# **Editorials**

# Monitoring Osteoporosis Treatment: DXA Should Not Be Routinely Repeated

HERBERT MUNCIE, MD, and LEANNE L. LEBLANC, MD Louisiana State University, New Orleans, Louisiana

Initiating treatment for osteoporosis is a relatively straight-forward clinical decision; however, determining if the patient has responded to treatment is a complex issue. The goal of osteoporosis treatment is reducing the patient's fracture risk.<sup>1</sup> Bone mineral density (BMD), as measured by dualenergy x-ray absorptiometry (DXA), is used as a surrogate marker for fracture risk; however, no studies have shown whether monitoring of therapy with repeat DXA actually reduces fractures. We believe that routine DXA to monitor therapy is unnecessary and a poor use of medical resources.

Most women significantly increase their BMD with treatment. In clinical trials, less than 10 percent of treated patients had a significant decrease in BMD.<sup>2</sup>

Among women whose BMD decreases, the most common cause is medication non-compliance, especially during the first three months of therapy. Compliance can be monitored by having a medical assistant assess therapy adherence<sup>3</sup> or by evaluating prescription refills.<sup>4</sup> Compliance is not an issue for physician-administered intravenous therapies. The least likely explanation for a decrease in BMD is nonresponse to therapy.<sup>5</sup>

Several organizations have made opinion-based recommendations about repeating DXA (*see accompanying table*).<sup>6-13</sup> A short-coming of expert opinion guidelines is the lack of data to support the recommendations. An evidence-based report in 2001 from the Agency for Healthcare Research and Quality discouraged retesting during the first year of therapy and cited insufficient evidence to determine the necessity of ever repeating the test.<sup>14</sup> That report has not been updated.

Many factors affect the accuracy of BMD testing, including intermachine variance; therefore, any repeat DXA ideally should be with the same machine.<sup>15</sup> Because all testing methods have variations in successive measurements due to random fluctuations, a statistically significant change in BMD must exceed the expected test-to-test variation. This statistically



This is one in a series of pro/con editorials discussing controversial issues in family medicine.

► See related editorial on page 749.



AAFP members may post comments about these editorials at http://www.aafp.org/afp/2010/1001/p749.html.

significant amount is referred to as the least significant change or the smallest detectible difference.<sup>16</sup> However, these effects take years to develop.

When outlying, seemingly extreme measurement results are repeated, they are often closer to the mean without any change in treatment; this phenomenon is called regression to the mean. Accordingly, repeating DXA in less than two years is unlikely to be clinically

## Table. Current Recommendations for Monitoring Osteoporosis Treatment

Organization	Recommendation
American Association of Clinical Endocrinologists <sup>6</sup>	Repeat yearly until stable, then every two years
Institute for Clinical Systems Improvement <sup>7</sup>	Acknowledges controversy; but if performed, repeat after one to two years of therapy
International Society for Clinical Densitometry <sup>8</sup>	Repeat based on each patient's clinical status, usually one year after starting therapy with longer intervals once therapeutic effect established
National Institutes of Health Consensus Development Panel on Osteoporosis Prevention, Diagnosis, and Therapy <sup>9</sup>	No specific recommendation
National Osteoporosis Foundation <sup>10</sup>	Serial testing in accordance with medical necessity and expected response, and in consideration of local regulatory requirements; usually one to two years after starting therapy
National Osteoporosis Guidelines Group (United Kingdom) <sup>11</sup>	No specific recommendation
North American Menopause Society <sup>12</sup>	Repeat every two years
Scientific Advisory Council of the Osteoporosis Society of Canada <sup>13</sup>	No specific recommendation

useful.<sup>17,18</sup> One study found that monitoring therapy during the first three years of bisphosphonate therapy is unnecessary and perhaps misleading.<sup>19</sup> Longitudinal data from Canada have challenged the need to repeat DXA in less than five years.<sup>20</sup>

An increase in BMD is associated with reduced fracture risk.<sup>21,22</sup> However, the relationship between BMD and fracture risk is not a linear one. Fracture risk decreases soon after beginning therapy, even preceding a measurable improvement in BMD.<sup>23,24</sup> Fracture risk can decrease with no change in BMD.<sup>25</sup> Studies have even shown a decreased fracture risk despite a slight decrease in BMD.<sup>26,27</sup>

Unless the physician knows how to adjust therapy based on repeat DXA, monitoring osteoporosis treatment via DXA is unlikely to be clinically necessary or beneficial. Currently, we assume that if the patient has not had a fracture and the BMD significantly increases, then no change in treatment is necessary. Most authorities recommend no change in treatment with a stable BMD.<sup>8</sup> Alternatively, if the BMD significantly worsens, should the therapy be changed? Proponents of repeat testing argue that a significant decrease in BMD would alert the physician to assess for secondary causes of osteoporosis, compliance with medication, or appropriate use of weight-bearing exercise.<sup>28</sup> All of these issues influence the treatment of osteoporosis, but most physicians can address these issues without using medical resources and repeating DXA.

Large test-to-test variance in BMD for the same person renders monitoring compliance to therapy via repeat DXA at least problematic, if not inaccurate.<sup>19</sup> Researchers have found no evidence that repeat DXA, up to eight years later, was better at predicting fracture risk than the initial test.<sup>29</sup> No study has addressed whether monitoring with repeat DXA improves compliance or BMD, or reduces fractures.

No outcomes-based answers are available to guide treatment changes based on repeat DXA. We urge physicians to continue osteoporosis treatment with medication and lifestyle changes, and we believe that additional routine DXA is unwarranted. Although this differs from expert guidelines, it is consistent with other published opinions.<sup>30</sup> Some monitoring of osteoporosis treatment may be helpful in the future, but it should be targeted to at-risk populations,<sup>31</sup> which have yet to be identified.

Address correspondence to Herbert Muncie, MD, at hmunci@lsuhsc. edu. Reprints are not available from the authors.

Author disclosure: Nothing to disclose.

#### **REFERENCES**

 Roux C, Garnero P, Thomas T, Sabatier JP, Orcel P, Audran M; Comité Scientifique du GRIO. Recommendations for monitoring antiresorptive therapies in postmenopausal osteoporosis. *Joint Bone Spine*. 2005;72(1):26-31.

- 2. Bonnick SL. Monitoring changes in bone density. *Womens Health (Lond Engl).* 2008;4:89-97.
- Clowes JA, Peel NF, Eastell R. The impact of monitoring on adherence and persistence with antiresorptive treatment for postmenopausal osteoporosis: a randomized controlled trial. J Clin Endocrinol Metab. 2004:89(3):1117-1123.
- Cramer JA, Silverman S. Persistence with bisphosphonate treatment for osteoporosis: finding the root of the problem. Am J Med. 2006;119(4 suppl 1):S12-S17.
- 5. Lewiecki EM. Nonresponders to osteoporosis therapy. *J Clin Densitom*. 2003;6(4):307-314.
- Hodgson SF, , et al.; AACE Osteoporosis Task Force. American Association of Clinical Endocrinologists medical guidelines for clinical practice for the prevention and treatment of postmenopausal osteoporosis: 2001 edition, with selected updates for 2003 [published correction appears in *Endocr Pract.* 2004;10(1):90]. *Endocr Pract.* 2003;9(6):544-564.
- Institute for Clinical Systems Improvement. Health care guideline: diagnosis and treatment of osteoporosis. http://www.icsi.org/osteoporosis/ diagnosis\_and\_treatment\_of\_osteoporosis\_\_3.html. Accessed July 10, 2009.
- Lenchik L, Kiebzak GM, Blunt BA; International Society for Clinical Densitometry Position Development Panel and Scientific Advisory Committee. What is the role of serial bone mineral density measurements in patient management? *J Clin Densitom*. 2002;5(suppl):S29-S38.
- NIH Consensus Development Panel on Osteoporosis Prevention, Diagnosis, and Therapy. Osteoporosis prevention, diagnosis, and therapy. *JAMA*. 2001;285(6):785-795.
- Clinician's guide to prevention and treatment of osteoporosis. Washington, DC: National Osteoporosis Foundation; 2008. http://www.nof.org/professionals/pdfs/NOF\_ClinicianGuide2009\_v7.pdf. Accessed July 10, 2009.
- 11. Osteoporosis clinical guideline for prevention and treatment. National Osteoporosis Guidelines Group; 2008. http://www.iofbonehealth.org/health-professionals/national-regional-guidelines/references.html#ef 12. Accessed May 9, 2010.
- North American Menopause Society. Management of postmenopausal osteoporosis: position statement of the North American Menopause Society. Menopause. 2002;9(2):84-101.
- Brown JP, Josse RG; Scientific Advisory Council of the Osteoporosis Society of Canada. 2002 clinical practice guidelines for the diagnosis and management of osteoporosis in Canada [published corrections appear in CMAJ. 2003;168(4):400, CMAJ. 2003;168(6):676, and CMAJ. 2003;168(5):544]. CMAJ. 2002;167(10 suppl):S1-S34.
- Nelson HD, Morris CD, Kraemer DF, et al. Osteoporosis in postmenopausal women: diagnosis and monitoring. Evidence Report/Technology Assessment No. 28. AHRQ Publication No. 01-E031. Rockville, Md.: Agency for Healthcare Research and Quality. January 2001. http:// www.ahrq.gov/clinic/epcsums/osteosum.htm. Accessed May 9, 2010.
- Kolta S, et al. Follow-up of individual patients on two DXA scanners of the same manufacturer. Osteoporosis Int. 2000;11(8):709-713.
- El Maghraoui A, Roux C. DXA scanning in clinical practice. QJM. 2008;101(8):605-617.
- Cummings SR, Palermo L, Browner W, et al.; Fracture Intervention Trial Research Group. Monitoring osteoporosis therapy with bone densitometry: misleading changes and regression to the mean. *JAMA*. 2000;283(10):1318-1321.
- 18. Morton V, Torgerson DJ. Regression to the mean: treatment effect without the intervention. *J Eval Clin Pract.* 2005;11(1):59-65.
- 19. Bell KJ, Hayen A, Macaskill P, et al. Value of routine monitoring of bone mineral density after starting bisphosphonate treatment: secondary analysis of trial data. *BMJ*. 2009;338:b2266.
- Berger C, Langsetmo L, Joseph L, et al.; Canadian Multicentre Osteoporosis Study Research Group. Change in bone mineral density as a function of age in women and men and association with the use of antiresorptive agents. CMAJ. 2008;178(13):1660-1668.

### **Editorials**

- 21. Cummings SR, Karpf DB, Harris F, et al. Improvement in spine bone density and reduction in risk of vertebral fractures during treatment with antiresorptive drugs. *Am J Med.* 2002;112(4):281-289.
- 22. Hochberg MC, Greenspan S, Wasnich RD, Miller P, Thompson DE, Ross PD. Changes in bone density and turnover explain the reductions in incidence of nonvertebral fractures that occur during treatment with antiresorptive agents. *J Clin Endocrinol Metab.* 2002;87:1586-1592.
- 23. Harris ST, Watts NB, Genant HK, et al.; Vertebral Efficacy with Risedronate Therapy (VERT) Study Group. Effects of risedronate treatment on vertebral and nonvertebral fractures in women with postmenopausal osteoporosis: a randomized controlled trial. *JAMA*. 1999;282(14):1344-1352.
- 24. Reginster J, Minne HW, Sorensen OH, et al.; Vertebral Efficacy with Risedronate Therapy (VERT) Study Group. Randomized trial of the effects of risedronate on vertebral fractures in women with established postmenopausal osteoporosis. Osteoporosis Int. 2000;11(1):83-91.
- Chapurlat RD, Palermo L, Ramsay P, Cummings SR. Risk of fracture among women who lose bone density during treatment with alendronate. The Fracture Intervention Trial. *Osteoporosis Int.* 2005; 16(7):842-848.

- 26. Watts NB, Cooper C, Lindsay R, et al. Relationship between changes in bone mineral density and vertebral fracture risk associated with risedronate: greater increases in bone mineral density do not relate to greater decreases in fracture risk. *J Clin Densitom*. 2004;7(3):255-261.
- 27. Watts NB, Geusens P, Barton IP, Felsenberg D. Relationship between changes in BMD and nonvertebral fracture incidence associated with risedronate: reduction in risk of nonvertebral fracture is not related to change in BMD. J Bone Miner Res. 2005;20(12):2097-2104.
- 28. Koval PG, Easterling L, Pettus D, Mackler L, Gottschall AB. Clinical inquiries. How should a DEXA scan be used to evaluate bisphosphonate therapy for osteoporosis? *J Fam Pract.* 2005;54(1):65, 69-71.
- Hillier TA, Stone KL, Bauer DC, et al. Evaluating the value of repeat bone mineral density measurement and prediction of fractures in older women: the study of osteoporotic fractures. *Arch Intern Med.* 2007;167(2):155-160.
- Compston J. Monitoring bone mineral density during antiresorptive treatment for osteoporosis. BMJ. 2009;338:b1276.
- 31. Curtis JR, Xi J, Westfall AO, et al. Improving the prediction of medication compliance: the example of bisphosphonates for osteoporosis. *Med Care.* 2009;47(3):334-341. ■