Author's response to reviews

Title: Perinatal HIV transmission and the cost-effectiveness of screening at 14 weeks gestation, at the onset of labour and the rapid testing of infants.

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Author's response to reviews: see over
Reviewer 1 Comments

Major Essential Revisions

1/ Describe US Virgin Islands in more detail: GDP per capita, total population, % female, % in reproductive age group, total fertility rate, HIV prevalence in pregnant women etc.

*Completed, page 5, paragraph 1*

2/ In providing a rationale for this study, need to better describe current practice ("sporadic"). How many (n and %) HIV-infected women are missing by current strategy. I think that this data may be included in the table but it is not entirely clear. A paragraph or two in the methods/background section is warranted.

*Completed, page 4, paragraph 2*

3/ Consider reducing the number of strategies. Discuss the options you have with experienced Obstetricians and/or Pediatricians to get a sense which of these strategies should be excluded. Or justify inclusion of each one.

*At the initiation of this study, screening options were discussed with Infectious disease specialists, Obstetricians and Pediatricians in not only the US Virgin Islands but also within Australia and the United States. After these discussions and further research, it was decided to include the 9 strategies.*

*There are 3 points of time during the perinatal screening where it is considered beneficial to screen women, with the earlier the women is screened the greater the effectiveness of the intervention. These time frames represent strategies B, C and D. The more times a woman has the opportunity to be screened for the HIV, the greater the likelihood an unknown case of HIV could be detected. However, the costs of each additional screening test offered have to be weighed against the additional intervention effectiveness. By offering screening at more than one point in time, it allows women who present at an earlier time frame to benefit from greater intervention effectiveness but still allows women to be screened who may not present for care at an earlier point in time. Offering screening at more than one point in time is represented by strategies E, F, G, H. It is also possible that even if a woman is screened, she may not have seroconverted at the time of testing or may contract the virus at a later time in her pregnancy. There is also a small chance that her initial test may have resulted in a false negative result. By repeating screening at a later opportunity, these women would still have their positive HIV status captured. These repeat screening options are represented by strategies I and J. Repeat screening is not offered between the onset of labour and the infant after birth because the time frame is too short for seroconversion or for the mother to contract the virus and the chance of a false negative were extremely small.*
The strategies chosen allow the unique characteristics of the US Virgin. Deleting any of these strategies would not allow us to comprehensively address perinatal HIV screening. Justification of the strategies is further discussed within the paper, page 4, paragraphs 1 and 2.

4/ Could you provide the reasoning for the use of the infant EIA (Orasure) shortly after birth. Is this to get an indirect assessment of the maternal status? What is the algorithm followed for those infants found to be seropositive? Western blot in the infants or the mothers or both? Would infants detected in this way get post exposure prophylaxis?

The use of the infant EIA shortly after birth is a way of indirectly testing for maternal status. If the infant EIA is found to be seropositive, both the mother and infant would be tested using a western blot. Until the results of the western blot are known, the infant would begin prophylactic therapy if the EIA was positive. It is most important that the prophylactic therapy begin within 24hrs of birth therefore the EIA needs to be completed within this timeframe.

5/ Consider shortening the Background and Discussion sections and replacing those cut with more results.

The background and discussion have been reviewed and shortened. We believe the results section, although quite short was complete in the first draft. We are not sure what additional results to include.

Minor Essential Revisions

1. References
   a. Reduce the total number of references (84)

   Completed

   b. Give a brief description in the methods of the few references describing US Virgin Island Data that are relied on to populate the models (especially those that may not be easily accessible to readers)

   Completed, page 6, paragraph 1. Data values were verified by local experts where relevant. This process involved the use of data from their clinical practice and their experience working in the USVI health system. This includes, for example, estimates of how long counseling might take and how many staff would be required for defined activities. Most likely and high and low estimates were elicited. We have added a sentence to the end of the first paragraph of the methods section to describe this.

   c. Formatting of citations (eg: references 51, 55, 61, 62)
1. Careful editing of the text is required prior to resubmission

   Completed

2. Table 1 and Table 2 Are favourable and unfavourable the low and high values respectively?

   The terminology in tables 1, 2, 3 and 4 has been changed from favourable and unfavourable to low and high respectively.

3. In results, describe what Table 5 and Figure 2 are showing.

   Completed, page 10, paragraph 1.

Discretionary Revisions

1. Reduce number of tables.

   Four of the five tables illustrate the variables and values in the model. We felt it was important to keep all of these tables to make the study as transparent as possible. The final table is that of the results which could not be deleted.

Reviewer 2 Comments

1/ Postma et al have published previously on repeat screening in AIDS (2002 or so), please discuss that one in relation to your findings on repeat screening.

   Completed

2/ The last section on page 8 should be rewritten. This is vague and it is not clear what exact assumptions were made here (LYG avoided case, earlier diagnosis mother seems all to be included but exactly how and what were the sources for the exact assumptions?)

   Completed, page 9

3/ Page 9: which probability distributions were used in the probabilistic sensitivity analysis?
For this study, probabilistic sensitivity analysis was not performed. One way sensitivity analysis was performed on all variables. A tornado analysis allowed the 8 most influential variables to be determined. A two-way sensitivity analysis was performed between each combination of the 8 most influential variables including a threshold analyses. In addition, a microsimulation was performed.

4/ Fig 1: it is said in the paper that it is assumed that if screening is denied once, screening is consistently denied also next times, so what is then the relevance of the “OR” models in this listing?

The statement above refers to the ‘AND’ strategies, strategies I and J where a woman is offered screening at 2 points in time even if she has been screened at the first offered opportunity. We assume however that if a woman denies screening at the first opportunity, she would also deny screening if offered at a second opportunity. The ‘OR’ strategies (strategies E, F, G and H) offer screening at the earliest opportunity and only offer screening once. For example, if a woman presents for screening during the first trimester, she would be offered screening at this time. Regardless whether she accepts or denies screening, she would not be offered at another point in time. If a woman did not attend prenatal care, she would be offered screening at the next earliest opportunity but again but not be offered screening a second time regardless of her acceptance or denial.

5/ My major concern is with Table 4 on the life expectancies, references 42, 82, and 83 are relatively old, they certainly do not justify a life expectancy of an HIV-infected child at 77.74 years, is there a difference between fast and slow progressors? How does 77.4 relate to life expectancy of mothers at only 12 years?

Very little research has been conducted on the benefits of prenatal HIV screening for the mother. The most relevant and recent data available was reference 42 (now reference 62). This reference stated that on average, mothers live an additional 12 years from the time of diagnosis with a normal diagnosis path and 12.7 additional years with an early diagnosis due to screening.

References 82 and 83 (Now reference 23) refers to the life expectancy in the US Virgin Islands which was interpreted at the life expectancy of a HIV negative infant (HIV-). The references have been confirmed to be current and accurate for the study year. The life expectancies of HIV+ infants is listed in Table 4 and is broken down by fast and normal progressors and by time in HIV phase versus time in AID’s phase.

Table 4 has been adjusted so that the life expectancy of HIV negative infants and HIV positive infants is clearer.