

Answering Reviewers

Dear Lian-Sheng Ma,

Thank you for the reviews and constructive feedback.

We fully agree with your comments and appreciate that they should be included in the manuscript.

We have made changes to incorporate all of your comments as per the below:

- Line 422 we have included the bold text below to emphasize the role that residual confounding may play:
Some of the observed geographic differences may be attributable to residual confounding **that cannot be fully accounted for in the current analysis**, rather than disparities in clinical practice.
- Line 429 we have included the statement to iterate the geographical generalisability limitations:
The study only included CCA patients diagnosed in England and therefore, without further research, it is unknown if our findings can be applied to other countries.
- Line 444 we have included the statement calling for further research:
Whilst it is possible that the geographic variation observed may be explained by factors that we are unable to account for in the present analysis, these findings provide a signal that further research is necessary to identify and address the complex and multifactorial nature of the observed geographic differences, including potential differences in clinical practice, healthcare access, and socioeconomic factors across different regions in England.

Sincerely,



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