Reviewer’s report

Title: Disparities in access to diagnosis and care in Blantyre, Malawi identified through enhanced tuberculosis surveillance and spatial analysis

Version: 0 Date: 10 Sep 2018

Reviewer: Sabine Belard

Reviewer's report:

The authors present a large study analysing TB registration and geolocation data from Blantyre, Malawi. Main findings are that poor neighborhoods and those furthest from TB clinics had lower TB case notification rates. The authors interpret these low case notification rates as a marker for low access to TB care and underdiagnosis of TB. Impressive efforts have been made to collect and relate TB and geolocation data over a study period of 3 years. I am not able to judge on the various statistical methods applied. However, I am missing some methodological information to fully understand and appreciate the presented findings. Please find some major and minor comments below.

Major comments:

1. It is difficult for the reader to differentiate between procedures that are part of routine patient care and study specific procedures. I understand the presented analyses include TB data from a new surveillance system (implemented at TB clinics) and TB data that were reported by patients or documented during TB work-up, both routine patient care data (including culture?). Did study specific procedures relate to geolocation only? The manuscript should more clearly present the framework and a consistent wording should be used/defined (e.g. routine and enhanced surveillance is mentioned probably meaning the same).

2. A more detailed characterization of the 18 health facilities where TB cases are registered and the general flow of TB cases should be provided. Are presumptive TB cases presenting to these health facilities for diagnostic TB work-up? Or are these health facilities only registering TB patients who have been diagnosed with TB elsewhere? Are patients diagnosed with TB elsewhere all referred to these facilities for registration and medication? Are these health facilities the only points of care where TB medication is provided/available? How is inpatient TB care linked to the registration facilities? How high do you estimate TB related mortality, i.e. may there be a substantial number of patients who died during inpatient care and before registration? Please include respective information.
3. The term "city-wide surveillance" is used repeatedly but parts of the city have been excluded from the analyses. Information on how catchment areas were chosen for inclusion should be specified in the methods section and also information on the (estimated) total population of Blantyre (percent coverage by the study) should be provided. Almost 25 percent of registered TB cases where not included in the analyses because patients were not residing within included catchment areas, this may be an important source of bias and this challenges the term "city-wide".

4. It remains unclear if "adults" were defined as patients older than 15 years for all aspects of the analyses; this should be clarified. As not specified in the manuscript I assume that population denominators included individuals aged younger than 15 years but enumerators for CNRs excluded patients aged older than 15 years. Please clarify. If denominators did not exclude individuals aged younger than 15 years (who accounted for up to 55% of the population in some catchment areas) this may be a source of bias as poorer populations may have more children accounting for lower CNRs.

Minor comments:

Abstract:

5. The abstract should include the number of TB registration clinics and the approximate coverage of the city population by the analyses.

6. The abstract should include mention that CNRs referred to adult/＞15y old population only.

7. The abstract mentions TB surveillance at all public and private TB treatment registration centres. In the manuscript there is no further mention of "private" facilities, please clarify.

Introduction:

8. Reference 10 appears to refer to the TB surveillance program but not to the stated HIV prevalence of 20% in Blantyre, please add a reference for HIV prevalence.

9. The last sentence of the introduction section reads very vague: "… we aimed … to identify the most important and modifiable barriers …". What potential barriers where identified / thought of prior to the study?
Methods:

10. What was the procedure if the head of a household was not present when the CHWs came for the interview? Please clarify.

11. Xpert status is mentioned as a collected variable but Xpert findings are not presented as results, please clarify.

12. The ratio of sputum smear positive to smear negative as a marker for late presentation - is this a valid marker in a population with such a high HIV prevalence / co-infection rate and a cohort with more than a third of patients being diagnosed with EPTB? Please comment.

13. How were re-treatment cases handled at TB registration? Were patients counted twice or was there a procedure to exclude multiple registrations of same patients? Adding information on the proportion of re-treatment cases to Table 1 would be valuable.

Results:

14. What is the rational for comparing the 3723 cases resident in CHW catchment areas with the 286 cases not living in CHW catchment areas (Table 1)? Would it not make more sense to compare the resident cases to all 4065 (7788 - 3723) cases captured by ePAL but not resident in a catchment area? Please clarify.

15. Why were sputum microcopy and culture not performed in around a quarter of cases? Was there an algorithm in place e.g. that patients who had started TB treatment during a preceding defined period would not need to provide a sputum? Please clarify.

16. HIV prevalence is high, but there is no distribution analysis for HIV status per catchment area; please comment.

Discussion:

17. Page 16, line 11: " … had higher TB CNRs …" should this not be "lower TB CNRs"; please check.

18. Page 16, starting line 18 to the end of the paragraph: "Areas in Blantyre …" it remains unclear to the reader if this would translate into higher rates of undiagnosed TB i.e. lower CNRs or if you suggest that these young men present late and thereby contribute to higher
CNRs because of longer infectiousness. Same for the last sentence of the paragraph, please clarify the assumed/derived hypotheses in terms of CNRs.

19. Paragraph on strengths and limitations: "...93% were successfully recorded and geolocated..." This statement appears limited by the high rate of missing sputum data; please comment.

20. Discussion of distance remains rather abstract as absolute measures for distance are not discussed (the only scale for distance in meters is provided in supplemental Table 1). For a better and more pragmatic understanding of the distance variable examples of "far" vs. "close" in absolute meters or kilometers would be helpful.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Not applicable

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

No

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
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I recommend additional statistical review

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