Author’s response to reviews

Title: Patient-Physician Relationships, Health Self-Efficacy, and Gynecologic Cancer Screening Among Women with Lynch Syndrome

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July 23, 2019

Dear Dr. Lubinski,

I am enclosing a revised manuscript submission to Hereditary Cancer in Clinical Practice entitled, “Patient-Physician Relationships, Health Self-Efficacy, and Gynecologic Cancer Screening Among Women with Lynch Syndrome.” My co-authors and I were grateful to have the opportunity to revise and resubmit our manuscript. We have incorporated the reviewer’s suggestions and believe the revised manuscript has been improved by the recommendations. Below, we have summarized the feedback and listed the changes made in the new version of the paper. The revisions to the manuscript are in tracked changes mode, for ease of review.
Reviewer #1:

The uptake, efficiency, and hence the benefit of cancer surveillance programmes including risk-reducing surgical procedures for patients with hereditary tumour syndromes is strongly influenced by a number of individual attitudes, personal and psychosocial factors, and the way in which physicians interact with and inform their patients. However, few studies only address these issues, although evaluating and understanding relevant factors may improve strategies to increase uptake and compliance with surveillance recommendations and thus help to better prevent advanced cancer in high-risk individuals.

The present study aims to explore the perception and attitudes of female Lynch syndrome mutation carriers regarding gynecologic cancer screening. The study has some limitations, the majority of which are already addressed by the authors. However, given the clinical relevance and the limited knowledge in this area, the work is of potential interest.

Specific comments:

1. Page 3: in LS, considerable gene-phenotype differences have been observed, in particular in MSH6 and PMS2 mutation carriers compared to MLH1 and MSH2 mutation carriers (see e.g. www.plsd.eu). Based on up-to-date prospective data, the life time risk for endometrial cancer ranges from 26-57% and for ovarian cancer between 0-17%, depending on the affected gene. So, I would recommend to provide a range rather than just one risk figure.

   Thank you for this recommendation. We have updated our paper’s introduction and replaced the risk figures we provided for lifetime risk of endometrial and ovarian cancer with ranges. We obtained these data from the most recent version of the National Comprehensive Cancer Network (NCCN) guidelines published in 2018 (reference #5 in our paper). We now state “The lifetime risk of endometrial and ovarian cancer in women with LS is estimated at 15-60% and 1-24%, respectively” based on the NCCN Guidelines.

2. The authors did not give any information about the mutated gene and mutation type present in their patients; however, in view of the different gene specific cancer risks it would be important to provide this information, e.g. in an additional table.

   We agree this is important information to include. We have now provided the information about the gene impacted in regard to cancer risk in Table 1 and also described this in the text, in the Baseline Characteristics section.
3. Page 4, participants: the reason for mutation testing is not mentioned. How many patients were tested because of a clinical suspicion of LS (affected index patients) and how many were tested in an asymptomatic state (predictive testing of relatives)? The reason for testing may also influence the attitude and compliance regarding screening procedures. This also refers to page 6, Baseline characteristics, "a minority reported prior cancer diagnosis". What does that mean? That a minority are clinically affected index patients and the majority of probands are healthy mutation carriers?

We now have clarified that 14% percent of participants had received genetic testing because of a clinical suspicion of LS (i.e., affected index patients), while 86% received predictive testing for known LS mutation in the family. Given this, we have now removed the sentence that a “minority reported prior cancer diagnosis.”

4. Page 6, Gynecological cancer screening behaviours: the figures for TVUS and pelvic US are provided, but how many patients obtain at least one type of US examination, i.e. TVUS or pelvic or both?

We have added this information to the results, in the Gynecological Cancer Screening Behaviours section. Approximately 61.2% of participants reported undergoing either TVUS or pelvic ultrasound and 42.9% reported undergoing both TVUS and pelvic ultrasound.

5. It would be interesting to know why the probands enrolled in this study did not choose risk reducing surgery. Are many of those too young to consider this preventive treatment or do they have specific concerns? In addition, it would be important to know why just a minority of probands underwent endometrial biopsies although this surveillance is recommended by NCCN. Is endometrial biopsy not offered by many physicians outside specialised expert centers? Is it not considered to be effective by the patients or considered to be too laborious or displeasing?

We thank the reviewer for these questions. Regarding why participants did not choose risk-reducing surgery, this is an interesting question for which we do not have data. Our questionnaires focused on screening behaviours and we weren’t sure what we would find when we first started data collection. This would be an interesting question for a follow-up study.

Regarding why only a minority of participants underwent endometrial biopsy, at the time of data collection for this study guidelines were not implemented in Canada for endometrial biopsy in women with Lynch syndrome.
Reviewer #2:

Are there informations about optional recommendations of prophylactic gynecological surgery by the physicians available?

We thank the reviewer for this interesting question. Unfortunately, we do not have any information about the recommendations to patients about prophylactic gynecological surgery from their physicians, although that would have been useful data to collect. This will be an important follow-up question for future research.

Please let us know if there are any further revisions that you would like us to undertake. We also made some minor edits to the paper that were primarily grammatical in nature. Again, we are very grateful to the reviewer for these suggestions and hope that this has significantly improved the quality of the manuscript.

Sincerely,

Tae Hart, PhD