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Patterns of Bone Density Evaluation in a Community Population Treated with Aromatase Inhibitors

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Abstract

Background—Aromatase inhibitors (AIs) increase risk of bone loss and fracture. Guidelines recommend routine bone density screening for women on AIs, but there are few data regarding the incorporation of these guidelines into clinical practice. We assessed bone density testing in a community-based cohort of breast cancer patients treated with AIs.

Methods—Using encounter and pharmacy data from WellPoint plans in the HealthCore Integrated Research Database, we assessed bone density testing among 9138 women aged ≥50 years with breast cancer who were treated with AIs between 2002 and 2008. We used multivariable logistic regression to identify factors associated with baseline bone density testing in women initiating an AI, and, among a subset of 2086 women treated with AIs for at least 2 years, with testing during the first 2 years of therapy.

Results—Only 41.6% of women underwent bone density testing when initiating AI therapy. Rates of bone density testing increased over time, but were lower for women who were older, lived in the Northeast (vs. other regions), had been treated with prior proton pump inhibitor or tamoxifen therapy, lived in areas with lower educational attainment, or were enrolled in a health maintenance organization (vs. other insurance types) (all P<.05). Among women treated with AIs for at least 2 years, 59.9% of women underwent bone density testing during the first 2 years of AI therapy. Rates of testing were lower for women living in the Midwest or West (vs. Northeast), living in areas with lower education levels, enrolled in health maintenance organizations (vs. other insurance types) and with prior tamoxifen use.

Conclusions—Most women initiating AI therapy, and 40% of those on long-term therapy, did not undergo recommended bone density evaluation in this community-based population. Attention is needed to ensure that unnecessary fractures are avoided in breast cancer patients taking AIs.

Keywords

Aromatase inhibitor; breast cancer; bone density

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Recognition of the increased risk of fracture in patients treated with aromatase inhibitors has led to the development of guidelines for management of bone integrity in patients treated with these agents. The American Society of Clinical Oncology convened an expert panel in 2002 to review available evidence and provide recommendations for maintaining bone health in women with breast cancer [1]. The panelists concluded that women treated with aromatase inhibitors were at high risk of bone-related complications and recommended regular monitoring of bone density to assess the need for bisphosphonate therapy. They also suggested that oncologists take a more active role in monitoring bone density and treating bone loss, rather than leaving management of bone health to primary care providers. The National Comprehensive Cancer Network also began to recommend bone density testing for women treated with aromatase inhibitors in the NCCN Breast Cancer Clinical Practice Guidelines in 2005 [2]. The NCCN convened a multidisciplinary task force on bone health in cancer care in early 2006 and in 2009 [3, 4], and recommended baseline and regular follow up bone density testing for women treated with an aromatase inhibitor, as well as the use of pharmacologic therapy and lifestyle modification for patients with osteopenia and osteoporosis. Finally, guidelines published by Hadji et al in 2008 [5] and updated in 2011[6] also recommend baseline bone density evaluation as well as repeat testing every 1–2 years.

Although guidelines recommend routine bone density testing in breast cancer patients being treated with aromatase inhibitors, there are few data evaluating the incorporation of these recommendations into clinical practice. We sought to evaluate patterns of bone density testing in a population of community-based breast cancer patients treated with these agents.

METHODS

Data

We obtained data from the HealthCore Integrated Research Database (HIRD^{SM}) from 2001 through 2008, from which we identified patients with an index diagnosis of breast cancer during 2002 through 2007. HealthCore is an independent subsidiary of WellPoint, Inc, and the HIRD, one of the largest fully integrated commercial payer databases in the U.S., contains data on inpatient and outpatient visits, prescriptions filled, and laboratory and radiographic testing for patients enrolled in large health plans across the United States. At the time of this study, the HIRD contained approximately 30 million members (including individuals aged >65 years) enrolled in indemnity plans, preferred provider organizations, health maintenance organizations, and point of service plans.

Cohort

We identified 49,697 women aged ≥50 years who were enrolled a minimum of 6–12 months before the first of at least 2 diagnosis codes for breast cancer during 2002–2007. We excluded 5234 women with codes for metastatic cancers through 2008. Among the remaining 44,463 women, we used pharmacy data to assess use of aromatase inhibitors (anastrozole, exemestane, or letrozole) and identified 9138 women who initiated treatment with an aromatase inhibitor during 2002 through 2008. The first observed pharmacy dispensing of an aromatase inhibitor was used as the index date.

Bone density testing

Bone density testing was ascertained based on administrative codes [7]. These included Current Procedural Terminology (CPT) codes 76070, 76071, 76075, 76076, 76077, 76078, 76977, 77078, 77079, 77080, 77081, 77082, 77083, 78350, 78351, and G0131, International Classification of Diseases, 9th edition (ICD-9) Procedure code 88.98 and ICD-9 Diagnosis code V82.81. We ascertained bone density at baseline, defined as the period from 6 months before the index date through 6 months after, for all women. In addition, among a subset of

2086 women who received at least 2 years of continuous aromatase inhibitor therapy (who initiated an aromatase inhibitor in 2002–2006), we ascertained receipt of any bone density testing during the initial 2 years of aromatase inhibitor therapy.

Independent variables

We obtained data on each woman's age, insurance product, and zip code of residence from HealthCore. We linked the zip codes to 2000 U.S. Census data to identify Census Region (Northeast, Midwest, South, West), urban/rural location of residence (large metropolitan, smaller metropolitan, large urban, small urban, rural, unknown), and socioeconomic characteristics of the residence zip code, including the proportion of adults with at least a high school education, median household income, proportion of residents of black race, and proportion of residents of Hispanic ethnicity (categorized in quartiles). We also classified patients' insurance product type (health maintenance organization, preferred provider organization, point of service/fee-for-service, other) and documented the year the patient initiated aromatase inhibitor therapy.

We characterized comorbid illnesses based on inpatient and outpatient encounters during the year before the index date using the Klabunde modification of the Charlson score, categorized as 0, 1, 2, ≥3 [8, 9]. We also created indicator variables for use of proton pump inhibitors and bisphosphonates during the year before the first dose of aromatase inhibitor therapy. Proton pump inhibitors have been associated with fracture risk [10], and bisphosphonate use suggests that patients are already being treated for bone loss. Finally, we identified whether patients had been on tamoxifen in the year before initiating aromatase inhibitor therapy since tamoxifen increases bone density [11], which may influence testing behavior.

Statistical analyses

Women were censored on December 31, 2008 (the last date for which data were available) or sooner if they died or disenrolled from the plan.

Our primary analysis examined factors associated with bone density testing at baseline (during the period six months before to six months after a first prescription for an aromatase inhibitor was filled). Relationships between patient characteristics and rates of bone density screening were evaluated using multivariable logistic regression. Independent variables included all variables described above.

We next assessed bone density testing among a subset of 2086 women who received at least 2 years of continuous aromatase inhibitor therapy. We used multivariable logistic regression to assess factors associated with receipt of bone density testing during the first 2 years of aromatase inhibitor therapy. In sensitivity analyses, we also assessed bone density testing from 6 months before the first dose of an aromatase inhibitor through the 2 years of therapy for this cohort treated with aromatase inhibitors continuously for at least 2 years.

RESULTS

Characteristics of the 9138 patients who filled an initial prescription for an aromatase inhibitor during the study period are listed in Table 1. The mean (standard deviation) age was 64.6 (8.5) years, the majority of women initiated aromatase inhibitor therapy after 2004, 90% had a Charlson Comorbidity score of 0, 12% were taking bisphosphonates in the year before aromatase inhibitor initiation, and 18% had taken tamoxifen before initiating an aromatase inhibitor.

Characteristics of patients continuously treated with an aromatase inhibitor for at least 2 years are listed in Table 2. Characteristics were overall similar to those of patients filling an initial prescription for an aromatase inhibitor, although the proportion of patients who had previously taken tamoxifen was slightly higher (22%). As in the full cohort, 12% of patients were treated with a bisphosphonate in the year before aromatase inhibitor initiation. In this cohort of patients treated with at least 2 years of aromatase inhibitor therapy, an additional 6% of patients (N=115) initiated bisphosphonate therapy during the first 2 years of treatment with an aromatase inhibitor.

Baseline bone density evaluation

Overall, 41.6% of women underwent bone density testing in the period 6 months prior to initiation of an aromatase inhibitor through 6 months after the first dose. The unadjusted proportion of women who received bone density testing is also included in Table 1. The proportion of women who underwent baseline bone density testing increased during the study period, with 26.6% of women undergoing bone density testing in 2002 and 44.7% in 2008 ($p<0.001$).

Factors associated with undergoing baseline bone density testing in adjusted analyses are included Table 1 (right columns). Women who were younger, lived in the Midwest, South, or West (vs. Northeast), initiated aromatase inhibitor therapy in later years, or had a Charlson comorbidity score of 1 (vs. 0) were more likely to undergo bone density testing. Women treated with a proton pump inhibitor at baseline were less likely to undergo bone density testing, although this finding was of borderline statistical significance (P=.054). Women who were on a bisphosphonate in the year before starting aromatase inhibitor therapy were more likely to undergo baseline bone density testing. Women who were enrolled in a health maintenance organization (vs. other plan types), lived in areas with fewer high school graduates or with a higher proportion of black residents (quartile 2 vs. 1) were significantly less likely to undergo baseline bone density evaluation, as were women treated with tamoxifen prior to initiating an aromatase inhibitor.

Bone density evaluation during long-term aromatase inhibitor use

Among the 2086 women who filled prescriptions for an aromatase inhibitor for at least 2 years, 59.9% underwent bone density testing during the initial 2 years of aromatase inhibitor therapy. The unadjusted proportion of women undergoing bone density testing by each patient characteristic is included in Table 2.

Factors associated with bone density testing in this group in adjusted analyses are also included in Table 2 (right columns). Women living in the Midwest or West (vs. Northeast) and women enrolled in a health maintenance organization (vs. other insurance types), women living in areas with the fewest high school graduates, and those who had used tamoxifen before aromatase inhibitor therapy were significantly less likely than others to undergo bone density evaluation during long-term aromatase inhibitor therapy. Other factors were not significantly associated with bone density testing.

In sensitivity analyses where we assessed bone density testing during the 6 months before through 2 years after initiation of an aromatase inhibitor for this subset of women, we found that 69.5% of women had undergone bone density testing, and the associations of patient factors and bone density testing were similar.

DISCUSSION

Since 2003, guidelines have recommended that women treated with aromatase inhibitors undergo regular bone density evaluation [1, 3]. To our knowledge, our study provides the

first data evaluating the incorporation of these guidelines into routine clinical practice. In our cohort of privately insured women with breast cancer, only 41.6% of patients initiating therapy with an aromatase inhibitor underwent baseline evaluation of bone density, and 40.1% of patients treated with an aromatase inhibitor for at least 2 years did not undergo bone density testing during their first 2 years of therapy. Although rates of bone density testing did increase over time, only 44.7% of patients who initiated an aromatase inhibitor in 2008 (the last year included in our analysis) underwent baseline bone density testing.

Several patient characteristics were associated with an increased likelihood of undergoing baseline bone density testing. Women who were older and women treated with proton pump inhibitors, who may be at increased risk of fractures, were significantly less likely than younger women to undergo baseline bone density testing. Women living in areas with fewer high school graduates or more black residents, and women living in the Northeast were also less likely than other women to undergo baseline bone density testing, suggesting that where one lives could be more important than clinical risk factors in determining receipt of recommended care. Women enrolled in health maintenance organizations (vs. other plan types) were also less likely to undergo baseline bone density, a surprising finding, since patients in health maintenance organizations typically receive more preventive care than other patients. The lower rates of testing among women who received tamoxifen prior to aromatase inhibitor therapy may have been influenced by the favorable effect of tamoxifen on bone density.

Among long-term aromatase inhibitor users, we found fewer characteristics associated with bone density testing, which may be partly related to decreased power due to our smaller sample size. Nevertheless, as for baseline bone density testing, we found lower rates of bone density testing among women enrolled in a health maintenance organization, women living in areas with fewer high school graduates, and women previously treated with tamoxifen. In this analysis, unlike the analysis of baseline bone density testing, we observed that women living in the Northeast had higher rates of bone density testing than women in other areas.

Two prior reports have used the Survival, Epidemiology, and End Results (SEER)-Medicare database to compare rates of bone density testing in older breast cancer survivors and age-matched controls. These studies found that 8.6% of 5662 older long-term breast cancer survivors and 6.8% of age-matched controls underwent bone density testing during a one-year study period in the late 1990's [12]; these rates increased over time with 18.2% of older breast cancer survivors undergoing bone density testing in 2002 [13], compared with 17.5% of controls. The higher rates of testing that we observed likely reflect our focus on women initiating aromatase inhibitor therapy and the more recent study period. To our knowledge, our study represents the first evaluation of bone density evaluation practices in community-based patients initiating treatment with aromatase inhibitors.

Aromatase inhibitors have largely become the hormonal therapy of choice for postmenopausal women diagnosed with early-stage, hormone receptor-positive breast cancer. The drugs were initially granted accelerated approval by the FDA for use in the adjuvant setting in 2002, with full approval granted in 2005. Randomized trials have demonstrated that aromatase inhibitors are relatively safe drugs with low rates of discontinuation due to adverse events.[14–16] However, use of the drugs can lead to bone loss and fracture. Fracture rates in patients treated with aromatase inhibitors have ranged from 2.4% in the Arimidex-Nolvadex (ARNO) 95/Austrian Breast and Colorectal Study Group (ABCSG) 8 studies [17], where an aromatase inhibitor was given after 2 years of tamoxifen, to 11% in the Anastrozole or Tamoxifen Alone or in Combination (ATAC) study [18], where patients were treated with 5 years of aromatase inhibitor therapy.

A number of studies have shown that aromatase inhibitor-induced bone loss can be prevented or ameliorated with the use of concomitant bisphosphonates [19–22]. For example, the Zometa-Femara Synergy Trial (Z-FAST) demonstrated that postmenopausal women initiating adjuvant letrozole who were randomized to immediate zoledronic acid experienced less bone loss compared to women randomized to delayed zoledronic acid [22]. These findings were confirmed in the ZO-FAST [21] and E-ZO-FAST [19] trials. None of these studies demonstrated differences in fracture rates, although the absolute risk of fractures was low, and the studies were likely underpowered to assess a difference. Despite these results, concern over long-term side effects of bisphosphonates, such as osteonecrosis of the jaw and spontaneous hip fracture, as well as the lack of difference in fracture rates, have limited the routine incorporation of concomitant bisphosphonate therapy into the adjuvant treatment of women initiating aromatase inhibitors for early breast cancer. For example, in our study, only 18% of women received any bisphosphonate before or during the first 2 years of treatment with an aromatase inhibitor. It is not possible to determine from our data whether these women initiated bisphosphonates in response to a decrease in bone density or to prevent this from happening, but the low rates suggest that most women initiating an aromatase inhibitor are not routinely started on bisphosphonate therapy. It is worth noting that neither ASCO [1] nor the NCCN [3] recommends routine use of bisphosphonates in patients treated with an aromatase inhibitor, unless dictated by bone loss.

Ongoing studies are evaluating the additional benefits of prolonged aromatase inhibitor therapy, given for durations of 10 years or more, on the risk of breast cancer recurrence [23]. The impact of prolonged aromatase inhibition on bone integrity is not yet known, but careful attention to decrements in bone density will be important, as the rate of decline among women in randomized controlled trials suggests that many women will develop osteoporosis with prolonged aromatase inhibitor therapy. Bisphosphonates are likely to benefit these women, based on evidence for reducing fractures among individuals with postmenopausal osteoporosis [24].

Our study suggests that many women initiating and receiving long-term aromatase inhibitor therapy do not undergo recommended bone density evaluation. If these patterns continue, many women who are cured of their early-stage breast cancers could develop bone loss and fractures as a result of their cancer therapy. A recent study of 228 breast cancer survivors who developed hip fractures following breast cancer therapy demonstrated significant functional decline in the ensuing 12 months, with difficulties in performing many activities of daily living [25]. Given the morbidity and mortality that is associated with hip and other fractures, it will be increasingly important that bone-protective guidelines are incorporated more widely into oncology practices. Increased awareness of the impact of aromatase inhibitors on bone density among medical oncologists, and better communication about these side effects to primary care physicians who often coordinate bone density evaluation, will be essential in ensuring that breast cancer patients taking aromatase inhibitors undergo adequate bone density screening.

A few limitations of our study should be acknowledged. Our analyses included data from 2002–2008. Since aromatase inhibitors were granted accelerated FDA approval in 2002 for use in the adjuvant setting and full approval for this purpose in 2005, physicians may not have been as aware of the impact of the drugs on bone density in the first years of our study period. Although the ATAC study demonstrated an increased risk of fracture in patients treated with anastrozole compared to those taking tamoxifen and guidelines began to recommend bone density evaluation in patients taking aromatase inhibitors as early as 2003, several studies documenting the extent of bone loss seen with the drugs, such as the Z-FAST [22] and ZO-FAST [21] trials, were not published until later in this period. Thus, our data may not be completely representative of current practices of bone density evaluation in

women treated with aromatase inhibitors. We were also only able to determine whether bone density testing was performed; it is possible that bone density testing was discussed or ordered for patients by their treating physicians, but that patients did not undergo recommended testing. Additionally, although most women initiating adjuvant endocrine therapy should continue treatment for at least 5 years, only 23% of women in our cohort continued on aromatase inhibitors for 2 or more years. This relatively small number is likely related to censoring of our data at the end of 2008 and to nonadherence with aromatase inhibitor therapy [26], since we focused on women who were continuously treated with aromatase inhibitors. Other limitations included incomplete information about the physicians who prescribed aromatase inhibitors and about the physicians who ordered bone density testing, restriction of the study population to women with private health insurance, and lack of information about race/ethnicity and socioeconomic status at the individual level.

In conclusion, our data suggest that many breast cancer patients treated with aromatase inhibitors are not undergoing recommended bone density testing. Testing rates appear to be lower in some individuals who are at increased risk of bone-related complications, including older women and women treated with medications that could increase fracture risk. Although data suggest that concomitant use of bisphosphonates can prevent aromatase inhibitor-induced bone loss, this practice has not become part of routine clinical practice. Thus, increased awareness of the detrimental effects of aromatase inhibitors on bone density and better adherence to screening guidelines are needed to prevent unnecessary fractures in breast cancer patients treated with aromatase inhibitors.

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Table 1

Characteristics of the cohort and receipt of bone density testing at baseline among women initiating aromatase inhibitor therapy in 2002–2008, N=9138

	N (%)	Unadjusted proportion of women with bone density testing	P value*	Adjusted Odds Ratio (95% Confidence Interval*)	P value†
	9138	41.6			
Age			<0.001		
51–59	2748 (30)	44.5		1.00	-
60–63	2168 (24)	45.3		1.03 (0.91 to 1.15)	0.66
64–68	1940 (21)	41.1		0.85 (0.75 to 0.96)	0.01
69+	2282 (25)	34.9		0.64 (0.56 to 0.72)	<0.001
Census Region			<0.001		
Northeast	1999 (22)	37.0		1.00	-
Midwest	992 (11)	48.6		1.83 (1.57 to 2.12)	<0.001
South	1719 (19)	45.2		1.26 (1.06 to 1.50)	0.009
West	4428 (48)	40.1		1.20 (1.04 to 1.39)	0.01
Year first dose of AI			<0.001		
2002	658 (7)	26.6		1.00	-
2003	650 (7)	36.2		1.52 (1.20 to 1.94)	<0.001
2004	1341 (15)	41.5		1.97 (1.60 to 2.44)	<0.001
2005	1833 (20)	45.6		2.26 (1.84 to 2.78)	<0.001
2006	2048 (22)	44.1		2.16 (1.76 to 2.65)	<0.001
2007	2250 (25)	41.4		1.94 (1.58 to 2.39)	<0.001
2008	358 (4)	44.7		2.02 (1.53 to 2.68)	<0.001
Charlson Comorbidity Index*			0.02		
0	8242 (90)	41.2		1.00	-
1	729 (8)	46.8		1.28 (1.09 to 1.50)	0.002
2	114 (1)	37.7		1.05 (0.71 to 1.57)	0.80
≥3	53 (1)	35.9		0.87 (0.49 to 1.56)	0.64
Proton pump inhibitor in year before AI			0.006		
No	8386 (92)	42.0		1.00	-

	N (%)	Unadjusted proportion of women with bone density testing	P value*	Adjusted Odds Ratio (95% Confidence Interval*)	P value†
Yes	752 (8)	36.8		0.86 (0.73 to 1.00)	0.054
Bisphosphonates in year before AI			<0.001		
No	8067 (88)	40.8		1.00	-
Yes	1071 (12)	47.6		1.33 (1.16 to 1.51)	<0.001
Tamoxifen use before AI			0.054		
No	7503 (82)	42.0		1.00	-
Yes	1635 (18)	39.5		0.86 (0.76 to 0.97)	0.01
Insurance product			<0.001		
Health maintenance	1681 (18)	30.5		1.00	-
Preferred provider	5772 (63)	43.9		1.90 (1.69 to 2.15)	<0.001
Point of service/fee-for-	1089 (12)	39.7		1.61 (1.36 to 1.91)	<0.001
Other	596 (7)	53.9		3.26 (2.67 to 3.99)	<.001
% with high school degree in zip code of residence, quartiles			<0.001		
Quartile 1 (lowest)	1945 (21)	36.9		1.00	-
Quartile 2	1854 (20)	42.1		1.33 (1.16 to 1.53)	<0.001
Quartile 3	2151 (24)	41.6		1.32 (1.15 to 1.52)	<0.001
Quartile 4 (highest)	2230 (24)	45.6		1.54 (1.31 to 1.80)	<0.001
Unknown	958 (10)	40.8		1.04 (0.84 to 1.28)	0.74
% African Americans in zip code of residence, quartiles			0.04		
Quartile 1 (lowest)	1945 (21)	43.2		1.00	-
Quartile 2	2158 (24)	43.2		1.00 (0.87 to 1.14)	0.95
Quartile 3	2115 (23)	39.1		0.82 (0.71 to 0.94)	0.003
Quartile 4	1962 (21)	41.3		0.91 (0.78 to 1.05)	0.20
Unknown	958 (10)	40.8		1.04 (0.84 to 1.28)	0.74
% Hispanics in zip code of residence, quartiles			<0.001		
Quartile 1 (lowest)	1683 (18)	45.0		1.00	-
Quartile 2	1980 (22)	43.9		1.00 (0.86 to 1.16)	0.98
Quartile 3	2301 (25)	41.3		0.99 (0.84 to 1.17)	0.90
Quartile 4	2216 (24)	37.6		1.09 (0.90 to 1.33)	0.36

	N (%)	Unadjusted proportion of women with bone density testing	P value*	Adjusted Odds Ratio (95% Confidence Interval*)	P value†
Unknown	958 (10)	40.8		1.04 (0.84 to 1.28)	0.74

*Using the chi square test.

†Using logistic regression and adjusting for all variables in the table.

AI=Aromatase inhibitor

Table 2

Characteristics of women who took an AI for at least 2 years and receipt of bone density testing during first 2 years of treatment among women initiating bone density therapy in 2002–2006, N=2086

	N (%)	Unadjusted proportion of women with bone density testing	P value*	Adjusted Odds Ratio (95% Confidence Interval*)	P value†
	2086	59.9			
Age			0.33		
51–59	621 (30)	59.9		1.00	-
60–63	615 (29)	62.6		1.17 (0.92 to 1.49)	0.21
64–68	434 (21)	57.1		0.98 (0.75 to 1.29)	0.89
69+	416 (20)	58.9		0.98 (0.73 to 1.31)	0.87
Census Region			<0.001		
Northeast	194 (9)	71.1		1.00	-
Midwest	187 (9)	66.8		0.57 (0.35 to 0.93)	0.02
South	346 (17)	67.4		0.85 (0.56 to 1.29)	0.44
West	1359 (65)	55.6		0.54 (0.36 to 0.82)	0.004
Year first dose of AI			0.005		
2002	271 (13)	59.8		1.00	-
2003	282 (14)	51.8		0.73 (0.51 to 1.04)	0.08
2004	491 (24)	57.6		0.93 (0.67 to 1.28)	0.65
2005	561 (27)	61.7		0.94 (0.68 to 1.30)	0.71
2006	481 (23)	65.1		1.06 (0.76 to 1.50)	0.73
Charlson Comorbidity Index*			0.89		
0	1911 (92)	59.8		1.00	-
1	142 (7)	62.7		1.06 (0.73 to 1.54)	0.75
2	22 (2)	59.1		0.78 (0.32 to 1.90)	0.59
≥3	11 (1)	54.6		0.66 (0.20 to 2.23)	0.50
Proton pump inhibitor in year before AI			0.22		
No	1939 (93)	60.3		1.00	-
Yes	147 (7)	55.1		0.77 (0.54 to 1.10)	0.15

	N (%)	Unadjusted proportion of women with bone density testing	P value*	Adjusted Odds Ratio (95% Confidence Interval*)	P value†
Bisphosphonates in year before AI			0.20		
No	1833 (88)	59.4		1.00	-
Yes	253 (12)	63.6		1.26 (0.94 to 1.68)	0.12
Tamoxifen use before AI			0.004		
No	1622 (78)	61.6		1.00	-
Yes	464 (22)	54.1		0.75 (0.60 to 0.94)	0.01
Insurance product			<0.001		
Health maintenance organization	375 (18)	38.7		1.00	-
Preferred provider organization	1308 (63)	65.5		3.10 (2.41 to 3.99)	<0.001
Point of service/fee-for- service	232 (11)	57.3		1.98 (1.40 to 2.82)	<0.001
Other	171 (8)	67.3		3.52 (2.34 to 5.31)	<0.001
% with high school degree in zip code of residence, quartiles			<0.001		
Quartile 1 (lowest)	429 (21)	50.6		1.00	-
Quartile 2	397 (19)	64.0		1.67 (1.23 to 2.26)	<0.001
Quartile 3	493 (24)	58.0		1.26 (0.93 to 1.69)	0.13
Quartile 4 (highest)	649 (31)	64.1		1.49 (1.05 to 2.10)	0.02
Unknown	118 (6)	65.3		1.00 (0.58 to 1.73)	0.99
% African Americans in zip code of residence, quartiles			0.18		
Quartile 1 (lowest)	474 (23)	62.9		1.00	-
Quartile 2	554 (26)	58.7		0.94 (0.72 to 1.23)	0.64
Quartile 3	517 (25)	56.5		0.89 (0.67 to 1.17)	0.40
Quartile 4 (highest)	423 (20)	61.0		0.99 (0.72 to 1.36)	0.97
Unknown	118 (6)	65.3		1.00 (0.58 to 1.73)	0.99
% Hispanics in zip code of residence, quartiles			<0.001		
Quartile 1 (lowest)	305 (15)	68.9		1.00	-
Quartile 2	436 (21)	65.8		0.94 (0.64 to 1.37)	0.74
Quartile 3	599 (29)	61.6		0.91 (0.60 to 1.38)	0.66
Quartile 4 (highest)	628 (30)	48.9		0.68 (0.43 to 1.06)	0.09
Unknown	118 (6)	65.3		1.00 (0.58 to 1.73)	0.99

* Using the chi square test.

† Using logistic regression and adjusting for all variables in the table.
AI=Aromatase inhibitor