Reviewer's report

**Title:** Increased cancer risk in type 2 diabetes mellitus: results from a cohort study in Tyrol/Austria

**Version:** 1  **Date:** 17 March 2014

**Reviewer:** Angela Pesatori

Reviewer's report:

This study describes an association between type 2 diabetes and some specific cancer sites using a record linkage method in Austrian population. The findings generally confirmed those of the previous literature on this topic but do not overcome limitations related to potential biases, confounders and modifiers well described in Johnson JA et al, Diabetologia 2011.

The authors should clearly state this main limitation of their design at the beginning of the paper and in the abstract.

MAYOR COMPULSORY REVISION

1) The study population is not clearly defined.

Pag 5, 3rd line, the authors state: “All cases diagnosed in the DRT since 2005 have been registered in a prospective manner” What this sentence really mean?

And below in the methods section: “Registration was performed prospectively for all patients diagnosed since 2005… the exact date of diagnosis could not obtained for all patients registered retrospectively, meaning diagnosis before 2005”

These definitions are confusing. It seems that the study population includes subjects attending out patients department since 2005. For all these subjects the authors tried to verify year of first diagnosis even if before 2005. This means that the study population includes

a) incident cases with a first diagnosis after 2005

b) some prevalent cases with diagnosis before 2005

c) and, in addition, that the latter subgroup (b) is in some way affected by survival, i.e subjects with diabetes who died before 2005 are not included. This is what I understand from their description but, may be, do I misunderstand something?

To clarify this issue is important since it can influence both statistical methods and results.

2) The authors perform analysis by first year of entry in the DRT?

Even if for a third of the population the year of diabetes diagnosis is unknown, I would prefer analysis by time since year of first diabetes diagnosis. This can help to better discuss the possibility of reverse causation.
3) Discussion

First sentence, please report results separately for males and females: “an association between liver and pancreas for both males and females, kidney cancer among males and postmenopausal breast cancer and uterus in females”

Second part of the discussion, pag 10, third paragraph. After the statement “causality of the association between diabetes and cancer is far from being the aim of our study” the authors list some methodological limitations and difficulties in interpreting studies on diabetes and cancer, but they miss to specifically refers how these limitations can affect their findings.

For example the highest risk for pancreatic cancer in the first year after entry in the DRT can be related to reverse causality whereas the persisting increased risk for liver cancer it is unlikely due to reverse causality. (the authors just quote this result very quickly at pag 9, but without any further comment)

In addition the generally highest risks observed in the first year after entry could be related to ascertainment bias, please comment.

4) Tables and figures

Results can be reported in one single table separately by gender (so join table 2 and 3). Figures 1 is useless since it’s just a graphical representation of tables 2 and 3. Please improve the format of the tables with lines under the title, at the end of the table and complete footnotes

MINOR

2) pag 5 instead of using the exact date is better to use year of first diagnosis since this is what is registered (the complete date is always missing)

3) pag 6 Please explain why do you prefer to use last cancer diagnosis instead of first cancer.

4) Table 1, I would also characteristics for patient without a well defined date of diagnosis.

Please specify as a footnote which are “late complications”

In this table please show some distribution of diabetes cases by year of diagnosis (quinquennium?)

5) Figure 2 and 3, please extend the title at least indicating: SIR and 95%CI are reported

Level of interest: An article of limited interest

Quality of written English: Acceptable

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

No competing interest