**Reviewer’s report**

**Title:** Comparative Efficacy of Six Therapies for Hypopharyngeal and Laryngeal Neoplasms: a Network Meta-analysis

**Version:** 0  **Date:** 26 Feb 2018

**Reviewer:** Henry Park

**Reviewer's report:**

This is an interesting network meta-analysis analyzing the effects of 6 different management strategies for laryngeal/hypopharyngeal cancers. It is quite an ambitious undertaking. However, I do have some concerns about the study design as well as the applicability of this work to clinical practice.

**Major issues:**

- The populations of the included studies are quite heterogeneous. Stage IV hypopharyngeal cancer is treated very differently than stage I glottic laryngeal cancer, as are many of the stages in between, and the associated prognoses are also very different as well. Ranking all the management strategies 1 through 6 for each outcome seems challenging to do in a manner that is clinically meaningful for such a heterogeneous group of diseases and patients.

- How (and why) are hazard ratios being separately calculated for 3-year and 5-year outcomes? Typically these are done not for discrete time points but for the hazard function overall, so that OS is one outcome and DFS is another outcome. I am also confused why 5-year overall survival rate is listed as a separate outcome from overall survival as well, and so this should be clarified. With 5 outcome measures and 6 interventions (especially when they are all quite similar), the results and conclusions certainly become more difficult to follow as well.

- The actual endpoints provided by each study should be comprehensively listed in Table 1 so we can see exactly what the primary data showed. This would make for a very wide table but one that is necessary during any evaluation of a meta-analysis.

- Is there room for sensitivity analyses (even the standard ones used for meta-analyses, like meta-regression, or excluding studies published before a certain year or that only had certain stages of disease) to ensure robustness of the conclusions?
- Is there any other way to quantitatively examine heterogeneity other than heat plots in NMAs?

Minor issues:

- RT should be specified as "RT alone" when discussed as a management strategy (same with surgery alone and TLM alone); the conclusions of the abstract make it sound like RT is detrimental in general, whereas it is really just RT alone performed poorly overall

- "Chemotherapy radiotherapy" in the abstract should called "chemoradiotherapy"

- OS, DFS, and OSR should be defined in the captions for Table 2 and Table 3.

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.

Unable to assess

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?
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