Reviewer's report

Title: Comparative Effectiveness and Cost-Effectiveness of Antiretroviral Therapy and Pre-exposure Prophylaxis for HIV Prevention in South Africa

Version: 1 Date: 27 October 2013

Reviewer: James G. Kahn

Reviewer's report:

This is a generally excellent assessment of the cost-effectiveness of PrEP and ART for HIV in South Africa. I like the modeling approach and the clarity of exposition in the narrative. I find the results (the cost-effectiveness of ART and PrEP general/focused, alone and in combination) credible and informative. This paper should make a very useful contribution to the literature in this area. Its findings are not unique, but provide important confirmation and added detail to existing work.

My concerns have to do with presentation of results, and in particular the use of tables and figures, as well as making CE ratios incremental, temporal presentation, and costing the focusing of PrEP. I consider all of these reviews mandatory.

(1) The labeling in the tables and figures is not intuitive, using letters and abbreviations that require footnotes which are, in turn, not entirely explanatory and clear. Table 2 (outcomes) is an example of this. I strongly recommend making each table and figure understandable on its own.

(2) The figure legends are too brief. In my view, each figure legend should guide the interpretation of the figure, so that the reader can make sense of it without reference to the text.

(3) Cost-effectiveness ratios for different options are compared with the status quo. I believe that the more appropriate comparison is with the next least expensive option, i.e., stepwise incremental. Thus, for example, the cost-effectiveness of universal ART might be in comparison with guideline ART, indicating the added health benefit and cost of the incremental ART expansion.

(4) I couldn’t understand the following paragraph, perhaps because of the underlined portion which suggests that a “smaller program scale” leads to a “large proportion” of coverage, which seems to contradict the term “smaller scale”. Please clarify.

“Scaling up General PrEP alone to 100% while keeping ART at current recruitment levels would avert 63% of new infections over 20 years. Most of PrEP’s benefits are achieved with smaller scale General PrEP programs: increasing PrEP coverage from 50% to 100% in the general population for any given ART level averts only an additional 2%-7% of new infections. This is...
because a large proportion of uninfected individuals will start PrEP over the time horizon even with a smaller program scale, and the incremental benefits of an initially less aggressive program approach the benefits of a more aggressive program over time.”

(5) I’d really like to see results over time – costs and QALYs in particular. For example, the fact that universal ART looks attractive at 20 years is important, and consistent with past work. However, the time required to achieve the favorable results is unclear … I strongly suspect initially unfavorable results, with steady improvements over time due to HIV infections averted. If the time horizon were extended to 30 or 40 years, there might even be net savings.

(6) Focused PrEP is attractive, if, as the authors note, it is “feasible”. However, as far as I can tell, there is no attempt to estimate the cost of efforts required to implement focused PrEP. I.e., identifying individuals at high risk, initially and over time. I suspect this is largely an unknown. If true, I recommend wide sensitivity analyses on the cost of focused PrEP. How much added cost of focusing would put PrEP back into similar CE range as general PrEP?

Quality of written English: Acceptable

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

Declaration of competing interests:

I have no financial interests related to his manuscript. Dr. Alistar worked for me for 6 months, on work unrelated to this. I have no other competing interests.