Reviewer's report

Title: Epidemiology of infections by HIV, syphilis, gonorrhea and lymphogranuloma venereum in a large city: a population-based incidence study

Version: 4
Date: 8 July 2015

Reviewer: Heidi Bauer

Reviewer's report:

See numbered comments to author.
Major revisions are described in General Comment #2 and Specific Comment 13.
Minor revisions include General Comment #3 and Specific Comments 1 and 12.
All others are Discretionary

This report includes surveillance data for HIV, syphilis, gonorrhea and LGV from Barcelona, Spain, 2007 through 2011. Using census and population based survey data, the authors are able to calculate rates and trends by sexual orientation and education level.

General comments:

1. The ratio of gonorrhea to syphilis cases is strikingly different from other western countries. In the US, the ratio is ~20:1, UK is ~8:1, other European countries have about 1.7-2:1. The ratio in Barcelona is close to 1:1. What is the explanation for this? Are these measurements of true disease incidence or do they reflect clinical practice patterns related to diagnosis, screening, or presumptive treatment without laboratory confirmation? Is most gonococcal infection symptomatic? What are the clinical and laboratory practices related to screening extragenital sites (throat and rectum) among MSM for asymptomatic infection?

2. There are many challenges and limitations to using surveillance data that need to be addressed more explicitly in the manuscript. In particular, reporting may be incomplete leading to an underestimate of the overall disease burden in addition to potential biases if reporting is differential across different provider types or populations. Additionally, measurements of STD burden are strongly influenced by clinical practice since most of these infections do not cause symptoms. Changing test technologies may increase the sensitivity of detection or the ability to use noninvasive specimens for screening. Increased rates of screening, including screening of extragenital sites among MSM, will increase the observed burden of disease. Conversely, if providers generally treat presumptively without testing, burden may be underestimated using surveillance data. Increased patient awareness and changes in the access to or use of care also influence observed disease burden. In addition to including these issues in the discussion of limitations, it would be useful if information were provided in the method section related to any relevant changes in diagnostic test technology,
clinical practice, and adherence to reporting requirements. For example, lack of routine screening for gonorrhea may explain the relatively lower rates of gonorrhea infection. What is known about clinical practice patterns in Barcelona that would provide some context for interpreting these data?

3. If at all possible, including more recent data — through 2014 or even 2013 — would strengthen the manuscript considerably.

Specific comments:

1. Methods, page 6. It would be useful to separate the men who have sex with both males and females from the men who have sex with men only. This provides a better measure of risk to females in the population. Additionally, understanding trends over time in the proportion MSM versus MSM&W might also be informative, particularly these trends in younger age groups.

2. Methods, page 6. Please clarify the meaning of "global sex specific rates". If these are the rates in Barcelona by country of birth, please state this explicitly.

3. Results. In the narrative for each disease, it would be useful to know the proportion of MSM cases with female partners.

4. Results, page 8. Please include sub-Saharan Africa as a category in both the Methods and Table 1.

Tables and Figures:

5. Table 1. The lower age limit appears to be 15. Were there no cases under the age of 15 or were these cases excluded?

6. Table 1. "More than 45 years" should be inclusive of cases age 45. Consider "45 years or older".

7. Figure 1. WOMEN. For all of the graphs except the one for women, the y-axis is adjusted according to the data. Using a maximum value of 10 would better display the trend for females.

8. Figure 1. MEN. Comparing the overall HIV trends for males with the trends for MSM and MSW, the increase seen from 2007 to 2009 does not seem to be explained by increases in HIV for either MSM or MSW over this timeframe. Similarly the decline in syphilis from 2010 to 2011 is not consistent with the trends displayed in the other figures. Consider the possibility that the red and blue lines in this figure are mislabeled.

9. For all the figures, it would be helpful to make consistent color assignments to the different diseases displayed. Comparing across Figure 2 and 3 is challenging.

10. Figure 3. Why is HIV not included?

11. Figure 3. According to Figure 2, the peak gonorrhea rate overall among MSW exceeded 20 per 100,000. How is it possible that only one strata for MSW in
Figure 3 barely exceeded 10?

Comment:

12. Discussion, page 12. While it is likely true that the increase of STDs may be due to the effectiveness of HIV treatment and less concern about HIV transmission, HIV is also increasing in Barcelona, which means there is also a failure of HIV prevention strategies (e.g. sero-sorting/positioning, treatment as prevention, pre/post-exposure prophylaxis, etc). This should be acknowledge and discussed explicitly.

13. Discussion, page 13. Please include a more extensive description of the limitations of using surveillance data (see #2 above).

14. Discussion, page 13. Do you have future plans to examine the interrelated risk of HIV and STDs by matching individual cases across surveillance databases?

15. Conclusion, page 14. The last sentence seems to reiterate core public health measures for STD prevention rather than interventions driven by the findings of this study. How did the results of this analysis inform program priorities? What was done differently? What programs were initiated or terminated?

Level of interest: An article of importance in its field

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