Reviewer’s report

Title: Quantification of Cancer Risk in Glomerulonephritis

Version: 0 Date: 12 Sep 2017

Reviewer: Matthew Abramowitz

Reviewer’s report:

Heaf et al. examine the association of a variety of glomerulonephritis diagnoses with cancer both pre- and post-diagnosis. This is an important topic but it is not clear what conclusions can be drawn from this paper. While the authors mention a number of limitations, they are not sufficiently addressed. I have the following comments.

1. There are many comparisons made. Each table in the paper has 100-150 cells breaking down a total of 911 cancer cases. This is a tremendous amount of data, but it is difficult to draw conclusions about the association of any specific GN diagnosis with cancer, and especially with a specific type of cancer.

2. The involvement of time is also confusing and the directionality of the GN-cancer association is not entirely clear. It is unclear what the significance is of cancers diagnosed 5-10 years before the GN diagnosis. The authors do not address the possibility that certain cancers could have been incidental and only diagnosed because of increased surveillance after the GN diagnosis. It is also possible that some indolent GN diagnoses could have been made because of increased surveillance of cancer patients, with hematuria or proteinuria detected on a urinalysis.

3. The use of registry data is a significant limitation. Given the weight given to the GN diagnosis in these analyses, the kappa 0.61 for GN diagnosis is not reassuring. The authors are also unable to account for the effects of immunosuppression on cancer risk after the GN diagnosis.

4. The authors give meaning to the differences between their current findings and of the prior study, but given the large number of comparisons, this may simply be due to chance. Similarly, the sentence on page 7, line 32 - that finding associations only for some GNs and cancers argues against a coincidental association - is incorrect. This is to be expected given the many comparisons.

5. Given these limitations, the authors recommendations for clinical care at the bottom of page 7 are too strong and are not justified by their data.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No
Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

No

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

No

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

Quality of written English
Please indicate the quality of language in the manuscript:

Acceptable

Declaration of competing interests
Please complete a declaration of competing interests, considering the following questions:

1. Have you in the past five years received reimbursements, fees, funding, or salary from an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

2. Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

3. Do you hold or are you currently applying for any patents relating to the content of the manuscript?

4. Have you received reimbursements, fees, funding, or salary from an organization that holds or has applied for patents relating to the content of the manuscript?

5. Do you have any other financial competing interests?

6. Do you have any non-financial competing interests in relation to this paper?

If you can answer no to all of the above, write 'I declare that I have no competing interests' below. If your reply is yes to any, please give details below.
I declare that I have no competing interests

I agree to the open peer review policy of the journal. I understand that my name will be included on my report to the authors and, if the manuscript is accepted for publication, my named report including any attachments I upload will be posted on the website along with the authors' responses. I agree for my report to be made available under an Open Access Creative Commons CC-BY license (http://creativecommons.org/licenses/by/4.0/). I understand that any comments which I do not wish to be included in my named report can be included as confidential comments to the editors, which will not be published.

I agree to the open peer review policy of the journal