Reviewer's report

Title: Timing of treatment interruption among latently infected tuberculosis cases treated with a nine-month course of daily isoniazid: findings from a time to event analysis

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Reviewer: Lisa Ronald

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This manuscript is an analysis of the timing and predictors of interruption of a standard 9-month isoniazid treatment regimen for latent tuberculosis infection, in order to prevent development of active TB disease. The authors analyzed data from an LTBI treatment registry in Florida with data collected in 2009-2015. They used Cox proportional hazards models to evaluate predictors of time to treatment interruption. The paper is well-written. Some comments to clarify:

1. The data were obtained from LTBI registry data pooled across 67 county health units. Additional information about the LTBI registry in the methods section would be helpful. Does the catchment population for these data cover all of the health units in Florida, and how complete is this registry likely to be for LTBI testing and treatment information for the catchment population? Is there mandatory reporting for LTBI testing and treatment to the health units? Additionally, where were the treatment outcomes definitions were obtained from, ie. was treatment completed, lost-to-follow-up, etc. a clinician-defined outcome within the registry? Also, it would be helpful to provide a comment in the methods section that data are not available regarding drug dispensation—this is mentioned later in the limitations section, but it would be helpful to have this mentioned earlier.

2. The reported prevalence %'s for some of the risk factors (diabetes, immuno-suppression) seems low. Is the co-morbidity risk factor data in this registry self-reported or clinician-reported, and is there any indication about how complete the risk factor data is? This may warrant further discussion in the limitations section.

3. Did the authors have any data regarding age? It would have been interesting to see how the outcomes differed across age groups (particularly completion and adverse event frequencies in older age groups).

4. The authors excluded a large number of people from the analysis (almost 40% of people listed as initiating INH therapy were excluded from the analysis, with 23% excluded due to missing treatment start date and 13% with a medical plan open for more than 9 months). Some LTBI treatment guidelines identify treatment completion as 240 doses
within 12 months. Did the authors do any sensitivity analyses to test the impact of an expanded time window regarding treatment completion, and whether inclusion of people with a treatment plan open for >9 months changed the conclusions? I understand that this was a time-to-event analysis, but would extension of the window to 12 months as a sensitivity capture most of these excluded people?

5. Re: Figure 1, there are a reported 19,726 people testing positive for TST and/or IGRA and of these, 15,602 are listed as initiating INH therapy. Figure 1 shows that 992 never initiated treatment, what about the other 3,132 who were candidates for INH therapy but didn't initiate treatment? Also a suggestion for Figure 1- if the authors can add an additional final box with # completing treatment, it would make the LTBI care cascade data clearer (# eligible, # initiating, and # completing).

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

Yes

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

Yes

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

Yes

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