

# Do inhaled steroids increase the risk of osteoporosis?

## EVIDENCE-BASED ANSWER

The use of inhaled corticosteroids at conventional doses for asthma and chronic obstructive pulmonary disease (COPD) does not appear to be associated with significant bone loss at 2 to 3 years of follow-up (strength of recommendation [SOR]: **A**, systematic reviews and randomized controlled trials [RCTs]). However, higher doses of inhaled

corticosteroids may be associated with negative bone density changes at up to 4 years of follow-up (SOR: **C**, RCTs without change in fracture rates). No evidence exists to evaluate whether nasal steroids increase the risks of bone loss. Longer-term effects of prolonged use of inhaled steroids on BMD or fracture risk are undetermined with current evidence.

## CLINICAL COMMENTARY

### Encourage weight-bearing and aerobic exercise to all asthma or COPD patients

Asthma and COPD are prevalent among the underserved patients I see. Inhaled steroids are difficult for these patients to obtain. Once they feel better, many stop using the steroid until symptoms return.

Although we do not usually prescribe at the higher doses described in the review, our goal has always been long-term treatment. If these medications can cause osteoporosis with longer use, it may become an additional deterrent to adherence.

However, consistent use may reduce the use of oral steroids for acute exacerbations, potentially even reducing bone loss.

Encourage weight-bearing and aerobic exercise for osteoporosis prevention and balance exercises to prevent falls for all asthma or COPD patients. These exercises may be prudent prevention for both lung disease and osteoporotic fractures.

**José E. Rodríguez, MD**

Florida State University College of Medicine,  
Tallahassee

## Evidence summary

Inhaled corticosteroids are the primary therapy for asthma and are commonly prescribed for chronic obstructive pulmonary disease. The use of oral steroids is a well-known risk factor for osteoporosis, but the effects of inhaled corticosteroids on bone mineral density (BMD) are not well defined.

## No significant changes seen in BMD at moderate doses

Our search found evidence pertaining to the use of inhaled pulmonary steroids, but no evidence meeting our inclusion criteria about the effect of inhaled nasal steroids. We located a Cochrane review, 1 other meta-analysis, and 2 individual RCTs that were not included in the systematic reviews. Three of the 7 RCTs

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**Fereshteh Gerayli, MD**

Johnson City Family Practice  
Residency, East Tennessee  
State University, Johnson City

**Bridget Loven, MLIS**

Carolinas Healthcare System  
and Charlotte Area Health  
Education Center, Charlotte, NC

included in the 2002 Cochrane review met our inclusion criteria for evaluating the impact of inhaled corticosteroids on BMD or fracture rate for adults with asthma or COPD.

All 3 RCTs (792 subjects total) examined the effect of conventional doses of inhaled corticosteroids on BMD and 2 of the RCTs (892 participants total) collected fracture data. No demonstrable effect was seen on vertebral fracture (odds ratio [OR]=1.87; 95% confidence interval [CI], 0.5–7.03) or BMD at 2 years follow-up.<sup>1</sup> The subjects were otherwise healthy people with asthma or COPD with an average age of 40 years; men outnumbered women 2 to 1.

A fair-quality 2004 meta-analysis of 14 randomized trials (2300 participants) included 2 studies (448 subjects) that overlapped with the Cochrane review. There were no significant changes in BMD with moderately high doses of inhaled corticosteroids at 1 to 3 years follow-up.<sup>2</sup>

Annual changes in lumbar and femoral neck BMD (–0.23% and –0.17%, respectively) were not statistically significant. Mean changes in lumbar BMD were not significantly different from controls (–0.02). A fair-quality 2004 RCT did not demonstrate any clinically relevant effect on BMD at 2 years follow-up. This study used 800 mcg/day of fluticasone for patients with mild asthma.<sup>3</sup>

### **BMD changes found at higher doses**

There is, however, some evidence that higher doses of inhaled corticosteroids can result in adverse BMD changes. In a high-quality RCT of 412 participants, aged 40 to 69 years, with mild to moderate COPD, use of higher-dose triamcinolone (1200 mcg/day) was associated with decreased lumbar and femoral neck BMD over 3 to 4 years.<sup>4</sup> The differences in BMD between the inhaled corticosteroids and placebo groups at the femoral neck

and lumbar spine were 1.78% ( $P<.001$ ) and 1.33% ( $P=.007$ ), respectively. However, the risk of fracture or height loss did not increase at follow-up.

A large fair-quality RCT from 2001 included in both meta-analyses demonstrated a dose-related fall in BMD within the subjects over 2 years at the lumbar spine (standard deviation, 3.4%;  $P<.010$ ). This finding remained statistically significant after adjusting for asthma severity, but BMD changes were not different between the inhaled corticosteroids and placebo groups. However, this finding may be the result of higher oral corticosteroids use in the reference group.<sup>5</sup>

### **Limitations of these studies**

These studies, though, have limitations. The follow-up periods for all of these studies are less than 5 years, and thus the longer-term effects of prolonged use of inhaled corticosteroids on BMD or fracture risk cannot be determined with this evidence. Furthermore, the study populations were relatively young, with few other risk factors (they were, for example, predominantly male) than populations at highest risk for osteoporosis and fracture. These factors limit interpretation of the data for long-term inhaled corticosteroids use, particularly in populations with higher baseline osteoporosis risk—older persons with chronic lung disease who take inhaled corticosteroids for more than 2 to 3 years. We need better and longer-term studies to help advise our patients about the risks and benefits of inhaled corticosteroids therapy.

### **Recommendations from others**

The New Zealand Guideline Group says the risk of reduced BMD increased with long-term, high-dose inhaled corticosteroids.<sup>6</sup> The Institute for Clinical Systems Improvement guidelines recommends considering osteoporosis

### **FAST TRACK**

**Inhaled steroids at conventional doses do not seem to cause significant bone loss; higher doses might**

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prevention measures for those who have been (or will be) taking a daily high-dose inhaled glucocorticoid for several years as glucocorticoid use compounds fracture risk beyond that determined solely by BMD.<sup>7</sup>

#### REFERENCES

1. Jones A, Fay JK, Burr M, et al. Inhaled corticosteroid effects on bone metabolism in asthma and chronic obstructive pulmonary disease. *Cochrane Database Syst Rev* 1, 2006.
2. Halpern MT, Schmier JK, Van Kerkhove MD, et al. Impact of long term inhaled corticosteroid therapy on bone mineral density: results of a meta-analysis. *Ann Allergy Asthma Immunol* 2004; 92:201–207.
3. Kemp JP, Osur S, Shrewsbury SB, et al. Potential effects of fluticasone propionate on bone mineral density in patients with asthma: A 2-year randomized, double-blind, placebo-controlled trial. *Mayo Clin Proc* 2004; 79:458–466.
4. Scanlon PD, Connett JE, Wise RA, et al. Loss of bone density with inhaled triamcinolone in Lung Health Study II. *Am J Respir Crit Care Med* 2004; 170:1302–1309.
5. Tattersfield AE, Town GI, Johnell O, et al. Bone mineral density in subjects with mild asthma randomised to treatment with inhaled corticosteroids or non-corticosteroid treatment for two years. *Thorax* 2001; 56:272–278.
6. New Zealand Guidelines Group. The diagnosis and treatment of adult asthma. Wellington, NZ: New Zealand Guidelines Group; 2002 Sep. 101 p. Available at: [www.guideline.gov/summary/summary.aspx?doc\\_id=3462](http://www.guideline.gov/summary/summary.aspx?doc_id=3462) (NCG: 2688). Accessed on January 18, 2007.
7. Institute for Clinical Systems Improvement. Diagnosis and treatment of osteoporosis. Bloomington, Minn: Institute for Clinical Systems Improvement; 2005 Sep. 61 p. Available at: [www.guideline.gov/summary/summary.aspx?doc\\_id=9626](http://www.guideline.gov/summary/summary.aspx?doc_id=9626) (NCG: 5146). Accessed on January 18, 2007.