Reviewer’s report

Title: Cost-effectiverness of novel vaccines for tuberculosis control: a decision analysis study

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Reviewer: Motasim H.Y Badri

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Cost-effectiveness of novel vaccine for tuberculosis control: a decision analysis study
Tseng et al

This is a well done study assessing the cost implications of an important healthcare intervention that is presumed to have a significant public health impact, particularly in the developing countries. The authors took great care and commendable efforts in designing their study and presenting their findings, and in undertaking measures to address the issue of uncertainty typically associated with studies based on the decision analysis methodology. The manuscript is succinct and clear. However there remain minor issues that would benefit from further clarification by the authors.

Major comments:

1. Although might arguably represent a reasonable estimate, the 70% efficacy of the BCG replacement vaccine is a hopeful and untested estimate that has no evidence to substantiate it. Till credible efficacy evidence emerges, the debate around this issue will be a pre-mature and inexact science. Of a particular concern in this study, the articles cited are relatively old and do not provide sufficient evidence of efficacy.

2. In different parts of the results section the authors mentioned that their objective is to assess the efficacy of the vaccine in preventing rapid progression to TB disease after initial infection. However they declare in the 2nd paragraph page 7 that some of the sensitivity analyses conducted accounted for (1) acquisition of initial infection following exposure to Mycobacterium TB and (2) late reactivation of longstanding latent TB infection. Where the evidence of these estimates come from? Instead of branching out to other potential mechanisms for vaccine action that lack evidence, it will be more prudent to focus the study on the effect of the vaccine in preventing rapid progression to active TB disease.

3. In the 2nd paragraph, page 6 the authors declare that the status quo was modeled to presumably reduce the risk of primary progression to TB meningitis or disseminated disease during early childhood. Why the effect of this vaccine on PTB was not considered? Children are usually falsely considered to contribute little to the maintenance of PTB epidemic. An autopsy study conducted in Zambia demonstrated that TB rivals acute pneumonia as a major cause of death from

4. One of the assumptions made in the analysis is that the vaccine will have no effect on the development of active TB in persons with clinical AIDS. Patients with AIDS represent a significant proportion of HIV infected patients in Sub-Saharan Africa, and are at increased risk of developing active TB. What is the scientific rationale for assuming that the vaccine will not have effect in these patients?

5. Why Haitian health care costs were used in the analysis conducted? Does that mean no such data exist in Zambia and no efforts were made to estimate these costs? If “data regarding the number of healthcare visits and out-of-pocket expenditures for patients and families in the diagnostic, hospitalization, treatment, and follow-up phases were collected and analyzed” were collected and included in the analyses, then what do these “Haitian health care cost” represent/include?

6. When the 30-year simulation analysis was conducted, was the Zambian population live-expectancy considered? If the protective effect of the vaccine at birth was assumed to be immediate, and would then linearly wane in 10 years time when a booster will be provided at age 10, how the 30 years time-span was chosen? In other words is this arbitrary or have some rationale behind it? This needs to be substantiated.

7. Why “development cost” is a worry in this type of study? Does development cost stand for the perceived cost of the vaccine, or because they represent an “opportunity” cost in the “Zambian” context? Is there a better methodology for estimating the cost of this presumed vaccine?

8. One of the major limitations of the analysis presented in this study is that it is focusing on a vaccination that will be administered at birth and does not account for those who are already infected or have active TB disease. This needs to be clearly acknowledged.

Minor comments:

1. What does “key TB pathogenetic factors” means? (e.g.; 1st paragraph of the Sensitivity analysis section – page 10.) These factors need to be explained/listed.

2. The TB cases and the TB-related deaths averted should be expressed per 100/1000.

3. What does sub-optimal provider/patient adherence (1st paragraph page 4) means? Why/how the “provider” is implicated in adherence?

4. 1st paragraph page 5: “currently available information”: give details for this information and cite a reference.

**Level of interest:** An article of importance in its field
Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

I declare that I have no competing interests