Reviewer's report

Title: The Effect of Metformin and Thiazolidinedione use on Lung Cancer in Diabetics

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Reviewer: Douglas Arenberg

Reviewer's report:

The authors present a retrospective case control analysis of diabetic patients with lung cancer to discern whether there is a relationship between use of thiazolidinedione (TZD) or metformin use and lung cancer incidence. They find that cases (lung cancer patients) had a lower likelihood if current and long term use of metformin or TZD-class agents. the protective affect proved to be more robust with metformin.

The advantages of their findings are the large number of cases, the individual chart level review of cancer cases, and the adjustment for known risk factors for lung cancer (age, tobacco, gender, etc.)

The drawbacks, acknowledged by the authors in their discussion, is the retrospective nature of the study which does not permit drawing conclusions completely free of bias, or isolation of all possible confounders.

The hypothesis generating nature of this study is acknowledged by the authors and their contention- that drugs of the class studied here may have potential as chemopreventive agents for those at risk for lung cancer, warranting further investigation- is supported by their data.

Major Compulsory Revisions: None

Minor Essential Revisions:

My biggest concern, acknowledged by the authors, is whether the data for use and duration of use of metformin and TZD class drugs can be adjusted for BMI, which is a "risk factor" for use of the drugs, and a protective factor in lung cancer risk models. It seems to have been done for the lung cancer patient s (no difference in BMI among cases with and without past exposure), but can this be done on the case-control comparison (or were cases matched to controls by BMI?) If so, please include or clarify this analysis.

Discretionary Revisions:

Also, I would like to see the authors provide data describing the percentage of the ~93,000 diabetics from their EMR that used either of the class of drugs, both or neither. This perspective on the total population of diabetics would be helpful to give the reader a "10,000 foot view" of the patients in this study.
Level of interest: An article of importance in its field

Quality of written English: Acceptable

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

Declaration of competing interests:
I have no competing interests to declare.