Reviewer's report

Title: Syphilis epidemiology in Norway, 1992-2008: resurgence among men who have sex with men

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Reviewer: David D Templeton

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The manuscript is of interest and supports what is being seen around the world, especially in cities with large MSM populations: (1) there is a resurgence of syphilis, disproportionately affecting MSM, and (2) HIV-infected MSM are the subpopulation at especially high risk.

As it relies on surveillance data, notified by both clinicians and laboratories, it appears the data are comprehensive and reliable.

What is unclear and requires clarification in methods section is how notifiers know that the infection was acquired within the previous year if the patient is asymptomatic. This is especially relevant to the results section "Women" paragraph: "Women seem to be more frequently diagnosed as late as the early latent stage". How was early latent syphilis defined? By definition this is syphilis infection acquired within 1 year (i.e. a documented negative test within 1 year of the current test) and no symptoms or signs of syphilis. This means that each individual categorised as early latent syphilis would have to have a documented negative syphilis test within the previous year. The text does not state if this is the case. Unless these criteria are satisfied, the authors cannot attribute a proportion of syphilis diagnoses as being in the early latent stage and this would be a major limitation of the current analysis. The methods section states "First positive syphilis tests" are notified, so it appears that no previous syphilis test result would be available, making the diagnosis of early latent syphilis in an asymptomatic individual impossible.

If this major issue is adequately addressed, I think the manuscript is interesting, valuable and should be published, however the length should be substantially reduced prior to publication (especially the introduction and discussion sections). The first 3 paragraphs of the introduction could be condensed into a brief 3-4 line summary of syphilis rather than detailing the natural history which is not of particular relevance to this paper.

The discussion is also unnecessarily long.

Specific comments:

Abstract, results: were no cases at all diagnosed in MSM in 1992-94? Could another explanation of the huge increases in early syphilis among MSM and other populations be that the notifications system has improved or that sexual
behaviour reporting has improved?

Methods

Paragraph 2: "could the authors please clarify the sentence "A single co-existent STI can be reported with HIV as a priority"? I had to read this several times before I realised what was meant. Suggest change to: "Data on co-existing STIs is collected, however, only one other STI can be reported on data collection forms. If the patient also has HIV, notification of their HIV diagnosis as the co-existing STI is prioritised"

Paragraph 3: "For the purpose of this study, we denoted men who had been infected with syphilis by another man "men having sex with men" (MSM). Could the authors please clarify this further. What is the specific question asked of clinicians regarding gender of partners? For example is it any sex with men, over a specific time period? i.e. can the authors categorically state that syphilis was acquired by MSM contact based on the data reported by clinicians?

Results:

Paragraph 2: please state "p-trend" if the statistical test applied (average 3.8 cases/year increase) was a test for trend and "95% CI" rather than only "CI"

MSM paragraph, line 5, "most of the cases" would have to be >50%, not 43%
Line 6/7: The proportion of HIV co-infected increased [add: over time] and state p-trend <0.001

Men infected heterosexually paragraph:
"No obvious time trend was observed": please state p-trend value for the reader
"More than half was older...." should read "were older"

"Women" paragraph, line 1: remove comma after "Among 56 women"

Table one:
Please indicate whether p-values are p for trend (i.e. age) or p for heterogeneity (i.e. birthplace)
Table two could be removed and the finding briefly stated in the text, as it adds little to the paper

Discussion

Paragraph one, line 2: "...MSM, including HIV positive" suggest changing to "....disproportionately affecting HIV positive" as one-quarter had HIV

Paragraph one, line 3-4 (and results section "Women" paragraph): "Women seem to be more frequently diagnosed as late as the early latent stage". This is unclear. More frequently diagnosed than who? And how was early latent syphilis defined? (see earlier comment)
"get infected" line 3, paragraph one and elsewhere in discussion is too strong a phrase as the risk factors are based on limited behavioural data. Suggest changing to "appear to be infected by", "reported being infected by" or "were likely to have been infected by"

Prostitutes: should be changed throughout the text to "sex workers" which is now the accepted terminology

Paragraph 3, 3rd sentence: "each year about 100 cases are reported by laboratories, but not clinicians". The authors include 562 early or congenital cases over a 16-year period notified. However, by my calculations, 100 cases a year equates to 1600 cases during the study period which would be three quarters of all syphilis cases diagnosed in Norway during this time period. Obviously the limited information on these presumed late latent cases precludes further analysis, but the large majority of syphilis cases diagnosed late is notable and deserves further comment

Paragraph 7 could be removed as the 4 cases of congenital syphilis, 2 of which were in adopted children from abroad is not noteworthy (except to say that it is very rare in Norway)

Paragraph 8&9 deal with oral sex as a possible risk factor for syphilis acquisition. Although this is noteworthy and probably accounts for a substantial minority of syphilis infections in MSM (see Jin et al. Med J Aust 2005; 183 (4): 179-183) condoms use for oral sex among MSM is very rare in all settings and reference to low condom use for oral sex could be removed. Paragraph 8 is confusing to read and requires clarification. Could the fact that more heterosexual men than MSM are diagnosed in the primary stage reflect the chancre being painless, and therefore more likely to pass un-noticed in anal or oral areas among MSM, compared with penile chancres in heterosexuals? The authors could comment on this.

Paragraphs 10-13 could be condensed to one short paragraph briefly outlining the contents of table 2 and concluding that overseas sexual contact is a key risk factor for heterosexually-acquired syphilis in Norway. That is the important message here and does not require so much discussion.

Paragraph 14 does not add to the discussion and should be removed

Paragraph 15 regarding frequency of testing to control syphilis among MSM and HIV positive is of key importance. Suggest keeping from line 2 'An evaluation..." to " ideally 2-4- times a year" and putting in final conclusion paragraph.

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

Quality of written English: Needs some language corrections before being published
**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