Reviewer's report

Title: Use of Beta-blockers and Mortality Following Ovarian Cancer Diagnosis: A Population-Based Cohort Study

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Reviewer: Elena Diaz

Reviewer's report:

Comment 1: The authors should be commended on a well-designed and statistically sound study that addresses an important question. The large sample size is certainly a strength of this study and the authors have done an excellent job of utilizing the resources available through the Danish medical system that allow this type of large cohort study to be performed.

Minor Essential Revisions:
Comment 2: Minor grammatical error: on page 10, line 22, should read "platinum- and taxane-based...".

Discretionary Revisions:
Comment 3: In the first paragraph of the discussion, the authors focus primarily on data from nasopharyngeal carcinoma. Although it makes sense to include some of this data since it is their own prior work, there is also a body of similar data in ovarian cancer that they only briefly refer to in one sentence (page 10, line 12). I would recommend that the authors consider shifting the focus of this first paragraph in the discussion towards prior published pre-clinical data about this topic in ovarian cancer, specifically since that is the disease being investigated in this paper.

Comment 4: Consider rewording the sentence on page 11, lines 3-4 to be clearer. One possibility would be, "Finally, and most importantly, because the authors decided that to be considered exposed a patient had to have used beta-blockers for at least 6 months, they also had to have survived at least 6 months, and therefore immortal time bias may entirely explain the increased survival among beta-blocker users."

Comment 5:
Table 1 includes a large amount of comorbidity data that makes the table a bit difficult to read. I am not sure that it is necessary to include all of it. Some of these comorbidity data are referred to in the discussion section when the authors explain that they tried to adjust partly for lifestyle factors that may have influenced outcome by using some of these comorbidities such as history of obesity, COPD, and ischemic heart disease as a proxy for lifestyle factors. I think it makes sense to include data about these comorbid conditions in the table since this data is discussed in the text of the manuscript. However, there are several
other comorbidities in Table 1 that are not discussed within the manuscript and thus it is not clear why they are included in the table. Some examples are tremor, anxiety, esophageal varices, migraines, and hysterectomy. Many of these such as tremor, migraines, and anxiety seem more like indications for beta-blocker use than actual co-morbidities that may influence survival. Since the authors also used the Charlson Comorbidity Index to report any significant difference in co-morbidities between non-users, current users, and previous users, they may consider cutting out some of the more detailed comorbidity data to make the table easier to read and more concise. If the authors do indeed feel that it is important to include all of this co-morbidity data then I would urge them to discuss its importance in the text of the manuscript.

Comment 6: Similarly, in Table 1 there is a large amount of data regarding comedications, however there is no discussion in the manuscript about why this data is important. The authors mention that current and previous users of beta-blockers more frequently used the comedications identified, but they do not explain why this is clinically significant. For example, does it matter if these patients were also taking anxiolytics and/or antipsychotics? The authors should make it clear why they are including this data if they choose to include it in the table.

**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 declare that I have no competing interests.