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Patient Reported Reasons for Non-Adherence to Recommended Osteoporosis Pharmacotherapy

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Abstract

Objectives—As many as half of the patients recommended for osteoporosis pharmacotherapy do not take their medications. We examined patient characteristics associated with non-adherence to

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Potential Conflicts of Interest Disclosure

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Previous Presentations

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recommended pharmacotherapy, as well as their reasons for non-adherence in order to identify intervention targets.

Methods—Data come from the Patient Activation after DXA Result Notification (PAADRN) study, a randomized controlled trial of 7,749 patients 50 years old or older presenting for DXA at three health centers in the United States. We focused on the 790 patients who reported receiving a recommendation for new pharmacotherapy at baseline. Using Pearson Chi-squared tests for categorical variables, two sample t-tests for continuous variables, and multivariable multinomial logistic regression, we compared those who reported starting the recommended medication (adherers) to temporary non-adherers and non-adherers on demographics, health habits, DXA impression, FRAX risk, and osteoporosis knowledge, and examined their stated reasons for non-adherence.

Results—Mean age was 66.8 (SD = 8.9), 87.2% were women, and 84.2% were white. One-fourth (24.8%) reported that they did not start their recommended pharmacotherapy. In the unadjusted analyses, the only factor significantly associated with non-adherence was osteoporosis knowledge, with those having better knowledge less likely to take their medications ($p < 0.05$). The most common reasons for non-adherence were fear of side effects (53.3%), a dislike of taking medicine (25.3%), and the belief that the medicine would not help their condition (16.7%).

Conclusion—One in four patients recommended for osteoporosis pharmacotherapy declined treatment because they feared potential side effects, don't like taking medicine, or felt that the medication would not help their condition. Improved patient counseling regarding the potential side effects of osteoporosis treatment and the risk-benefit ratio for these medications may increase adherence.

Introduction

Osteoporosis is a progressive disease of the skeletal system that is associated with decreased bone mass that leads to bone fragility and increased fracture risk. Currently, about 10.2 million adults 50 years old and older have osteoporosis and another 43.4 million have low bone mass (osteopenia).¹ Fractures that result from osteoporosis contribute to functional decline, greater morbidity, the need for nursing care, and increased mortality.²⁻⁴ The direct and indirect costs of osteoporotic fractures are a substantial burden on individuals, families, and society.

For most patients with osteoporosis or osteopenia, guidelines developed by the National Osteoporosis Foundation (NOF) recommend the use of osteoporosis medications, primarily bisphosphonates, to slow disease progression. Adherence to these medications is associated with decreased fracture rates within three years of initiation.⁵⁻⁹ Similarly, adherence to treatments over longer periods (up to 14 years) is associated with reduced fracture rates, with individuals who were non-adherent for longer periods having greater fracture risks than those who were non-adherent for shorter periods.¹⁰

To quantify the impact that bisphosphonates have had on fracture reduction, Ethel and colleagues reviewed seven years of data from two large claims databases. They estimated that approximately 144,000 fractures were prevented in women 45 years old and older who adhered to pharmacotherapy.¹¹ Despite evidence that adherence to osteoporosis medications

can significantly reduce fracture risk and the subsequent morbidity, mortality, and costs, adherence to these medications has been suboptimal with estimated non-adherence rates between 30% and 50% of patients prescribed pharmacotherapy.¹²

Predictors of non-adherence include drug type, cost, dosing regimen, adverse effects, provider follow-up, the asymptomatic nature of the disease, and patient beliefs about safety and the necessity of medication.^{13–17} Identifying the characteristics of patients mostly likely to be non-adherent and their reasons for being non-adherent may help healthcare providers, such as pharmacists, appropriately tailor patient counseling and education efforts to maximize adherence. To our knowledge PAADRN (Patient Activation after DXA Result Notification) is the first prospective study that has provided patient-identified reasons for non-adherence in addition to known predictors of adherence.

Objective

Our goal was to identify reasons patients stated for not starting osteoporosis treatment prescribed by their healthcare provider, and to identify patient characteristics that might predict non-adherence.

Methods

Study Design and Participants

PAADRN was a double-blinded, pragmatic randomized controlled trial examining the effects of a patient-activation intervention on osteoporosis pharmacotherapy, patient satisfaction, osteoporosis knowledge, and quality of life. The study design, randomization procedures, outcome measures and the results for several of the primary outcomes have previously been reported.^{18–22} The study protocols and consent procedures were approved by each participating site's institutional review board.

We enrolled patients presenting for DXA at three sites: the University of Iowa Hospitals and Clinics (UI), the University of Alabama at Birmingham (UAB), and Kaiser Permanente of Georgia (KPGA). We screened patients who were 50 years old and older presenting for DXA at these sites between February 2012 and August 2014. We excluded those who were unable to read or speak English, prisoners, and patients with cognitive impairment that would prevent them from providing informed consent. Within blocks based on their prior DXA ordering volume, physicians were randomized to three groups resulting in their patients being assigned to receive a personalized DXA result letter and an educational osteoporosis brochure, or to receive usual care per the practice of their provider or organization. For these analyses, we included only patients whose providers recommended that they begin pharmacotherapy for osteoporosis or osteopenia based on their index DXA.

Measures

Patients completed a baseline interview and were then contacted at 12- and 52-weeks post-DXA for follow-up interviews. At baseline, information was collected regarding patient demographics, health history, health habits, prior osteoporosis diagnosis or treatment,

osteoporosis knowledge using the Osteoporosis and You scale (scale items are provided in Table 1)²³, patient activation, osteoporosis health beliefs and osteoporosis self-efficacy. We also collected results from their index DXA including T-scores, femoral neck BMD, and the interpreting physician's impression (normal, osteopenia or osteoporosis). Based on information from the patient survey and DXA results, FRAX 10-year fracture risks were calculated for all patients (FRAX, online v3.6).²⁴ The 12- and 52-week follow-up interviews included many of the same measures used in the baseline interview. Additionally, patients were asked if their provider recommended a new or different medication. Patients who reported receiving a new or different recommendation for osteoporosis pharmacotherapy were asked if they had started it. Those who stated they did not start the new medication were asked why they did not start it as an open-ended question. Interviewers then categorized these patient reports according to the Medicare Current Beneficiary Survey protocol (i.e. afraid of medicine reactions/contraindications, didn't think medicine would help condition, not covered by insurance plan) and read that categorization back to the patient for their confirmation.²⁵ Non-adherence was defined as not taking a medication that was prescribed for bone health.

Statistical Analysis

We compared those who reported starting the recommended medication (adherers) and those who did not (non-adherers and temporary non-adherers) on demographics, health habits, DXA impression, FRAX risk, and osteoporosis knowledge using Pearson Chi-squared tests for categorical variables, and F-tests for continuous variables. We used multiple multinomial logistic regression with backwards selection (due to the small sample size) to evaluate the effects of these characteristics on adherence vs. temporary non-adherence vs. non-adherence. Finally, we present patients' reasons for non-adherence grouped by the medication that they were prescribed.

Results

Participant Characteristics

Of the 7,749 PAADRN patients, 790 reported at 12-weeks post-DXA that their healthcare provider had prescribed a new or different osteoporosis medication. The mean age of this group was 66.8 years (± 8.9), 87.2% were women, and 84.2% were White. One-fourth (24.8%, $n = 196$) reported that they did not start the newly prescribed medication at the time of their interview. We sub-classified the 196 non-adherers based on their reasons for non-adherence, with 46 (5.8%) indicating only temporary non-adherence (such as waiting until another procedure was performed, waiting to schedule an infusion appointment, or waiting to see if the medicine would be covered by their insurance) and 150 (19.0%) indicating that they decided not to take the prescribed medication at all. We then looked at the 46 temporary non-adherers at 52-weeks post-DXA to see if they had started the recommended medication and found that 21 (45.6%) had done so, while 16 (34.8%) still had not started a medication and 9 (19.6%) were lost to follow-up. Of the 21 temporary non-adherers who became adherers by 52-weeks post-DXA, 20 (95.2%) were on the medication that had originally been prescribed for them.

Predictors of Non-adherence

In the unadjusted analyses the only factor significantly associated with non-adherence was osteoporosis knowledge (overall $p < 0.05$, Table 1). Pairwise comparisons indicated that temporary non-adherers had significantly more correct responses on the knowledge scale than did adherers ($p = 0.017$), and also had a trend toward more correct responses than non-adherers (p value = 0.121). When looking at the individual items in the osteoporosis knowledge scale, both temporary non-adherers and adherers were more likely to recognize that osteoporosis is a preventable disease than adherers ($p = 0.015$ and $p = 0.069$, respectively). The final model (not shown) from the backwards selection multivariable multinomial logistic regression revealed only two statistically significant effects. Temporary non-adherers had better osteoporosis knowledge than adherers (adjusted odds ratio [AOR] = 1.128, $p = 0.027$), and non-adherers had greater self-efficacy for exercise (AOR = 1.116, $p = 0.033$).

Reasons for Non-adherence

Table 2 shows the drugs prescribed for adherers, temporary non-adherers, and non-adherers, and the reasons that patients reported for not starting each of these medications. Overall, fear of side effects or contraindications was the most frequently reported reason (53.3%) for non-adherence to newly prescribed osteoporosis medications. The next two most frequently cited reasons were not liking to take medicines (25.3%) and thinking that the medicine would not help their condition (16.7%).

Discussion

Understanding factors associated with patient non-adherence to recommended osteoporosis pharmacotherapy and the reasons for that non-adherence may facilitate tailoring interventions and counseling to improve pharmacotherapy acceptance. We found that of the 7,749 patients 790 had been recommended to start new or different osteoporosis medications after their study DXA. Of these 790 patients, 5.8% were temporarily non-adherent and 19.0% were non-adherent. Patients who had better osteoporosis knowledge were more likely to be temporary non-adherers than adherers, and patients who had greater self-efficacy for exercise were more likely to be non-adherers than adherers. The most common reasons offered by patients for their non-adherence were the fear of side effects or contraindications 53.3%, a dislike for taking medications (25.3%), and believing that the prescribed medication would not improve their condition (16.7%). These reasons support existing literature that describes predictors of non-adherence.^{15,26–28}

It is possible that due to their significantly better osteoporosis knowledge, temporary non-adherers may have realized that lifestyle changes can have important impacts on bone health and that patients with greater self-efficacy for exercise may have tried to make such changes rather than starting pharmacotherapy. This explanation is further supported by the fact that both temporary non-adherers and non-adherers were more likely to correctly identify osteoporosis as a preventable disease. That said, only 4.7% of non-adherent patients reported that they were trying lifestyle changes in lieu of medication.

Alternatively, our results may indicate that it is difficult for the general population to discern the difference between prevention and treatment. Individuals who don't know that osteoporosis is preventable may be adherent to medications because they assume that they will always have the disease and must take osteoporosis medications as the only way to treat the condition. Conversely, non-adherers with better osteoporosis knowledge may have been more aware of the potential side effects of osteoporosis medications, particularly those associated with bisphosphonates. That would be consistent with the fact that 46.4% reported a fear of side effects as their reason for non-adherence, and with the numerous reports of rare cases of osteonecrosis of the jaw, atypical femur fractures, and esophageal cancer that were brought to public attention in the mid to late 2000s as a result of bisphosphonate use. Indeed, Jha et al. reported spikes in news coverage and Internet search activity for bisphosphonates after several significant landmarks in media reports of pharmaceutical litigation regarding these adverse effects.²⁹ This was followed by a 50% decrease in bisphosphonate use reported in data from the Medical Expenditure Panel Survey. Although the more common side effects of bisphosphonates, such as gastrointestinal disturbance, may be easily avoided by following proper administration instructions, the bad publicity that bisphosphonates received from these very rare side effects may have lingered in patients' minds and led to their non-adherence.

The third most common reason for non-adherence was a dislike for taking medications, voiced by 22.4%. Because of the asymptomatic nature of osteoporosis prior to a fracture, patients may be less likely to prioritize this disease above others that have a more direct impact on their daily living. This is consistent with patterns for other silent diseases including diabetes, hypertension, and dyslipidemia.³⁰ Similarly, another frequent reason for non-adherence was disbelief that the medicine would actually help with their osteoporosis or that the medication was necessary, which further reflects the fact that patients did not feel that treating their osteoporosis or osteopenia was important. Because patient beliefs about the necessity of prescribed medications are known predictors of adherence, interventions to improve adherence should include educational efforts about the efficacy of osteoporosis pharmacotherapy.^{31–35}

Finally, it is important to note that our 24.8% non-adherence rate of (5.8% temporary non-adherence and 19.0% non-adherent) is somewhat lower than previously reported rates. A review of the literature by Kothawala et. al found non-adherence rates ranged between 30–50%.¹² That review, however, looked at studies about the initiation of a medication, as well as persistence, compliance, and refill history using pharmacy refill records, chart reviews, and patient self-reports, and included studies focused on a single or variety of classes of osteoporosis therapy making direct comparisons to our results less informative. Furthermore, participation in the PAADRN clinical trial may have affected our patients' behaviors regarding their bone health, making them somewhat more likely to follow their healthcare provider's recommendations.

Studies across disease states have shown that pharmacist medication counseling and monitoring can increase adherence.^{36–44} Pharmacist-led interventions to increase adherence include face-to-face counseling, automatic refill reminders, intensive pharmaceutical care and monitoring, and recommendations to prescribers to switch to medications that have

more reasonable administration regimens. For example, in Dutch communities the use of software to detect suboptimal adherence to bisphosphonates and subsequent pharmacist counseling showed a significant decrease in discontinuation of therapy at one year compared to usual care (31.7% vs. 16.1% $p < 0.001$).^{45,46} In that study, patients also reported greater satisfaction and increased osteoporosis knowledge. Such programs could be implemented in U.S. pharmacies.

Although no single intervention strategy has been shown to be superior, the evidence clearly demonstrates that pharmacist interventions can play a large role in improving adherence rates.^{47–50} Pharmacists are the most easily accessible health professional, have frequent contact with patients, and have the expertise to guide medication counseling. Understanding patients' reasons for non-adherence should facilitate the development of tailored pharmacist-led strategies to improve patient adherence to osteoporosis medications.

Limitations

Although this is an important descriptive study of patient reported reasons for non-adherence, there are several limitations to note. Our analysis involved a relatively small sample of the larger PAADRN cohort, making it harder to detect differences between our three groups. Second, the outcomes used for this sub-analysis all relied on patient reports. Patient reports may have inaccuracies, such as non-adherent patients feeling too embarrassed or fearful to be truthful about not following their healthcare provider's instructions. Furthermore, the osteoporosis knowledge measure consisted of questions regarding the nature and severity of osteoporosis, but not about its treatment options. This limited our ability to directly link better osteoporosis knowledge specifically to their better knowledge of treatment options. Third, although we allowed patients to verbalize their own reasons for non-adherence before the interviewers categorized and then confirmed that categorization with the patient, we did not ask follow-up questions. Thus, we don't know if participants were responding based on their past experiences, and we don't know if it was a real or perceived risk that influenced their non-adherence. Finally, temporary non-adherence from non-adherence, attrition between 12-weeks and 52-weeks post-DXA made it impossible to determine whether all temporary non-adherers eventually became adherent to the medication that was originally recommended.

Conclusion

Adherence to osteoporosis medications is crucial to prevent patient, family, and societal burdens of the disease. Patients with better osteoporosis knowledge were more likely to be temporary non-adherers to recommended pharmacological treatment. Non-adherers reported that they declined treatment because they feared the side effects, don't like to take medications, or didn't believe that the medication would help. These findings suggest that improved patient counseling regarding the side effects of osteoporosis treatment and the risk-benefit ratio for these medications could increase adherence rates. As the final healthcare contact involved with new prescriptions, pharmacists play a crucial role in influencing adherence and should implement tailored counseling to achieve maximum adherence to osteoporosis medications.

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KEY POINTS**Background**

- Adherence to prescribed osteoporosis pharmacotherapy can reduce fracture risk and decrease morbidity and health care costs for patients with osteoporosis or low-bone density.
- Despite the proven efficacy of these drugs, 30% to 50% of patients prescribed osteoporosis pharmacotherapy do not start their medications.

Findings

- 24.8% of individuals prescribed osteoporosis pharmacotherapy report that they do not start their treatment because of the fear of side effects (53.3%) or the belief that the medication will not help their condition (16.7%).
- Non-adherers to osteoporosis medications scored significantly higher on an osteoporosis knowledge scale than adherers.
- These findings suggest that pharmacist interventions such as patient counseling regarding the side effects of osteoporosis treatment and the risk-benefit ratio for these medications could increase adherence rates.

Table 1

Number (Percent) of Adherent, Temporarily Non-Adherent, and Non-Adherent Patients by Patient and Study Characteristics

Characteristics	Reported Taking the Medication (N= 594; 75.2%)	Reported Temporarily Not Taking the Medication (N= 46; 5.8%)	Reported Not Taking the Medication (N= 150; 19.0%)	P - value *
Site				
A	133 (22.4)	12 (26.1)	28 (18.7)	0.203
B	294 (49.5)	25 (54.3)	68 (45.3)	
C	167 (28.1)	9 (19.6)	54 (36 .0)	
Age				
< 65	229 (38.6)	24 (52.2)	65 (43.3)	0.134
>=65	365 (61.4)	22 (47.8)	85 (56.7)	
Gender				
Men	82 (13.8)	4 (8.7)	15 (10.0)	0.319
Women	512 (86.2)	42 (91.3)	135 (90 .0)	
Race/Ethnicity				
White	503 (84.7)	41 (89.1)	121 (80.7)	0.302
Black	80 (13.5)	3 (6.5)	26 (17.3)	
Other	11 (1.9)	2 (4.3)	3 (2.0)	
Study DXA Results				
Normal	27 (4.5)	14 (30.4)	7 (4.7)	0.305
Low BMD	204 (34.3)	32 (69.6)	60 (40)	
Osteoporosis	363 (61.1)	0 (0.0)	83 (55.3)	
FRAX Risk				
High	205 (34.5)	17 (37)	46 (30.7)	0.682
Moderate	226 (38 .0)	20 (43.5)	60 (40 .0)	
Low	163 (27.4)	9 (19.6)	44 (29.3)	
One or more comorbidities	168 (28.3)	13 (28.3)	33 (22 .0)	0.297
Correct responses on the osteoporosis knowledge scale				
Number of Correct Responses, Mean (SD)	7.99 (1.6)	8.43 (1.2)	7.81 (1.8)	0.040
Individual osteoporosis knowledge questions				
Age - related height loss is a symptom of osteoporosis	493 (83.8)	40 (87.0)	124 (83.2)	0.831
For women, the risk of having osteoporosis is higher after menopause	541 (91.5)	44 (95.7)	132 (89.8)	0.458
I have a greater chance of having osteoporosis if my mother or father has/had it	418 (71.0)	38 (82.6)	111 (74.5)	0.190
Eating foods high in calcium and vitamin D can help slow the rate of bone loss	551 (93.1)	42 (91.3)	143 (95.3)	0.512
Exercising every day can help slow the rate of bone loss	547 (92.6)	46 (100.0)	143 (95.3)	0.086
There is no way to prevent osteoporosis, number (%)	247 (42.3)	28 (60.9)	74 (50.7)	0.016

Characteristics	Reported Taking the Medication (N= 594; 75.2%)	Reported Temporarily Not Taking the Medication (N= 46; 5.8%)	Reported Not Taking the Medication (N= 150; 19.0%)	P - value *
A woman/man may have osteoporosis for years but not know this until she/he breaks a bone	534 (90.4)	44 (95.7)	135 (90)	0.476
If a woman/man has osteoporosis, something as simple as lifting a bag of groceries can break a bone	496 (84.1)	38 (82.6)	121 (81.8)	0.782
Bones cannot be rebuilt once they thin from osteoporosis	337 (57.1)	30 (65.2)	90 (60.0)	0.493
The health problems caused by osteoporosis can be life-threatening	426 (72.6)	38 (82.6)	116 (78.9)	0.121
Osteoporosis Self - Efficacy Exercise at 12 Weeks, Mean (SD)	7.98 (2.23)	8.05 (2.07)	7.64 (2.19)	0.160
Osteoporosis Self - Efficacy Diet at 12 Weeks, Mean (SD)	8.54 (1.77)	8.74 (1.53)	8.58 (1.60)	0.777
Correctly Identified DXA Impression	394 (66.3)	35 (76.1)	104 (69.3)	0.342
Smoking				
Current smoker	76 (12.8)	5 (10.9)	11 (7.3)	0.323
Past smoker	202 (34)	13 (28.3)	57 (38 .0)	
Non - smoker	316 (53.2)	28 (60.9)	82 (54.7)	
Current alcohol user	263 (44.4)	20 (43.5)	68 (45.3)	0.967
Taking calcium supplements	476 (80.3)	36 (78.3)	113 (75.8)	0.482
Intervention				
Intervention	274 (46.1)	26 (56.5)	65 (43.3)	0.291
Usual Care	320 (53.9)	20 (43.5)	85 (56.7)	

* P values are based on unadjusted analysis

Table 2

Reasons for Non-adherence by Prescribed Drug

		Bisphosphonates					Other Drugs				
	Number (%)	A	B	C	D	E	F	G	H	I	Drug Not Known
Patients by adherence category											
Number of patients who were prescribed osteoporosis drugs	790 (100.0)	358	86	49	40	19	26	7	54	31	162
Number of patients who were adherent	594 (75.2)	278	61	36	29	12	20	5	42	21	105
Number of patients who were temporarily non-adherent	46 (5.8)	12	13	3	3	2	0	0	7	1	8
Number of patients who were non-adherent	150 (19.0)	68	12	10	8	5	6	2	5	9	49
Reasons for non-adherence											
Was afraid of medicine reactions/contraindications	80 (53.3)	47	3	3	5	2	2	1	1	4	12
Don't like to take medicine	38 (25.3)	22	1	1	3	2	1	0	0	2	6
Didn't think medicine would help condition	25 (16.7)	17	1	0	1	0	0	1	0	0	5
Didn't think medicine was necessary	15 (10.0)	9	0	0	1	1	0	0	0	0	4
Getting second opinion or more info from doctor	15 (10.0)	3	3	0	0	1	1	0	1	0	6
Thought it would cost too much	14 (9.3)	5	0	2	1	0	0	0	0	1	5
Not covered by insurance plan / not on plan formulary	12 (8.0)	1	3	2	2	0	1	0	0	0	3
Used another medicine as a substitution	9 (6.0)	6	0	0	1	0	1	0	0	0	1
Just did not want to	9 (6.0)	2	1	0	1	0	0	0	0	2	3
Don't Know	7 (4.7)	1	0	0	0	0	0	0	2	2	2
Trying lifestyle changes first	7 (4.7)	6	0	0	0	0	0	0	0	0	1
Trouble obtaining medicine	6 (4.0)	0	0	1	0	0	0	0	0	1	4
Inconvenient dosing regimen	4 (2.7)	4	0	0	0	0	0	0	0	0	0
Other health condition	3 (2.0)	2	0	0	0	0	0	0	0	0	1

A: Alendronic acid

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- B: Zoledronic acid
- C: Risedronic acid
- D: Ibandronic acid
- E: Raloxifene
- F: Teriparatide
- G: Calcitonin
- H: Denosumab
- I: Estrogen