Reviewer's report

Title: Using population attributable risk to choose HIV prevention strategies in gay men

Version: 1 Date: 28 December 2010

Reviewer: Bruce R Schackman

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Major Compulsory Revisions

1. The authors should provide a clearer explanation of how to interpret the PAR results for readers unfamiliar with this method, beyond stating that it “controls for confounding among factors.” In Tables 2 and 3, the sums of the PARs for each risk factor are greater than the PARs for all risk factors, presumably because individuals can have more than one risk factor. Please explain how the PAR calculation for an individual risk factor takes into account this phenomenon. In Table 2, for example, 131 of 626 HIV cases are attributable to 10+ casual partners. Does this mean that if all individuals had less than 10 partners, 131 cases would be avoided even though some of those cases were still engaging in other risk factors?

2. The cost calculation is unclear, and it is inadequate because costs are not discounted. Discounting correctly takes account of increasing ARV costs as HIV progresses and delays between infection and entering treatment. If the issues described below cannot be adequately addressed, the authors should consider eliminating the cost results from the paper.

   a. In the methods section, I was unable to follow the calculation of HIV costs that led to an estimated average health care cost (ARV cost?) per HIV-infected person of $15,553. A table or figure might make this easier to follow. In the first sentence only ARV costs are considered, but the second sentence describes “total average costs per person per year” and presents numbers that are substantially lower than the annual costs of ARVs.

   b. The sources of several assumptions are not documented for this calculation, specifically the proportions of HIV-infected on first, second, and third line ART and the proportions of untreated and treated HIV-infected stratified by CD4 cell count. If the sources are estimates, then sensitivity analyses should be considered to reflect the uncertainty around the estimates.

   c. By lumping all costs into the average of $15,553, the authors do not correctly account for the time value of the lag time between infection and diagnosis (see for example citation 20), and between diagnosis and initiation on ARVs. These lag times before initiation on ART need to be accounted for by discounting to present value (Gold et al. recommend an annual discount rate of 3%). In other words, avoiding an infection does not immediately save ARV costs because
these costs would not have been incurred until ARVs would have been initiated, and a dollar saved today is worth more than a dollar saved in the future.

d. By lumping all costs into the average of $15,553, the authors also ignore the fact that costs become more expensive with time on treatment, as evidenced by the differences in ARV costs between first, second, and third-line that they cite. ARV costs need to be discounted to present value to reflect the fact that higher costs occur in later years. In other words, avoiding a future sequence of first, second, and third-line treatment is not equal to the average cost of ARV treatment for the current HIV-infected population.

Minor Essential Revisions

1. In the Conclusion section, the authors state that anal warts are now vaccine preventable. I do not believe any randomized study results have been published about the effectiveness of HPV vaccination in gay men. In addition, because the vaccine is only effective in individuals without prior HPV infection with the relevant sub-types, it is unlikely to be useful for a large majority of adult gay men. The language should be adjusted accordingly.

Discretionary revisions

1. Define PAR in the abstract the first time it is used

2. Methods section, STIs: it would be helpful to explain that the associations found by Jin et al. were after adjustment for risk behavior, since anal warts and gonorrhea are obviously associated with risk behavior. Is there a potential biological explanation for this association?

3. In the Discussion section the authors state as a limitation that participants in the HIM cohort were not randomly selected. This should be reported more clearly in the methods section in the cohort description, beyond the statement that participants were recruited primarily from community-based sources.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests: I declare that I have no competing interest