

Compliance and persistence with osteoporosis therapies: we can do better



Deborah T Gold* &
Stuart L Silverman

*Author for correspondence
Duke University Medical
Center, Departments of
Psychiatry and Behavioral
Sciences,
and
Sociology, Center for Aging,
Box 3003, Durham, NC
27710, USA
Tel.: +1 919 660 7530;
Fax: +1 919 668 0453;
drg@geri.duke.edu

'The aging of the US population virtually guarantees that the prevalence of osteoporosis and the incidence of related fractures will both skyrocket.'

Osteoporosis is a skeletal disorder responsible for atraumatic fractures that lead to deformity, pain and reduced quality of life. According to the National Osteoporosis Foundation (NOF), over 40 million Americans either have or are at risk of this disease. Those with or at risk of osteoporosis are of both genders and all races, ethnic backgrounds, educational and income levels [101]. Although women in the peri- and post-menopause are at greatest risk for osteoporosis, every adult over 65 years of age can develop this disease. And because Americans are living longer, on average, than ever before, many more adults aged 65 years and over will experience bone loss. One out of two post-menopausal women and one out of four men over 65 years of age will experience at least one osteoporotic (fragility) fracture in her or his lifetime [1]. The aging of the US population virtually guarantees that the prevalence of osteoporosis and the incidence of related fractures will both skyrocket.

In response to increasing awareness of osteoporosis as a threat to the public health, former US Surgeon General, Richard Carmona, commissioned a report, published in 2004, entitled Bone Health and Osteoporosis: A Surgeon General's Report [102]. The report indicated that America's bone health was "in jeopardy" and could only be expected to worsen with our aging population. However, in a note of hopefulness, the report also indicated the following [102]:

"Today, however, advances in scientific knowledge have ushered in a new era in bone health, one in which bone diseases can be prevented in the vast majority of individuals and identified early and treated effectively in those who do get them".

What a comforting statement for those with and at risk of osteoporosis as well as for those

who treat it! All we need to do is utilize our existing knowledge about medications, calcium and vitamin D supplementation, exercise and positive health behaviors, and this public health disaster can be averted!

So why, 3 years later, are fracture rates still rising and the economic and psychosocial costs of this debilitating disease growing exponentially? One answer to this question is poor compliance and persistence with pharmaceutical therapies that prevent and/or treat osteoporosis while reducing risk of fractures. Interestingly, the Surgeon General's report mentions issues of compliance only peripherally but does note that frequency of dosing could be a key to solving the compliance problem and therefore improving the bone health of America.

The issues of compliance and persistence with osteoporosis medications have entered the research literature only recently. Other than some articles in the 1980s and early 1990s on compliance with estrogen, the literature on patient compliance with osteoporosis medications did not burgeon until we were several years into the 21st Century. Articles such as McCombs and colleagues examined compliance rates in users of hormone therapy, bisphosphonates and raloxifene and concluded that, after 1 year, patient compliance was poor; however, reasons for poor compliance were not examined [2].

Solomon and colleagues also found that long-term compliance with osteoporosis drugs was poor (45% of their sample had stopped taking osteoporosis medications at 1 year) [3]. However, after adjusting the models for patient characteristics such as sex, age and number of comorbid conditions that independently predicted compliance, almost no additional variance was explained. Siris and others reported that adherence to bisphosphonate therapy significantly reduced fractures at 24 months [4]. Finally Gold and colleagues, analyzing claims data, also found that persistence was related to reduced risk of fracture [5].

A major turning point occurred in the literature on compliance with osteoporosis therapy when once-weekly alendronate was approved by the US FDA for the prevention and treatment of osteoporosis in postmenopausal women and

to increase bone mass in men (2000). Soon thereafter, once-weekly risedronate won FDA approval for the same indications (2002). Because of the change in medication frequency, many believed that compliance and persistence must certainly improve. Almost overnight, dosing interval took over as the key (and sometimes only) variable explaining compliance and persistence. Persistence with weekly medications was compared with that of daily medications, and studies found that weekly medications improved medication-taking behaviors [6,7]. When monthly ibandronate was FDA approved (in 2005), compliance and persistence questions became more complex but still focused on dosing interval as the critical factor influencing persistence. Some studies found that a longer dosing interval improved compliance and persistence (for example [8]) while others reported findings to suggest that the monthly dosing interval was not significantly better in persistence than weekly or daily therapies (for example [9]).

Different dosing intervals and methods of administration of osteoporosis medication proliferated. Oral bisphosphonates came in daily, weekly, monthly and two consecutive days a month versions; injectable drugs (teriparatide and ibandronate) had daily or every 3-month intervals. Most recently, the FDA approved a once-yearly infusion of zoledronic acid – a dosing interval that would require patients and healthcare providers to merely remember annually to treat osteoporosis.

As these studies have shown us, dosing intervals can play an important role in helping patients with osteoporosis comply and persist with their medication regimens. However, dosing interval is not the only factor that influences behavior of patients in taking their medications as directed. Virtually every article that discusses compliance and persistence with osteoporosis medications points out that overall compliance and persistence – even with substantial intervals between doses – are poor [10].

What happens when patients practice good compliance and persistence? In an excellent article, Siris and colleagues found that women who complied up to 50% of the time with their medication demonstrated only marginal effects from their bisphosphonates, while those who complied 80% of the time demonstrated a significant reduction in fracture rates [4]. In a study of claims data, Caro and colleagues found that patients

who complied with their osteoporosis therapy demonstrated a significantly reduced fracture rate when compared with their noncompliant peers [11]. And in a study by Weycker and others, those who are compliant more than 90% of the time demonstrated significantly reduced fracture risk [12].

‘... studies found that weekly medications improved medication-taking behaviors’.

Exactly why patients do not comply with their healthcare professionals’ recommendations has not yet been adequately investigated. But there are some common factors that reduce compliance: high medication costs, complex medication regimens, substantial side effects, drug interactions, comorbid conditions treated with multiple medications and poor patient–provider communication [13,14]. And some patients simply forget!

What are the negative consequences of poor persistence with osteoporosis therapies? According to Cramer and Silverman, poor persistence with bisphosphonates can lead to smaller decreases in bone turnover, smaller improvements in bone mineral density, as well as higher rates of fracture and disability [15]. In the long term, they say, poor compliance leads to increased healthcare costs because adverse events such as fractures are more likely to occur. Furthermore, all of these consequences cumulate to substantially reduce a patient’s quality of life.

Despite the many challenges people with osteoporosis face in taking their medications as directed by their healthcare professionals, the future of compliance and persistence with osteoporosis medications is getting brighter all the time. With the FDA approval of once-yearly zoledronic acid, patients can now select dosing intervals that work best with their lives. In addition, healthcare professionals need to educate patients about the importance of compliance and how best to achieve it. Educational programs combined with reminder systems that can be set up in individual physicians’ offices by allied healthcare professionals (e-mail reminders and phone contacts) can have a positive impact on patient behaviors. As an example, a study of medication compliance demonstrated that nurse monitoring of patients with osteoporosis increased compliance with raloxifene by 57% [16].

Despite the many published reports on poor medication compliance by patients with osteoporosis, there should be substantial hope that these behaviors can be changed in the future. Patient options for mode of delivery and dosing intervals should make the onerous task of taking medication somewhat easier. Further, medications that are now available for the treatment of osteoporosis are remarkably effective at increasing bone density and reducing fractures. All of these positives should signal a brighter future for medication compliance and persistence in osteoporosis, and they can be translated into real-world behaviors that will reduce future

fractures if providers and patients work together to conquer osteoporosis.

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Affiliations

- Deborah T Gold, PhD
Duke University Medical Center, Departments of Psychiatry and Behavioral Sciences, and
Sociology, Center for Aging, Box 3003, Durham, NC 27710, USA
Tel.: +1 919 660 7530;
Fax: +1 919 668 0453;
dvg@geri.duke.edu
- Stuart L Silverman, MD, FACP, FACP
UCLA, Cedars Sinai Medical Center, Greater Los Angeles Veterans Administration Health System, Los Angeles, CA, USA
Tel.: +1 310 358 2234;
Fax: +1 310 659 2841;
stuart@omcresearch.org