

# Do Bisphosphonates Cause Atypical Femoral Fractures?

*Analysis provides reassurance about intermediate-term safety.*

Several uncontrolled case series have described atypical subtrochanteric or femoral shaft fractures after long-term bisphosphonate therapy; the presumed mechanism is oversuppression of bone turnover ([JW Gen Med Dec 15 2009](#)). However, those reports do not establish causality. Now, researchers have examined whether an excess of such fractures occurred in three previously published randomized trials of bisphosphonate therapy for osteoporosis. The analysis was supported by the makers of alendronate and zoledronic acid.

The trials included about 7800 bisphosphonate recipients and 7500 placebo recipients: 3900 patients received zoledronic acid for 3 years, 3200 patients received alendronate for 4 years, and 660 patients received alendronate for 10 years. Overall, six bisphosphonate recipients and four placebo recipients experienced subtrochanteric or femoral shaft fractures — a nonsignificant difference.

**Comment:** This report provides considerable reassurance that intermediate-term use of bisphosphonates does not elevate risk for atypical femoral fractures. However, at least two concerns remain. First, most women in the trials used bisphosphonates for only 3 to 4 years. Second, patients taking multiple antiresorptive drugs or complicating drugs (e.g., corticosteroids) were underrepresented in these trials. Because of lingering uncertainty about longer-term exposure to bisphosphonates, some experts recommend a "drug holiday" after 5 to 10 years of bisphosphonate therapy. An excellent discussion of this issue — with specific recommendations — was recently published by Watts and Diab (*J Clin Endocrinol Metab* 2010; 95:1555). Among other things, they remind us that bisphosphonates should not be prescribed to low-risk patients, for whom even small risks would likely outweigh benefits.

— [Allan S. Brett, MD](#)

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