Can we withdraw treatment in post-menopausal osteoporosis?

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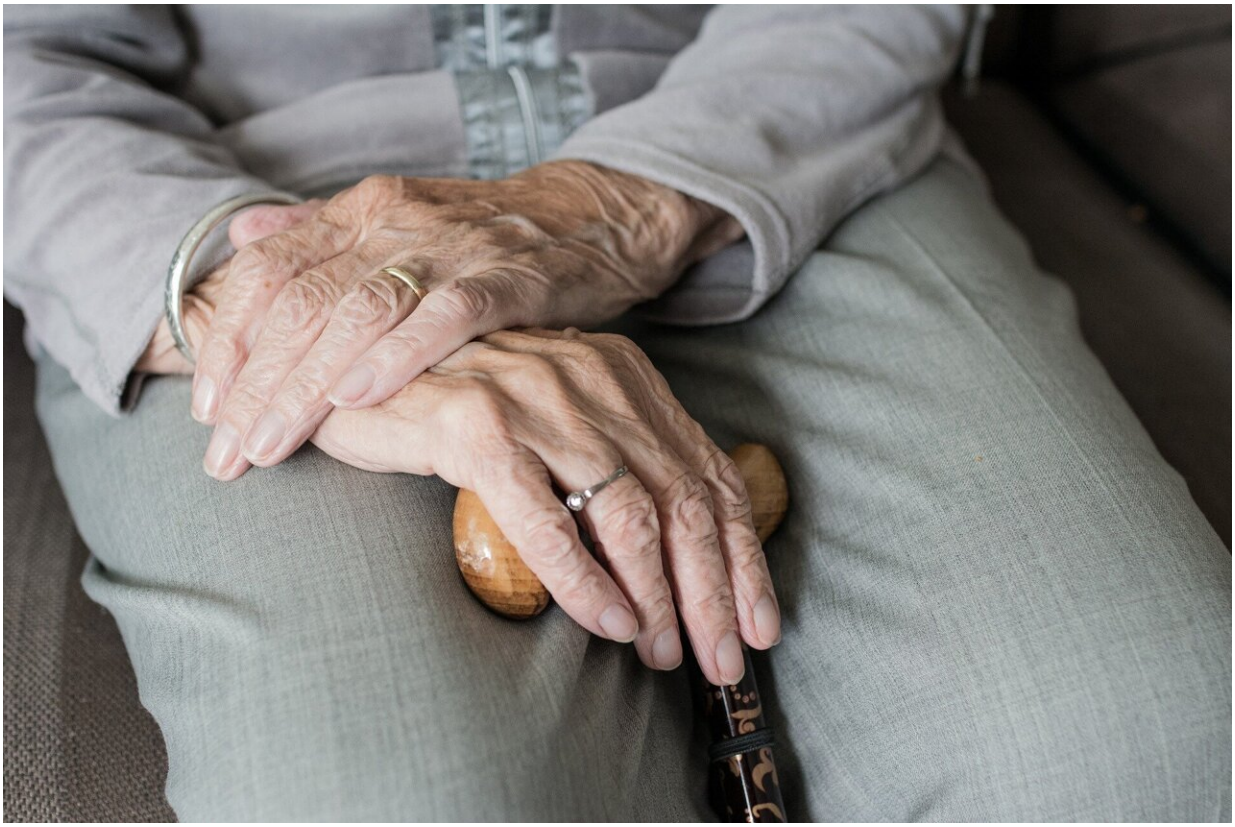

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Bisphosphonates are the recommended first-line treatment in post-menopausal osteoporosis, with denosumab recommended second-line. Based on the length of clinical trials for bisphosphonates, these drugs are

usually prescribed for 3–5 years, or longer in patients who remain at high risk, and recent recommendations suggest long-term discontinuation after this period.

However, data from the US suggest long-term discontinuation of bisphosphonates is associated with increased fracture risk. Until now, similar data from Europe has been lacking. New data on this topic is being shared at the 2024 congress of EULAR—The European Alliance of Associations for Rheumatology.

Osteoporosis is characterized by low bone mineral density and bone fragility. During menopause, falling estrogen levels impair normal bone turnover, with an average reduction in bone mineral density of 10%. This is compounded by the age-related bone loss that occurs in both men and women. With an aging population, post-menopausal osteoporosis represents a growing health problem.

The new data is from a case-control cohort study of over 128,000 women included in the French national claim database. The main aim was to estimate the incidence of long-term discontinuation of bisphosphonates—either oral or intravenous formulations—and denosumab among women with post-menopausal osteoporosis. A secondary aim was to compare the risk of fragility fractures in women with long-term discontinuation with the risk for women continuing treatment.

Overall, 55.1%, 68.9%, and 42.5% of women prescribed oral bisphosphonates, intravenous bisphosphonates, or denosumab had at least one long-term discontinuation recorded. These discontinuations typically occurred in a woman's mid- to late 70s, and after a mean treatment duration of 3.7–4.8 years. Crucially, when analyzed by calendar year, there was an upward trend in the incidence of long-term discontinuations, increasing from 1.6–17.6% in 2015 to 12.1–29.5% in

2020.

Compared with continuous treatment, long-term discontinuation increased the risk of fragility fracture by 12.4% and 92.3% for those stopping bisphosphonates or denosumab, respectively. This increased risk was observed for almost all fracture sites, with the exception of fractures in the distal forearm in women taking oral bisphosphonates.

The highest increase was seen in hip fractures, with increases of 19.0% and 108.3% among women with long-term discontinuation of bisphosphonates or denosumab, respectively. No significant differences were seen between women with long-term discontinuation versus continuous treatment of intravenous bisphosphonates. The trends in occurrence of fragility fracture did not change when death was included as a competing event.

These findings are important for several reasons. Firstly, while discontinuation of denosumab is not recommended, 42.5% of women in the study stopped denosumab for at least 1 year, with a resultant doubling of fracture risk. Furthermore, the increased fracture risk observed after treatment discontinuation differed for oral versus intravenous bisphosphonates. This may warrant further investigation and clarification in the guidelines to ensure optimal management of women with post-menopausal osteoporosis in routine clinical practice.

More information: Laborey M, et al. Risk of fragility fracture after long-term discontinuation of osteoporosis treatment in post-menopausal osteoporosis women in France: a population-based study conducted on the nationwide claim database (SNDS). Presented at EULAR 2024; OP0035. Ann Rheum Dis 2024; DOI: 10.1136/annrheumdis-2024-eular.2841