These findings suggest that patients may not need to understand the scientific definition of placebo in order to use the information to make judgments about drug efficacy. Terms such as “without the drug” deserve additional study.

Helen W. Sullivan, PhD, MPH
Amie C. O’Donoghue, PhD
Kathryn J. Aikin, PhD

Author Affiliations: Office of Prescription Drug Promotion, Center for Drug Evaluation and Research, Food and Drug Administration, Silver Spring, Maryland (Sullivan, O’Donoghue, Aikin).

Corresponding Author: Helen W. Sullivan, PhD, MPH, Office of Prescription Drug Promotion, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave, Silver Spring, MD 20993 (helen.sullivan@fda.hhs.gov).


Author Contributions: Dr Sullivan had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: All authors.

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"Due" for a Scan: Examining the Utility of Monitoring Densitometry

Opinions differ on the utility of monitoring dual-energy x-ray absorptiometry (DXA) to assess responses to treatment for low bone mineral density (BMD). Some argue that routine monitoring DXA may be unnecessary because approximately 98% of postmenopausal women treated with alendronate sodium experience an increase in BMD, and variation in subsequent BMD measurements by DXA may obscure the treatment effects.

This study aimed to understand the utility of monitoring DXA scans by assessing (1) clinician rationale for ordering monitoring DXA and (2) the treatment changes that follow among average-risk women who are receiving treatment for low BMD.
We hypothesized that monitoring DXA would rarely lead to treatment changes.

Methods | We identified 1782 patients at the University of Colorado Hospital, Aurora, who had undergone more than 1 DXA scan between January 1, 2003, and December 31, 2011. After excluding men (n = 120), those receiving medications or with conditions known to cause secondary osteoporosis (n = 580), and women not receiving treatment (n = 533), 549 women receiving treatment for low BMD remained. Of these, we reviewed the medical records from a random sample of 92 patients. Clinician rationale for ordering monitoring DXA and the treatment changes that followed were assessed.

Monitoring DXA was defined as any DXA performed on a patient being treated for low BMD, excluding the first DXA scan. All other scans were considered to be screening studies.

To explore clinician rationale for ordering monitoring DXA, we reviewed all the documentation within 6 months prior to the DXA scan or at the last clinical encounter. Quotations from the ordering clinician were recorded and categorized by topic. Changes in treatment following DXA were recorded as being due to monitoring DXA or due to factors other than monitoring DXA (Figure).

Results | Of 1647 DXA scans in 549 patients, the mean (SD) number of scans per patient was 3.0 (1.1) (range, 2-10 scans), with a mean interval of 2.4 years between scans. The mean age of our population was 68.4 years, 70 patients (76%) were white, and 91 (99%) were treated with bisphosphonates. For the 92 patients under review, a total of 196 monitoring DXA scans were performed. The mean 10-year probability of hip or major osteoporotic fracture as determined by the Fracture Risk Assessment Tool (FRAX; World Health Organization) was 3.5% and 13.3%, respectively.

The primary rationale for ordering scans was that they were “due” (177 of 196 scans [90%]). Other rationale for monitoring DXA and representative quotations from the ordering clinician are reported in the Table. Most scans (165 [84%]) resulted in no treatment changes (Figure, A). Among the 36 scans showing a significant decrease in BMD, 26 (72%) resulted in no treatment changes (Figure, B).
Discussion | Our data indicate that clinicians frequently order monitoring DXA scans out of a perception that they are due and rarely make changes in treatment based on the results. Even when DXA showed a significant decrease in BMD, treatment changes were uncommon. We are aware of no other studies that have assessed clinician rationale for ordering monitoring DXA or treatment changes that follow interpretation of the results.

We suspect that the frequency of monitoring DXA reflects adherence to professional guidelines, many of which recommend routine monitoring every 1 or 2 years while the patient is receiving treatment. Nonetheless, clinicians may feel uncomfortable escalating treatment on the basis of BMD changes because decreases in BMD during treatment do not reliably predict future fracture risk. Notably, most patients who lose BMD during the first year of treatment regain much of that in the following year even if the treatment is not changed. The findings from this single-center study, however, may not be generalizable to other institutions.

How often monitoring DXA should be used is uncertain, although finite health resources and our obligation to avoid unnecessary interventions require us to reconsider routine use of monitoring DXA among average-risk women who are receiving treatment for low BMD.

Brandon P. Combs, MD
Michelle Rappaport, BA
Tanner J. Caverly, MD
Daniel D. Matlock, MD, MPH

Author Affiliations: Division of General Internal Medicine, University of Colorado Denver School of Medicine, Aurora (Combs, Rappaport, Caverly, Matlock).

Corresponding Author: Brandon P. Combs, MD, Division of General Internal Medicine, University of Colorado Denver School of Medicine, 2011 E Lowry Blvd, Ste 120, Denver, CO 80220 (brandon.combs@ucdenver.edu).


Author Contributions: Dr Combs had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Combs, Caverly, Matlock.

Acquisition of data: Combs, Rappaport.

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Transparency Interrupted: The Curtailment of the European Medicines Agency’s Policy on Access to Documents

A colleague and I recently reported on the first 2 years of the European Medicines Agency’s (EMA’s) November 2010 freedom of information policy on access to documents.1 The policy made a wide range of regulatory documents potentially accessible to anyone who asked for them, including clinical study reports. As of November 19, 2012, the EMA had released approximately 1.66 million pages of clinical trial data and other documents in response to 457 requests.1

On April 25, 2013, the General Court of the European Union, in 2 interim decisions, ordered the EMA not to provide documents in response to 3 specific requests. The injunction followed legal action by AbbVie (Wilmington, Delaware) about 2 separate requests for clinical study reports for adalimumab (Humira), a drug for rheumatoid arthritis, and legal action by InterMune (Brisbane, California) about a request for similar documents on pirfenidone (Esbriet), a drug for idiopathic pulmonary fibrosis. Both companies contended that the requested EMA documents contain commercially confidential information.2,3 The EMA had planned to provide the documents, consistent with the view that “clinical trial data should not be considered commercial confidential information.”4 A hearing on the case may not be held until 2014.5

On April 30, the EMA responded to the court order by declaring an intention to “continue with its policy to grant access to documents” but that “requests for access to documents similar to those contested by AbbVie and InterMune will be considered on a case-by-case basis.”6 In addition, the EMA confirmed that it would continue to develop a forthcoming policy on proactive publication of clinical trial data, pending the final decision of the court, and has since released a draft policy for public comment.7

I recently obtained a logfile (Appendix in Supplement) from the EMA of all 728 requests for documents handled under its policy through June 4, 2013. The logfile showed that on May 28, 2013, the EMA rejected requests for documents related to 54 products. Academia/research institutes (27 requests), health care professionals (11), legal professionals (11), the pharmaceutical industry (8), and media (3) made the requests. (I received 1 such rejection letter, which cited the on-