Reviewer’s report

Title: Pre-diagnostic metabolite concentrations and prostate cancer risk in 1077 cases and 1077 matched controls in the European Prospective Investigation into Cancer and Nutrition

Version: 0 Date: 09 Feb 2017

Reviewer: Elizabeth Want

Reviewer’s report:

* The authors do not discuss PSA in the introduction - this should be included. Why are there limitations to PSA? This would set the scene more for the current study.

* There should be more detailed critical analysis of previous findings in the Introduction.

* Methods - what is EPIC? Why was it established? What findings have arisen from EPIC to date?

* How much variation is there within each disease grade? How subjective is the scoring? I presume disease heterogeneity will play a large part in the difficulties of finding consistently significantly changed metabolites.

* Do the authors know the effect of citrate on any of the analytes being measured here? Could the use of citrate in the plasma collection tubes impact upon quantification of the metabolites?

* Did the authors consider using a different control population, e.g. a benign condition? Some of the changes could be due to patients being healthy versus diseased rather than being specific to cancer.

* The figures are not very visually interesting - could the authors find some different ways to display the data?

* Perhaps some biological pathways could be included showing the relevant metabolites?

* The results need to be put more in context with metabolite changes observed in other cancers. For example, are the lipid changes seen here specific to prostate cancer? I imagine not.

* Limitations as well as advantages of using a targeted assay should be discussed.

* What future work should be considered? Is there other work that can be performed as part of the EPIC project?

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.
Yes

**Does the work include the necessary controls?**  
If not, please specify which controls are required in your comments to the authors.

Yes

**Are the conclusions drawn adequately supported by the data shown?**  
If not, please explain in your comments to the authors.

Yes

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**  
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

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