

# Real-World Challenges of Treating Osteoporosis

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All patients being considered for osteoporosis therapy should be counseled on risk factor reduction, including the importance of calcium and vitamin D intake, physical activity, and other lifestyle-based strategies. These simple yet critical prevention strategies are the cornerstone of effective management in patients with, or at risk for, osteoporosis and osteoporosis-related fractures.

The decision to initiate pharmacologic treatment should consider clinical assessments, bone mineral density (BMD), diagnostic workups, risk of fracture, and clinical judgment. Clinical guidelines also provide direction for selecting patients who would most benefit from treatment. The National Osteoporosis Foundation (NOF) recommends that treatment be considered in postmenopausal women and men age 50 and older with the following:<sup>1</sup>

- Hip or vertebral (clinical or morphometric) fracture
- T-score of  $-2.5$  or less at the femoral neck or spine after appropriate evaluation to exclude secondary causes of osteoporosis
- Low bone mass (T-score between  $-1.0$  and  $-2.5$  at the femoral neck or spine) and a 10-year probability of a hip fracture of 3% or greater or a 10-year probability of major osteoporosis-related fracture of 20% or greater based on the US-adapted World Health Organization FRAX algorithm

The most recent American Association of Clinical Endocrinologists (AACE) postmenopausal osteoporosis guidelines endorse the NOF recommendations for initiation of treatment in postmenopausal women.<sup>2</sup>

## Pharmacologic Therapies

On a microscopic level, the skeleton is an extremely dynamic tissue where bone remodeling is ongoing, and activated osteoclasts resorb bone while osteoblasts generate bone matrix.<sup>3</sup> This process serves to repair microdamage and ensure skeletal strength. Numerous systemic mediators regulate bone cell activity, including endogenous parathyroid hormone, vitamin D metabolites, prostaglandins, cortisol, and hormones. Several steps in this complex bone remodeling process can be targeted with pharmacotherapy to inhibit resorption or augment bone formation.<sup>1</sup>

## Abstract

Numerous treatments have been shown to significantly reduce the risk of osteoporosis-related fracture. Treating patients with osteoporosis therapies after an initial osteoporotic fracture can reduce the risk of future fractures 40% to 60%, resulting in significant cost reductions. But despite the availability of effective management strategies, osteoporosis management is still suboptimal. Barriers to providing quality care include knowledge, competency, and performance on the part of healthcare professionals, and knowledge and adherence to therapy on the part of patients. Addressing these barriers and treating patients appropriately can help address the potential health and economic consequences of osteoporosis.

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For author information and disclosures, see end of text.

**Table 1.** Pharmacotherapies Approved for the Prevention and/or Management of Osteoporosis<sup>1,29</sup>

Agent	Indication				Dosage Form(s)	Frequency of Administration
	Women: Prevention	Women: Treatment	Men: Treatment	Glucocorticoid-Induced		
Alendronate	X	X	X	X	Oral tablet Oral liquid	Daily Weekly
Ibandronate	X	X			Oral tablet	Daily Monthly
Ibandronate		X			IV injection	Every 3 months
Risedronate	X	X	X	X	Oral tablet	Daily Weekly Twice monthly Monthly
Zoledronic acid	X	X	X	X	IV infusion	Yearly
Calcitonin		X			Nasal spray SC injection	Daily Every other day
Estrogen/hormone therapy	X				Oral tablet Transdermal	Daily
Raloxifene	X	X			Oral tablet	Daily
Teriparatide		X	X	X	SC injection	Daily
Denosumab		X			SC injection	Every 6 months

IV indicates intravenous; SC, subcutaneous.

A variety of pharmacologic agents are available for the prevention and/or treatment of osteoporosis and related fractures (Table 1). Antiresorptive agents (eg, bisphosphonates, calcitonin, estrogen/hormone therapy, raloxifene, and denosumab) inhibit osteoclastic activity, thereby reducing bone turnover and maintaining bone mass, while anabolic therapy (eg, teriparatide) improves bone turnover by increasing osteoblastic activity to a greater degree than osteoclastic activity.<sup>1,4,5</sup>

**Bisphosphonates**

The bisphosphonates alendronate, ibandronate, risedronate, and zoledronic acid are all approved by the Food and Drug Administration (FDA) for the prevention and treatment of postmenopausal osteoporosis. Alendronate was the first approved bisphosphonate and is available as a daily or weekly oral medication.<sup>1,6</sup> Alendronate is also approved for the treatment of osteoporosis in men and for treatment of glucocorticoid-induced osteoporosis (GIOP).<sup>1,7,8</sup> In the United States, a generic formulation of alendronate is also available.<sup>1</sup> Risedronate, which is available as a daily, weekly, or monthly oral medication, is also indicated for the treatment of osteoporosis in men, and the prevention and treatment of GIOP in men and women.<sup>1,9,10</sup> Ibandronate is available as a daily or monthly oral tablet, or an intravenous (IV) injection that is given every 3 months.<sup>1</sup> While the oral formulation of ibandronate is approved for both the prevention and treatment of postmenopausal osteoporosis, the IV injection is only

approved for the treatment of postmenopausal osteoporosis.<sup>1</sup> Zoledronic acid is the most recently approved bisphosphonate, and is administered by IV infusion once per year for the treatment of osteoporosis and once every 2 years for the prevention of osteoporosis.<sup>1</sup> It is also indicated to prevent and treat GIOP in men and women, and to prevent recurrent fracture in patients who have already suffered a low-trauma hip fracture.<sup>1,11</sup>

Oral bisphosphonates should be taken first thing in the morning on an empty stomach with a full glass of water, and it is recommended that the patient remain upright and not eat or drink anything for 30 minutes to 1 hour after ingesting the medication. This dosing regimen has served to reduce the potentially serious adverse reaction of esophageal erosion that was evident early in use. Unfortunately, this regimen can be construed as too complicated by many patients. The advent of newer weekly and monthly dosing regimens available for most bisphosphonates has helped to ease some of the burden associated with dosing regimens (by decreasing frequency of dosing) and made them easier to incorporate and follow. In addition, newer agents (ibandronate and zoledronic acid) are available via IV administration. While this route of administration may help address difficulties associated with oral dosing regimens, they may pose different challenges for patients. For example, administration requires frequent office visits (every 3 months for ibandronate and yearly for zoledronic acid) and an injection, both of which may be off-putting to patients.

Bisphosphonates are highly effective in reducing fracture rates, and the effects are maintained for several years after discontinuation of therapy. Alendronate has been shown to reduce fractures at the spine, hip, and other sites by approximately 50% as compared with placebo.<sup>12,13</sup> Data demonstrate that risedronate reduces fracture rates at the spine, hip, and other sites by an estimated 50% to 60%.<sup>14</sup> Ibandronate has not been shown to reduce hip or other site fractures, but has demonstrated a high efficacy in reducing vertebral fractures (approximately 50%-60%).<sup>15,16</sup> Studies show that zoledronic acid is very effective in reducing vertebral fractures (about 75%), and demonstrates a more modest effect on reducing hip and all-site fractures (about 25%-35%).<sup>11</sup>

Adverse events associated with bisphosphonate therapy may include gastrointestinal issues, such as difficulty swallowing, gastric ulcers, and esophageal inflammation.<sup>1</sup> In addition, because bisphosphonates are effective in suppressing bone resorption, there are concerns that bone quality may be compromised. Some case reports identified patients who sustained fractures while taking bisphosphonates, possibly due to oversuppression of bone turnover.<sup>17</sup> Another concern associated with bisphosphonates is osteonecrosis of the jaw, which is a rare condition primarily associated with high-dose IV bisphosphonates commonly used in the treatment of malignancies, reduction of bone pain, and malignancy-related hypercalcemia.<sup>18</sup> It is important to consider, though, that while osteonecrosis of the jaw is uncommon in these patients receiving high-dose IV bisphosphonates, it is even more rare among healthy patients who take bisphosphonates for the prevention or treatment of osteoporosis.<sup>19</sup>

### **Calcitonin**

Calcitonin is approved for the treatment, but not prevention, of osteoporosis in women who are at least 5 years postmenopausal.<sup>1</sup> It is available as either an intranasally administered formulation or a subcutaneous injection.<sup>1</sup> While calcitonin is an inhibitor of bone resorption, the associated reduction in bone turnover with calcitonin is much less than that seen with other antiresorptive agents.<sup>20</sup> As such, calcitonin is not considered first-line therapy in the treatment of osteoporosis and is often reserved as an alternative option for women who cannot use or choose not to use one of the other medications available for treating osteoporosis.<sup>21</sup> Nasal calcitonin is generally well-tolerated, and adverse events may include nasal irritation or rhinitis, while adverse reactions reported with the injectable formulation include local inflammation, nausea, and flushing of the face or hands.<sup>1,21</sup>

### **Estrogen/Hormone Therapy**

During menopause, a decrease in estrogen production is associated with an increase in bone resorption leading to an increased risk of fracture. Estrogen/hormone therapy helps minimize that increase in bone resorption, and has been shown to increase BMD.<sup>21</sup> Data from the Women's Health Initiative showed a reduction in both vertebral and non-vertebral fractures in women receiving both estrogen plus progestin and in women taking estrogen alone; however, data from the same trial identified the potential for increased risks for coronary heart disease, venous thromboembolism (VTE)-related events, stroke, and breast cancer.<sup>21-23</sup> Subsequent analyses and more recent studies have demonstrated that the use of hormone therapy in women who are transitioning to postmenopause is not associated with an increased risk for cardiovascular disease.<sup>24,25</sup>

Various estrogen/hormone therapies are approved for the prevention of osteoporosis associated with menopause.<sup>1</sup> While the North American Menopause Society (NAMS) supports the extended use of hormone-based therapies for the prevention of bone loss and/or reduction in fracture risk when other agents are not suitable or result in adverse effects, they also recommend the use of these agents at the lowest effective dose consistent with treatment goals.<sup>21</sup> The NOF advises that when estrogen therapy or hormone therapy is considered solely for the prevention of osteoporosis, non-estrogen treatments should first be carefully considered.<sup>1</sup>

### **Raloxifene**

Raloxifene, which is a daily oral medication, is the only estrogen agonist/antagonist approved for the prevention and treatment of postmenopausal osteoporosis.<sup>1</sup> While raloxifene is not an estrogen, it works via the estrogen receptor and has estrogen agonist effects on bone. It has been shown to be effective in reducing vertebral fractures (approximately 30%-50%) and in increasing BMD at both the hip and spine.<sup>1</sup> Raloxifene is also indicated for the reduction of the risk of invasive breast cancer in postmenopausal women with osteoporosis.<sup>1</sup> Hot flashes are an adverse reaction associated with the use of raloxifene, which may be reason enough for some patients to select an alternative medication, especially for postmenopausal women already experiencing this symptom. In addition, patients receiving raloxifene have an increased risk of deep vein thrombosis, similar to that seen with the use of estrogen.<sup>1</sup>

### **Parathyroid Hormone**

Teriparatide (recombinant human parathyroid hormone analog) is the only anabolic agent approved for the treatment of osteoporosis in postmenopausal women and men at

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high risk of fracture, and is administered via daily subcutaneous injection.<sup>1</sup> It is also indicated for treatment in men and women at high risk of fracture with osteoporosis related to the sustained use of systemic glucocorticoid therapy, and to increase bone mass in men with primary or hypogonadal osteoporosis at high risk for fracture.<sup>1</sup> Unlike the antiresorptive agents, teriparatide increases bone remodeling, leading to increases in bone formation that are greater than bone resorption and, ultimately, increased bone density. Teriparatide has demonstrated efficacy in increasing vertebral, femoral neck, and total body BMD, as well as in reducing the risk of vertebral and nonvertebral fractures.<sup>26</sup> While teriparatide is generally well tolerated, dizziness and leg cramps have been reported as adverse events.<sup>1</sup> Teriparatide is contraindicated in patients with an increased risk of osteosarcoma and is not recommended for individuals with prior radiation therapy of the skeleton, bone metastases, a history of skeletal malignancy, or hypercalcemia.<sup>1</sup> The safety and efficacy of teriparatide has not been demonstrated beyond 2 years of treatment, and it is common practice to follow teriparatide therapy with an antiresorptive agent.<sup>1</sup>

### **Denosumab**

Denosumab, a monoclonal antibody, is the most recently approved osteoporosis-related medication. While it is considered an antiresorptive agent, denosumab works via a novel mechanism of action. It binds to RANKL (a protein essential for the formation, function, and survival of osteoclasts), preventing the activation of RANK on the surface of osteoclasts, and ultimately inhibiting the formation of osteoclasts, thereby decreasing bone resorption.<sup>27</sup> Denosumab is administered as a subcutaneous injection every 6 months, and is indicated for the treatment of osteoporosis in postmenopausal women with a high risk of fracture, such as those with a history of fracture, women with multiple risk factors for fracture, or patients who failed or are intolerant of other available therapies.<sup>28</sup> Data from a 3-year study of postmenopausal women with osteoporosis demonstrated a 68% relative decrease in the risk of vertebral fracture, a 40% relative decrease in the risk of hip fracture, and a 20% relative decrease in the risk of nonvertebral fracture with the use of denosumab versus placebo.<sup>27</sup> The most common adverse events observed with denosumab use include back and musculoskeletal pain, elevated cholesterol, and cystitis.<sup>27</sup>

### **Combination Therapy**

Combining osteoporosis medications (usually a bisphosphonate with a non-bisphosphonate) may be necessary to improve bone density effectively, although potential safety

concerns and lack of supporting data may limit this practice to only those with very severe cases of osteoporosis. In general, the concomitant use of 2 antiresorptive agents has shown greater increases in BMD compared with either agent alone; however, there are limited data evaluating the impact of combination therapy on fracture reduction and on long-term safety.<sup>29-31</sup> With regard to combining teriparatide (an anabolic agent) and an antiresorptive, the response varies. While combination therapy using teriparatide and raloxifene may enhance the bone-forming effects of teriparatide, the combination of teriparatide with alendronate seems to blunt the effects of teriparatide.<sup>32,33</sup> Treatment decisions concerning combination therapy should also weigh the potential gains against the additional costs, potential adverse effects, and potential for oversuppression of bone associated with the use of multiple therapies.

### **Emerging and Novel Agents**

Several agents are currently under investigation for the prevention and/or treatment of osteoporosis and new potential targets for treatment have been identified as a result of improved knowledge of bone pathophysiology, bone remodeling, bone cells, and intracellular signaling pathways. Antiresorptive agents currently in development include the estrogen agonists/antagonists, bazedoxifene and lasofoxifene; and odanacatib, an inhibitor of cathepsin K, which is a protease that degrades bone matrix.<sup>34,35</sup>

In addition, modifications to human parathyroid hormone are under investigation in an effort to generate additional anabolic agents with greater efficacy. The identification of new pathways involved in bone formation is also directing clinical research efforts toward the development of anabolic agents with novel targets. The signaling pathways involved in bone formation, particularly the Wnt-pathway, hold promise as potential treatment targets in those conditions that are characterized by an inability to attain sufficient bone formation.<sup>36,37</sup> Current focuses of research include antibodies that may work against naturally occurring Wnt-pathway antagonists and calcilytic agents, which are modulators of parathyroid hormone production.<sup>37</sup>

### **Selecting Appropriate Pharmacologic Therapy**

While available guidelines discuss and tend to agree regarding patients in whom pharmacologic treatment for osteoporosis should be initiated, there is often vagueness around selection of an appropriate agent. For instance, NOF guidelines provide discussion around which patients should be considered for therapy and the available pharmacologic agents, but do not specify which treatments should be used

**Table 2.** Treatment Recommendations From the AACE Postmenopausal Osteoporosis Guidelines<sup>2</sup>

<b>First-line options</b>	<ul style="list-style-type: none"> <li>• Alendronate</li> <li>• Risedronate</li> <li>• Zoledronic acid</li> <li>• Denosumab</li> </ul>
<b>Second-line options</b>	<ul style="list-style-type: none"> <li>• Ibandronate</li> <li>• Raloxifene<sup>a</sup></li> </ul>
<b>Third-line options</b>	<ul style="list-style-type: none"> <li>• Raloxifene<sup>a</sup></li> </ul>
<b>Last-line options</b>	<ul style="list-style-type: none"> <li>• Calcitonin</li> </ul>
<b>Patients with very high risk of fracture or patients in whom bisphosphonate therapy has failed</b>	<ul style="list-style-type: none"> <li>• Teriparatide</li> </ul>
<small>AACE indicates American Association of Clinical Endocrinologists.  <sup>a</sup>Raloxifene is identified as either a second- or third-line agent.</small>	

for which patients and in which order. The AACE guidelines (Table 2) and NAMS position statement (Table 3) do provide some suggestions related to which agents should be used when, but without confirmation of a treatment algorithm and in light of variations between guidelines and patients, these recommendations may not be as valuable.<sup>2,21</sup> Most guidelines do agree, however, that treatment for osteoporosis needs to be long term in most women. While the development of a single, definitive treatment algorithm may not be possible, clinicians may benefit from some guideline consensus related to selection of treatment, offering general recommendations while still allowing for providers to incorporate patient-specific factors and their own clinical judgment into decisions around therapy.

**Monitoring Treatment Efficacy**

Monitoring the efficacy of pharmacologic therapy is another key element in the treatment of osteoporosis. The NOF recommends that for patients receiving pharmacotherapy for osteoporosis, BMD should be evaluated regularly using dual-energy X-ray absorptiometry (DXA), to assess adher-

ence, persistence, and effectiveness of treatment.<sup>1</sup> A BMD test should be performed at least every 2 years, or more frequently should it be necessary in certain patients and clinical scenarios or until findings are stable.<sup>1</sup> Both the AACE guidelines and the NAMS position statement recommend repeat BMD assessments every 1 to 2 years until the patient is stable.<sup>2,20</sup> In addition, when possible, follow-up of patients should be done in the same facility, with the same machine, and preferably with the same technician to minimize variability as much as possible.<sup>2</sup> This continual assessment of BMD allows for routine evaluation of the need for pharmacotherapy, and allows for modifications to be made as necessary.<sup>1</sup> For instance, as a patient ages, the need for therapy may change and an agent with a different route of administration or mechanism of action may be required.

**Barriers to Optimal Osteoporosis Management**

Despite the availability of clear guidelines for the assessment and diagnosis of osteoporosis, and a number of effective therapies, the disease remains underdiagnosed and undertreated. While there may be no single clear culprit for this discrepancy in care, several types of barriers may collectively serve to influence this suboptimal care, including those related to available treatments, those related to providers, and those related to patients.

Treatment-related barriers include cumbersome dosing requirements and adverse reaction profiles. Oral bisphosphonates, which may be considered first-line therapy and are the most frequently used medications for patients with osteoporosis, require patients to take them on an empty stomach, to remain upright for at least 30 minutes after ingestion, and to avoid intake of food and beverages for at least an hour. This complicated routine, performed on a daily, weekly, or monthly basis, can wear on a patient’s patience. Injectable bisphosphonate alternatives pose their own problems, as they require patients to endure frequent injections, and plan

**Table 3.** Treatment Recommendations From the 2010 North American Menopause Society Position Statement on the Management of Osteoporosis in Postmenopausal Women<sup>21</sup>

<b>Bisphosphonates</b>	<ul style="list-style-type: none"> <li>• First-line therapy for postmenopausal women with osteoporosis</li> </ul>
<b>Raloxifene</b>	<ul style="list-style-type: none"> <li>• Consider for postmenopausal women with low bone mass</li> <li>• Consider for younger postmenopausal women with osteoporosis</li> </ul>
<b>Teriparatide</b>	<ul style="list-style-type: none"> <li>• Reserve for postmenopausal women who are at high risk for fracture</li> </ul>
<b>Hormone therapy</b>	<ul style="list-style-type: none"> <li>• Primarily used to treat moderate to severe menopause-related symptoms, but can be considered for continued use for bone effects once symptoms cease</li> <li>• May be treatment option for a few years of early postmenopause</li> </ul>
<b>Calcitonin</b>	<ul style="list-style-type: none"> <li>• Not first-line therapy, but may be used in women with osteoporosis who are more than 5 years beyond menopause</li> </ul>

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frequent trips to their healthcare providers for administration. Teriparatide requires a daily subcutaneous injection, which is also a burden for patients.

In addition to complications related to administration, side effect profiles of many agents make them less than desirable. For example, bisphosphonates have been associated with gastrointestinal side effects, and more recently concerns related to osteonecrosis of the jaw and peripheral fractures related to oversuppression of bone. Raloxifene is known to cause hot flashes in patients, which may be especially concerning to postmenopausal women as they may already be experiencing hot flashes. Hormone therapies may be of concern to patients due to the controversies around their potential association with risk of other conditions, such as VTE events and stroke.

General barriers for clinicians may include the lack of definitive guidelines for selecting therapy for patients at risk for or with osteoporosis. Another point to consider is lack of continuity of care. Although most patients present to an orthopedic surgeon for the treatment of a fracture, studies have found that orthopedic surgeons feel primary care physicians are primarily responsible for any investigation and subsequent medical treatment for the fracture.<sup>38</sup> Additionally, primary care physicians and general practitioners may not be fully convinced that the efficacy of available osteoporosis therapies is worth the attendant costs and associated risks.<sup>39</sup>

Patient-related barriers to optimal osteoporosis management may include misconceptions around the need for treatment once a fracture has healed.<sup>39</sup> Additionally, since osteoporosis medications do not provide physical evidence that they are working, many patients may not feel that the medications are effective or necessary. These patient perceptions and beliefs may lead to a significant lack of adherence and persistence with osteoporosis management regimens, and ultimately an undertreated patient population.

### Addressing Adherence and Persistence

Regardless of disease or condition, adherence with recommended therapies is essential to treatment success. This issue is especially important for chronic, asymptomatic diseases such as osteoporosis, where nonadherence can result in debilitating fractures. Adherence (the extent to which a patient acts in accordance with dosing regimens) and persistence (the extent to which a patient continues treatment for a prescribed length of time) with osteoporosis therapies have long been problematic. Despite improvements in dosing regimens seen with newer agents, many women discontinue their osteoporosis treatment within the first year of therapy.<sup>40</sup> Regardless of the agent, higher adherence and persistence rates mean better

patient outcomes and lower adherence and persistence rates mean more fractures.

Several factors may contribute to poor adherence and persistence with regard to osteoporosis medications, including troublesome side effects, complexity of dosing, doubt about efficacy or safety of therapy, out-of-pocket costs, and underestimation of fracture risk. Clinicians play a vital role in addressing these issues with their patients with osteoporosis, and may play a significant role in improving adherence and persistence.

Since a variety of factors contribute to medication nonadherence, a multifaceted approach is necessary to improve adherence. Strategies for improving adherence begin with identification of the problem. Clinicians should look for signs of nonadherence such as lack of improvement in BMD or missed refills, and they should promote open communication with patients by asking if they are taking their medications. In addition, discussions with patients should be nonconfrontational and aim to uncover barriers to adherence that the patient may be experiencing. Providers should also take the time to emphasize the value of the therapy in preventing fractures and potential repercussions associated with nonadherence. In addition to effective patient-provider communication, other strategies for improved adherence include prescribing medications with simplified dosing schedules, educating and employing caregivers and family members on the importance of maintaining adherence, and providing access to adequate patient education. It is important for physicians to individualize therapy, as well as follow up with patients to ensure they are taking their medication as prescribed and to identify reasons for medication nonadherence.<sup>41</sup>

### Managed Care Organization Perspective

Managed care organizations (MCOs) recognize that there is a significant cost and illness burden associated with osteoporosis. The condition is responsible for more than 2.0 million fractures per year, including more than 300,000 hip fractures, 400,000 wrist fractures, 600,000 vertebral fractures, and 700,000 fractures at other sites.<sup>1</sup> Additionally, in 2005, osteoporosis-related fractures were responsible for an estimated \$19 billion in costs, and by 2025, experts predict that these costs will rise to approximately \$25.3 billion.<sup>1</sup>

There are significant life impact issues associated with osteoporosis as well. The consequences of bone disease can include pain, loss of productivity, impairment of functional states, and loss of independence. Patients who are disabled from osteoporotic fractures have higher risk for pressure

ulcers, pneumonia, and urinary tract infection. Fractures can also result in depression, loss of self-esteem, and fear of falling and suffering another fracture.<sup>4</sup>

Despite the availability of multiple treatments for osteoporosis, “real-world” adherence with osteoporosis medications tends to be suboptimal. Multiple analytic studies in the literature showed that less than 50% of osteoporotic women treated with bisphosphonates (both daily and weekly doses) were adherent to therapy as defined by a medication possession ratio (MPR) of less than 80%.<sup>42,43</sup> The study by Huybrechts et al showed that nonadherence (as defined by an MPR of less than 80%) was associated with a statistically significant higher risk of fracture (16.7%). This study also showed that nonadherence with osteoporosis therapy was associated with a 37.2% higher rate of all-cause hospitalizations per patient month and an increase in patient cost (\$600 vs \$340 per patient per month,  $P < .001$ ).<sup>43</sup> More recently, a study by Halpern et al published in January 2011 showed that in both commercial and Medicare plans, low medication adherence with osteoporosis therapy (as defined by an MPR of less than 80%) is associated with undesirable clinical and economic consequences. In the Halpern et al study, commercial members with low adherence had a 37% higher risk of fracture and Medicare members with low adherence had 18% greater all-cause medical costs and 34% more all-cause hospitalizations.<sup>44</sup>

It is clear from studies such as these that there are both economic and clinical advantages to MCOs that can appropriately manage access to and adherence with osteoporosis therapy. To that end, MCOs must develop policies and formularies that balance appropriate patient access to all medically appropriate therapies with the need to manage the cost of therapy in this category.

## Conclusion

Osteoporosis is a potentially debilitating disease with significant health and economic consequences. With the availability of screening protocols and clinical guidelines, providers have the tools necessary to effectively assess patient risk for osteoporosis and related fractures, and to implement therapy. There are a myriad of pharmacologic agents currently available and in development to help improve outcomes for patients with or at risk for osteoporosis and related fractures. It is imperative that providers continue to utilize available resources to improve the diagnosis and management of osteoporosis. The incorporation of strategies to identify and improve patient adherence with therapy is crucial for reducing the risk of fracture as well as helping to address the potential health and economic consequences associated with osteoporosis.

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