Reviewer's report

Title: Time-series analysis of tuberculosis in Singapore

Version: 2
Date: 22 August 2014

Reviewer: Gavin Koh

Reviewer's report:

No major revisions requested.

Minor essential revision:
* It is stated that seasonality was found in TB incidence. It is not clear to me from the figure whether peak incidence follows summer in the Northern hemisphere or vice-versa. Seasonality is one of the major conclusions presented in the abstract, so I should like to see the data presented in the main body of the manuscript instead of as a supplementary figure, please.
* Please discuss the public health implications of these findings in the Discussion section of the manuscript. For example, the STEP programme is mentioned in the introduction and then not again. It is important for the reader to understand the broader relevance of this study (e.g., how does this change public health policy/interventions?), which only the authors can provide.
* Although HIV incidence is noted to be low, this is not referenced in the manuscript (page 13). Please provide context to the general reader who is unfamiliar with the situation in Singapore, by referencing a manuscript or report with current HIV incidence and historical trends.

Discretionary revisions:

One of the main conclusions is that the TB incidence is falling in the non-resident population. However, no explanation for this is offered.

Although country-of-origin is not available, I note that migrants to Singapore can divided into two broad groups, who are the work permit holders (generally manual labourers or domestic workers) and the employment pass holders (professionals and other white collar workers). Publicly available statistics from the Ministry of Manpower show that the number of Employment Pass holders in Singapore has increased faster than the number of Work Permit holders. This seems to me a perfectly plausible explanation for the apparent fall in TB incidence in the non-resident group. This is the link to the MOM website:

The second major conclusion is that there is seasonality in TB incidence in Singapore, which is surprising, seeing as Singapore is on the equator and therefore does not experience seasons as such. However, Singaporeans are highly mobile and air travel from Singapore is easily available. One could speculate that:
1. Travel to endemic countries at holiday time may be a driver of seasonality, by increasing exposure to the TB in a seasonal fashion. Singapore has a 6-week school vacation in November/December of each year that could drive this.

2. Travel to temperate climates may expose Singaporeans to environmental drivers of seasonality that they would otherwise not be exposed to in Singapore (e.g., winter crowding; reduced sunlight in winter and therefore reduced vitamin D, etc.).

Would the authors like to comment on the plausibility of these hypotheses, please?

Minor comment:
Page 6; lines 6, 7: "The situation is complicated further by the spread of multidrug-resistant (MDR) TB[3], a particular problem in South East Asia." I feel that this statement is slightly misleading. While MDR-TB may be a problem in SEA, I think it is a particular problem in Eastern Europe and the former Soviet bloc countries. I am not even sure whether this statement is relevant to the manuscript as a whole, since the manuscript does not deal with MDR-TB.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

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

Declaration of competing interests:

I am an employee of GlaxoSmithKline which is developing TB drugs on a not-for-profit basis.