Reviewer's report

Title: Factors Associated with Default from Treatment among Tuberculosis Patients in Nairobi Province, Kenya: A Case Control Study

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Reviewer: Kelly Dooley

Reviewer's report:

In this manuscript, the authors address reasons for treatment default among tuberculosis patients in Nairobi, Kenya. As treatment default is a contributor to continued TB transmission and negatively impacts TB control efforts, it is worthwhile to look at region-specific risk factors for default to be able to address them appropriately. In this study, the authors conducted a chart review of defaulters (cases) and completers (controls) of treatment (n=1978) and also conducted an interview with some of the cases and controls to enhance their understanding of risk factors for default (n=274). The article could use some restructuring so the reader can follow which results are from the 1978 and which are from the subset of 274 that underwent interviews. Here are some suggestions:

Major compulsory revisions:

(1) In the methods section, it would be easier for the reader to follow if this were divided into sections, such as Patient Population, Study procedures, and Statistical analysis. The study procedures section should separate the larger chart review from the smaller substudy involving questionnaire.

(2) In the methods section, a description of how the 1978 were chosen from among all defaulters at the study clinic sites would be helpful (what does purposefully sampled mean exactly?). Further, among those 1978, how many of those randomly selected to participate in the interview actually participated? Perhaps this could be described in the results. For example, "of 2000 defaulters in the study clinics over the study period, we randomly selected 1000 for inclusion in the study, and of these 945 charts were available for abstraction. Of the 945, 200 were randomly selected to participate in an interview, and 120 could be found and agreed to participate." This helps show possible areas of bias.

(3) In the results section, it is difficult to figure out which data apply to the chart review study of 1978 people and which data are from the analyses involving the 274 patients who participated in the interview. I would suggest reorganization of the data into sections so the reader always knows which group is being described.

(4) In the results section, the sub-sections "Factors attributed to default", "factors associated with default", and "predictive factors for default" are similar, and it is unclear how they differ from each other. Perhaps this would be better organized
into "Patient Characteristics", "Timing of default", "Risk factors for default" (put univariate and multivariate analyses here), "knowledge and beliefs about TB and impact on default".

(5) The discussion section could be reworked to give a little more punch. A major worrisome finding of this study is that people seem to default early and at a time when there is no evidence that they have converted their sputum from positive to negative. Why, do you speculate, do people default early in Kenya and Brazil but late in Nigeria and Ethiopia? This must have something to do with treatment delivery structure or tracking of defaulters. I would discuss this more fully.

(6) I would consider restructuring the discussion section to tackle patient factors, treatment delivery factors, and knowledge/beliefs separately. This will make the discussion flow better. Many of the factors described in this section have been described in other studies. It would be very interesting for readers to know what is different about this urban Kenyan population. For example, use of herbal medications may be an issue in Kenya but not in many other settings. This is important and is not really described in the default literature.

Minor compulsory revisions:

(1) In the background section, the comment that poor adherence to treatment results in prolonged infectiousness, relapse, or death should have an associated citation. Further, the statement that default can foster emergence of resistance is under debate. For instance, the Pablos-mendez paper cited states that resistance is more common among defaulters, but the confidence interval is 0.7 - 44. If there are more recent papers in support of this supposition, they should be cited.

(2) In the last paragraph of the background section, the results of the study are described. These should be removed from this section and left for the results section. Instead, the three goals of the study: to determine the timing of treatment default among defaulters; to determine risk factors for treatment default; and to evaluate health attitudes and beliefs associated with default should be described.

(3) Were controls and cases matched on treatment period or just on study site?

(4) Please specify that the study population consisted of adult and children if that is the case (age range begins at 1 year old). Were children included in the univariate and multivariate analyses? Many of the factors studied, of course, would not apply to them.

(5) A brief description of how TB is treated in Kenya would be helpful. For instance, is the first 2 months daily HRZE delivered via DOTS as an outpatient and the next 4-6 months not observed and given less frequently? This may help when thinking about reasons people default early in treatment in your study but late in treatment in other studies.

(6) It would be helpful to see the 8 questions about knowledge about TB -- perhaps this could be added as a table.
(7) In the methods section, the sample size was calculated using an assumption of a 10% default rate. Yet in this case-control study, 50% were defaulters and 50% were controls, by definition, so this part of the statement can be removed (the rest reads well).

(8) The section "Limitation" in the methods section might be better-placed in the discussion section. I would suggest a discussion of study limitations in the discussion, in general.

(9) In the results section "Characteristics of study population", a large part of the data presented here are also in the table. Would recommend removing from the text and referring to the table to save space for discussion and other things.

(10) Were the interviews conducted using a closed format, or were they conducted using open-ended questions in a semi-qualitative format? This should be described in the methods section.

(11) In figure 2, were these responses mutually exclusive? That is to say, could a patient default due to alcohol and stigma, or did the respondent have to pick the one most important reason for default?

(12) In figure 1, the # at risk and # who defaulted should be added.

(13) In the "factors attributed to default" section, it states that medical reasons for default included "misdiagnosis" or "multidrug resistant TB". Can these individuals be considered defaulters?

Discretionary revisions:

(1) There are many studies about reasons for default. In the background section, some ideas about why reasons for default may be different in Kenya than in other settings would help set the stage for the study and describe why it may be different than others of its kind.

(2) Table 3 number of significant figures in numbers presented should be consistent.

(3) The findings that patients with HIV more commonly default are interesting and are further evidence that HIV and TB care should be better integrated. Authors could consider discussing this a little.

Level of interest: An article whose findings are important to those with closely related research interests

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.