Reviewer's report

Title: Estimating age-based antiretroviral therapy costs for HIV-infected children in resource-limited settings based on World Health Organization weight-based dosing recommendations

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Reviewer: Nicolas Menzies

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General

This paper describes an approach for estimating the costs of pediatric ARV regimens for HIV treatment, based on child age and regimen recommendations. The paper appears well written and the analysis generally sound.

Major Compulsory Revisions

None

Minor Essential Revisions

1. Page 4, paragraph 2: expensive cold-chain systems are mentioned as part of the complications of estimating ART costs for children, yet are not addressed by the approach. It would be useful to reframe this part of the introduction focusing on the problems to which the method provides a solution.

2. Page 5, paragraph 1: it is implied that citation 21 examined pediatric HIV treatment costs in South Africa, but this study was conducted in other countries, so I think this needs to be reworded.

3. Page 8, paragraph 3: The authors need to justify the assumption that “the weight distribution for HIV-infected children of a given age will be narrower than for children of the same age in the general population”. At the moment this adjustment is simply stated.

4. Same section: a couple of assumptions are required to go from weight to age-based dosing. It would be useful to test the sensitivity of the results to these assumptions – e.g. test alternate values for the z-score adjustment and report the impact on final costs. I assume the results will be reasonably robust to these changes, but need to check.

5. Comparison to GPRM estimates: the ideal source of validation would be empirical data from a program. I am not exactly sure how the GPRM estimates are calculated, but my strong suspicion is that they are based on a similar calculation to the approach described in this paper, though maybe cruder. There is, as far as I can see, no way would they (GPRM) have the level of reporting data needed to calculate some kind of empirical estimate (and if they were,
shouldn’t CE analysts just be using estimates from the GPRM? As a consequence, I don’t think the GPRM estimates validate the current approach. It might be reasonable to keep them as some kind of corroboration of the results presented here, but it needs to be clear what they represent. Of note, where a major difference is observed between GPRM estimates and those in this manuscript (i.e. for LPV/r), it would be useful to tease out the cause a bit. I agree with the hypothesis noted in the discussion section (i.e. a difference in prices), but is it possible to confirm this (as far as I remember the price estimates are available in GPRM)?

6. Page 13, paragraph 2: It is incorrect to state that this approach estimates costs from a healthcare system perspective. This is clear from the very next sentence (regarding the costs not included). This approach estimates the cost of drugs dispensed to patients.

7. I assume the Excel document is intended to be downloadable as a resource for users of this approach? If so, this is great, but there needs to be better documentation – step by step instructions – about how the tool should be used. In similar exercises I have seen a short user manual inserted as the first tab of such a document, but there might be better approaches. It might also be useful to lock cells that the user should not adjust. If this Excel document is not meant to be available for download, please ignore this comment.

8. A more general concern is that this approach is presented as a method for estimating the costs of pediatric ARVs, as might be useful for program planners and cost-effectiveness analysts, but does not include a number of considerations which will all increase the total cost to the program / health system – shipping, insurance, storage, transport, wastage, shrinkage, expiration, etc – individually these can be minor considerations but they add up. The authors mention these issues in the discussion section but I think it needs to be raised earlier, as I could see the naïve user simply ignoring them. The ideal solution would be to provide some basis for estimating these additional costs, but I realize this may not be easy, and some of these cost will differ substantially by country.

Discretionary Revisions

9. Page 8, last paragraph: I don’t think you need to mention the specific Excel functions you used, though would be worthwhile confirming that this is not one of the functions where Excel is known to give erroneous answers (don’t need to include in text, but should check).

10. It would be useful to rework the results section a bit: at the moment it reads like a brief recapitulation of the methods (though I realize is this is somewhat a result of the nature of the analysis).

11. Page 12, first paragraph: “uniformly increase” is somewhat unclear. I assume the intended idea is that costs do not increase monotonically. Also, if this is due to a switch away from liquids it might be useful to say that explicitly.

12. Page 14, first paragraph: typo “over a several ages”.
13. Page 15, first paragraph: “full capacity” this seems not quite right – an underfunded program might hit full capacity very quickly, but I am not sure this is the intended idea. Also in next sentence, perhaps “about” instead of “surrounding”?

14. Table 4: it is important to be clear about the content of a table, but the footnote for this table could be more concise (seems to fully reiterate the relevant section of the methods).

15. It is my understanding that an issue with liquid formulations is the need to dispense ‘whole’ bottles, such that even if the total weight-based dosage for a dispensing period is 185ml, if the bottle contains 240ml then 55ml automatically goes to waste. If this is still true (the authors will likely have a better understanding of the current situation) it could be incorporated into the estimation approach, or otherwise noted in the text.

16. Occasionally it is mentioned that policy-makers might use this tool. I am not sure that this is the case, and perhaps the intended audience should be restricted to analysts and budget administrators (as the authors mention in the conclusion).

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**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.