Reviewer's report

Title: Use of metformin or other antidiabetic drugs is not associated with a decreased risk of thyroid cancer: a case-control study

Version: 2
Date: 10 March 2015
Reviewer: Rachel Stankowski

Reviewer's report:

Major Compulsory Revisions
1. Introduction, Page 3, Line 17: Please clarify whether "also in thyroid cancer" refers to a thyroid cancer cell line or to thyroid cancer patients. Based on later mentions of reference number 20, it appears that you are referring to a cell line or cell lines here.
2. Materials and Methods, Page 5, Line 11: How do you define "active history" over the three year period? Is there a requirement for number or frequency of visits?
3. Materials and Methods, Page 6, Line 8: Were prescriptions typically of the same length? For example, is everyone with 10 prescriptions for a drug taking the drug for the same duration or is it possible that one person had 10 x 3-month prescriptions and another had 10 x 1-month prescriptions? Perhaps it's more standardized in the UK in the US... if so, please ignore!
4. Tables 2 and 3: In the footnotes for both tables, it is unclear what you mean when you say that the OR was adjusted for "each other." Please clarify.

Minor Essential Revisions
1. Discussion, Page 9, Line 16: It is unclear to me what "model I" is referring to--something from the Tseng article referenced? Please clarify.
3. Some inconsistency throughout the article regarding use of antidiabetic vs. anti-diabetic; please make consistent.
4. Table 1: Word "no" appears to be missing for CHF and IHD.

Discretionary Revisions
1. Discussion, Page 9, Lines 1 - 3: Since the finding regarding a potential association between metformin exposure and thyroid cancer was insignificant, you might consider softening this statement. For example, "In the relatively small number of patients with long-term metformin exposure, there was some suggestion of a possible association between metformin and thyroid cancer, although this finding was not significant." Not a required changed, it just seems a bit strong for the data presented.
2. Discussion, Page 9, Line 12: Phrase "similar to our findings" regarding
exposure to sulfonylureas, similar to the above, seems too strong to me considering that none of the findings were statistically significant.

3. The Discussion section seems a bit unfocused and strays from the major point of the study, which was to determine whether use of metformin or other anti-diabetes drugs are associated with thyroid cancer risk. There seems to be a lot of emphasis placed on the other covariates examined and the discussion strays from the diabetes focus. Perhaps a single paragraph describing how your findings regarding other covariates is consistent with the literature would be more appropriate?

4. Your concluding sentence might be a more appropriate tie in to your original objective if you modified it to include both metformin and the other anti-diabetes medications you assessed. For example, "In conclusion, neither metformin nor any other anti-diabetes medication examined was associated with thyroid cancer in this population-based observational study."

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

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests.