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: Epco Hasker

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

The authors describe a case control study investigating default from TB treatment, conducted in Nairobi Kenya. In a first stage they sampled all defaulters registered between January 2005 and March 2007 in 30 purposively sampled high output facilities in Nairobi as well as 1033 controls, i.e. patients who did successfully complete treatment. For these patients they extracted routinely available information from their medical records, in particular demographic factors and factors related to treatment and follow-up examinations.

From this larger study group, 120 cases and 154 controls were randomly sampled and subjected to a structured interview. At this stage data was collected on socio-economic status, side effects experienced, knowledge about TB, alcohol consumption, use of herbal medications.

Most patients who defaulted (59%) did so within the first 3 months of treatment. Of 391 defaulters that were smear positive at the start of treatment, 187 (48%) had defaulted before sputum smear conversion had been documented.

The authors distinguish between ‘factors attributed to default’ and ‘factors associated with default’. In the former category they classify inadequate knowledge about TB treatment, long distance to health facility, feeling better after some weeks of treatment, side effects of anti-TB drugs, preference for herbal treatments, alcohol use and medical reasons. With the exception of side effects, all these were significantly associated with default.

Among ‘factors associated with default’ the authors classify demographic characteristics (age, sex), HIV co-infection and having a history of default, all of which are significantly associated with default.

Based on their findings the authors recommend to better inform patients on TB treatment and they suggest some ways to improve the way in which treatment is administered. They also recommend to inform patients not to use alcohol during treatment. And to refrain from using herbal treatment.

Major comments:

Although this is in principle an interesting study, there are some major shortcomings that need to be addressed. There are some methodological issues
related to the process of sampling and data collection. Findings could also be presented in a much more structured manner, using a conceptual framework e.g. as described by Munro (PLoS Med 2007; 4(7):e238) or as described in chapter 5 of ADHERENCE TO LONG-TERM THERAPIES, Evidence for action; WHO 2003.

Background:

- The authors state that: ‘studies on TB treatment default in Nairobi, and the country at large, have not been documented’. There are however a number of published studies on default from TB treatment from other sub Saharan African countries, it would be good to present here the main factors identified in those studies.

Methods:

- As the authors admit in their ‘limitation’ paragraph, the fact that patients were selected from purposively sampled high-volume public facilities may lead to a selection bias. They need to provide more detail on proportions of the total caseload of Nairobi being treated in those facilities. Also in the analysis they need to explore whether there were differences in results between the facilities; if there were none, they need to mention this.

- It is not clear how controls were sampled. Cases (945) were apparently all defaulters identified in the study period but we may assume that the 1033 controls are a sample of a larger group. How many patients completed treatment in the study period and how were the 1033 sampled?

- Were cases and controls matched by facility, was there any other matching done? Has this matching been taken into account in the analysis?

- In the next stage, 120 cases and 154 controls were identified and interviewed. How were they selected? Did all those sampled participate? Were there no patients (especially among the defaulters) that could not be traced, refused to participate or had died?

- How has alcohol use been defined? Any alcohol use, problematic alcohol use, alcoholism?

- The criteria used to assess knowledge about TB are not always relevant. ‘Having attended a public health lecture’, ‘TB history among household members or friends’ or ‘suspected TB at onset’ are irrelevant. The important issues are whether patients know that TB is curable and whether they know for how long, how and where they will be treated.

Results:

- In table 1 patients are classified as ‘Return after default’ and ‘Others’, this is confusing because ‘Other’ in the standard WHO terminology has a different meaning. I assume the ‘Others’ here are ‘New cases’, if so please use the case definitions as indicated in ‘Treatment of tuberculosis: guidelines – 4th ed. WHO/HTM/TB/2009.420.

- In the section ‘Duration of treatment before default’ it would be better to
distinguish between default in the first two months (intensive phase) and default later in treatment (continuation phase). More detail could be provided here but the three month cut off has little practical significance. Probably there is default during the intensive phase and another peak upon transition from intensive to continuation phase.

• I do not understand the distinction between ‘Factors attributed to default’ and ‘Factors associated with default’. If a factor is attributed to the default it is the result rather than the cause of default. It seems as if the authors tried here to capture the patients perspective but how did they do so? Were the questions open or were the patients just asked e.g. whether or not they had used herbal medicine?

• For age, only two strata are considered with 30 years as cut off. This is not very informative, for age to be useful as a risk marker the increased risk should be pinned down to a much narrower group so specific interventions can be devised.

• In the ‘factors associated with default’ section, half of the second paragraph is about factors related to knowledge among defaulters. This in itself is not so interesting, it only becomes interesting if it can be compared to figures among controls. For this purpose, as I said earlier in my comments to the ‘methods’ section, I do not think the way knowledge was summarized is appropriate.

Discussion:

• The discussion is too much a repetition of the results with hardly any new elements. I would recommend to structure it according to a clear conceptual framework (see earlier comment in ‘results’ section). Also I would recommend to present results from the literature on default from TB treatment in sub Saharan Africa in the ‘background’ section and use the ‘discussion’ section to contrast the findings in the study to those found from the literature. In it's current from the discussion is not of much use for the TB program management in Nairobi or wherever.

Conclusion:

• As with the discussion, this is again mainly repeating the results. The ‘conclusion’ and ‘recommendations' sections can be merged into one.

• The statement ‘use of alcohol during treatment should be discouraged’ is not very useful. It’s unlikely to have any effect on problem drinkers. Better would be to devise targeted interventions aimed at assuring adherence in persons abusing alcohol.

• The recommendation to discourage patients from use of non-conventional medicines, including herbal medication, does not follow logically from the results of this study. The authors have demonstrated an association between default and use of herbal medicine but how certain are they about the causality? It could very well be that defaulters turned to herbal treatment because of being dissatisfied with allopathic treatment.

Minor comments
Background:
  • In the second paragraph the authors state that up to 2006 the treatment success rate stagnated at 80%, does that mean that it has since improved? What is the current level?
  • The authors report a 16.7% defaulter rate for Nairobi, how does this relate to defaulter rates in other parts of the country, was there a special reason to sample in Nairobi only?
  • The last two sentences of the section should be moved to the ‘results’ section.

Methods
  • The sentence: ‘Kaplan-Meier survival analysis method was used to determine probabilities of defaulters continuing with the treatment program over different durations’ is a bit unclear.
  • The ‘limitation’ section can be moved to the discussion, taking into account my earlier remarks about the need for more detail.

Results
  • In the first paragraph, ‘characteristics of the study population’, the percentages apparently refer to all those enrolled. This is not very meaningful since this is an artificial population in which cases are overrepresented. Better present separate figures for cases and controls.
  • The figures in the paragraph ‘Factors attributed to default’ are slightly different from those in table 2. Moreover it is not meaningful in a case control study to provide combined figures for cases and controls because this is an artificially composed population.
  • Figure 1 is not easy to interpret, it could be helpful to add gridlines so readers can see at one glance which proportion of defaulters had abandoned treatment at which time.

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: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests: I declare that I have no competing interests.