Reviewer's report

Title: Time-series analysis of tuberculosis in Singapore

Version: 2 Date: 28 August 2014

Reviewer: Lisa Szatkowski

Reviewer's report:

1. Is the question posed by the authors well defined?

- Minor essential revision: The authors give a good background to the topic and the situation local to Singapore. However, I do feel that the first objective could be defined more clearly – what demographic factors does the work consider? It is a little confusing to then refer to ‘macro level factors’ in the following sentence – it may be best to be consistent in the use of terminology.

2. Are the methods appropriate and well described?

Major Compulsory Revisions:

Annual analysis:
- Relatively little detail is provided regarding the analysis of the annual TB cases. I suspect the majority of readers will not be familiar with ARIMA analysis, and thus I would like to see the modelling procedure described more fully, but using language which is not too technical. It would also be useful to provide a key reference to enable the audience to read further about the type of analysis used if they so wish. What population characteristics were entered as explanatory variables in the models? How exactly did you adjust for population at risk? Please justify your choice of lag periods (plus clarify why in the methods section you state you considered lags 0-5, but then on the following page state lags of 0-4 years). Please explain what model validation procedures you used.

Monthly analysis:
- Please clarify in the methods exactly which models you built e.g. for different strata of the population, what the outcome variable was, what exposure variables were included in the model
- Was your assumption of a linear temporal trend in the monthly TB risk appropriate—the graphs in Figure 2 suggest a non-linear model may be more appropriate? Please explain whether you considered using a non-linear modelling approach. A Generalised Additive Mixed Model (Wood 2006, Hastie and Tibshirani 1990) may be a more appropriate modelling approach to use.
- Please provide a reference for your use of a cosine component to model periodicity, and clarify in your methods exactly what periodicity this is modelling.

3. Are the data sound?
- Minor essential revision: The study uses routinely-collected laboratory data, which is appropriate to the study design. However, I would like to see some more detailed discussion about the strengths and weaknesses of these data, building upon the limited comments the authors have made already (sentence starting “Since the data are from a passive surveillance system…”). Please elaborate further on the potential biases which might affect these data. Were the data collection/recording/extraction procedures consistent across the whole of the time period? If not, any changes may introduce a confounding effect assessment of the association between changing demographic factors and the outcome.

- Minor essential revision: Please report results to the same degree of accuracy throughout (including in the supplementary material) e.g. 3 decimal places is adequate for p-values, 1 or 2 decimal places for percentages etc.

4. Does the manuscript adhere to the relevant standards for reporting and data deposition?
- To the best of my knowledge, there are no agreed standards for the reporting of time series analyses.
- Major Compulsory Revision: I would like to see a table of results included in the paper summarising the estimates of effect from the various models, along with 95% CIs and p-values.

5. Are the discussion and conclusions well balanced and adequately supported by the data?
- Major Compulsory Revision: The discussion and conclusions are supported by the data, but I would like to see more of a nuanced discussion with regard to study power (see point below).

6. Are limitations of the work clearly stated?
- As I have noted above I would like to see some more discussion about the strengths and limitations of the data used.
- Major Compulsory Revision: Detailed discussion of the limitations of the modelling approach is warranted, particularly with regard to study power. With relatively a short time series (particularly with the annual data) does the failure to find any significant associations between demographic factors and TB incidence simply reflect a lack of data?

7. Do the authors clearly acknowledge any work upon which they are building both published and unpublished?
- I am not familiar with the field of TB epidemiology and so do not feel able to answer this question

8. Do the title and abstract accurately convey what has been found?
- Minor essential revision: The title could arguably be more information – analysis of what about TB in Singapore?

9. Is the writing acceptable?
- Minor essential revision: There are just a few minor errors in written English and thus an additional proof-read is recommended.

**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:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests