

# Long-term inhaled corticosteroid use increases fracture risk in lung disease patients

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Patients with chronic obstructive pulmonary disease (COPD) who use inhaled corticosteroids to improve breathing for more than six months have a 27 percent increased risk of bone fractures, new Johns Hopkins-led research suggests.

Because the research subjects were mostly men age 60 and older, the findings raise perhaps more troubling questions about the medication's effects on women with COPD, a group already at a significantly higher risk than men for fractures.

"There are millions of COPD patients who use long-term [inhaled corticosteroids](#) in the United States and millions more across the world," says Sonal Singh, M.D., M.P.H., an assistant professor of [general internal medicine](#) at the Johns Hopkins University School of Medicine and the senior author of the study published online in the journal *Thorax*. "The number of people who are getting fractures because of these medications is quite large."

The inhaled corticosteroids evaluated were fluticasone, sold in combination with salmeterol as Advair, and budesonide, sold in combination with formoterol as Symbicort. Although applied through the mouth, the body absorbs corticosteroids, which have long been linked to a decline in [bone density](#). Until now, no reliable association had been found to fractures in patients with COPD, Singh says.

Singh and his colleagues reviewed and analyzed two different sets of research studies comparing inhaled corticosteroids to a placebo in COPD patients. One study looked at 16 long-term double-blind [randomized controlled trials](#) with more than 17,500 participants; the other examined seven observational studies with 69,000 participants. In both, the researchers found a significantly increased risk of fractures for those using inhaled

corticosteroids. The observational studies also found evidence of dose-response that fracture risk increased as steroid dosage increased.

Recent research has linked other popular medications to increased fracture risk, notably [proton-pump inhibitors](#) given for heartburn and some diabetes drugs, such as rosiglitazone (Avandia) and pioglitazone (Actos).

Inhaled corticosteroids are used to reduce the frequency of hospitalizations in patients with moderate to severe COPD. "Patients need to know about this risk along with the benefits of these inhaled medications," Singh says. "People who continue to use inhaled corticosteroids should pay attention to bone health and consider the lowest possible dose for the shortest possible time. The risks may be somewhat mitigated with bone-building drugs."

Patients with COPD, the researchers note, are already at a high risk of osteoporosis and fractures, which may stem from nutritional deficiencies or previous corticosteroid use. At larger doses, adverse effects of inhaled corticosteroids may come close to that of oral steroids, which are well known to increase bone loss and decrease bone formation.

Singh says he would like the U.S. Food and Drug Administration to look into the issues discovered in this research by his team and his colleagues from the University of East Anglia in the United Kingdom and the University of Louisville in the United States.

Although many asthma patients also take inhaled corticosteroids, Singh says his research does not apply to that mostly younger cohort since they were not included in the study.

Singh says he is most concerned about those who were not the focus of this study: women.

"It was surprising to find an increased risk of fractures in this study where two-thirds of the participants were men over the age of 60," Singh says. "It really makes us wonder what is happening to women with COPD who use inhalers, because older women are already at a much higher [fracture risk](#) than men."

Provided by Johns Hopkins Medical Institutions

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