Compliance and Persistence with Osteoporosis Therapies

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Regardless of disease or condition, adherence with recommended therapies is essential. This statement seems obvious, yet millions of Americans either don’t take their prescribed medications or take them incorrectly on a daily basis. In his 2004 Report on Bone Health and Osteoporosis, Surgeon General Richard Carmona indicated that the bone health of Americans was at severe risk. He suggested that the risk could be lowered substantially if only Americans would use existing therapies appropriately.

With chronic asymptomatic diseases such as osteoporosis, this issue is of particular importance. Patients must take medications consistently to avoid the fractures that can devastate their lives. And yet, studies show that compliance and persistence with medication regimens are poor. In this issue of Osteoporosis Clinical Updates, we will discuss the consequences of poor compliance and persistence with osteoporosis therapy. After that, we will take a look at methods proven to increase compliance and persistence that healthcare providers can easily incorporate into their practices.

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WHAT DO WE MEAN BY COMPLIANCE AND PERSISTENCE?

Recently, a working group of the International Society of Pharmacoeconomics and Outcomes Research (ISPOR) developed definitions to clarify the language used to describe patient use of prescribed therapeutic programs. Following a treatment plan is made up of two parts: compliance and persistence. Compliance is defined as the extent to which a patient acts in accordance with the prescribed interval and dosing regimen: the timing, dosage and administration frequency. Persistence is defined as the extent to which a patient continues treatment for the prescribed length of time; in other words, the duration of time from initiation to discontinuation of therapy.

Unfortunately, there is tremendous confusion over the use of terms related to this subject. Many studies done between 2000 and 2004 use the term adherence instead of compliance and persistence. Some studies suggest that adherence is the overall term and defines both parts of the equation: that is, compliance + persistence = adherence. However, as noted above, compliance and persistence are the preferred terms and we will use them in this issue to avoid further confusion.

History of Compliance and Persistence with Osteoporosis Treatments

Compliance and persistence with osteoporosis therapies have always been problematic. This is not a recent phenomenon born of the complex regimens necessary for taking some of the medications. Prior to 1995, there were only two hormonal therapies approved for the prevention/treatment of osteoporosis: estrogen and calcitonin. Estrogen was approved for prevention and treatment of osteoporosis. Clinical Updates is a publication of the National Osteoporosis Foundation (NOF). Use and reproduction of this publication for educational purposes is permitted and encouraged without permission, with proper citation. This publication may not be used for commercial gain. NOF is a non-profit, 501(c)(3) educational organization. Suggested citation: National Osteoporosis Foundation, Osteoporosis Clinical Updates. Issue Title. Washington, DC; Year.

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Statement of Educational Purpose

Osteoporosis Clinical Updates is published to improve osteoporosis patient care by providing clinicians with state-of-the-art information and pragmatic strategies on prevention, diagnosis, and treatment that they may apply in clinical practice.

Overall Objectives

Despite the availability of effective prevention, diagnostic, and treatment protocols for osteoporosis, research indicates that it is significantly underdiagnosed and undertreated in the general population. Through this publication, NOF encourages participants to incorporate current evidence and expert recommendations into clinical practice to improve the bone health of their patients.

Upon completion of each issue of Osteoporosis Clinical Updates, participants should be able to:

• Recognize current concepts in osteoporosis research and clinical practice
• Identify implications of these concepts for osteoporosis patient care
• Adopt evidence-based strategies to study, prevent, and/or treat osteoporosis
• Improve patient care practices by integrating new data and/or techniques

Intended Audience

This continuing education activity is intended for health professionals who care for patients at risk for or suffering from osteoporosis practicing in primary care, endocrinology, geriatrics, gynecology, internal medicine, obstetrics, orthopedics, osteopathy, pediatrics, psychiatry, radiology, rheumatology, and/or physical therapy.

This includes physicians, nurse practitioners, registered nurses, pharmacists, physician assistants, technologists, researchers, public health professionals and health educators with an interest in osteoporosis and bone health.

Activity Objectives

Upon completion of this CE material, the participant should be able to:

• Recognize the critical problem of low compliance and persistence with osteoporosis medications.
• Identify the most common reasons for nonpersistence and noncompliance with fracture-reduction medication.
• Explain the consequences of noncompliance and nonpersistence with osteoporosis medications.
• Recognize signs of noncompliance and nonpersistence in patients in your care.
• Implement strategies for improving patient medication compliance and persistence.
poor, regardless of dosing interval, although small improvements have been seen in some cases.\textsuperscript{1,7,8,9} For example, once-weekly dosing has been shown to improve both compliance and persistence over daily dosing.\textsuperscript{7-14} Improvements have been seen in persistence with monthly dosing as well.\textsuperscript{14}

A large retrospective study of managed care claims databases found a 38\% reduction in discontinuation of therapy in patients on monthly ibandronate vs. weekly alendronate.\textsuperscript{15} However, despite these improvements, overall compliance and persistence are still suboptimal. Regardless of dosing frequency, roughly one-half of women discontinue their treatment within the first year of therapy.\textsuperscript{16} In addition to bisphosphonates, two other classes of medication, an estrogen agonist/antagonist, formerly referred to as a selective estrogen receptor modulator or SERM, (raloxifene) and an anabolic agent (teriparatide) are available. Both have higher rates of compliance and persistence than bisphosphonates.\textsuperscript{17,18}

Daily subcutaneous teriparatide (parathyroid hormone) has higher rates of compliance than the self-administered bisphosphonates: 91\% (3 month), 89\% (12 months), and 82\% (18 months).\textsuperscript{18} In addition, teriparatide shows very high rates of persistence at 12-18 months and likely higher than that with oral medications.\textsuperscript{19} It has been speculated that the high compliance rates with teriparatide are due to the fact that patients on this drug have more severe osteoporosis with the highest fracture risk. These patients also know exactly how long they will be on the drug (it is approved for a maximum of 2 years). It’s likely that when there is an end in sight, compliance is somewhat easier.

Results of Poor Compliance and Persistence

The results of poor compliance and persistence are well documented. Higher compliance and persistence rates mean better patient outcomes. Lower compliance and persistence rates

\begin{figure}[h]
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\caption{Patient Self-Reported Compliance with Fracture-Prevention Medication. Six-month self-reported compliance rates of 785 women surveyed regarding adherence to fracture-prevention medication. (Huas D, Debiais F, Blotman F, et. al. 2010;10:26-33.)}
\end{figure}
mean more fractures. One study of Canadian claims data found that compliance greater than 80% significantly reduced fractures. Another study of a managed care database found that low compliance resulted in a 17% increase in fractures and a 37% increase in all-cause hospitalizations.

Two studies of claims data from large US health plan databases found that fracture risk decreased as compliance increased. One study of five years of claims data found that patients who were refill compliant and persistent showed 20-45% relative risk reductions in fractures.

Taken to its logical conclusion, this translates into roughly 390,000 fractures prevented per year in the US alone given high rates of compliance and persistence with osteoporosis medications, regardless of prescribed dosing and type of drug.

A large study conducted in the Netherlands looked at the outcomes of 8,845 new female users of alendronate, risedronate or etidronate aged 50 and older. It found that patients who were persistent with their bisphosphonate treatment reduced their risk of hospitalization for osteoporotic fractures by 20 to 30%. The protective effect was highest (30%) in patients who used bisphosphonates consistently for more than one year.

**Figure 2.** Retrospective analysis of claims data from a large healthcare plan examining relationship between persistence with alendronate therapy and fracture risk. Patients with 24 months of follow-up were stratified into persistent (>6 months therapy) and nonpersistent cohorts (<6 months therapy). Nonpersistence was defined as >30-day gap in medication supply. (Gold D et al. CMRO 2007)

Causes of Poor Compliance and Persistence with Osteoporosis Treatments

What are the causes of poor compliance and persistence? One study surveying prescription users at a large national pharmacy chain found that the most commonly cited cause of discontinuing weekly or monthly bisphosphonate therapy was the occurrence of troublesome side effects (67%), including stomachache, heartburn, and nausea. In the same study, the second most frequently cited reason for ceasing therapy was doubt about the drug’s safety and effectiveness.

Out-of-pocket costs were also cited by patients as a concern that led to their discontinuing treatment, but not at a statistically significant rate.

Several studies have found a correlation between persistence and patients’ perception of their need for fracture-prevention medication. One study of patients with low bone mineral density or osteoporosis observed that almost half did not begin prescribed therapy because they did not believe it was necessary. This study also found that, among those who did initiate therapy, the most common reasons cited for discontinuation (non-persistence) were adverse effects and complexity of dosing.

Of the 34% of patients who reported non-persistence with oral bisphosphonates surveyed in another large study, low perceived need, along with fears about long-term safety and possible side effects, current smoking, and lack of confidence in their ability to successfully maintain the treatment plan were strongly associated with nonpersistence. Interestingly, the survey found that this last factor, called medication self-efficacy, was the strongest predictor of noncompliance (such as missed doses) in the patients surveyed. Patients who believed the fracture-prevention medication was safe and necessary and who had initiated treatment were noncompliant, either intentionally or unintentionally, because they felt they couldn’t manage the regimen in their daily life.

Motivating Better Compliance and Persistence

How can clinicians improve patient compliance and persistence with osteoporosis medications? First, clinicians need to be aware that more than half of their patients are likely to fail treatment because of not taking their medications as prescribed. Physicians tend to be too
optimistic about patient compliance and persistence. In a recent study, physicians estimated that 67% of their patients were compliant and persistent; however, only 40% actually were, as indicated by pharmacy records. This is important because, if healthcare providers assume patients are compliant and persistent, they may miss opportunities to improved medication-taking behaviors.

Second, clinicians can ensure that patients understand the benefits of treatment and potential consequences of nontreatment: fracture, pain, disability, and deformity. Reviewing current research on a medication’s outcomes helps motivate patients to get started on their treatment. Any doubts about the medication’s safety and effectiveness can be identified and answered.

Third, clinicians can address the issue of side effects. Patients should know what to expect, why the medication must be taken as prescribed in order to work, and how to mitigate the most troubling side effects.

This two-pronged approach addresses the patient’s fears and focuses on his/her personal stake in maintaining the treatment plan. To support patient compliance and persistence, a treatment plan must be clear, straightforward and as simple as possible.

Healthcare providers should review the treatment plan during each patient visit to confirm that the patient understands it and to address any concerns that have arisen about how, when and under what circumstances the medication must be taken. In the process, the plan can be tailored as needed to fit the patient’s preferences, further improving the odds that the patient will be able to follow the plan.

Because osteoporosis is a silent disease, with no outward symptoms short of fracture, patients do not have immediate symptom relief to motivate and reassure them of the treatment’s effectiveness. This is where follow-up BMD and measurement of biochemical markers of bone turnover can be of great assistance. Providing concrete evidence that the medication is reducing a patient’s bone turnover rate can be a powerful tool in motivating the patient to follow the prescribed medication regimen.

Monitoring compliance and persistence requires watching for behaviors typically associated with not taking medications appropriately. Red flags such as missed appointments, unfilled prescriptions, and lack
The best improvements in compliance and persistence for patients with chronic diseases like osteoporosis appear to come with repeated face-to-face educational interventions provided by clinicians or knowledgeable healthcare support staff. To this end, the 2004 Surgeon General’s report on bone health and osteoporosis stated: “Nurse practitioners, nurse midwives and physician assistants can contribute significantly to the provision of bone health care. They can educate patients and monitor compliance with treatment.”

**Patient Cases: Improving Compliance and Persistence in Clinical Practice**

In the following case studies, we will discuss issues related to medication compliance and persistence in typical patients.

**Case Study 1: 70-Year-Old Woman with Poor Response to Treatment**

The first patient we will discuss is very typical of those seen in clinical practice. She is a 70-year-old woman with a diagnosis of osteoporosis by DXA. Two years ago, she was started on an oral bisphosphonate. At that time, her clinician instructed her on how, when, and for how long she should take her medication. The patient appeared willing to follow the regimen.

On her current DXA, two years after initiating therapy, the patient’s follow-up bone density report shows a decrease of 5% at the spine and 3% at the hip. In addition, the patient’s urine bone turnover marker (NTX) is 95 (normal is <75).

What could be going on with this patient? It is likely that the patient is noncompliant/nonpersistent with her medication regimen. She is probably either not taking her oral bisphosphonate as prescribed or has stopped taking it altogether. The clinician pursues this possibility, asking questions to discover if the patient is experiencing side effects that may have made it difficult for her to continue her medication as directed.

The patient reports that she has had heartburn taking the oral bisphosphonate. She explains that the heartburn kept her awake at night until she stopped taking the drug. The patient goes on to express financial concerns, including declines in the national economy and rising costs for name-brand drug co-pays.

of response to treatment can signal discontinuation or inconsistent use of medication. One factor common to all of these recommendations is time spent with the patient. Studies have shown the effectiveness of patient education in improving medication compliance and persistence.

Given the constraints of most healthcare providers today, carving out the time to counsel patients can pose a real challenge. Studies have shown modest improvements in therapeutic compliance and persistence with the use of videotaped patient education instruction, but have not found written materials in the absence of counseling to be effective.
What can be done to improve this patient’s compliance, persistence and bone health?

In order to get this patient back on track with her medication plan, three things need to happen: first, her side effects need to be addressed; second, her financial concerns related to the medication need to be dealt with; and third, she needs to see evidence of the need for this therapy.

After referring the patient for a barium swallow test, the clinician confirms that the patient has a mild case of GERD. The physician discusses lifestyle modifications that the patient can make that may help alleviate the symptoms of GERD, including elevating the head of the patient’s bed, avoiding eating within three hours of bedtime and avoiding tobacco, alcohol, caffeine, chocolate, peppermint and fatty foods. In addition, the physician changes the patient’s dosing schedule from daily oral bisphosphonates to weekly.

The clinician asks the patient to report back in one month on her heartburn symptoms, explaining that medications may be needed to address them if the lifestyle modifications and medication dosing change don’t alleviate her symptoms.

To address the patient’s concerns regarding the increased cost of insurance co-pays for name-brand drugs, the physician writes the patient a prescription for the generic version of alendronate weekly 70 mg.

And last, the clinician explains the mechanism of the drug on bones, how long it takes to have an effect, how to tell if it’s working and how fracture rates rise if the drug isn’t taken as directed. With this overview, the clinician discusses how measurements of biochemical markers of bone turnover can indicate whether or not the drug is working. The physician then measures the patient’s biochemical markers and schedules a follow-up to check on her progress in six months time.

Taking these measures and following the patient over time promises to improve her compliance and persistence with treatment and, in so doing, improve her long-term bone health.

Case Study 2: 60-Year-Old Woman with Poor Medication Persistence

The second patient we will discuss is a 60-year-old postmenopausal woman diagnosed three years ago with osteoporosis.

CME Program Eligibility

Method of Participation in the Learning Process: Clinician learners will read and analyze the subject matter, conduct additional informal research through related internet searches on the subject matter, and complete a post-test assessment of knowledge and skills gained as a result of the activity.

After participating in this activity, the reader has the option of taking a post-test with a passing grade of 70% or better to qualify for continuing education credit for this activity. It is estimated it will take 1.0 hour(s) to complete the reading and take the post-test. Continuing education credit will be available for two years from the date of publication.

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The National Osteoporosis Foundation is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians. The National Osteoporosis Foundation designates this educational activity for a maximum of 1.0 AMA PRA Category 1 Credit(s)™. Physicians should only claim credit commensurate with the extent of their participation in the activity.

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Statement Regarding Off-Label Use

Any publication of the Osteoporosis Clinical Updates that discusses off-label use of any medications or devices will be disclosed to the participant.
The clinician is notified that the practice’s patient prescription-refill-tracking system indicates the patient has not filled her prescription for osteoporosis medication in several months.

*What can the clinician do to help improve this patient’s compliance and persistence with her medication?*

Studies have shown that nurse monitoring and follow up helps to motivate patients to take their medicine as directed. The clinician’s staff contacts the patient to schedule a consultation.

At the consultation, the clinician reviews the patient’s BMD history and explains the risk of fracture that she incurs by not persisting with her medication regimen. The clinician explains the use of biochemical markers of bone turnover and what they can reveal about a patient’s response to treatment. The clinician measures the patient’s biochemical markers of bone turnover and schedules a follow-up measurement for three months later to track response to therapy. Research has shown that a positive response to antiresorptive therapy, as indicated by markers of bone turnover, motivates higher persistence and compliance in patients.

*How can the clinician follow the patient’s persistence and compliance?*

This clinician is on the right track using a system to follow patient prescription refills. This is an excellent tool for indicating patient persistence with medication. However, it is not sufficient in itself to ensure that patients are compliant and persistent. Individual consultation, done via e-mail, phone call or in person, as well as follow-up assessment of BMD, biomarkers, etc., are needed both to ensure that patients are following their prescribed medication regimens and to make any needed modifications to the treatment plan.

**References**


### Strategies to Improve Medication Adherence

- Involve family members in maintaining the medication regimen.
- Provide written and verbal instructions.
- Assess the patient on areas of the regimen that are going to be challenging.
- Assess if the patient is physically able to maintain the regimen, i.e., handle the syringe, open the pill container.
- Discuss the cost of the medication and the patient’s ability to pay for it.
- Offer aids to adherence such as calendar stickers, pill dispenser.
- Ask about adherence at each office visit.
- Contact the patient if an appointment is missed.


For many people, the beginning of a new year is an important time for making resolutions to engage in healthy behaviors. The National Osteoporosis Foundation (NOF) supports you in making a commitment to your health and encourages you to think of yourself as having vibrant good health.

- To help you reach your health goals, we have affirmations to share with you from our Staying Power Kit. You can use them to help embrace healthy changes in your life.
- I have osteoporosis, and I know that it's beatable and treatable.
- I plan to live a long and healthy life. Having strong bones is important in achieving this goal, and I am willing and able to do what it takes.
- I stay focused on my strengths. Knowing that I have strengths motivates me to do my best every day for my health and well being.
- I think positive thoughts about my physical and emotional health. I seek out and choose to have friendships with people who support me. Having strong, positive relationships keeps me healthy.
- I exercise regularly. My bones and entire body appreciate my effort. I become stronger and more flexible each day.
- I forgive myself for past unhealthy behaviors and focus on the things I can do now. I know that what I do today brings strength to my body and soul.
- I reward myself in healthy ways. One of my favorite activities is to take walks by myself or with a friend several times a week. I can focus on the beauty of nature or on pleasurable conversation while I do something positive for myself.
- My bone health is worth my time and attention. I love myself enough to take good care of my health.
- My bones are an essential part of my body. Bones give shape to my body, and they support and protect my internal organs. I respect and care for my bones and treat them well.
- I am careful with movements and activities. I care enough about my bones to protect them.
- I welcome people into my life, and strangers become friends. Osteoporosis does not isolate nor keep me from having relationships with friends and family.
- I approach the future one day at a time, and I remember to appreciate each day as I live it. I feel good about my bones and my health.
- I accept help graciously and positively. Everyone needs a little help from time to time. I am grateful that there are people to help me. And, I help others in turn.
- I make my bones stronger by exercising regularly, remembering to get enough calcium and vitamin D and taking my medicine as directed.
- When I take my medicine, I visualize it strengthening my spine, hips and other bones in my body. I see strong healthy bones.
- I take pleasure in each new day. I plan and take part in activities, gatherings and social events that bring me pleasure. I take pleasure in knowing that I can have strong healthy bones.
- When I look in the mirror, I remember to STAND TALL. I feel good about myself.
Making Sure Patients Understand How to Take Their Medications

Visiting a healthcare provider is an overwhelming and confusing experience for many patients. While a patient may indicate that they fully understand your instructions on how to take a medication, this may not always be the case. There are many things you can do to improve your patients’ ability to understand and remember the instructions for taking a medication. One of these methods is called “teach back.”

“Teach back” requires your patients to demonstrate whether or not they fully understand the instructions you have given them. After prescribing a medication, you can employ “teach back” simply by saying, “I want to make sure my instructions on how to take your Fosamax® tablets were clear. Please describe to me how you are going to take the medication.” In this example, you are putting the blame for poor understanding on yourself, the clinician, rather than the patient.1

In the case of weekly alendronate (Fosamax®) tablets, patients should be able to describe that they will take the medication on the same day each week, on an empty stomach, first thing in the morning, with 8 oz. of plain water and no other liquid, and that they must wait at least 30 minutes before eating, drinking or taking any other medication. In addition, they also must be able to demonstrate that they will remain upright which means that they must sit or stand during this interval.

Such instructions can be complicated and difficult to remember for any patient, regardless of age, income, education level, etc. If a patient is not able to demonstrate a clear understanding of the medication’s instructions, try drawing pictures and using more simple language. You should repeat this process until the patient can demonstrate a clear understanding of the instructions.

While “teach back” may seem time consuming, it should only take a minute or two. Start by practicing the method on one or two patients a day until you feel more comfortable. Studies show that clinicians who use “teach back” do not spend more time with patients that those who do not use this method.2 “Teach back” can help prevent serious medication errors as well as unnecessary follow-up phone calls and visits. This method can also help your patients to improve their compliance and persistence with their prescribed medications.

Osteoporosis International

Osteoporosis International is the leading scientific journal for clinical research in osteoporosis and related bone diseases. Published monthly, the journal is an international, multidisciplinary joint initiative of NOF and the International Osteoporosis Foundation.

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A Guide to Osteoporosis Medicines
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