Author’s response to reviews

Title: Prognostic factors for rural endometrial cancer patients in a population-based cohort

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Reviewer reports:

Keiichiro Nakamura (Reviewer 1): I think that this paper is suitable for acceptance.

We thank the reviewer for their kind words.
Reviewer 2 (Reviewer 2): PEER REVIEWER ASSESSMENTS:

OBJECTIVE - Full research articles: is there a clear objective that addresses a testable research question(s) (brief or other article types: is there a clear objective)?

Yes - there is a clear objective

DESIGN - Is the current approach (including controls and analysis protocols) appropriate for the objective?

Yes - the approach is appropriate

EXECUTION - Are the experiments and analyses performed with technical rigor to allow confidence in the results?

Yes - experiments and analyses were performed appropriately

Statistics - Is the use of statistics in the manuscript appropriate?

Yes - appropriate statistical analyses have been used in the study

INTERPRETATION - Is the current interpretation/discussion of the results reasonable and not overstated?

No - there are minor issues

OVERALL MANUSCRIPT POTENTIAL - Is the current version of this work technically sound? If not, can revisions be made to make the work technically sound?

Probably - with minor revisions

PEER REVIEWER COMMENTS:

GENERAL COMMENTS: My overall impression of the study is the authors have asked a clinically relevant research question and they were successful in leveraging the Utah Cancer Registry and Utah Population database to look for an answer. The interpretations of the study findings might probably be the most challenging part for the readers.

REQUESTED REVISIONS:
In the Abstract, the statement saying 'Rural endometrial cancer patients were older at cancer diagnosis, and had higher comorbidities …', however, in the Table 1, more patients in the rural area have fewer medical comorbidity (see Table 1. CCI category score 0, 63.9% for rural region vs 60.7% for urban patients).

We thank the reviewer for their attention to detail and have updated the abstract.

In Table 4, under the category of Histology, urban patients with carcinosarcoma had numerically 2.4-fold increased risk of death as compared to the endometrioid adenocarcinoma histology. This phenomenon is not seen in the rural area patients. And urban patients who received either surgery + radiation + chemotherapy or other combination, had at least numerically greater risk of death when compared to rural patients. Therefore, it may be too simplistic to conclude that 'the risk of mortality is greater among rural patients.' in the conclusions.

While we agree with the reviewer that is it too simplistic to make that conclusion, we could only find in the abstract and discussion section where we address the risk of mortality greater among rural patients with advanced stage endometrial cancer. We have tried to clarify the language to ensure readers understand that we are addressing advanced stage endometrial cancer patients on this point and not all rural endometrial cancer patients.

Note: This reviewer report can be downloaded - see attached pdf file.

Sherri Stewart (Reviewer 3): This is a well written manuscript discussing differing survival trends from uterine/endometrial cancer among urban and rural women in Utah. It adds to the literature on the topic, and is especially important because as the authors note, uterine cancer is one of a few cancers that has been increasing in recent years. While the methods and conclusions are sound, the authors are very limited by the small sample size of their rural population to make more significant associations. This is noted by the authors, and for me doesn't take away from the importance of this article, given the increasing cancer trends. I have a couple specific suggestions for authors to consider:

1) I suggest adding a couple of sentences to the intro and perhaps discussion to note the specific treatment modalities for endometrial cancer. It may help to provide context to the findings given that chemotherapy and/or radiation treatments are done over a longer period of time compared to surgery. It's possible that rural cancer patients may have difficulty with the continued and cyclical nature of these treatments with regard to easy geographic access/instrumental support, etc. This could help explain why late stage rural patients have a higher risk of death compared to urban.

We have added sentences on this to both the introduction (page 1, lines 93-95) and discussion (page 9, lines 230-231).
2) Also, on Pg 9 in the Discussion, it is likely best to not refer to screening for high-risk individuals, because this is not a universally accepted or mandated guideline. Removing these sentences will not take away from the paper.

We have removed this from the discussion.

3) Likewise, I would consider deleting the sentences in lines 227-231, Pg 9, Discussion about death rates, and Figure 1. Survival is the much better measure for endometrial cancer because it is highly survivable, as shown by the author's comprehensive survival analysis and death percentages listed in Table 1. An unadjusted Kaplan-Meier survival curve would likely add more to the paper than the current Figure 1.

We agree with the reviewer on this point and have deleted those sentences. We have replaced the figures with unadjusted Kaplan-Meier survival curves as the reviewer suggested.