Reviewer's report

Title: Cost-Utility Analysis of Drug Treatments in Patients with HBeAg Positive Chronic Hepatitis B in Thailand

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Reviewer: Andriy Danyliv

Reviewer's report:

General comment
Overall, this is a well written and interesting paper with potentially important results. However, it could benefit from several improvements and clarifications which are listed below.

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Major compulsory revisions

Background
1) The choice of common comparator, palliative care, comes somewhat unexpectedly. Probably due to lack of justification, this comparator might seem to be appropriate. Is palliative care the ‘usual care’ for patients with CBH? The authors should better explain the background and the choice of palliative care as a comparator.

Methods
2) The underlying calculations of the cost for each state are somewhat obscure. The authors have clear reference to the cost in the states of complications (compensated cirrhosis, decompensated cirrhosis and HCC). But for other states, including CHB, the authors provide the sources of unit cost for drugs and diagnostic tests. However, the link between unit cost and lifetime (70 years) cost of a state (say CHB) is not clear. The readers should be better convinced in the reliability of the calculations by knowing what the assumptions for the service and drug utilization were, how this was projected at the 70-year time horizon, whether discounting was applied (this is presented later in the text which is slightly confusing) etc. These explanations could potentially be presented in an appendix.

3) It is not very clear how the parameters in the sensitivity analysis were varied. What ranges were used in one-way analysis? Which distributions were applied in PSA? This information could be presented in Table 2.

Results:
4) Table 3 with the results is lost.

Discussion
5) The author mention in the Method section that the costs of the treatment of the
adverse drug events were not included in the study. To my mind, this point should be discussed in more detail to show what effect it might have had on the cost-effectiveness results, especially if the cheap generic drugs result in more adverse (side) effects.

Conclusion

6) It seems that the prioritization of the three therapies, i.e. which is preferred and when, should be reflected in the Conclusion.

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Minor Essential Revisions

7) Figure3:
- Are other drug therapies omitted due to presentation convenience? If so, please, indicate this in the text.
- Why is the technology described as “generic lamivudine with the addition of tenofovir based on the road map guideline” which is different from the “generic lamivudine with the addition of tenofovir when drug resistance occurred”, but is also dominant compared to palliative care, not on the graph? It is only much later in the Discussion that it is said that the cost of the former is higher while the effects do not differ. It would be better to mention it when presenting Figure 3, or to incorporate the former technology in the Figure.

8) Methods: I presume time invariant survival rates (or death rates) were applied. It is better to mention this.

9) Language: Although the level of English is rather good, some of the sentences are not clearly constructed. Most of the attention should be paid to the Discussion.

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Minor Discretionary Comments

10) Abstract: Define the abbreviation HBV when first mentioned.
11) Methods, Paragraph 2: sentence 2 is not very clear.
12) Methods\Cost: “All direct non-medical and indirect costs were obtained from a systematic review in Thailand.” Is there a reference? Further on, systematic review is mentioned one more time, but no references are provided.
13) Results \ Uncertainty analysis: “The willingness to pay (WTP) threshold for a QALY gained for the adoption of health technologies and interventions is shown by the vertical dashed lines.” It does not sound correct to say that the WTP threshold is gained.

Discussion:

14) “In addition, when considering the provision of CHB treatment to HBeAg positive CHB patients above 30 years of age (i.e., 40-70 years), these three interventions were still dominant and cost-saving interventions compared with palliative care. Therefore, providing these three interventions in elderly HBeAg
positive CHB patients would still be very beneficial.” I do not understand why the word ‘still’ is used here.

15) “Thus, lamivudine should be considered to be the first line drug for the treatment of HBeAg positive CHB patients who require the treatment based on the aforementioned criteria.” Patients over 30 y.o.? 

16) “After the consideration of the NLED committees, it was announced that tenofovir was to be included in the NLED for CHB patients with drug resistance due to nucleoside analog such as lamivudine and tenofovir with the specification that it should be used as an add-on but not as a monotherapy.” Something is wrong with this sentence.

**Level of interest:** An article of importance in its field

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests.