within 6 months postfracture, and 138 with Paget's disease). The remaining 15,685 hip fracture patients were studied. Ninety percent were female and 98% were Caucasian. The mean age of the cohort was 83.6 years (SD 6.6), and their mean income was \$10,265 (SD \$3,491).

Proportion treated. Over the 10-year study period, 21% (95% CI 20.8–22.1) of patients were treated within 6 months of their hip fracture. Treatment increased from 7% (95% CI 5.6–7.7) in 1995 to 31% (95% CI 28.6–33.6) in 2002, and then remained stable through 2004 (30%, 95% CI 26.7–33.8). This trend was similar for men and women, but fewer men were treated (Figure 1A). Similar trends were observed in the treatment-naïve subgroup (Figure 1B). Among the subgroup of those with no history of osteoporosis treatment within 6 months prior to hip fracture, treatment increased from 4% (95% CI 3.1–4.7) in 1995 to 17% (95% CI 14.5–18.9) in 2002, with no subsequent increase through 2004.

Physician specialty was identified for 94% (n = 3038) of the 3231 treated patients. Over time, the proportion of hip fracture patients treated by endocrinologists/rheumatologists, orthopedic surgeons, and obstetricians/gynecologists each declined (p for trend < 0.05; Table 1). In contrast, we observed no change over time in the proportion of patients treated by geriatricians (p for trend = 0.6 overall, p for trend = 0.4 treatment-naïve subgroup), and an increase in the proportion of patients treated by other physicians (p for trend < 0.001). Geriatricians treated the majority of their patients with calcitonin, and specialists in obstetrics/gynecology treated the majority of their patients with HT (Table 2). Other physicians preferred bisphosphonates.

Prescribing patterns. Over the decade studied, bisphosphonates led other treatments in the frequency of prescribing, except during 1997–99, when calcitonin was the most common (Figure 2). Etidronate comprised one-third of bisphosphonate prescribing in 1995. Since 1995, less than 0.1% of bisphosphonate prescribing was for etidronate. Among bisphosphonate users, weekly dosing increased from 26% in 2000 to 100% in 2004. We observed no change in use of combination therapy over time, ranging from 1% to 3% (p for trend = 0.33). Treatment with HT decreased from 22% of female hip fracture patients in 1995 to fewer than 4% in 2002, with no subsequent change through 2004. Although raloxifene prescribing doubled from 4% of female patients treated in 1998 to 8% in 1999, we observed little change in its use between 1999 and 2004, ranging from 7% to 10% (p for trend from 1998 to 2004 = 0.15). Similar osteoporosis drug pre-

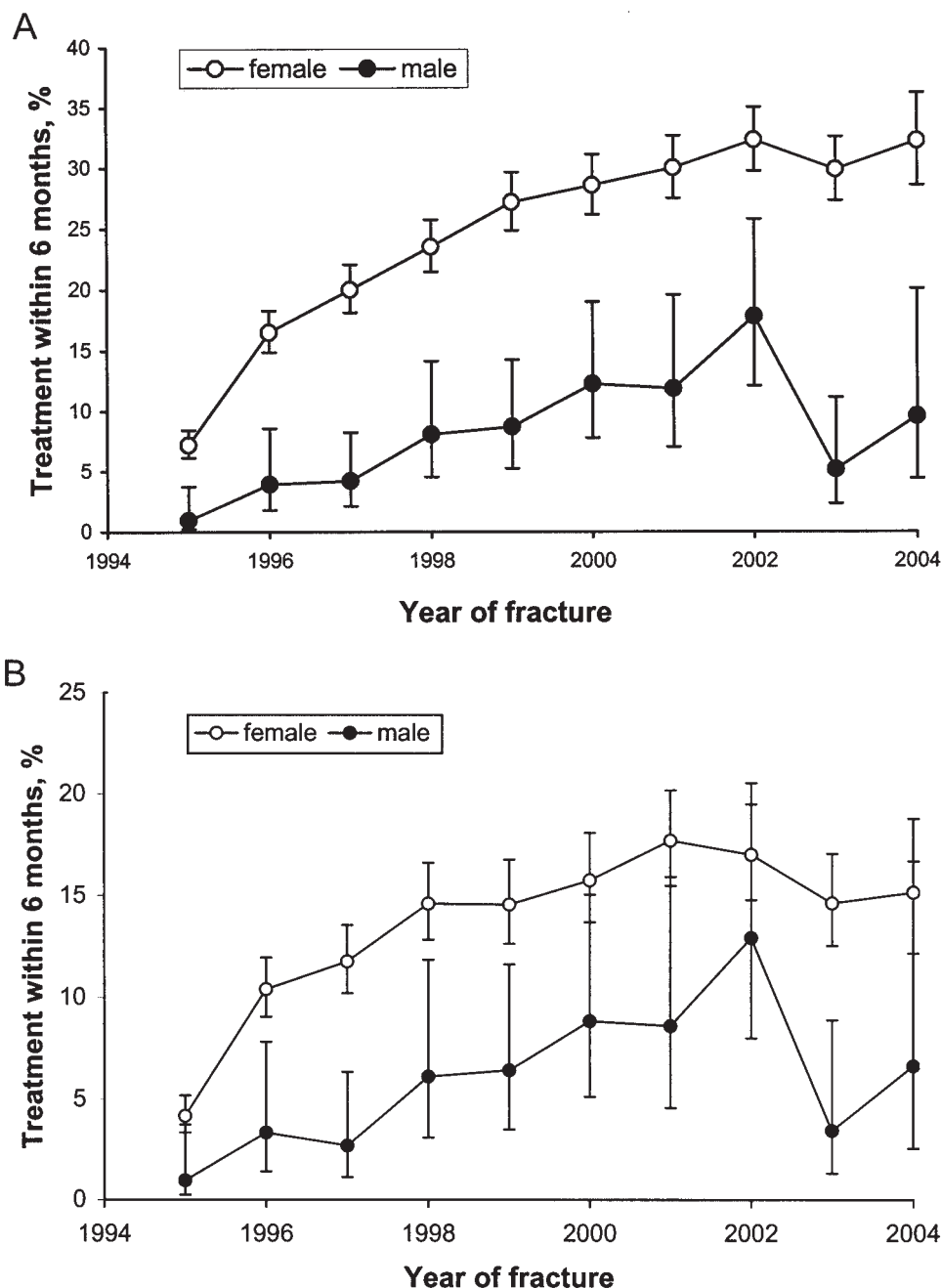


Figure 1. Proportion of hip fracture patients treated (oral bisphosphonate, calcitonin, hormone therapy, raloxifene, and/or teriparatide) within 6 months, by sex and year, 1995-2004. A. overall; B. treatment-naïve subgroup. Estimates calculated using Kaplan-Meier methods, censoring patients on their date of death or 6 months postfracture. Error bars indicate 95% confidence intervals.

scribing patterns were observed when restricted to new users (data not shown).

Treatment changes postfracture. Half the patients treated postfracture had also been treated before their fracture ($n = 1645$). Among the 1606 patients treated with a single agent prior to their hip fracture, 18% changed therapy postfracture. Both sexes switched in similar proportions ($p = 0.34$), and we found

no trend over time (p for trend = 0.24). However, significantly more patients changed therapy if a different physician prescribed treatment (26%) compared to those treated by the same physician pre- and postfracture (13%; $p < 0.0001$). There was no difference in the proportion changing therapy by drug class among those treated by the same physician pre- and post-hip fracture ($p = 0.39$; Figure 3).

Table 1. Prescriber specialty* among hip fracture patients treated within 6 months, 1995–2004. Data are the proportion treated each year, by the specialty of the prescribing physician (columns sum to 100).

	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004
Overall, n = 3038										
Endocrinology/rheumatology	14.9	10.9	8.7	5.3	4.7	6.1	5.2	5.6	5.2	3.5
Orthopedic surgery	5.2	5.6	5.8	7.3	4.4	3.3	3.2	2.4	2.5	0.6
Obstetrics/gynecology	6.7	1.3	1.9	2.2	2.5	1.1	0.3	0.8	1.2	1.2
Geriatrics	7.5	9.2	9.0	7.3	9.9	11.1	7.6	10.2	8.3	9.9
Other (including family/general practice)	65.7	72.9	74.7	77.8	78.7	78.3	83.7	81.0	82.7	84.8
Treatment-naïve, n = 1489										
Endocrinology/rheumatology	12.0	9.5	6.6	1.5	4.2	2.9	4.7	6.1	3.9	6.2
Orthopedic surgery	8.0	7.8	8.4	10.0	7.1	3.5	3.5	3.1	3.1	0.0
Obstetrics/gynecology	4.0	0.6	1.2	2.0	0.0	1.2	0.0	0.0	0.8	0.0
Geriatrics	5.3	9.5	8.4	9.0	11.3	10.5	5.2	10.4	9.3	13.8
Other (including family/general practice)	70.7	72.6	75.3	77.5	77.4	82.0	86.6	80.4	82.9	80.0

* Prescriber specialty available for 94% of those treated by linking medical license number to the American Medical Association Masterfile^{11,12}.

Table 2. Drug class preference by prescriber specialty*. Data are the proportion treated by specialty of the prescribing physician (rows sum to 100).

	Bisphosphonate	Calcitonin	Hormone Therapy	Raloxifene	Teriparatide	Combination
Overall, n = 3038						
Endocrinology/rheumatology	59.5	32.5	3.5	3.0	1.0	0.5
Orthopedic surgery	68.0	27.2	3.2	0.8	0.0	0.8
Obstetrics/gynecology	22.4	8.2	63.3	4.1	0.0	2.0
Geriatrics	41.3	44.6	5.8	5.1	0.0	3.3
Other (including family/general practice)	50.1	34.3	7.8	5.6	0.1	2.1
Treatment-naïve, n = 1489						
Endocrinology/rheumatology	63.3	32.9	1.3	2.5	0.0	0.0
Orthopedic surgery	67.8	29.9	1.1	0.0	0.0	1.1
Obstetrics/gynecology	15.4	23.1	46.2	7.7	0.0	7.7
Geriatrics	42.0	49.3	2.2	3.6	0.7	2.2
Other (including family/general practice)	52.4	39.6	2.7	3.8	0.0	1.5

* Prescriber specialty available for 94% of those treated by linking medical license number to the American Medical Association Masterfile^{11,12}.

DISCUSSION

Prescribing practices changed substantially over the 10 years of study. We found that the proportion of patients treated with osteoporosis drugs within 6 months of their hip fracture increased 4-fold from 1995 to 2004, yet remained low with fewer than one-third receiving pharmacotherapy. We document an increase in bisphosphonate prescribing, a decline in calcitonin and HT prescribing, and little change in patterns of raloxifene prescribing or the proportion changing therapy postfracture. Bisphosphonates led other treatments in the frequency of prescribing, except during 1997–99, when calcitonin was the most common. There are several possible explanations for this observation. Early postmarketing surveillance of alendronate raised concerns about its gastrointestinal tolerability¹³. Bisphosphonate dosing instructions are also complex and may have been perceived as too difficult, particularly in hip fracture patients. Nasal calcitonin, on the other hand, is administered by daily nasal spray with minimal adverse effects. In addition, raloxifene received US Food and Drug Administration (FDA) approval in 1997, providing physicians

and patients with new treatment options. Calcitonin prescribing lost favor to bisphosphonates in 2000. At that time, weekly bisphosphonate dosing and a new bisphosphonate (risedronate) entered the market. Part of the drop in popularity of calcitonin may also be attributed to a clinical trial finding no protection from nonvertebral fractures¹⁴. Since 2000, bisphosphonates have dominated post-hip fracture prescribing, and as of 2004, all bisphosphonate prescriptions were for weekly dosing. Teriparatide is the only agent, other than bisphosphonates, shown to prevent nonvertebral fracture among those with established osteoporosis^{10,15}. Teriparatide received FDA approval for severe osteoporosis in November 2002, and is administered by daily injection. It is thus not surprising that few patients in our cohort were treated with teriparatide.

Prior studies examining prescribing trends have documented a decline in use of HT since the publication of the Women's Health Initiative (WHI) results^{16–18}. We also found that HT use declined over time. However, since few hip fracture patients in our cohort were treated with HT before the WHI results were released^{9,19}, it is difficult to determine whether or

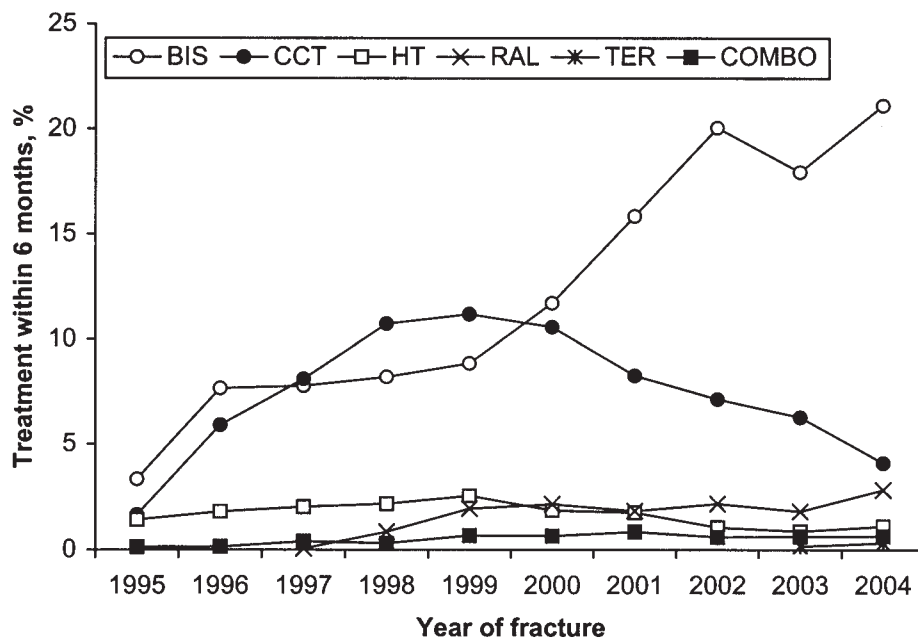


Figure 2. Proportion of hip fracture patients treated within 6 months, by drug class, 1995-2004. BIS: oral bisphosphonate, CCT: calcitonin, HT: hormone therapy, RAL: raloxifene, TER: teriparatide, COMBO: combination therapy, treatment with 2 or more osteoporosis drug classes.

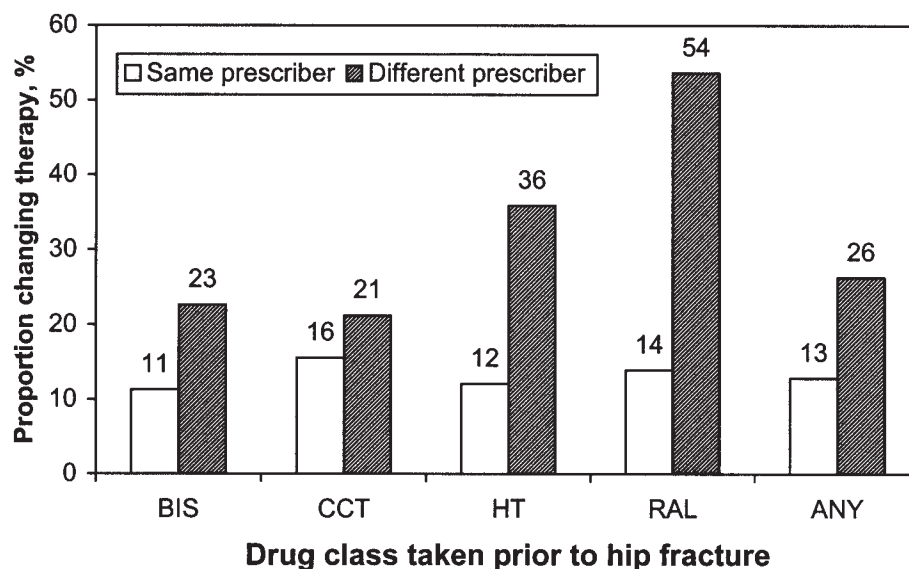


Figure 3. Proportion changing treatment postfracture, among those treated with a single agent prior to fracture, by drug class; one patient was taking teriparatide prior to fracture. This patient continued teriparatide postfracture (no change in therapy), treated by a different prescriber. BIS: oral bisphosphonate, CCT: calcitonin, HT: hormone therapy, RAL: raloxifene, ANY: all patients treated with any agent prefracture.

not WHI influenced post-hip fracture prescribing patterns. Raloxifene increases the risk of deep vein thrombosis to a degree similar to HT¹⁰, and there is no evidence to support its use for nonvertebral fracture prevention⁸. Despite this, the proportion of women treated with raloxifene remained relatively stable from 1998 to 2004, comprising on average 8% of

those treated. It is unknown what proportion of raloxifene users had contraindications or were previously intolerant to bisphosphonates. We thus cannot comment on the appropriateness of raloxifene prescribing in our study.

We also document trends and preferences for prescribing by physician specialty. Although we observed no change in

the proportion of patients treated by geriatricians over time, the proportion of patients treated by endocrinologists/rheumatologists, orthopedic surgeons, and obstetricians/gynecologists declined, and the proportion treated by other prescribers increased. The majority of physicians prescribed bisphosphonates. However, geriatricians treated the majority of their patients with calcitonin and obstetricians/gynecologists with HT. Unfortunately, due to limited numbers, we could not assess trends in prescribing preferences by physician specialty over time.

Current guidelines for managing osteoporosis and preventing fragility fractures do not include recommendations for treatment changes among those who fracture on therapy^{1,10}. We found that 13% of patients treated by the same provider and 26% treated by a different provider changed therapy after sustaining a hip fracture. Despite the introduction of several new agents, there was no trend in the proportion changing therapy postfracture over time. Osteoporosis guidelines provide no explicit recommendation and since no randomized controlled trials have examined the effects of changing therapy postfracture, it is unclear what course of action to take when a patient fractures on therapy. More data regarding the benefits of changing treatment postfracture are needed.

Consistent with prior findings⁵, we document that post-hip fracture treatment is particularly poor among men. Although osteoporosis is gaining attention as an important health problem among elderly men²⁰, osteoporosis continues to be perceived as a health issue affecting older women^{21,22}. In general, men have poor knowledge about osteoporosis, and do not perceive themselves to be susceptible to osteoporosis^{23,24}. Family physicians have also commented that men are “not thought about” when it comes to osteoporosis²². Post-hip fracture treatment with osteoporosis drugs is also complicated by the lack of consensus regarding how to define osteoporosis among men, and that there are fewer treatment options²⁰. Indeed, only recently has there been a trial supporting the benefits of bisphosphonate prescribing among men to reduce fracture risk²⁵. Therefore, although postfracture prescribing has improved over time in both sexes, further work is required to help reduce the burden of osteoporosis among women and men, particularly postfracture.

Our data also suggest that improvements in the proportion of hip fracture patients treated with osteoporosis drugs have leveled off in recent years. Our finding that fewer than one-third of hip fracture patients received pharmacotherapy is concerning, but not unexpected⁵⁻⁷. The lack of coordination between those who provide fracture care and those who provide osteoporosis management is well documented^{6,26}. Recent data suggest that multifaceted systems approaches may be needed to improve postfracture treatment rates²⁶⁻²⁹.

Several limitations of our study are worth noting. First, we are limited to drugs dispensed and cannot comment on treatment prescribed but not dispensed. Similarly, it is possible that some patients were provided with free drug samples.

However, our 6-month period of observation postfracture should minimize such underreporting. Second, we do not have information regarding treatment with nonpharmacological or nonprescription strategies, such as calcium or vitamin D supplementation, hip protectors, or fall-prevention programs. We thus cannot comment on trends in the use of nonprescription strategies. Third, in categorizing combination therapy as agents dispensed on the same date, we may have underestimated the proportion on combination therapy. However, our definition of combination therapy is reasonable, whereas drugs dispensed on the same day are clearly being used in combination, theoretical overlap of days covered does not necessarily indicate concurrent treatment.

Fourth, by studying hip fractures, we assume that all cases are candidates for treatment with osteoporosis drugs. However, some patients may have had BMD testing with normal findings and thus been appropriately managed without pharmaceutical intervention. We also may have misclassified some fractures as osteoporosis-related for other reasons, such as by identifying our hip fracture cohort solely on the basis of diagnostic codes (thus including pathological and traumatic fractures). However, prior evidence suggests that the positive predictive value for hip fractures is just as high based on diagnostic code alone compared to including procedural codes, yet the sensitivity is better³⁰. Twelve percent of our eligible hip fracture sample did not have a relevant procedural code. Stratified by year, there were no differences in treatment based on whether or not a procedural code was present. In addition, over the 10-year study period, only 2.5% of hip fractures ($n = 249$) were identified by pathological fracture diagnosis (ICD-9-CM 733.14) alone, and fewer than 1% were associated with severe trauma codes (ICD-9-CM E820.xx–E848.xx).

Fifth, we cannot comment on the intentions of the prescribing physician, nor the appropriateness of osteoporosis treatment in our study. For example, HT is often prescribed for reasons other than bone health³¹, and neither calcitonin nor raloxifene has documented nonvertebral fracture efficacy⁸. Regardless, our results document prescribing trends over a period of 10 years, during which time several new pharmaceutical agents and data regarding their efficacy became available. We also document improvements in hip fracture treatment with antiresorptive agents with proven nonvertebral fracture efficacy, finding that treatment with bisphosphonate increased over time.

Sixth, in requiring that each patient has a prescription claim during the followup period, we are limited by missing data due to loss of PACE coverage (e.g., became Medicaid-eligible, left the state of Pennsylvania, first 100 days of nursing home residency). If there are systematic differences between those who lost PACE coverage during followup and those for whom we had complete data, then our estimates of treatment over time may be misleading.

Finally, the study cohort comprised frail adults aged 65 or

more years enrolled in a drug benefit program for low income residents of Pennsylvania. Hip fracture patients are generally old and have several comorbidities; we thus believe that our overall findings of the patterns of osteoporosis drug prescribing are relevant. In addition, by studying a population-based cohort of hip fracture patients with complete drug coverage, our results may be more generalizable than prior studies focusing on care after discharge from limited samples of hospitals⁵⁻⁷. Nonetheless, we cannot comment on the generalizability of our results to seniors with different types of drug coverage. Pennsylvania was also identified as the top state in osteoporosis management in women who had a fracture by the National Committee for Quality Assurance, with 24.4% being managed in 2005 (BMD test and/or treatment within 6 months of fracture) compared to the national average of 20.1%³². The proportion of hip fracture patients treated within 6 months of hip fracture may thus be higher than other areas of the United States. In addition, osteoporosis management in women post-fracture was added as a quality indicator by the National Committee for Quality Assurance in 2004³². Therefore, unlike our finding that osteoporosis treatment rates post-hip fracture have leveled off with about one-third being treated, if effective quality improvement interventions are implemented, treatment rates may increase in coming years.

We observed that prescribing practices changed substantially over time with the introduction of several new medications. The proportion of hip fracture patients treated with osteoporosis drugs increased over time, but leveled off in recent years, and remains low, with fewer than one-third receiving pharmacotherapy. Effective quality improvement interventions are needed to maximize postfracture treatment rates.

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