

## HOW PUBLICATION BIAS MAY OVERESTIMATE THE RISK OF SERIOUS ADVERSE EVENTS ASSOCIATED WITH BISPHOSPHONATE USE

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### CONTEXT AND OBJECTIVE

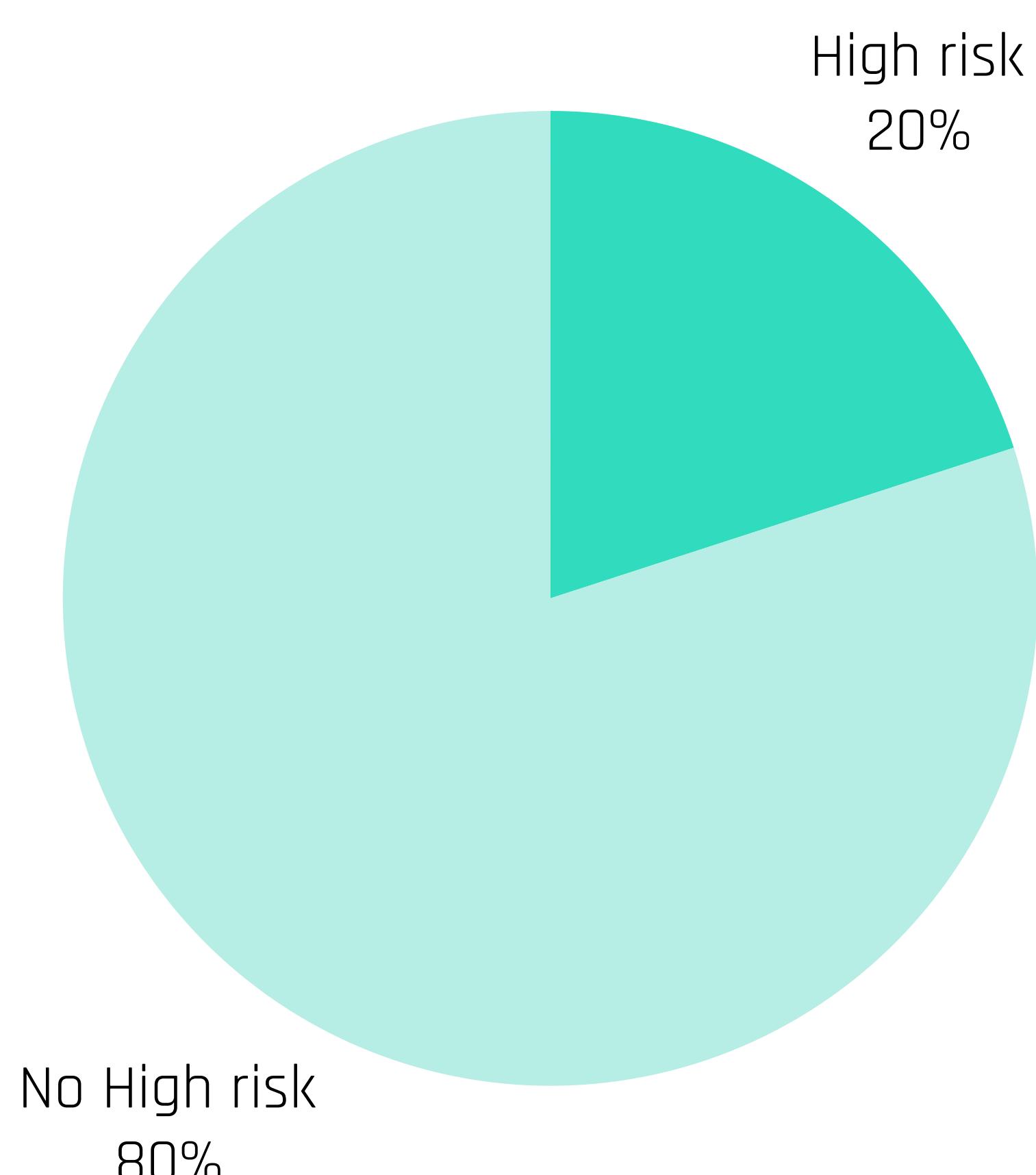
The first study investigating the association between bisphosphonates (BP) and osteonecrosis of the jaw (ONJ) was published in 2006, and a recent meta-epidemiologic analysis (2024) identified the presence of publication bias. However, its temporal evolution has not been evaluated. The aim of this study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

### METHODOLOGY

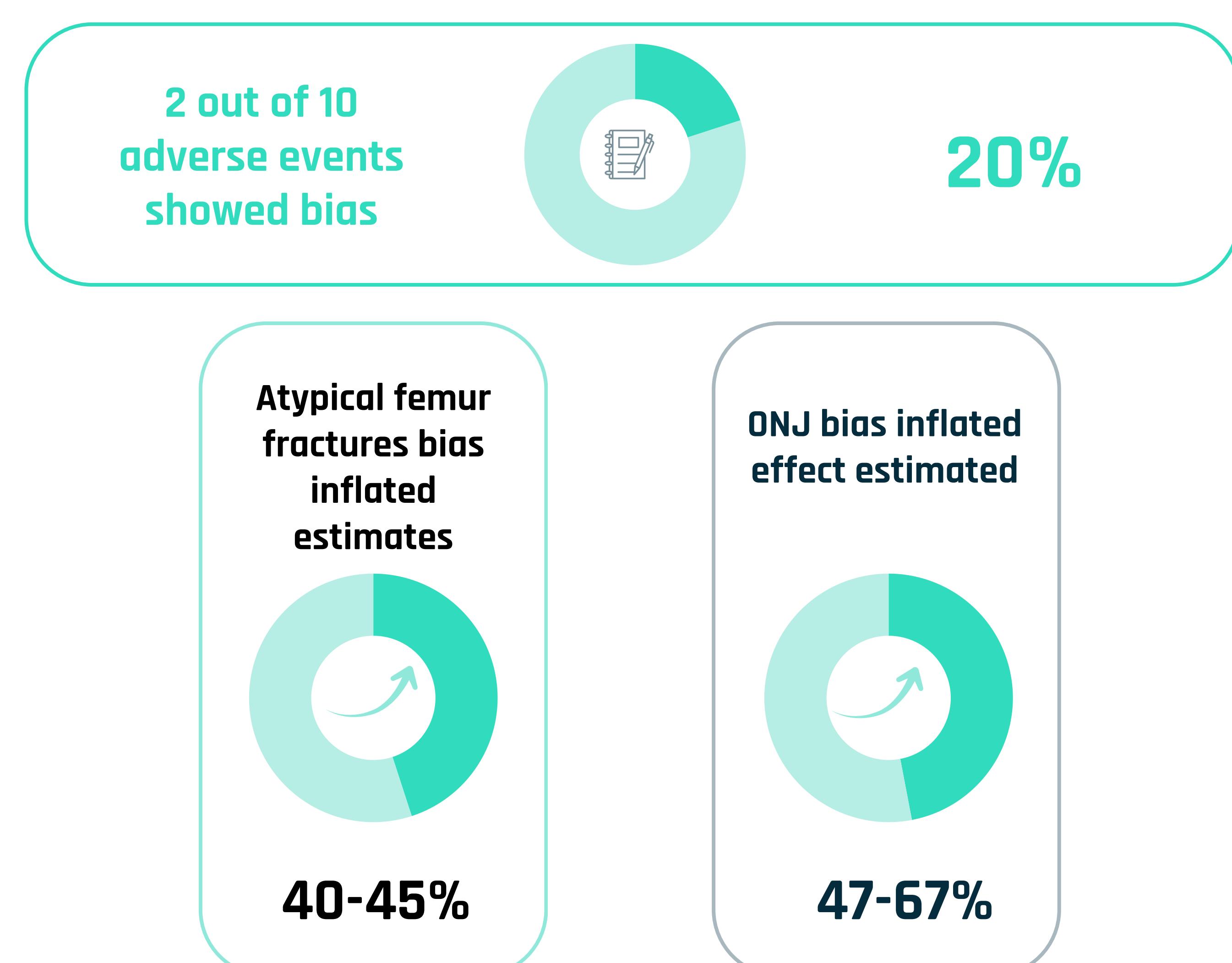
A systematic review was conducted to identify studies assessing the BP-ONJ association. A cumulative year-by-year meta-analysis was performed to estimate the crude odds ratio (OR) over time. Publication bias was evaluated using Egger's test and visual inspection of funnel plots. If bias was detected, 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

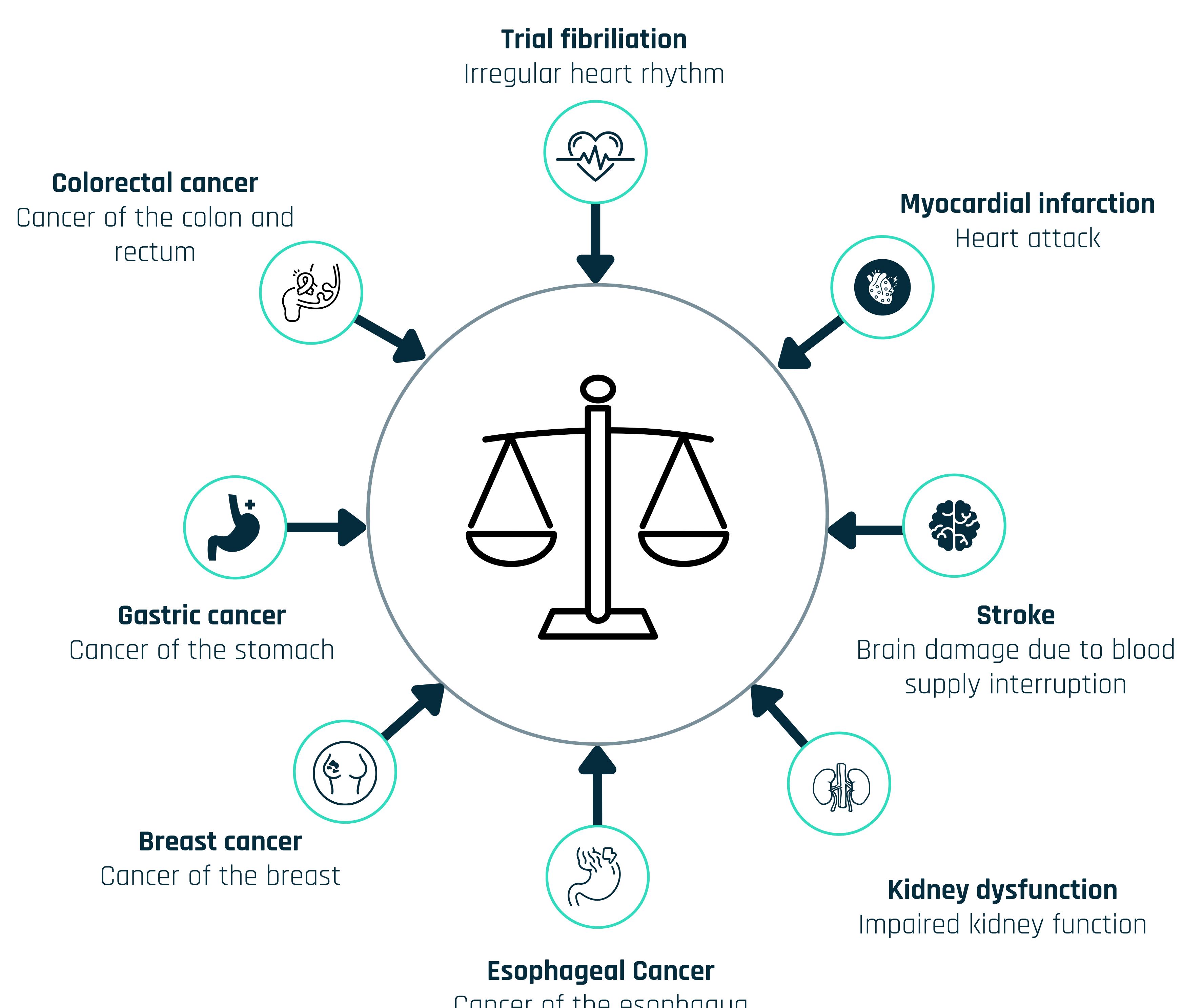
The analysis included 42 systematic reviews totaling 112 clinical studies (58% were observational) for 10 AE.



**Figure 1 - Publication bias in adverse Events**



**Figure 2 - Absence of Publication Bias in Adverse Events**



### CONCLUSION

High risk of publication bias was detected for atypical femur fractures and osteonecrosis of the jaw, with associations with bisphosphonates use disappearing after adjustment. This bias may lead to a distorted assessment of the risk-benefit balance.



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