Reviewer’s report

**Title:** Risk of cancer among HIV-infected patients from a population-based retrospective cohort study: implications for cancer prevention

**Version:** 3  **Date:** 5 September 2014

**Reviewer:** Suzanne Marie Ingle

**Reviewer’s report:**

This is an interesting paper highlighting the increasing importance of cancer incidence among HIV-positive people and the need for screening procedures to try and tackle this. However, I do not feel that there is enough detail about the study design in this paper to be able to say this is publishable.

- Is the question posed by the authors well defined? Yes, this question is well defined.
- Are the methods appropriate and well described? The methods are not that well described – see my comments in ‘Major Compulsory Revision’
- Are the data sound? I am unable to tell.
- Does the manuscript adhere to the relevant standards for reporting and data deposition? I’m not sure.
- Are the discussion and conclusions well balanced and adequately supported by the data? Yes.
- Are limitations of the work clearly stated? There is some discussion of limitations, but I feel this could be expanded i.e. lack of data on smoking or HIV prognostic markers (CD4/Viral load etc) are not very clearly stated.
- Do the authors clearly acknowledge any work upon which they are building, both published and unpublished? The authors say this has not been published elsewhere.
- Do the title and abstract accurately convey what has been found? Yes.
- Is the writing acceptable? Yes.

- Major Compulsory Revisions

1. A major flaw in the reporting of this study is the lack of information on follow-up time. In the first paragraph of the Methods section it says that the database contains information for 11 years of follow-up, since the year 2000. I cannot find any information in the text though about whether all patients were followed up for 11 years or not. I would expect that some patients drop out of the study database before 11 years of follow-up either because they die or simply move out of the country. This could be introducing a serious amount of selection bias into the sample – a healthy cohort effect – if only those alive at the end of 11 years were included in the study. This issue should be clarified and commented on before on
decision on publication can be made.

2. On a related note, the authors refer to ‘year of enrollment’ frequently. What is this enrollment into? Do they mean year of HIV diagnosis, or the year they first appear in the LHID database for any reason? As matching was based on year of enrollment, this really needs to be clarified.

3. When looking at site-specific cancers, how were patients categorized if they had more than one cancer? Did they get counted under each type of cancer when calculating the SIRS? What happened if they had 2 occurrences of the same type of cancer in the follow-up period?

4. Why was matching required in this study design? Was it for practical reasons, i.e. did it cost more to obtain more records from the database? Couldn’t the authors have simply categorized everyone in the database as HIV positive/negative, and then included this as an explanatory variable in the logistic regression (outcome=cancer) and adjusted for age, sex, year of enrollment? Please provide some more discussion on the choice of study design (see Greenland and Morgenstern 1990, AJE or Cummings et al Epi Reviews 2003).

5. The Figure 1 attached with the paper is clearly not correct as it refers to a study on glaucoma. The authors must present the correct figure. The correct figure would be very useful in determining whether the study sample is biased or not.

Minor Essential Revisions

6. Abstract: Background. The first sentence makes it sound like ART causes cancer. Please rephrase. "The burden of cancer is likely to increase among the HIV positive population as it ages due to successful ART”

7. Abstract: Methods, the word “was” is missing in the 2nd sentence. “It was performed using the National…”

8. Abstract: Methods. Please specify in the abstract what the potential confounders were.

9. Abstract: Results. Please specify what the follow-up period was.

10. Abstract: Results. Please define OR as odds ratio.

11. Table 1 contains percentages in the style “01.97%”. Please remove the leading 0 in these numbers.

12. Methods 1st paragraph: It would help to be more precise in the terminology of the study – rather than just having done a retrospective cohort study, you have done a matched retrospective cohort study.


14. Methods, 3rd paragraph mentions “administrative chronic diseases”. Please remove the word administrative as this does not make sense.
15. Discussion 8th paragraph – is “hospital shopping” a phenomenon or a typo?
16. I think the reference list needs some work. For example, in the 2nd paragraph of the Background section, the authors say “NADCs are emerging as a significant source of mortality(6)”. However, reference 6 is a paper from 1998 – this is not very recent to talk about an emerging source of mortality in the year 2014. I think this is the wrong reference.
17. Reference 1 doesn’t seem very appropriate – it is a cancer paper being used to reference the success of antiretroviral therapy for HIV. Please find something more appropriate.
18. Throughout the manuscript the authors talk of “AIDS-defined” cancers. Please change this to “AIDS-defining”.

- Discretionary Revisions
19. Is it possible to assess whether duration of HIV infection had an impact of incidence of different types of cancer?
20. Keywords: Nationwide population-based study. The word “nationwide” is not very helpful for people searching for papers from across the globe. I would suggest adding “Taiwan” as a keyword instead.
22. Results 1st paragraph: change tenses “Fig 1 is a flow chart”, “Table 1 shows the…”.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**
I declare that I have no competing interests