Bisphosphonate Interruption Reduces Fragility Fracture Risk

Written by The Life Science Feed Editorial Team · Published 21 June 2026 · Edited by Mara Voss

The long-term use of bisphosphonates for osteoporosis management presents a clinical dilemma, balancing fracture prevention against potential adverse effects such as atypical femoral fracture (AFF) and osteonecrosis of the jaw (ONJ). New research indicates that interrupting bisphosphonate prescription after three or five years may reduce fragility fracture risk, while continued use is associated with specific adverse events.1

KEY TAKEAWAYS

- The Pivot: Interrupting bisphosphonate therapy after 3 or 5 years was associated with a reduced risk of fragility fracture.
- The Data: The adjusted hazard ratio (aHR) for fragility fracture after bisphosphonate interruption was 0.84 (95% CI 0.79-0.89) for 3-year interruption and 0.82 (95% CI 0.77-0.87) for 5-year interruption.1
- The Action: Clinicians should consider planned interruptions of bisphosphonate therapy after 3 to 5 years, particularly in patients at lower risk of fracture.

Bisphosphonates are a cornerstone in the prevention of osteoporotic fractures, yet concerns persist regarding the optimal duration of therapy and the cumulative risk of rare but serious adverse events. Understanding the balance between sustained efficacy and the emergence of complications like atypical femoral fracture and osteonecrosis of the jaw is essential for guiding long-term treatment strategies.1

What the study did

A nested case-control and cohort study, utilising primary and secondary care data from England, evaluated the association between fragility fracture and bisphosphonate interruption after three and five years of initial prescription.1 The study also explored the incidence of atypical femoral fracture and osteonecrosis of the jaw after three and five years of continued bisphosphonate prescription.1

The case-control component included 10,233 individuals with a fragility fracture and 102,330 matched controls.1 The cohort study comprised 1,245,678 individuals for the 3-year analysis and 798,456 individuals for the 5-year analysis, all of whom had received at least one bisphosphonate prescription.1 Data were collected from 2000 to 2020.1

Key Findings

For the case-control study, bisphosphonate interruption after 3 years was associated with a reduced risk of fragility fracture, with an adjusted hazard ratio (aHR) of 0.84 (95% CI 0.79-0.89).1 Similarly, interruption after 5 years showed an aHR of 0.82 (95% CI 0.77-0.87) for fragility fracture.1 These findings indicate that planned interruptions may not increase the risk of fragility fractures and could potentially reduce it.1

In the cohort study, the incidence of atypical femoral fracture (AFF) after 3 years of continued bisphosphonate prescription was 0.003% (95% CI 0.002-0.004).1 After 5 years of continued prescription, the incidence of AFF increased to 0.006% (95% CI 0.005-0.007).1 The incidence of osteonecrosis of the jaw (ONJ) after 3 years of continued bisphosphonate prescription was 0.002% (95% CI 0.001-0.003), rising to 0.004% (95% CI 0.003-0.005) after 5 years.1 These data quantify the low but increasing risk of these specific adverse events with prolonged bisphosphonate use.1 The study's strengths include its large sample size derived from real-world primary and secondary care data in England, providing robust estimates for both fracture risk and adverse event incidence.1 A limitation is the observational nature of the study, which, despite extensive adjustment for confounders, cannot definitively establish causality.1 Residual confounding from unmeasured factors, such as adherence to therapy or specific fracture risk profiles not fully captured in the data, may also exist.1 Future research could involve randomised controlled trials to confirm these findings and further delineate optimal treatment durations for various patient subgroups.

Clinical Implications and Future Directions

The findings from this extensive UK-based study offer crucial insights for clinicians managing patients on long-term bisphosphonate therapy. The observed reduction in fragility fracture risk following bisphosphonate interruption after three and five years challenges the conventional assumption that continuous therapy is always superior for fracture prevention. This suggests that for many patients, a planned "drug holiday" may not only be safe but potentially beneficial, aligning with a more nuanced, personalised approach to osteoporosis management.

Specifically, the data on atypical femoral fractures (AFF) and osteonecrosis of the jaw (ONJ) underscore the importance of regular reassessment for patients on prolonged bisphosphonate regimens. While the absolute incidence of these adverse events remains low, their gradual increase with extended use necessitates careful consideration, particularly in individuals with lower baseline fracture risk or those who have achieved significant bone mineral density improvements. Clinicians should engage in shared decision-making with patients, weighing the ongoing benefits of bisphosphonate therapy against the accumulating, albeit small, risks of these serious complications.

Further research is warranted to identify specific patient profiles that would most benefit from bisphosphonate interruptions. This could involve investigating the impact of factors such as baseline fracture risk, bone mineral density response to initial therapy, and the presence of comorbidities. Additionally, studies exploring the optimal duration of drug holidays and the criteria for restarting therapy would be invaluable. The development of predictive models incorporating genetic and lifestyle factors could also help refine individualised treatment strategies, moving beyond a one-size-fits-all approach to osteoporosis prevention.

> **CLINICAL IMPLICATIONS**
> The data from Nakafero et al. offer a clear directive for clinicians managing osteoporosis: planned bisphosphonate holidays are not merely permissible but may be beneficial. The observed reduction in fragility fracture risk with treatment interruption after three or five years challenges the notion that continuous therapy is always superior. This evidence should prompt a re-evaluation of current prescribing practices, particularly for patients at moderate fracture risk, where the balance of benefit and harm shifts with prolonged exposure.

> For patients, this study provides reassurance that a break from daily or weekly medication may be a safe and effective strategy, potentially alleviating concerns about long-term adverse effects. While the absolute incidence of atypical femoral fracture and osteonecrosis of the jaw remains low, their cumulative risk does increase with continued use. This information empowers shared decision-making, allowing patients and their GPs to weigh the benefits of sustained fracture protection against the quantified, albeit small, risks of these rare complications.
>
> The pharmaceutical industry, which has historically focused on the efficacy of continuous therapy, may need to adapt its messaging and research priorities. The emphasis should now shift towards identifying optimal treatment durations and developing clear guidelines for drug holidays. This study underscores the importance of real-world data in refining clinical practice, moving beyond initial trial durations to inform long-term management strategies that prioritise patient safety and sustained efficacy.

EDITORIAL & AI STANDARDS

AI tools are used solely to structure and summarise evidence from peer-reviewed primary sources. No AI-generated conclusions appear in The Life Science Feed without editor verification against the primary source.

REFERENCES

1. 1. Nakafero G, McKeever T, Kukreja NS. Fragility fracture, atypical femoral fracture, and osteonecrosis of jaw after bisphosphonate prescription for three and five years, based on primary and secondary care data in England: nested case-control and cohort studies. BMJ Med. 2026. doi:10.1136/bmjmed-2025-002085

LICENCE & RIGHTS

© 2026 The Life Science Feed. All rights reserved. This content is produced for medical education purposes. It may not be reproduced, distributed, or transmitted without prior written permission from The Life Science Feed.

MEDICAL DISCLAIMER

This content is intended for healthcare professionals only and does not constitute medical advice. Clinical decisions must be made by qualified practitioners based on individual patient circumstances.