

# Prevention of Glucocorticoid-Induced Osteoporosis: Why Are We Doing So Poorly?



Glucocorticoid-induced osteoporosis (GIOP) is a significant public health issue. Up to 1% of adults are treated with glucocorticoids (GC), and GC increase the risk of fracture, even with doses of prednisone as low as 2.5 mg/day<sup>1</sup>. The increase in fracture risk begins early, within 3 to 6 months of onset of treatment, and glucocorticoids appear to lower the fracture threshold so that the increased fracture risk is at least in part independent of bone density<sup>1-3</sup>. There are effective strategies for prevention and treatment of GIOP, best documented for oral bisphosphonates along with supplemental calcium and vitamin D. Several national organizations have published guidelines incorporating these findings<sup>4-9</sup>.

In this issue of *The Journal*, Saag, *et al* report results of a retrospective cohort study among new users of glucocorticoids who received a mean dose of 11 mg prednisone for more than 6 months<sup>10</sup>. The authors evaluated the receipt of bone mass measurement and use of prescription medications to prevent GIOP over a 6-year time period beginning in 1996, the year of publication of the American College of Rheumatology (ACR) guidelines for the prevention and treatment of GIOP<sup>11</sup>. Early in this period (in 1997), Medicare coverage for dual-energy x-ray absorptiometry (DEXA) studies for patients receiving glucocorticoids was approved in the United States. Saag, *et al* document an increase in the receipt of a bone mass measurement in postmenopausal women and an increase in the use of antiosteoporotic medications, particularly among women ages 65 years and over.

While the findings of Saag, *et al* might seem encouraging, does this mean we are doing a good job of protecting our patients? Hardly. Looked at carefully, their results are not reassuring.

Saag, *et al* found that rates of DEXA nearly doubled from 10% in 1996–97 to 19% in 2000–01 among postmenopausal women, but this increase is not impressive. Rates of DEXA remained below 6% among women under age 50 years and

in men. As for the use of antiosteoporotic medications, this approached 50% for women ages 50 years and over, but was substantially less frequent in men and women under age 50. Put differently, even in the highest risk group, more than half received no antiosteoporotic treatment. Unfortunately, even this exaggerates the proportion of patients who receive adequate treatment. First, including estrogen as an antiosteoporotic medication may inadvertently inflate estimates of treatment rates, as estrogen could well have been prescribed for reasons other than for osteoporosis. As Saag, *et al* point out, the use of estrogen has decreased dramatically since publication of the Women's Health Initiative, and these women may now be at higher risk of fracture<sup>12</sup>. More importantly, the authors defined the use of antiosteoporotic medications as the receipt of "one or more" prescription treatments as documented within the pharmaceutical database. About half of patients who start osteoporosis treatment discontinue by the end of a year, so that many patients who begin prescription therapy obtain little benefit<sup>13</sup>. For these reasons, the results of Saag, *et al* overestimate the number of patients who receive adequate treatment.

Saag, *et al* confined their study to the population covered by the 1996 ACR guidelines, which included patients starting glucocorticoid therapy and expected to receive  $\geq 7.5$  mg/day of prednisone equivalent for more than 6 months. The ACR guidelines were updated in 2001 to recommend antiosteoporotic prescription medication for new users of GC at a dose of  $\geq 5$  mg/day for more than 3 months<sup>4</sup>. Had the Saag study been performed using these revised guidelines, their study would likely have documented even lower rates of prevention of GIOP.

Why are we doing so poorly? The following are some potential barriers to following the guidelines.

*Lack of awareness of the problem.* The introduction to the 2001 ACR guidelines states that low rates of treatment to prevent bone loss suggest "that physician awareness of

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bone loss and the increase in fracture risk caused by glucocorticoid treatment is low.”<sup>4</sup> While it strains credulity to think that physicians are unaware of these risks, some information on the extent of the risk, especially with low-dose GC therapy, is relatively new<sup>1</sup>.

*Lack of awareness of the treatment guidelines.* In the United States, the ACR guidelines were published in a rheumatology journal, and were not likely seen by primary care physicians or other specialists. Even if physicians know about the existence of a guideline, it is easy to forget about it at the time of the office visit<sup>14</sup>.

*The guidelines are confusing.* The published guidelines are inconsistent as to who should be treated. For example, there is disagreement whether the cutoff should be prednisone 5 mg/day for 3 or more months or 7.5 mg/day for 6 or more months. The guidelines differ as to whether new GC users should be treated automatically with bisphosphonates or have treatment decisions based on bone mass measurement. Suggested T-score cutoffs for treatment range from -1 to -2.5. Some guidelines differentiate between new and chronic GC users, while others do not. This distinction seems to add unnecessary complexity. Simplification of the guidelines might improve practice<sup>15</sup>.

*The guidelines are hard to implement.* Physicians may not have the time and skills to effect lifestyle modifications recommended by guidelines, such as those relating to nutrition and exercise. Time spent on counselling about fracture risk may be poorly reimbursed. Physicians may also feel the need to focus on underlying illness being treated with GC. In one study, patients receiving GC had a mean of 6 comorbid illnesses<sup>16</sup>. Limited access to bone densitometry may be a barrier to implementing the guidelines in some areas.

*Implementing the guidelines may lead to inappropriate treatment.* While there is no question that GC increase fracture risk and there are good data demonstrating improvements in bone density with intervention, there are no studies that address fracture prevention as a primary outcome. Based in part on analogy to the treatment of postmenopausal osteoporosis, there appears to be little doubt that treatment is effective in the reduction of fracture risk, but this has not been rigorously tested. We also do not have enough information to evaluate the cost-effectiveness of any specific strategy for prevention and treatment of GIOP, especially in premenopausal women and younger men receiving low doses of GC. The absolute risk of fracture in premenopausal women and younger men is low, so that an increased relative risk associated with GC therapy may not warrant intervention. In addition, we lack data on the safety of bisphosphonates in women who might become pregnant, so that caution in the treatment of premenopausal women is warranted<sup>17</sup>. Last, guidelines written to address a single issue such as GIOP may not adequately address the complexity of care required for older patients with multiple comorbid dis-

eases. For these patients, application of several guidelines each focused on different problems may result in excessive care<sup>18</sup>.

*Patients may not accept treatment.* Studies such as that by Saag, *et al* evaluate only whether the patient received a test or treatment. They do not address the critical role of the patient, who may decline to initiate therapy for many reasons, including lack of trust in the physician, lack of confidence in the effectiveness of the intervention, dissatisfaction with communication with the physician, fear of side effects, complexity of the dosing regimen, and cost of therapy. Patients, especially older patients with multiple medical problems, vary in regard to the importance they place on certain health outcomes, such as the prevention of GIOP, as well as the risk of adverse events and inconvenience they are willing to accept<sup>19</sup>. Analyses of administrative databases without chart review may underestimate the quality of care offered to patients, because such analyses do not take into account instances where appropriate care was offered, but not accepted<sup>20</sup>.

The article by Saag, *et al* is a helpful reminder that in spite of increasing rates of bone mass measurement and use of antiosteoporotic medication for patients receiving glucocorticoid treatment, we have a long way to go. It is now time for us to move beyond documenting undertreatment of GIOP, and to focus our efforts on understanding barriers to treatment and developing interventions to improve quality of care.

**ROBERT A. YOOD, MD,**  
Meyers Primary Care Institute;  
Department of Medicine,  
Saint Vincent Hospital;  
Chief of Rheumatology,  
Fallon Clinic,  
630 Plantation Street,  
Worcester, Massachusetts 01605, USA

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