Reviewer's report

Title: Cancer incidence in patients with type 2 diabetic mellitus: a population-based cohort study in Shanghai

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Reviewer: Pierre-Antoine Dugué

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Pierre-Antoine Dugué, 19 April 2015

The manuscript provides an estimation of the risk of common malignancies in Chinese patients with Type 2 diabetes. Although the subject is important and the sample size rather substantial (total of 1200 cases observed in 36,500 individuals), a certain number of revisions are required.

Major compulsory revisions:

1. The authors have used Standardized Incidence Ratios, but did not explain what variables were used for standardization.

2. Another study in China (Zhang et al. BMC Public Health 2012) found very similar results. Although briefly cited in the manuscript, it might be interesting to compare the results with the Zhang study, or other Chinese studies (Gong et al. World J Gastroenterol 2012? Ren et al. Public Health, 2009?, other studies?)

3. The authors conclude that cancer screening should be employed in diabetes patients. However, 1) very few malignancies can be successfully screened, 2) the benefit of population screening is usually evaluated through cost-effectiveness analysis (do author have knowledge of such an analysis for Chinese diabetic patients?) 3) because the results were not adjusted for other cancer risk factors, targeting diabetic patients for individualised screening might result in lower cost-effectiveness than expected based on the presented SIRs.

4. The SIRs were not adjusted for other cancer risk factors such as sedentary lifestyle, tobacco smoking, or obesity. Acting on those factors, or on diabetes management, might therefore constitute a more effective prevention strategy than screening for diabetes patients. The fact that SIRs appear to be equally high for malignancies not previously associated, or not strongly, with T2DM (prostate, bladder, kidney, brain and lung in women) and for those for which a more clear association was found (e.g. liver and pancreas) is an indication that other risk factors might play a substantial role. This should be discussed more carefully.

5. Several studies have concluded that the risk of prostate cancer was decreased in T2DM patients, but it was SIR=5.4 (highly significant) in the present study. This puzzling finding requires more discussion.
6. Because the results were not adjusted for other risk factors, the conclusions of the paper should be nuanced. E.g. in conclusion, L261 “the present study provides valuable evidence that TD2M increases the risk of cancer”.

7. I find the very strong age gradient presented in Table 4 quite surprising. Could authors check once again their results, and be very precise on the standardisation that was used for computing SIRs? If results are correct, the finding that individuals with diabetes aged over 70 have a significantly decreased risk of cancer should be made clear and discussed too.

8. The English writing must be considerably improved, for example by being read and corrected by a native English speaker. Extensive editing of the manuscript is also required.

Minor essential revisions

1. The sentence “Finally, lack of information on glucose-lowering medication use and lifestyle factors has limited our ability to evaluate the effect of these factors on cancer risk” should be rephrased to focus on the article’s objective.

2. The sentence “Considering the long sojourn time of cancers, it is difficult for us to distinguish the comorbidity of diabetes and cancer from their causal relationship” needs to be rephrased, explained, or deleted.

3. The sentence “The findings are consistent with those that show elevated risk in previous studies [17-19], but inconsistent with those that show no associations [20]” needs to be rephrased.

4. Did the type of enrolment (“comprehensive hospital”, regular check-up, free-screening in high-risk group) make a difference on the results?

5. Other parameters could have been investigated, such as the length of follow-up? Are there any other variables available to the authors that could have been investigated? Did authors have any information on diabetes onset date?

6. “Diabetes mellitus” is more common than “diabetic mellitus”, and might be preferred in the title of the manuscript.

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

Quality of written English: Not suitable for publication unless extensively edited

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