

# Bisphosphonates and Age-Related Macular Degeneration: A Propensity-Matched Cohort and Nested Case-Control Analysis

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**Objective.** To investigate the association between oral bisphosphonate (BP) use and the risk of developing age-related macular degeneration (AMD).

**Methods.** *Design:* a propensity score-matched hip fracture cohort. We also used a nested case control design to study dose-response according to medication possession ratio (MPR). *Setting:* UK primary care, using data from the Clinical Practice Research Datalink. *Participants:* Patients  $\geq 50$  years old with an incident hip fracture in 1999-2013, without previous history of AMD at hip fracture (index) date or in the following year. *Exposure:* BP use with a first prescription after follow-up initiation. BP use was further categorised according to medication possession ratio (MPR) in quartiles. *Outcomes:* Primary outcome was AMD. *Statistical methods:* Propensity scores were used to match 1:1 non-users and BP users. Covariates in the propensity score were index year, age, gender, BMI, smoking, alcohol drinking, region, drug confounders and comorbidities. Risk of AMD was analysed using subhazard ratios (sHR) and their 95% confidence intervals (CI), accounting for a competing risk with death. A nested matched 1:20 case-control was analysed using conditional logistic regression according to MPR quartiles.

**Results.** The 1:1 matched cohort had 6,208 BP-users and non-users, with 57 (1.8%) vs 39 (1.3%) AMD cases respectively. The sHR (CI) was 1.60 (0.95, 2.72) ( $P=0.08$ ). BP-users in the top quartile of MPR had the highest risk of AMD, with OR 5.70 (3.43-9.50) ( $P<0.01$ ) compared to non-users.

**Conclusions.** Overall, oral BP use was not associated with increased risk of AMD in a cohort of hip fracture patients, although the risk increased with higher MPR. More data are needed to confirm these findings.

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