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Characteristics associated with anti-osteoporosis medication use: data from the Global Longitudinal Study of Osteoporosis in Women (GLOW) USA cohort

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Abstract

Introduction—Many women at risk of fracture do not receive anti-osteoporosis medication (AOM), while others may be receiving unnecessary treatment.

Purpose—To examine the characteristics associated with AOM use among women at low and high risk of fracture.

Methods—The Global Longitudinal Study of Osteoporosis in Women (GLOW) is a prospective cohort study in which data were collected, via self-administered questionnaires, from 60,393 non-institutionalized women aged ≥55 years in 10 countries between October 1, 2006 and April 30, 2008. This is a cross-sectional analysis of baseline USA data, in which women were classified as having low fracture risk (<65 years; no FRAX risk factors) or high fracture risk (≥65 years; prior fracture or ≥2 other FRAX risk factors).

Results—Of 27,957 women, 3013 were at low risk of fracture and 3699 were at high risk. Only 35.7% of high-risk women reported AOM treatment, rising to 39.5% for those with self-reported osteopenia and 65.4% for those with self-reported osteoporosis. Conversely, 13.4% of low-risk women reported AOM, rising to 28.7% for osteopenia and 62.4% for osteoporosis. Characteristics associated with significantly higher AOM treatment rates among low-and high-risk women were:

osteoporosis (odds ratios 75.3 and 18.1, respectively), osteopenia (17.9 and 6.3), concern about osteoporosis (2.0 and 1.8), higher perceived risk of fracture (2.3 and 1.6), and higher vitality score (1.7 and 1.6).

Conclusion—Use of AOM is frequently inconsistent with published guidelines in both high -and low-risk women. Characteristics other than FRAX fracture risk appear to influence this use, particularly the presence of self-reported osteoporosis.

Keywords

Anti-osteoporosis medication; Fracture risk; Postmenopausal osteoporosis; Women

Introduction

Expert groups have published treatment guidelines for preventing osteoporosis-related fractures based on clinical risks and bone mineral density (BMD) determinations [1–3]. Despite such guidance, multiple studies have demonstrated that many women at increased fracture risk remain undertreated [4–9]. There is also a suggestion that women at low risk are sometimes treated unnecessarily [10].

Within a large cohort of postmenopausal women, we identified subgroups of women at high and low risk of fracture using clinical risk factors specified in the FRAX prediction model [11]. We then investigated whether, after accounting for fracture risk, any additional characteristics were associated with anti-osteoporosis medication (AOM) use and whether these differed between the high-and low-risk women.

Material and methods

The Global Longitudinal Study of Osteoporosis in Women (GLOW) is a large multinational prospective cohort study involving 60,393 women aged ≥55 years in 10 countries (Australia, Belgium, Canada, Germany, Italy, Netherlands, Spain, France, the UK, and the USA) [12]. Women who are patients at primary care practices at 17 different sites were surveyed. Women were eligible for inclusion if they had visited their physician in the previous 24 months, were not institutionalized, and had no cognitive impairment, language barrier, or illness preventing them from completing the survey questionnaire. The questions covered seven domains: patient characteristics/risk factors, perceptions about fracture risk and osteoporosis, medication use, comorbid conditions, healthcare use and access, physical activity, and physical function/quality of life. The overall aim of the GLOW study is to identify patterns of risk as well as of management and treatment of osteoporosis and fractures in this multinational cohort [12].

This study is a cross-sectional analysis of the baseline GLOW data for the cohort of women in the USA. Women were placed into one of two risk categories: low-risk women were those aged <65 years with no FRAX risk factors; while high-risk women were those aged ≥65 years with a prior fracture or ≥2 other FRAX risk factors (parental hip fracture, current smoker, ≥3 alcoholic drinks/day, rheumatoid arthritis, current corticosteroid use, body mass index [BMI] <20 kg/m^2, and secondary osteoporosis) [11]. Women who did not fit into

either of these two categories were not included in the analysis, although data for the entire USA cohort is also included. BMD, which is included in the FRAX risk model, was not accounted for in this study, as BMD data were not collected in GLOW.

The characteristics considered for potential association with treatment were: education, age (within risk strata), number of comorbid conditions, prescription drug coverage, concern about osteoporosis, self-perception of fracture risk, self-assessed health status, short form 36 (SF-36) physical function, and vitality score [13]. Baseline data were used for all of the characteristics. Treatment rates were also analyzed by self-reported diagnosis of osteoporosis or osteopenia. The outcome of interest was use of AOM (current use at baseline), defined as any of the following: alendronate, calcitonin, raloxifene, risedronate, teriparatide, or zoledronic acid. Women who were members of the USA cohort, but who were taking medications that are not approved in the USA were excluded from analysis. Women on raloxifene who also reported having cancer were excluded from the analysis, as cancer can be an indication for such use. Women on estrogen were excluded from the analysis, as it was not possible to determine whether they were on estrogen for osteoporosis or another indication.

Statistical methods

Means and standard deviations (SDs) are reported for continuous variables; while numbers and percentages are reported for discrete variables. Chi-square tests for significance were used to detect differences in treatment rates between risk groups. A p value <0.05 was considered significant. Odds ratios (ORs) with 95% confidence intervals (CIs) for characteristics associated with AOM treatment were calculated using logistic regression models for both risk groups. Study site and age were adjusted for in the models. All analyses were performed using SAS 9.2 (SAS Institute, Cary, NC, USA).

Results

Characteristics of the USA GLOW cohort, overall and according to risk group, are listed in Table 1. There were 27,957 women in the USA cohort, including 3013 in the low-risk group and 3699 in the high-risk group. High-risk women had lower vitality and physical function scores than low-risk women (Table 1). Fewer high-risk women listed no comorbid conditions and fewer rated their own health as excellent, very good, or good (Table 1). The numbers of high-and low-risk women who were very or somewhat concerned about osteoporosis were similar, but high-risk women were more likely to rate their own fracture risk as higher than others (Table 1).

Table 2 shows AOM treatment rates at baseline by risk factors for fracture for the whole USA cohort. Women with rheumatoid arthritis, current corticosteroid use, and prior fracture had the highest treatment rates (33–36%).

Overall, 13.4% and 35.7% of low-and high-risk women, respectively, reported treatment with AOM. Table 3 shows AOM reported treatment rates among low -and high -risk women, by various baseline factors. Factors that significantly increased reported AOM use among both low-and high-risk women were: concern about osteoporosis, higher perceived fracture

risk, higher vitality and physical function scores, and having prescription drug coverage (Table 3). However, having no comorbidities only significantly increased reported AOM usage among low-risk patients; while being white, being better educated, and having better general health only significantly increased reported AOM usage among high-risk patients (Table 3). Results from the whole GLOW USA cohort were generally similar to those in the low-and high-risk groups (Table 3).

Table 4 shows the percentages of women reporting AOM use, further categorized by self-reported osteoporosis, osteopenia, or neither. Not surprisingly, reported AOM treatment rates were much higher among women with self-reported osteoporosis or osteopenia than among those with neither condition, in both the low-and high-risk groups (Table 4). However, less than two-thirds of high-risk women with osteoporosis were actually receiving AOM. Results by risk factors were generally similar among these groups to the overall results shown in Table 3.

Results of the multivariable analysis are listed in Table 5. The most important factors for reported AOM treatment were self-reported osteoporosis or osteopenia, with higher ORs among low-risk women (ORs 75.3 and 17.9, respectively) than among high-risk women (ORs 18.1 and 6.3, respectively) (Table 5). Prescription drug coverage was important among low-risk women (OR 5.6), but not among high-risk women (OR 1.0). Concern about osteoporosis and higher perceived fracture risk approximately doubled the chance of receiving AOM in both risk groups, as did an above median vitality score (Table 5).

Discussion

The results from this large cohort of postmenopausal women show that established clinical risk factors are associated with AOM treatment. There was a 2.7-fold higher rate of reported treatment among high-versus low-risk women. As expected, self-reported osteoporosis was associated with the strongest likelihood of treatment, with self-reported osteopenia also highly associated with AOM use. However, our results suggest that certain other characteristics are also driving treatment. Concern about osteoporosis, perception of having a higher fracture risk than others, having fewer comorbid conditions, and having greater vitality each increased the likelihood of being treated, by 1.4–2.3-fold, regardless of fracture risk.

As an example, AOM use was somewhat higher among low-risk women who were very/somewhat concerned about osteoporosis (15.2%) than in high-risk women who were not concerned (11.9%). Additionally, 42.3% of women in the low-risk group with self-reported osteopenia who perceived their fracture risk as higher than others were treated with AOM, compared with only 37.8% of high-risk women with self-reported osteopenia who did not perceive themselves to be at high risk. The tendency for higher treatment rates among women with higher vitality and physical function scores, fewer comorbid conditions, and better reported general health suggests that healthier, more energized individuals may be stronger advocates for treatment or may focus more on AOM if they have fewer competing health concerns.

We also found that reported rates of AOM use were much higher among low-risk women with versus without prescription drug coverage, but that this difference was less pronounced among high-risk women. In contrast, race had little impact on AOM treatment among low-risk patients, but being white significantly increased the rate of treatment among high-risk patients.

Overall, the AOM treatment rates in our population were low. The reported treatment rate among all high-risk women was only 35.7%, increasing to 39.5% in women with self-reported osteopenia and to 65.4% for those with self-reported osteoporosis, which, while improved, still falls below suggested standards. The National Osteoporosis Foundation and the American Academy of Clinical Endocrinologists recommend treatment for postmenopausal women aged ≥50 years with: a hip or vertebral fracture; a T-score ≤–2.5 at the femoral neck or spine; a T-score between −1.0 and −2.5 at the femoral neck or spine and a 10-year probability of a hip fracture ≥3%; or a 10-year probability of a major hip fracture ≥20%, based on the USA-adapted World Health Organization [1,3]. The American College of Physicians recommends offering treatment to those with a diagnosis of osteoporosis and those who have experienced a fragility fracture[2].

While our data indicate substantial under-treatment, we also found that 8.9% of low-risk women without self-reported osteoporosis reported receiving AOM treatment. The National Osteoporosis Foundation does not recommend pharmacologic treatment for osteopenia in the absence of other risk factors [1]. However, in the low-risk group (i.e. those with no FRAX risk factors), 28.7% of women with self-reported osteopenia reported receiving AOM treatment. Therefore, it appears that there is a substantial group of women who are being treated with AOM who are not likely to benefit from treatment.

These findings are reminders that active treatment involves both physician and patient participation. Doctors must recognize risk and prescribe appropriately, but patient attitudes may also contribute. Study subjects in both the high-and low-risk groups who perceived that their fracture risk was increased were significantly more likely to report taking AOMs. Women who reported concern about osteoporosis were also more likely to report AOM use in both risk groups.

Previous studies have focused on predictors of receiving AOM treatment. Bessette et al. reported significant predictors of treatment following a fracture to be: low BMD, fracture site (hip, femur, pelvis, or wrist), use of calcium and vitamin D consumption at the time of fracture, and age ≥60 years [14]. Hamel et al. reported that a finding of osteoporosis or osteopenia by first BMD testing influenced the prescribing of bisphosphonates, while a pretest history of fracture did not[15]. Asche et al. also examined predictors of oral bisphosphonate prescriptions in postmenopausal women, and found that fracture history, older age, low T-score (≤–2.5), and oral corticosteroid use were associated with treatment with an oral bisphosphonate [16]. Onder et al. studied patients with a diagnosis of osteoporosis who were discharged from hospital [17]. Admission for a hip or vertebral fracture and corticosteroid treatment were associated with a higher rate of treatment, while older age, male sex, a greater number of comorbid conditions, and a greater number of medications were associated with a lower likelihood of AOM [17]. Data from Greenspan et

al., also using the GLOW cohort, demonstrated that self-reported osteoporosis and use of calcium were associated with a higher likelihood of being treated for osteoporosis among women who sustained incident fractures[18]. In line with our finding that there was a segment of the study population receiving treatment without a clear indication, Roux et al. found, in the Prospective Observational Study Investigating Bone Loss Experience in Europe (POSSIBLE EU) study, that 25% of patients were taking AOM despite having neither a previous fracture nor a dual energy X-ray absorptiometry (DXA) diagnosis [19]. They also found that nearly 25% of patients had no DXA diagnosis and no prior fracture, yet were taking AOM. This suggests that there are other factors driving treatment, such as clinical risk factors or other diagnostic modalities. None of this prior work considers the role that patient attitudes or reported health status may contribute to treatment.

Study limitations and strengths

As this is a cross-sectional study and the data are prevalence estimates, it remains uncertain whether characteristics such as “concern about osteoporosis” and “fracture risk” are predictive of treatment with AOM or whether they are the result of treatment.

These are self-reported data, which have not been verified by medical record review, so we do not know true doses or indications. The diagnoses of osteoporosis and osteopenia, for example, are presumably based on BMD testing, but lack numeric results. However, we do know that among those women who stated that they had osteoporosis, 94.6% also reported having had a BMD test, and among those who reported that they had osteopenia, 97.4% reported having had a BMD test. Moreover, it is not known whether women not reporting osteoporosis or osteopenia had normal BMD examinations or had not been tested. They may also have had appropriate indications for AOM that were not captured in our study (in particular unreported clinical risk factors for fractures). There are indications for AOM treatment other than FRAX risk factors, such as Paget’s disease and bone metastases. However, these indications are rare and are not likely to have had a significant effect on the results.

The strengths of this study include the large sample size and the uniform method of collecting data across study sites. Data were collected from patients of primary care physicians and there were few exclusion criteria. Physicians did not select specific patients for this study; they merely provided lists of active patients so the overall group to whom the questionnaires were sent initially should be representative of the practices.

Conclusions

The results of this study indicate low overall rates of treatment with AOM, but also reveal a number of women at low risk of fracture who were on AOM. Among the low -and high-risk women, rates of treatment were higher among healthier, higher-functioning women. Rates were also higher among women who felt they had a higher fracture risk than others and who were more concerned about osteoporosis regardless of actual fracture risk, suggesting that attitudes and beliefs of the women themselves, as well as FRAX risk factors, are affecting the likelihood of AOM treatment.

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Abbreviations

AOM	anti-osteoporosis medication
BMD	bone mineral density
BMI	body mass index
CI	confidence interval
DXA	dual energy X-ray absorptiometry
GLOW	Global Longitudinal Study of Osteoporosis in Women
OR	odds ratio
POSSIBLE EU	Prospective Observational Study Investigating Bone Loss Experience in Europe
SD	standard deviation
SF-35	short-form 36

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Table 1

Baseline characteristics of women in the GLOW USA cohort and in the low -and high-risk fracture groups.

	GLOW USA cohort (n=27,957)	Low risk[a] (n=3013)	High risk[b] (n=3699)
Age (years)	69 ± 9.1	60 ± 2.5	75 ± 7.0
BMI (kg/m^2)	28 ± 6.4	29 ± 6.8	27 ± 5.9
Vitality score	61 ± 20.4	66 ± 18.7	59 ± 21.0
Physical function score	72 ± 27.7	85 ± 20.0	65 ± 28.2
Number of co-morbidities			
0	4408 (19.3)	1011 (34.2)	435 (12.6)
≥1	18,400 (80.7)	1943 (65.8)	3025 (87.4)
General health			
Excellent, very good, or good	23,275 (84.4)	2805 (93.5)	2995 (81.7)
Fair or poor	4313 (15.6)	195 (6.5)	669 (18.3)
Prescription drug coverage			
Yes	25,591 (92.4)	2841 (94.5)	3411 (92.6)
No	2094 (7.6)	167 (5.5)	274 (7.4)
Concern about osteoporosis			
Very/somewhat	23,604 (85.1)	2603 (86.4)	3228 (87.7)
Not at all	4129 (14.9)	408 (13.6)	452 (12.3)
Perceived fracture risk			
Same or lower than others	21,702 (79.6)	2597 (87.1)	2474 (68.0)
Higher than others	5558 (20.4)	386 (12.9)	1166 (32.0)
Education			
High school or less	9211 (33.5)	441 (14.7)	1363 (37.6)
More than high school	18,246 (66.5)	2564 (85.3)	2265 (62.4)
Race			
White	23,925 (86.6)	2696 (90.0)	3372 (92.1)
Non-white	3706 (13.4)	299 (10.0)	290 (7.9)

Data are mean ± SD for continuous variables and number (%) for discrete variables.

BMI, body mass index; GLOW, Global Longitudinal study of Osteoporosis in Women; SD, standard deviation.

[a] Low risk: age <65 years, no FRAX risk factors, [c] not on estrogen.

[b] High risk: age ≥65 years and prior fracture or ≥2 FRAX risk factors, [c] not on estrogen.

[c] FRAX risk factors: parental hip fracture, current smoker, prior fracture, ≥3 alcoholic drinks/day, rheumatoid arthritis, current corticosteroid use, BMI <20 kg/m^2, secondary osteoporosis.

Table 2

AOM treatment rates at baseline by risk factors for fracture (n=27,957).

Risk factors for fracture	With risk factor	Without risk factor	p value
Parental hip fracture	27.5	21.5	<0.0001
Current smoker	17.9	22.8	<0.0001
Prior fracture	33.2	19.1	<0.0001
Alcohol ≥3 drinks/day	18.1	22.5	0.31
Rheumatoid arthritis	35.8	22.5	<0.0001
Current corticosteroid use	34.7	22.0	<0.0001
Secondary osteoporosis	20.2	23.2	<0.0001
BMI <20 kg/m^2	31.1	21.6	<0.0001

Data are %.

AOM, anti-osteoporosis medication; BMI, body mass index.

Table 3

Percentages of women receiving AOM by fracture risk factors

	GLOW USA cohort (n=27,957)		Low risk (n=3013)		High risk (n=3699)	
	%	p-value[a]	%	p-value[a]	%	p-value[a]
Total	22.4		13.4		35.7	
Education		0.94		0.96		0.007
High school or less	22.4		13.4		32.8	
More than high school	22.5		13.5		37.3	
Race		<0.0001		0.97		<0.0001
White	23.5		13.5		36.6	
Non-white	16.2		13.4		24.8	
Number of comorbidities		0.57		0.01		0.26
0	22.9		15.7		38.2	
≥1	22.5		12.1		35.4	
General health		0.01		0.2		0.03
Excellent/very good/good	22.7		13.6		36.7	
Fair/poor	21.0		10.5		32.1	
Prescription drug coverage		<0.0001		<0.0001		0.004
No	13.4		2.5		27.5	
Yes	23.2		14.0		36.5	
Concern about osteoporosis		<0.0001		<0.0001		<0.0001
Very/somewhat	25.2		15.2		39.0	
Not at all	6.3		2.0		11.9	
Perceived fracture risk		<0.0001		<0.0001		<0.0001
Same/lower than others	17.3		9.6		27.5	
Higher than others	43.5		40.5		53.6	
Vitality score		<0.0001		<0.001		0.001
≤median (62.5)	21.2		10.9		33.5	
>median (62.5)	24.0		15.6		39.0	
Physical function score		0.12		0.001		0.03
≤median (85)	22.0		10.0		34.4	

	GLOW USA cohort (n=27,957)		Low risk (n=3013)		High risk (n=3699)	
	%	p-value[a]	%	p-value[a]	%	p-value[a]
>median (85)	22.8		14.7		37.9	

AOM, anti-osteoporosis medication; GLOW, Global Longitudinal study of Osteoporosis in Women.

[a] p values are from chi-square tests of differences in percentage treated between rows within risk groups.

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Table 4

Percentages of women receiving AOM by diagnosis (osteoporosis, osteopenia, or neither) and fracture risk factors.

	n	Low risk			High risk		
		Osteopenia (n=745)	Osteoporosis (n=252)	Neither (n=2016)	Osteopenia (n=839)	Osteoporosis (n=1321)	Neither (n=1539)
Total	6538	28.7	62.4	1.6	39.5	65.4	7.6
Education							
High school or less	1751	28.9	51.0	2.4	35.4	60.5	8.5
More than high school	4711	28.7	65.3	1.4	40.7	68.3	6.9
Race							
White	5920	28.5	62.7	1.3	39.8	66.4	7.4
Non-white	566	34.0	62.5	3.3	30.3	49.4	10.0
Number of comorbidities							
0	1410	30.7	68.7	2.5	46.2	76.1	10.6
≥1	4849	27.6	58.7	1.2	38.1	64.7	7.2
General health							
Excellent/very good/good	5649	29.4	61.4	1.6	40.3	69.7	7.6
Fair/poor	843	13.8	70.0	1.4	37.0	50.5	8.3
Prescription drug coverage							
No	423	3.4	20.0	0.8	31.3	54.4	9.3
Yes	6096	29.8	64.3	1.6	39.9	66.4	7.5
Concern about osteoporosis							
Very/somewhat	5683	28.9	63.3	1.8	39.9	65.4	9.1
Not at all	836	21.7	20.0	0.5	30.8	69.8	2.8
Perceived fracture risk							
Same/lower than others	4944	24.8	56.0	1.5	37.8	61.0	7.3
Higher than others	1510	42.3	70.4	4.1	43.7	69.6	9.3
Vitality score							
≤median (62.5)	3578	23.3	54.5	1.1	36.0	61.3	6.2
>median (62.5)	2939	32.8	69.5	2.1	43.9	72.5	9.6
Physical function score							
≤median (85)	3087	23.7	51.6	1.9	37.1	62.9	7.5

	n	Low risk			High risk		
		Osteopenia (n=745)	Osteoporosis (n=252)	Neither (n=2016)	Osteopenia (n=839)	Osteoporosis (n=1321)	Neither (n=1539)
>median (85)	3433	30.0	66.1	1.5	42.7	70.5	7.8

Data are %.

AOM, anti-osteoporosis medication.

Table 5

Results from logistic regression: characteristics associated with treatment with AOM in low-and high-risk women (adjusted for study site)(n=6054)

	Low risk	High risk
Increasing age (5-year increments)	1.2 (0.9–1.6)	1.2 (1.1–1.3)
Diagnosis (self-reported) of osteoporosis vs. neither	75.3 (46.5–121.9)	18.1 (14.0–23.5)
Diagnosis (self-reported) of osteopenia vs. neither	17.9 (11.9–27.0)	6.3 (4.8–8.2)
More than high school education vs. high school or less	1.2 (0.8–1.8)	1.2 (1.0–1.5)
0 vs. ≥1 co-morbidities	1.4 (1.1–1.9)	1.5 (1.1–2.0)
Prescription drug coverage vs. not	5.6 (1.9–16.4)	1.0 (0.7–1.5)
Very/somewhat vs. not at all concerned about osteoporosis	2.0 (0.9–4.3)	1.8 (1.2–2.6)
Perceived higher vs. same/lower risk of fracture than others	2.3 (1.7–3.2)	1.6 (1.3–1.9)
> vs. ≤ median vitality	1.7 (1.2–2.2)	1.6 (1.3–1.9)
> vs. ≤ median physical function	1.2 (0.8–1.7)	1.2 (1.0–1.5)

Data are OR (95% CI).

CI, confidence interval; OR, odds ratio.