Reviewer’s report

Title: Online Cost-Effectiveness ANalysis (OCEAN): A user-friendly interface to conduct cost-effectiveness analyses for cervical cancer

Version: 2 Date: 23 Aug 2019

Reviewer: Monisha Sharma

Reviewer's report:

This is a very interesting tool for conducting CEAs that has the potential to be highly useful for policy makers. I have some suggestions that would be helpful to address before publication.

Model uses:
It is not clear from the paper who the intended users are of the online CEA tool. The tool is calibrated to Spain, which is a high-income setting. However the vast majority of cervical cancer burden occurs in developing settings. Most HPV modeling groups develop separate models that are used in developed vs developing countries because of the myriad of factors that affect the natural history in different settings. It would be useful to outline specific cases in which the tool could be used to inform policy decisions and to which settings the results can be applied.

Available support from developers:
The authors state "Despite the tool's ease of use and its design, thought to be usable for non-experienced users, the authors are available to provide some guidance in case it is needed." This sentence is a bit vague so it's not clear what level of support is available in parameterizing, conducting, and interpreting a CEA from the tool. Many other simplified models for diseases provide extensive user support. For example the WHO GOALS model for HIV provides a user training on the model and ongoing support use despite the model's ease of use. Although it is relatively easy to run the model, users without a background or understanding of CEAs could make incorrect model assumptions or misinterpret model results leading to potentially negative policy results. What steps will the developers take to prevent these occurrences? Further what level of ongoing developer support will be available to address bugs and issues as they arise?

Correctly specified model inputs:
What data is needed in order to produce accurate results from the model? Currently, the data in the model is populated with costs and incidence/prevalence data from Spain. If a user is not familiar with the inputs that he/she needs to change, it seems they could inadvertently use default inputs from Spain. What steps will the authors take to prevent this from occurring? Would it be possible to pre-populate the model with HPV prevalence and CC incidence data from many countries around the world (using ICO, registry, and Globocan) and allow the user to choose the country from a drop down menu? This is how HIV models including GOALS are set up to minimize errors in model specification. Further, users may not have the clinical or epidemiologic background to manipulate primary data into a form needed by the model or correct for biases (eg the proportion of sexually active young women in HPV prevalence surveys or the sensitivity/specificity of
precancer lesion detection). This highlights another reason that technical support from the authors in analyses is important.

Accuracy of model results:
The authors state that the tool output is very similar to that of a more sophisticated model for Spain but it would be useful to have more detail, including graphs comparing the results, or indications of how and why the results of the two models differ. More detail would be useful on the validation of this tool, particularly given its simplicity. It's not possible for a simple tool to match a more complex model exactly, so in what ways are the results inaccurate and how inaccurate? What are the implications of this? Specifically, graphs comparing the projected impact of CC screening on CC burden over time from the tool and a more complex model would be useful.

Lack of herd immunity:
This tool seems very useful to evaluate cervical cancer screening strategies. However, I'm concerned about the implications of using a linear model to assess the cost-effectiveness of HPV vaccination. The authors state several times in the manuscript that they intend to add in 9v-HPV and additional vaccine related cancers for evaluation. Modeling studies evaluating the impact of not considering herd immunity when projecting health benefits from HPV vaccination have found a substantial underestimating of cancers averted and a cost-effectiveness ratio that is too high. It would be useful if the authors could address this limitation and assess the difference between health benefits projected by the tool compared to a dynamic simulation model. My sense is that it would be better for policy makers interested in HPV vaccination to use a very simple dynamic compartmental model to assess projected impact of vaccines rather than a linear model.

Supplementary material:
It would be helpful if the supplementary material was more detailed, particularly since this is the first time this new tool is being published. Most modeling papers include supplementary information that is 50-100 pages of model specification, equations, rationale behind model assumptions, validation exercises, etc. References can be included for model parameters and costs reported in the supplement currently.

Language/grammar:
The paper can benefit from careful proofreading and improvements to language and readability. Grammatical editing by a native English speaker would be helpful. For example

Page 6: "That allow the tool to generate" should be "That allows(s) the tool to generate"

Further, much of the language could be tightened to be more concise. For example:

"In general, it is known that the mathematical models used in cost-effectiveness analyses are affected by a significant and non-negligible degree of uncertainty at different levels" could be changed to:

"Model-based projections are subject to uncertainty."
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

Does the work include the necessary controls?
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