Medication Adherence: A Challenge for Patients With Postmenopausal Osteoporosis and Other Chronic Illnesses

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ABSTRACT

OBJECTIVE: To define medication adherence and describe the limitations of various assessment methods, reasons for nonadherence to medications used to manage chronic illness, the impact of nonadherence to osteoporosis medications, and strategies for improving medication adherence.

BACKGROUND: Medication nonadherence is a major public health problem that adversely affects patient outcomes and increases health care utilization and costs. Postmenopausal osteoporosis is a chronic disease, and adherence to drug therapy used to manage the disease is as much of a challenge as it is in other chronic diseases.

SUMMARY: Medication adherence reflects both compliance and persistence. Direct assessment methods (e.g., observation, laboratory serum drug assays) are more accurate than indirect methods, but they are more costly and often impractical. Indirect methods include patient self-report and the use of prescription refill records, pill counts, and electronic monitoring devices. Medication adherence in patients with postmenopausal osteoporosis or other chronic illnesses is less than optimal. Adverse effects, financial constraints, miscommunication with the prescriber, and a perception that medications are unnecessary are among the possible reasons for medication nonadherence. Unintentional nonadherence is a passive process, often simply forgetting, and intentional nonadherence is an active process involving a deliberate choice, often based on adverse effects or a perceived lack of benefit.

CONCLUSIONS: Nonadherence to osteoporosis medications can adversely affect patient outcomes and increase health care utilization and costs. An individualized approach to improving medication adherence based on patient preferences and readiness to change is needed.

KEYWORDS: Intentional nonadherence, Medication adherence, Postmenopausal osteoporosis, Readiness to change, Unintentional nonadherence


Medication nonadherence is a major public health problem. Adherence to long-term therapy for chronic illnesses in developed countries averages 50%. The rates of adherence in developing countries are even lower. In people aged 60 years or older, rates of adherence to medication regimens range from 41% to 74%. Many patients have difficulty following treatment regimens.

The terms compliance, persistence, and adherence often are used interchangeably, but they have distinctly different meanings. Compliance is the consistency and accuracy with which a medication regimen is followed. Persistence is the length of time a regimen is continued. Adherence reflects both compliance and persistence.

Adherence, in general, results from an intricate and complex interaction among an individual, the environment, and the community. More specifically, medication adherence is the level of participation in a specific drug regimen once the patient agrees to that regimen. Improving medication adherence has the potential for a greater impact on the health of the population than improvements in medical therapy. Finances may be a barrier to adherence, especially for senior citizens on a fixed income. Programs to assess a patient’s ability to pay for medications and provide financial assistance if needed may improve medication adherence.

Assessment

Medication adherence has been assessed using several different methods. Direct assessment methods (e.g., direct observation, laboratory assays of serum drug concentrations or biochemical markers) are the most accurate methods for assessing medication adherence, but they are costly, cumbersome, and often impractical. Patient or caregiver self-report is the most traditional indirect assessment method, especially in clinical settings. However, this method lacks reliability and validity because many patients are reluctant to admit that they are nonadherent for fear of upsetting the prescriber.

Prescription refill records are an alternative source of information about medication adherence provided the prescriptions are obtained from only one pharmacy. This method is not useful if a patient obtains refills from multiple pharmacies, a phenomenon that has become more popular with the recent increase in mail-order pharmacies. Moreover, prescription refill records do not necessarily reflect whether the medication actually was taken. A reliance on refill records may overestimate adherence. Pill counts may be conducted to circumvent the shortcomings of prescription refill records. However, pill counts traditionally are unreliable and tend to overestimate adherence. Electronic monitoring devices record the times when a prescription container was opened. However, the data do not necessarily reflect whether
the medication was taken.

Pharmacists can evaluate medication adherence and establish a system of checks and balances using multiple assessment methods. For pharmacists interested in this area, a direct patient interview is recommended initially, with prescription refill information used as a screening tool to detect possible non-adherence. This approach may not be feasible for patients who use mail-order pharmacies because a conversation with the patient usually is not possible.

Open-ended, nonjudgmental questions are recommended in conducting patient interviews. Such questions should address how and when the medications are taken, especially with respect to meals. The patient might be asked to explain or demonstrate how the medications are kept organized (e.g., in a pill box or organizer) and how the medications are taken. The pharmacist might offer to contact the prescriber on behalf of the patient and make suggestions to simplify the medication regimen. The pharmacist also could ask about the patient’s means for paying for medications and offer to help the patient obtain assistance with out-of-pocket expenses if available.

Patient interviews can be instrumental in identifying and correcting key medication-related problems. For example, when a patient receiving a bisphosphonate complained about gastrointestinal discomfort, she was asked to explain and demonstrate how she took the medication. She understood that she needed to take each dose at least 30 minutes before the first food or beverage of the day, take the medication with a full glass of plain water, and stand or sit upright for at least 30 minutes after the dose. In demonstrating how she took the medication, the patient placed a tablet on her tongue, took a sip of water from an 8-ounce glass, and set the glass down. The patient had not understood that she needed to drink the entire glass of water. The patient said that no one ever told her to drink the entire glass of water. This patient is like many others who take instructions (or lack thereof in this case) literally.

Medication nonadherence should be suspected in elderly patients whose functional abilities have deteriorated. Impairment in cognitive function, vision, or hearing can interfere with medication adherence.

### Chronic Diseases

Medication nonadherence is a problem associated with nearly all chronic diseases (Table 1), including terminal illnesses (e.g., late-stage cancer or chronic obstructive pulmonary disease). A complex medication regimen increases the likelihood of nonadherence.

<table>
<thead>
<tr>
<th>Disease State</th>
<th>Mean (Range [%]) Medication Adherence Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cancer</td>
<td>80 (35-97)</td>
</tr>
<tr>
<td>Cardiovascular diseases (all)</td>
<td>71 (39-93)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>73 (39-93)</td>
</tr>
<tr>
<td>Psychiatric illnesses</td>
<td>78 (75-83)</td>
</tr>
<tr>
<td>Epilepsy</td>
<td>70 (46-88)</td>
</tr>
<tr>
<td>Glaucoma</td>
<td>78 (76-80)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>73 (66-85)</td>
</tr>
<tr>
<td>Asthma</td>
<td>55 (37-92)</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease</td>
<td>51 (50-52)</td>
</tr>
</tbody>
</table>

* Adapted from reference 8.

Medication adherence in 208 patients was evaluated by telephone interview 10 months after hospital discharge with an acute coronary syndrome. The average patient age was 65 years and 60% of patients were male. Medication adherence decreased from the time of discharge to the time of telephone contact (i.e., persistence was poor), regardless of the type of medication. The rate of adherence to beta-blockers was 90% at the time of discharge and 80% 10 months later. Adherence to angiotensin-converting enzyme (ACE) inhibitors decreased from 71% to 66% over the same time frame. Similarly, adherence to lipid-lowering therapy decreased from 83% to 76%, and adherence to low-dose aspirin decreased from 95% to 87% during the same 10-month time frame.

The most common reason, by far, for failure to adhere to the medication regimen was the impression that the physician did not want the medication continued (59% on beta-blockers, 48% on ACE inhibitors, 50% on lipid-lowering agents, and 63% on aspirin), which may reflect miscommunication between the physician and patient. Problems with or fear of adverse effects, a desire to try another medication, inability to afford the medication, and a perception that the medication was unnecessary are other reasons for nonadherence, but none accounts for more than 18% of the sample. The investigators concluded that ascertaining patient beliefs about illness and medication use may be helpful in developing strategies to improve adherence.

Another chronic condition associated with poor adherence to therapy is Parkinson’s disease. Parkinson’s disease is a neurologic disorder with a profound physical and psychological impact, and antiparkinsonian drug therapies often cause adverse effects that can reduce adherence. Medication adherence was evaluated using electronic monitoring over a 3-month period in 54 patients with Parkinson’s disease. The average age was 62 years, 56% of patients were male, and 61% received levodopa therapy. Poor medication adherence (defined as less than 80%) was associated with a young age, receipt of a large daily number of tablets of antiparkinsonian medication, depression, and a poor quality of life. The investigators concluded that a triad of depression, medication underuse, and poor quality of life may be self-perpetuating in socially isolated patients with Parkinson’s disease.

In a study of a “silent disease,” hypertension, rates of unintentional and intentional adherence were explored using...
The average patient age was 40 years and 50% patient self-reports in a Veterans Affairs study of 558 patients. Unintentional nonadherence is a passive process, often arising from a patient’s carelessness or forgetfulness, and intentional nonadherence is an active process, whereby a patient deliberately chooses to deviate from the treatment regimen. The average patient age was 63 years, 98% of patients were male, and 42% of patients were nonwhite. Approximately 31% of patients reported unintentional nonadherence and 9% of patients reported intentional nonadherence. Unintentional nonadherence was associated with a nonwhite race and less than a 10th-grade education. Intentional nonadherence was associated with a nonwhite race and 5 or more adverse effects. The investigators speculated that these patients may have decided to stop their drug therapy because the perceived benefits did not outweigh the many adverse effects. The investigators also concluded that different strategies are needed to overcome unintentional and intentional nonadherence problems because of the different patient characteristics associated with these 2 types of nonadherence.

Involuntary (i.e., unintentional) and voluntary (i.e., intentional) nonadherence also were evaluated in a study of 40 patients with inflammatory bowel disease (a diagnosis of Crohn’s disease or ulcerative colitis). The average patient age was 40 years and 50% of the patients were male. Two thirds of patients reported involuntary nonadherence, including 60% who blamed forgetfulness and 38% who attributed it to carelessness. Voluntary nonadherence was acknowledged by 35% of patients, including 25% who stopped taking the medication because they felt worse after taking it and 15% who stopped taking the medication because they felt better after taking it.

### Postmenopausal Osteoporosis

Postmenopausal osteoporosis is a chronic disease, and adherence to drug therapy used to manage the disease is as much of a challenge as it is in other chronic illnesses. Adherence to 3 different osteoporosis medications (hormone-replacement therapy [HRT], the bisphosphonate alendronate, and the selective estrogen receptor modulator raloxifene) was evaluated in 956 women with low bone mineral density (BMD) who were interviewed an average of 7 months after treatment initiation. The average patient age was 45 years. The rate of discontinuation of HRT (26%) was significantly higher ($P = 0.02$) than the discontinuation rates for alendronate (19%) and raloxifene (19%). Discontinuation was more likely in women with bothersome adverse effects or who thought that their BMD test results did not show osteoporosis. There were no significant differences between treatments in adherence after adjusting for adverse effects and patient characteristics.

In a retrospective study of more than 58,000 patients who initiated drug therapy for osteoporosis (estrogen alone, estrogen plus a progestin, a bisphosphonate, or raloxifene), the overall 1-year compliance rate was less than 25%. The average duration of continuous therapy was 221 days for raloxifene, 245 days for the bisphosphonate, 262 days for estrogen alone, and 292 days for estrogen plus a progestin ($P < 0.0001$). Compliance was associated with significant reductions in the risk of hip (odds ratio [OR] = 0.382, $P < 0.01$) and vertebral (OR = 0.601, $P < 0.05$) fractures, use of physician services ($P < 0.0001$), hospital outpatient services ($P < 0.05$), and hospital care ($P < 0.01$) compared with noncompliance.

Other studies also have shown a link between osteoporosis medication adherence and patient outcomes. In 11,249 women with osteoporosis and a mean age of 68 years who were followed for 2 years, there was a 16% lower fracture rate ($P = 0.004$) in adherent women who took at least 80% of doses of their osteoporosis medications compared with nonadherent women. Another study examined 6,825 women aged 45 years or older with a diagnosis of postmenopausal osteoporosis. Forty-eight percent were refill compliant, and 21% were persistent. The relative risk of fracture was 26% less in compliant women than in noncompliant women ($P < 0.0001$), and 21% lower in persistent women than in nonpersistent women ($P < 0.0069$).

### TABLE 2 Stages of Change in Health-Related Behavior *

<table>
<thead>
<tr>
<th>Stage of Change</th>
<th>Characteristics</th>
<th>Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Precontemplation</td>
<td>Patient has no intention of changing and is unaware of potential benefits</td>
<td>Provide information about benefits of change</td>
</tr>
<tr>
<td>Contemplation</td>
<td>Patient has begun to think about changing but is not yet serious about making a change</td>
<td>Discuss negative aspects of change</td>
</tr>
<tr>
<td>Preparation</td>
<td>Patient has made decision and commitment to change</td>
<td>Develop a treatment plan and discuss plans to change</td>
</tr>
<tr>
<td>Action</td>
<td>Patient has made overt efforts to change, but the change is not yet ingrained and relapses may occur</td>
<td>Support change by offering rewards</td>
</tr>
<tr>
<td>Maintenance</td>
<td>Patient has made a change, and change has been sustained for more than 6 months</td>
<td>Continue providing support and rewards</td>
</tr>
</tbody>
</table>

* Adapted from reference 29.
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osteoporosis treatment 1 year after initiation of therapy correlated with a significant increase in hip BMD ($P = 0.01$) and cross-linked N-telopeptide of type I collagen ($u$NTX, $P = 0.002$) but not in the lumbar spine ($P >0.05$). Additionally, in a study of postmenopausal women who were patients in a multispecialty practice affiliated with a health maintenance organization, those with compliance greater than or equal to 66% showed significant increases in spine ($P <0.005$) and hip ($P <0.004$) BMD.20

A study conducted in the Netherlands involving 8,845 women who were at least aged 50 years and who initiated use of bisphosphonates found that adherence to bisphosphonate therapy reduced the risk of hospitalization for fractures by 20% to 30%.21 The protective effect was greatest (30%) in patients who used bisphosphonates consistently for more than 1 year.

Research is needed to evaluate whether patient preferences for bisphosphonates that are administered monthly instead of weekly or daily (see the preceding article by O’Connell in this supplement) translate into greater adherence for long periods (i.e., improved persistence) and improved patient outcomes.22 Studies currently are under way to explore these outcomes.

### Strategies

There are 3 key requirements for improving adherence to osteoporosis drug therapy. First, patients must be educated about the disease and its treatment and must believe that the disease is a personal threat. Second, patients need to see evidence of the rationale for and positive results from treatment (e.g., BMD test results). Third, health care providers need to take into consideration patient preferences (e.g., preferences for weekly or monthly doses instead of daily doses, concerns about adverse effects). Efficacy usually takes priority over adverse effects and ease of medication administration, especially in patients with terminal illnesses. However, patients with nonterminal but chronic illnesses may be willing to compromise efficacy to avoid adverse effects. Positive reinforcement of adherence by such patients to the medication regimen is also vital.

The results of diagnostic testing provide justification for and motivation to adhere to osteoporosis treatment. When 1,014 patients who underwent diagnostic bone densitometry testing were surveyed about their knowledge of the test results, only 80% of the patients had been informed about the results. Only 63% of the 341 participants with a normal BMD, 31% of the 309 patients with osteopenia, and 50% of the 364 patients with a diagnosis of osteoporosis reported the results correctly.23 Patients with a low BMD (i.e., osteopenia or osteoporosis) who were able to correctly report their results were significantly more likely to have received a medication and continue to take it than patients who incorrectly reported their results.

Various strategies may be used to optimize medication adherence.24 Screening for indicators of nonadherence, including missed appointments and skipped prescription refills, can help identify problems.7 Strategies to improve adherence may involve counseling patients about the importance of the planned treatment regimen, enlisting the support of the patient’s family and friends, sending reminders about follow-up appointments, recognizing and reinforcing adherence efforts, simplifying the treatment regimen, addressing patient concerns about adverse effects, and maintaining a supportive provider-patient relationship.24 In addition, simple, clear instructions should be provided to patients about how and when to take medications. Input from the patient about his or her preferences should be elicited and accommodated to the extent possible.

Monitoring of drug therapy by nurses or other staff should be considered. Monitoring of raloxifene therapy in women with postmenopausal osteoporosis by nurses using a predefined protocol has been shown to improve patient adherence.25

### Theoretical Basis for Behavioral Change

The concept of self-management of chronic illness has been in the medical literature for many years and forms a solid theoretical basis for improving adherence.25 The individual patient must claim responsibility for self-care and accept the fact that he or she has a chronic illness and that treatment may improve his or her health status. Self-management involves making day-to-day decisions about one’s own care, and self-management education teaches problem-solving skills.26 Self-efficacy—the confidence to carry out a behavior needed to achieve a desired goal—is central to self-management.27 Adherence is likely to improve in patients with or at risk for osteoporosis if they embrace this self-management approach.
Adhering to prescribed osteoporosis drug therapy involves behavioral change, and readiness to change varies from one individual to another. Health-related behavioral changes are preceded by 5 stages of change (Table 2) that reflect readiness and motivation to change, according to the Transtheoretical Model of Change described years ago by Prochaska, based on a health-belief model. An individual may pass through all 5 stages of change quickly and implement the change promptly or spend a long time in a particular stage and fail to progress through subsequent stages.

A validated 2-item measure of the stage of change for medication adherence developed for patients with hypertension or human immunodeficiency virus infection might be adapted for patients with or at risk for osteoporosis (Figure 1). Efforts to improve medication adherence should be tailored to the stage of change for an individual (i.e., his or her readiness and motivation to change).

## Conclusion

Adherence to osteoporosis medications is less than optimal. Medication nonadherence can adversely affect patient outcomes and increase health care utilization and costs. An individualized approach to improving medication adherence based on patient preferences and readiness to change is needed.

## DISCLOSURES

This article is based on the proceedings of a symposium held on April 6, 2006, at the Academy of Managed Care Pharmacy’s 18th Annual Meeting and Showcase in Seattle, Washington, which was supported by an independent educational grant from Roche Laboratories and GlaxoSmithKline. The author received an honorarium from Roche Laboratories and GlaxoSmithKline for participation in the symposium. She reports that she is a speaker and consultant for GlaxoSmithKline, Roche, Procter & Gamble, sanofi-aventis, and Eli Lilly & Co. She also has conducted research that has been funded by Eli Lilly & Co.

## REFERENCES


