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JNCI J Natl Cancer Inst (2022) 114(10): djac083

https://doi.org/10.1093/jnci/djac083
First published online April 23, 2022
Response

Response to Lehrer and Rheinstein

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We thank Drs Lehrer and Rheinstein (1) for their interest in our study. We agree that results from the previous literature on the relationship between bisphosphonates and risk of epithelial ovarian cancer (EOC) have been mixed. However, we note that the meta-analysis cited by Lehrer and Rheinstein reported an identical effect estimate (relative risk = 0.81, 95% confidence interval = 0.58 to 1.14) (2) to our estimate (odds ratio = 0.81, 95% confidence interval = 0.75 to 0.88) for the association between ever-use of bisphosphonates and risk of EOC overall. Our study included more than 9000 cases, almost 40% more than the number of cases in the meta-analysis; thus, our estimate reached conventional levels of statistical significance. The other analysis referred to by Lehrer and Rheinstein from the QResearch database was included in the meta-analysis and was the only included study that reported an estimate greater than 1 (albeit nonstatistically significant) (3).

We read with interest the additional results presented by Drs Lehrer and Rheinstein; however, we find it difficult to put these data in context with the existing literature without further information. It appears that these results have not been adjusted for important confounders, particularly age. Age is strongly related to both bisphosphonate use and EOC (4), and therefore any apparent relationship could be due to bias from confounding.

Apart from the smaller sample sizes of previous studies, there were several additional limitations we were able to overcome in our study. First, we used dispensing data to ascertain bisphosphonate use rather than relying on self-report, which is known to be prone to error (5). In our study, we were also able to specifically look at use of nitrogen-based bisphosphonates. Perhaps of most importance, we were able to consider the individual histotypes of EOC. It is clear that these histotypes have different cells of origin and etiologies (4), so considering them separately in analyses is essential to clarifying our understanding of the factors that influence EOC development.

Funding

This work was supported by a project grant from the Australian National Health and Medical Research Council (NHMRC, APP1121151). PW was supported by NHMRC Investigator Grant GNT1173346. NP's salary was supported by a NHMRC grant (APP1185416). KT was supported by an Australian Government Research Training Program scholarship.

Notes

Role of the funder: The funders had no role in the writing of this manuscript or the decision to submit it for publication.

Disclosures: The authors have no conflicts of interest to disclose.

Author contributions: Writing—original draft—KT, SJ. Writing—review and editing: all authors.

Data Availability

No new data were generated or analyzed in support of this research.

Received: April 1, 2022; **Accepted:** April 8, 2022

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