“Never order a test you don’t know how to interpret.”
This was a basic principle of our medical education, and yet so easily we forget. In practice, when treatment is initiated for disease or for prevention, observation and monitoring usually are necessary to assure response and efficacy of treatment. However, routine monitoring of osteoporosis treatment may not fit this paradigm precisely because of the uncertainty surrounding the meaning of test results. Osteoporosis is a disease in which tertiary prevention (prevention of fractures) is the recommendation, rather than secondary (treatment of osteoporosis) or primary (treatment of osteopenia) prevention. The latter are highly suggestive, based on both lifestyle modification and pharmacotherapy.

The definition and measurement of osteoporosis is made via a dual-energy x-ray absorptiometry (DEXA) bone scan of bone density. The US Preventive Services Task Force (USPSTF) in 2002 stated:

The USPSTF found good evidence that the risk for osteoporosis and fracture increases with age and other factors, that bone density measurements accurately predict the risk for fractures in the short-term, and that treating asymptomatic women with osteoporosis reduces their risk for fracture. The USPSTF concludes that the benefits of screening and treatment are of at least moderate magnitude for women at increased risk by virtue of age or presence of other risk factors. American College of Obstetrics and Gynecology guidelines go further, suggesting a need for prevention and treatment of osteoporosis.

With these recommendations in place since at least 2002, a great number of DEXA scans have been performed and women treated via lifestyle changes and/or pharmacotherapy for osteopenia or osteoporosis. Having initiated treatment, patients should be evaluated by their physicians to determine the efficacy of their treatment. The USPSTF has suggested repeating bone density scans after 18 to 24 months of treatment initiation to determine whether there has been any improvement. However, there is little evidence to support this or another time interval for repeat scans, or even to determine the best method of evaluation. More disturbing is the fact that recommendations for evaluation of additional or further treatment have not been developed. Why are we retesting women for osteoporosis if we do not know how best to test them or what to do with the results?

### Gauging What We Don’t Know

To date there have been no studies examining the best methods or the best times to repeat bone density scans. Some experts suggest repeating the scan 12 months after start of treatment. However, there is debate as to whether this is a sufficient time period, as some women may not show improvement until the second year of treatment. Thus, although an improvement seen at 12 months would be reassuring, a negative value would not necessarily be cause to change medication. One study examined alendronate and found that, among women whose bone density had decreased by more than 4% in the first year of treatment, 83% showed improvement in the second year without any change in medication or treatment.

Some experts suggest a 2-year interval is necessary to measure any significant changes in bone density. Menopausal women normally lose bone density at a rate of 2% per year. And, approximately 15% of women on estrogen or alendronate experience continued bone loss in spite of therapy. A meta-analysis found that a small improvement in bone density may correlate in a small way with fewer fractures (0.03 relative risk of improvement). However, measuring bone density only every 2 years may cause clinicians to miss early losses.

Another method of measuring efficacy of treatment is to use various biochemical markers at the onset of treatment and then repeat the measurement in 6 months. However, there is no evidence to support that changes or decreases in bone turnover markers are related to or correlate with decreased risk of fractures.

Some experts believe no further monitoring is necessary because there is no evidence that increasing the doses, changing the medication, or combining medications improves bone density loss for patients who do not respond.
to initial therapy. There is no evidence that increasing the dose of the bisphosphonates or raloxifene over the starting dose decreases the risk of fractures. For those women at high risk for fractures and for those who have already had fractures, many experts suggest that additional use of estrogen, calcitonin, or parathyroid hormone in addition to bisphosphonates may improve bone density, although there is no evidence to support this claim, either. Despite all this, we currently treat women for osteopenia or osteoporosis without fractures, though in this population additional medication is not indicated. Additionally, with the recent evidence of the negative effects of estrogen use, its addition is not suggested except for the treatment of severely affected women.

Consistent therapeutic behavior suggests that evaluating treatment of osteoporosis or osteopenia via repeat bone density scans or monitoring of biologic markers is not warranted, or that we should only do follow-up testing for osteoporosis if it will change our management of the patient—a process for which there currently is little supporting evidence. Because there is no consensus about method of evaluation or treatment of failures, further investigation may not be reasonable. What is obvious is that further long-term investigation of treatment efficacy and treatment failures is essential.

References

Lou Bridges, MD PhD
Dawn L. Satterfield, PhD
Frank Vinicor, MD, MPH
Vince Winkle Prins, MD
Subhashini Yaturu, MD
Takao Ando, MD
Victor Buckwold, PhD
Ann Falsey, MD
Jennifer Cather, MD
Alan Elias, MD
Rachel Williams, PhD
Michael Fingerhood, MD, FACP
Yngvild Olsen, MD, MPH
Georgine Lamvu, MD, MPH
Vince Sorrell, MD
Jae Hee Kang, ScD
Muhammad Usman Mustafa, MD, MRCP(UK)
Kendrick A. Shunk, MD, PhD, FACC
Helen E. Cejtin, MD
Leslie S. Massad, MD
R. John Solaro, MD
W. Lane Duvall, MD
Jeffrey A. Cohen, MD
Robert J. Fox, MD
Robert J. Kaplan, MD
Neil C. Binkley, MD
Tara Shapiro, DO
Gunhilde Buchsbaum, MD
Mark Schifman, MD, MPH
Paula Insera, PhD
Wilbert S. Aronow, MD
Pasquale J. Palumbo, MD
Sanders J. Robins, MD
Arthur Burnett, MD
Nadeem U. Rahman, MD
Ariel Roguin, MD, PhD
Alfred E. Buxton, MD
Imran Saleem Virk, MD
Malanda Nsuami, MD, MPH
Javed Butler, MD, MPH
William C. Miller, MD, PhD, MPH
Fagen Xie, PhD
Ramesh K. Ramanathan, MD
Stuart M. Lichtman, MD, FACP
Stanley A. Gall, MD