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: 3
Date: 12 May 2015
Reviewer: jim yeung

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Major Compulsory Revisions (MCR):

1. Previous MCR 1: Please state the power (i.e., 1 - beta) for the statistical test that evaluate the significance of metformin as a factor associated with a decreased risk of thyroid cancer. Unless the power for the test is >80% (i.e., beta <0.2), one cannot conclude that "Use of metformin is not associated with a decreased risk of thyroid cancer", and the title of the article should be "Lack of evidence that use of metformin is associated with a decreased risk of thyroid cancer". I just want to emphasize the logic that not being able to find "A" in a limited effort does not mean that "A" does not exist.

2. Previous MCR 2: The clinical behavior of thyroid cancer is not just divided along the line of differentiated vs. poorly differentiated or anaplastic thyroid cancer. The biology, clinical behavior, treatment and prognosis of the differentiated thyroid cancers are all different. For example, medullary thyroid carcinoma arise from C cells of the thyroid and they do not uptake iodine. The majority of the thyroid cancer cases are papillary thyroid carcinoma. If it is impossible to identify the type of thyroid cancer in the data set, the word "differentiated" (page 11 line 26) should be replaced by "papillary thyroid".

3. Previous MCR 3: The authors only presented one side of the story. The following publications should also be cited and discussed:

   Plews et al. J. A Novel Dual AMPK Activator/mTOR Inhibitor Inhibits Thyroid Cancer Cell Growth. Clin Endocrinol Metab. 2015; 100(5):E748-56.


4. Previous MCR4: Hyperthyroidism and goiters are known risk factors for thyroid cancer. The a priori models were deficient by not including them. After reporting the results of the a priori models, what are the obstacles that will prevent analyzing a new model postpriori (post hoc) as long as the models are reported
as such with appropriate control for the type I error rate?

5. Previous Minor Essential Revision 2: The reference on page 10 line 17 (reference 40) is a review article. A reference with primary data to support that statement that "TZD inhibit proteolytic activity of dipeptidyl peptidase (DPP) IV" needs to be cited. Although TZDs may lower the circulating DPP IV level, I am not aware of any data showing that TZDs can inhibit DDP IV in intact thyroid cancer cells at concentrations reachable pharmacologically in humans.

**Level of interest:** An article of insufficient interest to warrant publication in a scientific/medical journal

**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