Reviewer's report

Title: Profiling of individuals responsible for local HIV-1 transmission

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Reviewer: Jorg Ruhe

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In their manuscript “Profiling of individuals responsible for local HIV-1 transmission”, Chalmet et al. use HIV RNA sequencing data combined with retrospectively obtained patient demographic and clinical data to characterize modes of HIV transmission within their community. Transmission clusters were detected especially among men-who-have-sex-with-men. Overall, the manuscript is well written. However, information on other important modes of HIV transmission such as intravenous drug use was not provided which makes the conclusions drawn less robust. I would like to make the following comments:

A. Major revisions

1. Page 2, lines 37-43: The authors listed several parameters that were associated with the outcome on bivariate analyses, but not on subsequent logistic regression analyses. These could be omitted in the abstract, but be mentioned later in the “Results” section.

2. Page 5, lines 97-98: One weakness of the study is the definition of other concomitant diseases. Presence of Chlamydia infection was defined as a positive serology. Please specify if IgG and/or IgM antibodies were determined. Syphilis was defined as the presence of a positive TPPA test. Both a positive TPPA test and a positive Chlamydia IgG only indicate that the patients were exposed to these organisms at some point. Active infection with either one could have been overcome at the time of HIV transmission. Other parameters such as a positive Chlamydia PCR and/or an elevated RPR/VDRL in a previously untreated patient obtained at the time the HIV serum sample was drawn would have been helpful. Similarly, the presence of a positive HBV core IgG (please specify if only IgG or both IgG and IgM antibodies were determined) does not necessarily correlate with the presence of acute or chronic hepatitis B infection at the time of HIV transmission. The authors acknowledged this by mentioning “past or present” infections with these agents on page 10, lines 212-213, but this should be discussed as a study weakness again in the discussion section.

The term “past or present” should also be added in the “Conclusions” section of the abstract as on page 2, line 46. The term “prevalence” is misleading in this context as it implies the presence of an active, ongoing infectious process.

3. Page 10, lines 209-210: Were any data available on HIV transmission through heterosexual contact and intravenous drug use? Are there any data available on...
drug use (IV or non-IV) within the MSM group? This information would be important, especially given the recommendations made by the authors. If not available, the potential bias introduced by the lack of these data should be mentioned as a study disadvantage in the discussion section and could be reflected in the study conclusions.

4. The discussion section should also mention the retrospective design of the study as a Study weakness.

5. Page 16, lines 339-342: It is often difficult to identify patients with acute HIV as they may present with only unspecific and mild clinical symptoms. As the long-term benefit of initiating HIV therapy in this early stage is still not exactly defined, a focus on early diagnosis and emphasis on protective measures such as safe sex and avoidance of needle sharing would also be important and could be mentioned in the discussion on “systematic early treatment”.

B. Minor revisions

6. Page 12, lines 259-263: Is any information available on these patients' country of origin? It would be interesting to know if patients with non-B infections came from many different geographic areas or if one or few areas/countries predominated.

7. Please comment on the p-value of 0.528 for the Hosmer-Lemeshow test on page 23 (Table 1).

**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.