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ACCUMULATING EVIDENCE: WHEN PUBLICATION BIAS PERSISTS

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CONTEXT AND OBJECTIVE

The first study investigating the association between bisphosphonates (BP) and osteonecrosis of the jaw (ONJ) was published in 2006, and a recent meta-epidemiologic analysis (2024) identified the presence of publication bias. However, its temporal evolution has not been evaluated. The aim of this study was to investigate the persistence and magnitude of publication bias over time.

METHODOLOGY

A systematic review was conducted to identify studies assessing the BP-ONJ association. A cumulative year-by-year meta-analysis was performed to estimate the crude odds ratio (OR) over time. Publication bias was evaluated using Egger's test and visual inspection of funnel plots. If bias was detected, the trim-and-fill method was applied to obtain an adjusted OR for publication bias. The impact of publication bias was quantified using the ratio of odds ratios (ROR) (adjusted OR / crude OR).

RESULTS/FINDINGS

A total of 44 studies assessing the association between bisphosphonates and osteonecrosis of the jaw (ONJ) between 2006 and 2025 were collected (Figure 1). Publication bias was detected from 2008 and remained present until 2025 (Figure 2). The ROR showed a gradual decrease in publication bias over time. In 2008, the ROR was 0.42, corresponding to a 58% overestimation of the BP-ONJ association. By 2025, the ROR had increased to 0.66, indicating a 24% overestimation. The magnitude of bias was higher in observational studies (40%) compared with randomized controlled trials (11%).

Figure 1 - Flow chart of studies selection

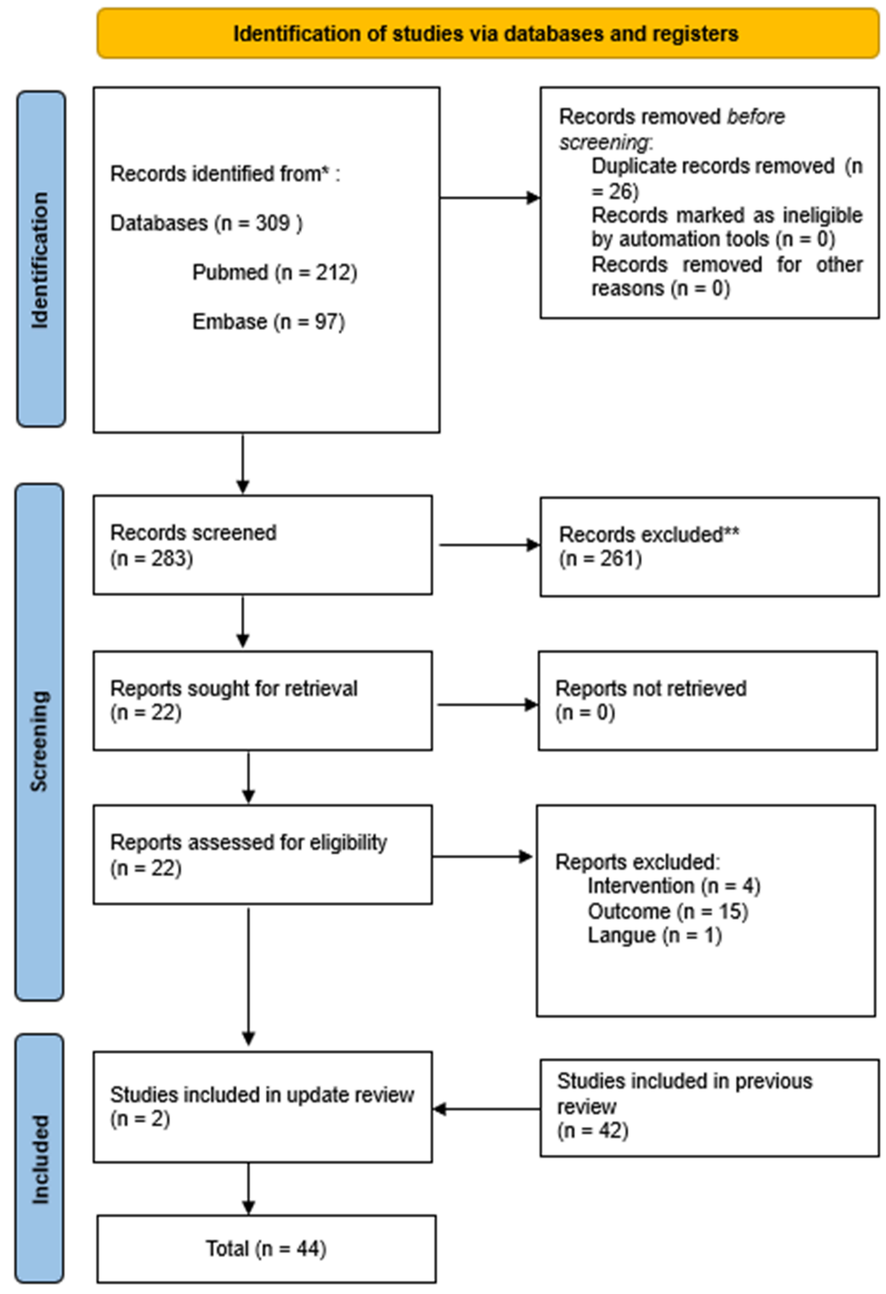
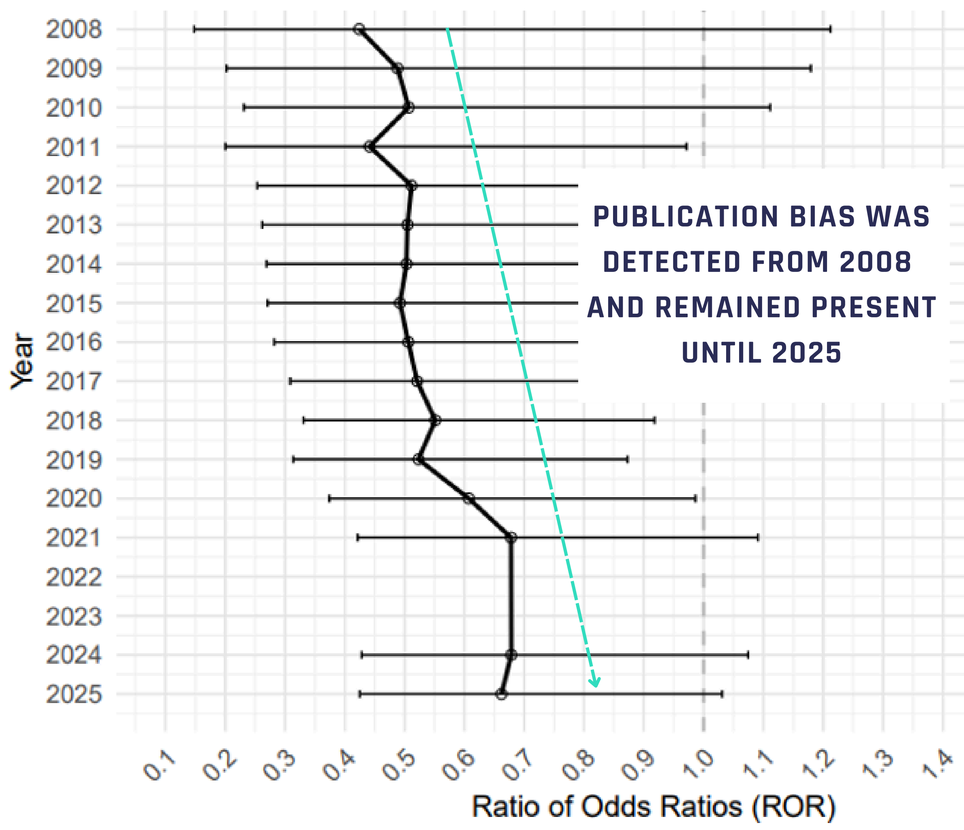


Figure 2 - Evolution of the ROR over time: Publication bias evolution



Year	n	OR_unajusted	OR_ajusted
2008	10	2.31[1.23; 4.33]	0.98[0.42; 2.27]
2009	11	2.05[1.19; 3.53]	1.00[0.50; 2.01]
2010	16	1.97[1.21; 3.21]	1.00[0.54; 1.84]
2011	21	2.22[1.36; 3.61]	0.98[0.53; 1.82]
2012	24	2.21[1.42; 3.43]	1.13[0.65; 1.95]
2013	26	2.09[1.39; 3.14]	1.05[0.63; 1.76]
2014	28	2.11[1.43; 3.12]	1.06[0.65; 1.74]
2015	30	2.18[1.50; 3.16]	1.07[0.67; 1.71]
2016	31	2.09[1.45; 3.01]	1.06[0.67; 1.67]
2017	36	2.07[1.49; 2.88]	1.08[0.72; 1.62]
2018	38	1.92[1.39; 2.64]	1.06[0.71; 1.57]
2019	39	2.01[1.46; 2.77]	1.05[0.71; 1.56]
2020	40	1.99[1.46; 2.72]	1.21[0.83; 1.75]
2021	42	1.91[1.39; 2.64]	1.30[0.91; 1.84]
2024	44	1.95[1.43; 2.66]	1.32[0.94; 1.86]
2025	46	2.00[1.48; 2.69]	1.32[0.95; 1.83]

CONCLUSION

Using ML methods for missing data imputation is a promising approach to improving the performance and robustness of predictive models in healthcare. However, the reviewed studies highlight remaining challenges, particularly in cases of high missingness. This warrants cautious interpretation and further methodological refinement.

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