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ORIGINAL ARTICLE

Predictors of oral bisphosphonate prescriptions in post-menopausal women with osteoporosis in a real-world setting in the USA

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Abstract
Summary We identified factors associated with oral bisphosphonate treatment in 50+-year-old female patients with a first fracture, osteoporosis diagnosis, or BMD ≤−2.5 in the Geisinger Health System electronic health record database. Treatment was positively associated with age, oral corticosteroids, and smoking, and negatively associated with body mass index and bone mineral density scores.
Introduction To identify factors associated with oral bisphosphonate treatment in patients with an indicator for post-menopausal osteoporosis.
Methods Females age 50+ years with a first fracture, osteoporosis diagnosis, or bone mineral density (BMD) ≤−2.5 (index date) were identified in the Geisinger Health System electronic health record database. Treatment was defined as an oral bisphosphonate prescription order (risedronate sodium, ibandronate sodium, or alendronate) ≤90 days post-index date. Treatment rates were assessed and a multivariate logistic model was used to identify predictors of treatment separately for patients with fracture (FRAC) and with diagnosis or low BMD (ICD-9-BMD).
Results The FRAC group had 2,003 female patients with a mean (SD) age of 69.0 (±11.3) years and the ICD-9-BMD group had 12,976 female patients with a mean (SD) age of 66.9 (±10.0) years. Within 90 days of the index date of fracture, diagnosis, or low BMD score, 188 (9.4%) patients in the FRAC group and 5,395 (41.6%) in the ICD-9-BMD group received treatment. Treatment was positively associated with age and oral corticosteroids and negatively associated with body mass index and subsequent BMD in both groups. Smoking currently was positively associated with treatment in the ICD-9-BMD group.
Conclusion Certain patient characteristics are predictors of physicians prescribing oral bisphosphonates. However, many patients remain untreated.

Keywords Bone mineral density · Fracture · Oral bisphosphonate · Osteoporosis · Real world data

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Introduction

Osteoporosis is a skeletal disorder characterized by low bone mineral density (BMD) and a disruption of normal bone architecture. It is a major risk factor for fracture, which leads to substantial morbidity and mortality [1]. Osteoporotic fractures are common; it is estimated that one half of all post-menopausal women will have a fracture in her lifetime [2]. Hip fractures reduce life expectancy, by 25% in one study [3], and are associated with a substantial decrease in quality of life [4]. The estimated societal cost of osteoporotic fractures in the USA was $13.8 billion in 1995 [5]. Osteoporosis will likely become increasingly burdensome as the proportion of the US population that is elderly increases.

The aim of treatment of established osteoporosis is to maintain and, ideally, to restore bone strength with the ultimate goal of preventing fractures. There are currently a number of FDA-approved agents for the treatment of osteoporosis including bisphosphonates (e.g., alendronate, ibandronate, or risedronate), raloxifene, teriparatide, and calcitonin. Estrogen replacement therapy is indicated for the prevention of osteoporosis. All of these agents have been shown to increase BMD and several have shown efficacy in fracture risk reduction [6].

Thus, drug therapy is a key therapeutic component in preventing osteoporosis fractures in patients at risk for fracture. However, it is estimated that only 36% of women with post-menopausal osteoporosis are treated with any agent for the prevention or treatment of osteoporosis, and specifically, only 16% were treated with bisphosphonate or calcitonin [7]. A number of studies have examined predictors of treatment to help understand what factors clinicians are weighting most heavily in determining whether to treat osteoporotic patients. Ideally, predictors of treatment should mirror predictors of fracture. Surprisingly, many of these studies have found that this is not necessarily the case. Increased age, oral corticosteroid usage, and smoking status are all risk factors for osteoporosis and fracture [8] but have often been found to have either a negative association or no association with treatment administration [9–20]. Yet several studies have found that either older patients are less likely to get treatment [12, 18, 22] or there is no association between age and treatment [20, 23].Low T-scores on BMD tests are strong predictors of fracture but are often not available for researchers. In this study, we distinguish osteoporotic patients based on having a fracture or having a low BMD T-score or a diagnosis code for osteoporosis. Few studies have examined factors associated with treatment in patients with these specific characteristics [11, 21]. As noted, the risk of fracture increases with age.

The objective of this study was to identify predictors of osteoporosis treatment. This was done separately for two subgroups of osteoporosis patients: (1) those with a fracture (FRAC group) (2) and those with either an International Classification of Diseases (ICD)-9 code for osteoporosis and/or a low (≤−2.5) T-score from a BMD test (ICD-9-BMD group). Potential predictors were included based on their association with bone health and fall risk. The evaluated predictors included weight, body mass index (BMI), smoking status, excessive alcohol consumption, a history of previous fractures, BMD T-score, comorbid conditions, and drug exposures. In this study, we focused specifically on prescribing for oral bisphosphonates (risedronate, alendronate, and ibandronate). Bisphosphonates are a commonly used class of prescription drugs for the treatment of osteoporosis [24], and in patients with low bone density, bisphosphonate have been shown to reduce fracture risk by 40–50% [25].

Methods

Study design

This study utilized a retrospective cohort design to evaluate the association between observable clinical characteristics and drug treatment for osteoporosis.

Data

We used data from the Geisinger Health System (GHS) from January 1, 2000–June 30, 2007. GHS was founded in 1915 and is a physician-led organization comprised of 650 plus physicians, 75 medical and surgical specialties, and 42 pediatric medical and surgical subspecialties. GHS, which also has one of the largest not for profit rural HMOs in the USA, has three existing hospitals (primary to quaternary care) and 41 community practice offices. The GHS service area is limited to the state Pennsylvania. The core of the data originates from an electronic medical record (EMR) infrastructure that contains longitudinal clinical patient data including lab results for nearly three million patients from 1996 to 2006. A unique feature of this dataset is the availability of diagnostic testing results. For the present study, we utilized results from BMD tests. The data was obtained through MedMining (a Geisinger Health System Business), which has developed a proprietary, Health Information Portability and Accountability Act compliant research database based on the GHS data.

Study population

The cohort population was selected based on specific criteria. Female patients age 50 and older were selected for inclusion into the study if they had at least one of three separate identifiers for osteoporosis from January 1, 2000 through June 30, 2007: (1) ICD-9 codes for osteoporosis (733.0, 733.00, 733.01, 733.03, 733.09); (2) a BMD T-score of −2.5 or less; or (3) a fracture on or after age 50 with no fracture in the 6 months prior. Locations for fractures were identified by ICD-9 codes (Table 1) for the clavicle, hip, humerus, pelvis, leg, wrist, and spine. The date of osteoporosis identification was designated as the patient's index date. Patients were excluded if they were not continuously active in the database for 365+days prior to and 365+days after the

Table 1 Fragility fracture (Inclusion and Outcome Criteria)

Fracture site	ICD-9-CM	
1. Clavicle (closed)	Closed	810.0x
2. Hip (closed)	Pathologic	733.14
	Transcervical	820.0x
	Pertrochanteric	820.2x
	Unspecified	820.8x
3. Humerus (closed)	Pathologic	733.11
	Upper end	812.0x
	Shaft/unspecified	812.2x
	Lower end	812.4x
4. Pelvis (closed)	Acetabulum	808.0x
	Pubis	808.2x
	Other specified	808.4x
	Unspecified	808.8x
5. Leg		
Femur (closed)	Pathologic	733.15
	Shaft/unspecified	821.0x
	Lower end	821.2x
Tibia/Fibula (closed)	Pathologic	733.16
	Upper end	823.0x
	Shaft	823.2x
	Unspecified	823.8x
6. Wrist (closed)	Pathologic	733.12
	Forearm upper end	813.0x
	Shaft	813.2x
	Lower end	813.4x
	Unspecified	813.8x
7. Spine/vertebral (closed)	Pathologic	733.13
	Cervical, closed	805.0x
	Dorsal, closed	805.2x
	Lumbar, closed	805.4x
	Unspecified, closed	805.8x

index date, if they had both a fracture and at least one of the other two osteoporosis identifiers, or if they had a diagnosis for a condition known to impact bone density and quality (i.e., Paget's disease (ICD-9: 731.xx), secondary malignant neoplasm of bone and bone marrow (ICD-9: 198.5), and osteomylitis (ICD-9: 730.xx)).

Statistical analysis

Patients were stratified into two groups, FRAC and ICD-9-BMD, based on reason for inclusion. Descriptive statistics, including proportion of patients treated, were used to characterize the baseline demographic and clinical characteristics of patients in both groups.

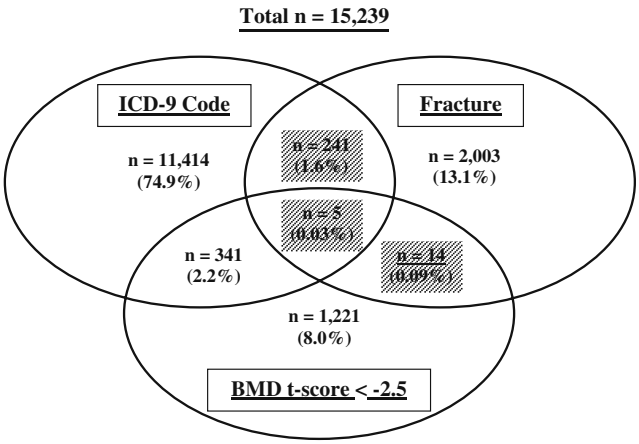
A logistic regression was used to identify predictors of osteoporosis treatment with an oral bisphosphonate (risedronate, alendronate, or ibandronate). Patients were identified as treated if they had a prescription for one of the three drugs on the index date or up to 90 days post-index date. Regressions were run separately for each of the two patient groups. Independent variables included age at index date (50–64, 65–74, and 75+), BMI ($\leq$24 kg/m^2, 25–29 kg/m^2, 30–34 kg/m^2, and 35+ kg/m^2), smoking status, excessive alcohol consumption, fall history, insurance status (Medicare, private insurance, or no insurance), presence of an order for a BMD test, and BMD T-score. The value for the BMD T-score variable was the test result for the hip, if available. If the hip T-score was not available, a spine test result was used, and if neither a hip or spine result was available, a forearm score was used. Values for the BMD T-score variable included test results within the first 90 days after the index date and was dichotomized based on whether the value was greater than or less than or equal to −2.5. Therefore, patients in the FRAC group, who by definition did not have a T-score $\leq$−2.5 on the index date, may still have a value for this variable below this threshold if it was measured in the first 90 days post-index. Furthermore, while it was not possible to link the cause of the fracture for patients in the FRAC group to a specific fall, if the fracture was the result of a fall, that fall would be captured by the fall history variable. Also included were diagnoses of comorbidities associated with bone health such as aortic atherosclerosis, diabetes, thyroid disease, and malnutrition. Indicators for the use of drugs over the study period whose exposures are associated with fracture risk were also included (e.g., chemotherapy, oral corticosteroids, thyroid replacement therapy, and furosemide therapy). Finally, a Charlson Comorbidity Index (CCI) score was calculated for each patient based on comorbidities documented on or one year prior to their index date [26].

Initially, a forward selection process was undertaken by running univariate regressions with each independent variable. Variables whose coefficients had p values of $\leq$0.10 were chosen to be included in the full multivariate regression. As a sensitivity analysis, calculations for proportion of treated patients as well as regression models were repeated using post-index date windows for defining treatment of 180 and 365 days.

All statistical tests were performed at a 0.05 significance level using Stata SE v. 9 (StataCorp, College Station, Texas) and SAS v. 9 (Cary, NC.)

Results

Figure 1 is a Venn diagram depicting the portion of patients with each of the three osteoporosis identifiers. The FRAC group consisted of 2,003 females and the ICD-9-BMD group was made up of 12,976 females. A total of 260



Note: Bone Mineral Density (BMD); International Classification of Diseases – 9 (ICD-9) Shaded patient counts were excluded from the final analysis.

Fig. 1 Venn diagram showing portion of patients with each osteoporosis identifier. Bone Mineral Density (BMD); International Classification of Diseases 9 (ICD-9) *Shaded* patient counts were excluded from the final analysis

patients, depicted in shaded regions in the figure, had both a fracture and either a low BMD T-score or an ICD-9 code for osteoporosis. These patients are included in Fig. 1 for illustrative purposes but were excluded from the analysis in order to isolate the two patient groups.

The mean age was 69.0 (SD±11.3) in the FRAC group and 66.9 (SD±10.0) in the ICD-9-BMD group (Table 2). A higher proportion of patients in the ICD-9-BMD group had a BMD ordered at any point in the study period compared to patients in the FRAC group (62.5% vs. 16.9%) and had lower average T-scores for each of the three sites (hip, −1 [SD±1.1] vs. −0.7 [SD±1.2]; spine, −1.3 [SD±1.0] vs. −0.8 [SD±1.5]; forearm, −1.5 [SD±1] vs. −1.2 [SD±1.1]). In both patient groups, most patients either had never smoked (ICD-9-BMD, 60.3%; FRAC, 58.9%) or were former smokers (ICD-9-BMD, 25.1%; FRAC, 58.9%). Most of the patients in the FRAC group had a CCI ≥3 (63%), 16.3% were taking an oral corticosteroid, and 2.5% had a diagnosis for rheumatoid arthritis. In the ICD-9-BMD group, 46% of the patients had a CCI ≥3, 14.4% were taking an oral corticosteroid, and 4.4% had a diagnosis of rheumatoid arthritis.

Only 188 (9.4%) of the patients in the FRAC group were prescribed treatment in the first 90 days post-index date, while 5,395 (41.6%) patients in the ICD-9-BMD group were treated during this same time period (Table 3). Treatment was prescribed for 13.4% and 18.5% of FRAC patients in the 180 days and 365 days following the index date, respectively. For the ICD-9-BMD patients, 45.9% had been prescribed treatment within 180 days while 49.3% had been prescribed treatment within 365 days.

In Table 4, results from the logistic regressions are presented for patients in the FRAC group. Baseline results for which treatment was defined as a prescription in the first 90 days following fracture are presented along with alternative treatment definitions of 180 and 365 days. Individuals between the ages of 65 and 74 were significantly more likely to get treatment (OR=1.77, p=0.009) compared with patients between 50 and 64. A low BMD T-score (≤−2.5) after fracture date was significantly associated with increased likelihood of receiving treatment (OR=4.90, p<0.001). Obese patients were less likely to receive treatment than underweight or normal weight patients (OR=0.53, p=0.03), and those taking an oral corticosteroid were more likely to receive treatment (OR=1.67, p=0.01). The effects of covariates on the likelihood of bisphosphonate treatment were similar using treatment windows of 180 and 365 days post-index date; however, more odds ratios reached statistical significance as the number of treated patients increased.

Results from logistic regressions for patients in the ICD-9-BMD are presented in Table 5. Treatment receipt was positively associated with age, with patients between the ages of 65 and 74 (OR=1.18, p<0.001) and 75 and older (OR=1.57, p<0.001) significantly more likely to receive treatment compared with patients between 50 and 64. A low BMD T-score (≤−2.5) was significantly associated with an increased likelihood of receiving treatment (OR=1.32, p=0.002). Patients who used to smoke (OR=0.76, p<0.001) or who never smoked (OR=0.72, p<0.001) were significantly less likely to receive treatment than those who currently smoke. BMI was negatively associated with treatment. Overweight (OR=0.81, p<0.001), obese (OR=0.54, p<0.001), and very obese (OR=0.46, p<0.001) patients were less likely to receive treatment than those who were underweight or normal weight. Patients with higher CCI (OR=0.96, p<0.001) were less likely to receive treatment, while those taking an oral corticosteroid (OR=1.34, p<0.001) and those with rheumatoid arthritis (OR=1.40, p<0.001) were more likely to receive treatment. Results were similar using treatment windows of 180 and 365 days.

Discussion

The purpose of this study was to quantify how fracture risk factors are associated with physicians prescribing bisphosphonate treatment in women with post-menopausal osteoporosis. The treatment rate was low, especially in the FRAC group, with merely 9.4% having a prescription order for an oral bisphosphonate in the first 90 days following a fracture and only 18.5% having such a prescription order if the follow-up period is extended to 1 year. This result is similar to those found in other studies where treatment rates have

Table 2 Baseline characteristics

	Fracture (n=2003)		Low BMD or ICD-9 (n=12,976)	
	n/mean	% or SD	n/mean	% or SD
Mean age (SD)	69.0	11.3	66.9	10.0
50–64	774	38.6	5,582	43.0
65–74	519	25.9	4,156	32.0
75+	710	35.4	3,238	25.0
Race (n, %)				
White	1,980	98.9	12,819	98.8
Black	6	0.3	38	0.3
Hispanic	5	0.2	32	0.2
Other	9	0.4	75	0.6
Unknown	3	0.1	12	0.1
Mean baseline BMD T-score (SD)				
Forearm	−1.2	1.1	−1.5	1.0
Hip	−0.7	1.2	−1	1.1
Spine	−0.8	1.5	−1.3	1.4
BMD T-score orders (n, %)	339	16.9	8,114	62.5
BMD T-score (n, %)				
≤−2.5	26	1.3	560	4.3
>−2.5 to ≤−1.0	115	5.7	3,581	27.6
≥−1.0 to ≤1.0	156	7.8	3,283	25.3
≥1.0	25	1.2	310	2.4
Missing	17	0.8	380	2.9
Unknown	1,664	83.1	4,862	37.5
Smoking				
Current smoker	185	9.2	1,285	9.9
Former smoker	486	24.3	3,262	25.1
Never smoker	1,179	58.9	7,828	60.3
Missing	153	7.6	601	4.6
Baseline BMI				
Under/normal weight	232	11.6	3,051	23.5
Over weight	363	18.1	3,312	25.5
Obese	402	20.1	2,790	21.5
Very obese	134	6.7	500	3.9
Missing	872	43.5	3,323	25.6
Insurance status (n, %)				
Medicaid	835	41.7	4,931	38.0
Medicare	709	35.4	4,710	36.3
Commercial	419	20.9	3,190	24.6
Self-pay	40	2.0	145	1.1
Excessive alcohol consumption (n, %)	8	0.4	32	0.2
Mean Charlson Comorbidity Index (SD)	2.3	1.1	2.0	1.1
0	217	10.8	2,015	15.5
1	263	13.1	2,545	19.6
2	254	12.7	2,356	18.2
3+	1,269	63.4	6,060	46.7
Oral corticosteroid (n, %)	327	16.3	1,870	14.4
Rheumatoid arthritis (n, %)	50	2.5	575	4.4
Fall history (n, %)	812	40.5	1,445	11.1

Table 2 (continued)

	Fracture (n=2003)		Low BMD or ICD-9 (n=12,976)	
	n/mean	% or SD	n/mean	% or SD
Aortic atherosclerosis (n, %)	41	2.0	151	1.2
Chemotherapy (n, %)	669	33.4	4,400	33.9
Diabetes (n, %)	657	32.8	2,844	21.9
Thyroid replacement therapy (n, %)	524	26.2	3,329	25.7
Thyroid disease (n, %)	842	42.0	5,201	40.1
Furosemide therapy (n, %)	695	34.7	2,693	20.8
Malnutrition (n, %)	291	14.5	1,393	10.7

SD standard deviation, *BMD* bone mineral density, *ICD-9* International Classification of Diseases 9, *BMI* body mass index

ranged from 16% to 26% in patients with fractures during 1 year follow-up periods [7, 27–30]. The rate of treatment within 90 days of diagnosis in the ICD-9-BMD group was also low (41.6%), and remained low at 1 year after diagnosis of osteoporosis (49.3%). These treatment rates all fall short of the estimates based on National Osteoporosis Foundation (NOF) guidelines [31]. Based on these guidelines, an estimated 72% of white women ages 65 and above should receive pharmacologic treatment for osteoporosis. Our findings are more consistent with the World Health Organization fracture risk assessment tool (FRAX™) guidelines which suggest that 23–46% of post-menopausal women should be treated for osteoporosis [32].

These results illustrate a potential gap in terms of clinical perception of fracture risk in a patient or benefits of therapy and treatment guidelines based on known fracture risk factors. Clinical guidelines recommend treatment in post-menopausal women with a BMD T-score of ≤−2.5 or a prior fragility fracture. Other post-menopausal women, who are candidates for treatment, are those with high fracture risk based on a high probability of a fracture within 10 years [31]. The FRAX™ model was developed to provide a measure of fracture risk based on known fracture risk factors with or without BMD scores [33]. These tools help clinicians quantify risk and therefore help to target patients for treatment. BMD tests are critical in making treatment decisions. Treatment recommendations from the National Center on Clinical Excellence recommend the use of alendronate in patients with a fragility fracture only if they have a T-score ≤−2.5 [34–36].

Thus, fracture risk factors should be drivers of treatment and, therefore, should also be treatment predictors, which was largely observed in this current study. Comparison of these results to those of fracture from other studies reveals some similarities but also many gaps. Low BMD T-scores, smoking, and weight are all significant predictors of fragility fracture which are shown here to be strongly associated with treatment. However, fall history, excessive alcohol consumption, comorbid conditions such as diabetes, thyroid disease, aortic atherosclerosis, and malnutrition, and drug exposures such as chemotherapy and thyroid replacement therapy have all been shown to be associated with fractures, but were not significant predictors of initiation of treatment in this study.

Several of our findings are substantially different from those found in earlier studies though consistent with what we would expect. Earlier studies have reported either no association between age and osteoporosis treatment or that treatment is negatively associated with age [12, 18, 20, 22, 23]. That age is positively associated with treatment in our study, while different from previous studies, makes clinical sense given the strong association of age and osteoporosis and fracture risk [15, 17]. Many other studies have also failed to find as association between oral steroid use and osteoporosis treatment [23, 37–39]. Again, our findings

Table 3 Frequency of patients treated at 90, 180, and 365 days after index date

Number of days from index date	Fracture (n=2,003)		Low BMD or ICD-9 (n=12,976)	
	n	%	n	%
90 days	188	9.4	5,395	41.6
180 days	268	13.4	5,954	45.9
365 days	371	18.5	6,395	49.3

BMD bone mineral density, *ICD-9* International Classification of Diseases

Table 4 Logistic regression for osteoporosis treatment—patients with fracture

	Number of days from index date for treatment definition					
	90 days		180 days		365 days	
	Odds ratio	*P* value	Odds ratio	*P* value	Odds ratio	*P* value
Age						
50–64 (ref)						
65–74	1.764	0.009	1.784	0.002	1.780	<0.001
75+	1.469	0.119	1.632	0.018	1.463	0.032
Race						
White (ref)						
Other	0.788	0.762	0.514	0.389	0.591	0.415
BMD T-score category						
≤−2.5	4.900	<0.001	3.441	0.007	5.750	<0.001
>−2.5 (ref)						
Unknown	0.128	<0.001	0.180	<0.001	0.295	<0.001
Smoking						
Current smoker (ref)						
Former smoker	0.798	0.474	0.882	0.644	1.031	0.898
Never smoker	0.930	0.799	0.954	0.852	1.059	0.795
Unknown	0.225	0.011	0.286	0.007	0.383	0.010
Baseline BMI						
Under/normal weight (ref)						
Over weight	0.804	0.428	0.774	0.274	0.802	0.274
Obese	0.532	0.031	0.584	0.027	0.462	<0.001
Very obese	0.545	0.146	0.465	0.035	0.301	<0.001
Missing	0.845	0.521	0.671	0.067	0.535	<0.001
Charlson Comorbidity Index	1.034	0.269	1.040	0.122	1.033	0.138
Oral corticosteroid	1.669	0.014	1.358	0.092	1.270	0.136
Rheumatoid arthritis	1.650	0.254	2.179	0.031	1.765	0.092

BMI body mass index, *BMD* bone mineral density

regarding oral corticosteroid use are consistent with physicians making prescription decisions based on known risk factors. At least one other study found that women with rheumatoid arthritis were less likely to receive treatment [12]. Once more, in finding that patients with this disease are more likely to receive treatment, our results are more consistent with expectations. Finally, while smoking status has not been a significant predictor of treatment in other studies [9, 12], it is in ours.

We found that BMI was negatively associated with treatment, while other studies have either found the same result [23] or no significant association between BMI and treatment [9, 11]. Our findings on BMD T-scores are consistent with several other studies [9–11, 13, 14, 16, 19]. However, previous studies looking at the association between BMD T-scores and treatment have used prospective data sources. This is the first study to find this result using a retrospective database.

Our results, particularly the low prescribing rates, suggest there is room for improvement in prescription drug prescribing for patients with osteoporosis. Efforts to raise clinician's awareness and adoption of the treatment guidelines put forth by the NOF could potentially help reduce fracture rates in women with post-menopausal osteoporosis.

Limitations

This study provides insight into predictors of post-menopausal osteoporosis treatment in a real-world setting by whether women had a prior fracture or a diagnosis or a low BMD T-score as indicators of osteoporosis. However, several limitations warrant mention. First, the EMR data represents care delivered to study patients within GHS; care delivered by non-GHS providers would likely not be included in the data unless reported by the patient and documented in the EMR, including prescription orders. As a health system, data is more likely to be comprehensive than an EMR that was located in a single site of care, such as an office based EMR system. The

Table 5 Logistic regression for osteoporosis treatment—patients with low BMD or ICD-9 code

	Number of days from index date for treatment definition					
	90 days		180 days		365 days	
	Odds ratio	*P* value	Odds ratio	*P* value	Odds ratio	*P* value
Age						
50–64 (ref)						
65–74	1.176	<0.001	1.197	<0.001	1.248	<0.001
75+	1.565	<0.001	1.524	<0.001	1.514	<0.001
Race						
White (ref)						
Other	1.369	0.059	1.289	0.127	1.197	0.281
BMD T-score category						
≤−2.5	1.322	0.002	1.533	<0.001	1.651	<0.001
>−2.5 (ref)						
Unknown	0.579	<0.001	0.591	<0.001	0.618	<0.001
Smoking						
Current smoker (ref)						
Former smoker	0.758	<0.001	0.754	<0.001	0.761	<0.001
Never smoker	0.715	<0.001	0.715	<0.001	0.711	<0.001
Unknown	0.336	<0.001	0.345	<0.001	0.356	<0.001
Baseline BMI						
Under/normal weight (ref)						
Over weight	0.805	<0.001	0.779	<0.001	0.739	<0.001
Obese	0.538	<0.001	0.513	<0.001	0.473	<0.001
Very obese	0.462	<0.001	0.394	<0.001	0.357	<0.001
Missing	0.726	<0.001	0.710	<0.001	0.701	<0.001
Charlson Comorbidity Index	0.955	<0.001	0.963	<0.001	0.968	<0.001
Oral corticosteroid	1.338	<0.001	1.336	<0.001	1.309	<0.001
Rheumatoid arthritis	1.395	<0.001	1.512	<0.001	1.732	<0.001

BMI body mass index, *BMD* bone mineral density, *ICD-9* International Classification of Diseases 9

disadvantage of using data from a single healthcare system is that the prescribing patterns and, thus, predictors of treatment may not reflect prescribing patterns of other health systems or of US prescribers overall. Similarly, included patents reside in a single geographic region. Thus, caution must be made in generalizing these findings to other populations or the USA as a whole.

Second, while this study did not include fractures that were most likely due to trauma, it is still not possible from the data to ascertain if fractures were fragility related or primarily the result of an injury. Thus, fracture as a criterion for defining osteoporosis in this study may lack sensitivity and may help to explain why treatment rates were low in the fracture group.

Finally, there is debate about whether antiresorptive treatment should be initiated immediately after fracture [40, 41]. One recent study showed that zoledronate did not delay union of hip fracture [42]. However, another study examining patients with a humerus fracture showed that bisphosphonate use increased the risk of non-union between 3 and 12 months after the fracture [43]. This suggests that providers may wait for fragility fractures to heal before initiating bisphosphonate therapy. While most fractures would be healed in 90 days, the sensitivity analyses of 180 and 365 days for the treatment window indicate that the choice of a 90 day treatment window versus a longer window did not impact predictors of treatment or overall treatment rate.

Conclusion

In this study, we found that many patient characteristics that indicate fracture risk were predictive of oral bisphosphonate treatment in a cohort of females age 50 and older with at least one indicator for osteoporosis. Many of these associations have not been found in previous studies. However, several other known risk factors for fracture and osteoporosis were not found to be significant predictors of

treatment, and the treatment rate for those with a prior fracture was low overall. This suggests that while prescribing patterns may be more consistent with recommendations than previously evidenced, there remains opportunity for improvement in the use of drug treatment to help avoid fractures in women with post-menopausal osteoporosis.

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