Author's response to reviews

Title: Factors associated with patient and health care system delay in diagnosis for tuberculosis in the province of Luanda, Angola

Authors:

Luigi Segagni Lusignani (luigi.segagnilusignani@meduniwien.ac.at)
Gianluca Quaglio (gianluca.quaglio@ospedaleuniverona.it)
Andrea Atzori (a.atzori@cuamm.org)
Joseph Nsuka (cuamm@cuamm.org)
Giovanni Putoto (g.putoto@cuamm.org)
Maria Da Conceição Palma (mariapalma58@yahoo.com)
Ross Grainger (rgraingerefl@gmail.com)
Fabio Manenti (f.manenti@cuamm.org)

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Author's response to reviews: see over
Dear Professor Harris,

I am grateful for the constructive suggestions of the reviewers, which have been closely followed in the revision of the manuscript. I am providing you with a point-by-point response to suggestions of the reviewers and a new version of the manuscript.

I look forward to hearing from you.

Yours sincerely,

Luigi Segagni Lusignani
NOTE:
Questions of the reviewers are reported here in italics. New phrases and sentences that have been inserted into the manuscript are in bold type.

REVIEWER #I: DENISE SILVA

Minor Essential Revisions
1-The authors should describe the statistical tests used in ‘Data Analysis’ section.
The Data Analysis section was redrafted as follows: Data were analysed using SPSS for windows version 17. Beyond descriptive statistics, associations between the dependent variables (patient delay and health system delay) and the independent variables were analysed by calculating the ORs test and respective 95% confidence intervals (CI). Responses to questions to assess TB knowledge were analysed by calculating their mean and interquartile scores. Using the mean score as a cut-off, the responses were categorised into good knowledge (above or equal the mean) and poor knowledge (below the mean) [26]. Independent variables that showed marginal associations (p<0.20) in the bivariate analysis were used in a logistic regression analysis in order to identify independent predictors of both patient delay > 30 days and health system delay > 15 days. The association of predictor variables with the dependent variables was assessed by using 95% CI and adjusted odds ratio (AOR). A p-value of <0.05 was regarded as statistically significant.

Major Compulsory Revisions
1-Why did the authors choose a cut-off point of > 30 days for patient delay and > 15 days for health care system delay?
The following explanation was integrated at page 5: The majority of the quantitative studies measured delay as a dichotomous variable, typically as approximately 1 month or more for patient delay [16,20-22], and 15 days for health system delay [16, 21, 23, 24]. In other studies median value of the observed data was used as a cut-off [24, 25]. Following the consultation with experts of the NTP and with treating physicians,...

2-The authors should explain what was considered a TB case. If the median health system delay was seven days, I supposed that culture was not used for diagnosis. And how smear-negative patients were diagnosed?
The following explanation was added in the text (page 5): According to the NTP, smear-positive pulmonary TB were defined the patients with two or more sputum smears for acid fast bacilli (AFB) or one sputum positive for AFB and radiological abnormalities consistent with active TB; smear-negative PTB were defined the patients with three negative sputum smears for AFB and radiological abnormality consistent with active TB or failure to respond to antibiotics trials. Extrapulmonary TB (EPTB) patients were defined the patients with TB in organs other than the lungs proven by histo-pathology or TB based on strong clinical evidence consistent with active EPTB and the decision by a physician to treat with a full course of anti-TB therapy.
3-Do the authors have any data on laboratory turn-around time? The question here is, does the lab play an important role in the delay in health system or is it only the clinical team that plays a role? If data on this is not available, it should be discussed in the limitations.

On the basis of the reviewer's suggestion the following phrase has been added in the limitations (page 13): Another limitation of the current study is that we are not able to provide data on laboratory turn-around time. So it is not possible to say if the lab plays an important role in the in health system delay.

REVIEWER #II: FEKADU ABEBE
Major compulsory revisions

Abstract:
1. Under methods, line 6, it reads “structured questionnaire were randomly administered to a cohort of TB patients” but on page 4 study design, “we performed a cross-sectional study during a three-month period from April to June 2008”. The authors should need to rewrite their study design both in the abstract and materials and methods.

In the Abstract, the Methods section has been rewritten as follow:
On a cross-sectional study, 385 TB patients who visited 21 DOTS clinics in Luanda were included consecutively. The time from the onset of symptoms to the first consultation of health providers (patients’ delay) and the time from the first consultation to the date of diagnosis (health system’s delay) were analysed. Bivariate and logistics regression were applied to analyse the risk factors of delays.

2. Under abstract Line 8, the authors state, “univariate and multivariate analysis were performed. Logistic regression analysis was applied to analyse risk factors of delays”. The authors need to clearly state which statistical method was used for what.

The Data Analysis section (page 7) was entirely redrafted.

Introduction
3. “Introduction” may change to “background” to follow BMC format

The correction has been made.

4. Paragraph 2, line 2 “it is estimated that every year there are 9.4 million-----tuberculosis (4). It is not clear whether this figure is global or for Angola?

The 9.4 million rate is the global incidence. The specification worldwide was added.

Methodology
5. The authors may need to give the rationale for excluding DOTS centers with less than 100 TB patients

The following explanation has been inserted on the text (page 4):...... and because they were located in difficult to reach peripheral rural areas.

6. The authors are required to give inclusion and exclusion criteria used for selecting their TB patients, and more importantly how the study participants were selected, instead of giving a 1967 book reference?

The following sentence was integrated in the text (page 5): All patients diagnosed with TB of all forms according to the national TB guidelines [Ministry of Angola 2006] and coming to the selected DOTS centres were included consecutively and interviewed just before starting treatment, up to reach the sample size defined for the single centre. Patients who started treatment prior to interview were excluded.

7. The authors need to show questions used to measure patients knowledge of TB and how the results were analyzed.
The following lines have been added (page 6): its cause, gravity and treatment (able to mention bacteria/germ/microbe as a cause of TB, to categorise TB as a transmissible disease, to recognise measures to prevent the transmission, to be able to mention that TB is a treatable disease and the approximate duration of treatment).

In addition, on Data Analysis section (page 6) the following lines have been added to explain how the results were analyzed: Responses to questions to assess TB knowledge were analysed by calculating their mean and interquartile scores. Using the mean score as a cut-off, the responses were categorised into good knowledge (above or equal the mean) and poor knowledge (below the mean). On this respect an additional reference has been added (current reference n.26) Legesse M, Ameni G, Mamo G, Medhin G, Shawel D, Bjune G, Abebe F. Knowledge and perception of pulmonary tuberculosis in pastoral communities in the middle and Lower Awash Valley of Afar region, Ethiopia. *BMC Public Health* 2010, 10:187

8. The authors are required to describe how they assessed perception levels and the quality of health services at the DOTS center?

On page 6 the following lines have been added to clarify this point: (taking into account the opening time of the centre, the waiting time in the centre, the attitude of the health personnel, do you consider to be; i) definitely satisfied, ii) to some extent satisfied or iii) not satisfied with DOTS centre care received?).

9. The authors are required to give a brief description (e.g distance from each other, setting, etc) of the 21 DOTS center selected.

The following description of the 21 DOTS centers was inserted at pages 5 and 6: Eight of the 21 DOTS centres were located in the suburban districts of the province (Samba, Cacuaco and Viana), where the population density for each district was less than 900 inhabitants per km$^2$ and the nearest health facility was more than 3 km away. Thirteen DOTS centres were settled in the urban districts where the density population was higher and the nearest health facility was less than 2 km away.

Results

10. “socio-economic characteristics of the study sample” may be replaced by “socio-economic characteristics of the study participants”

As suggested “Socio-economics characteristics of the patients” was replaced by “Socio-economic characteristics of the study participants”.

11. Although patient delay and health systems delay have been defined differently, the variables used to assess both patient delay and health system delay are the same. For instance, it is not clear how factors such as high volume of DOTS centers, density of inhabitants/health care workers, waiting time at the center, and center of first contact on patients delay will affect patient delay. Similarly it is not clear how factors such as sex, education, income, residence, occupation, distance, transport method, knowledge of TB affect health systems delay.

We agree with the Reviewer: his is an important point of many studies on TB delay and it is a limitation of the present study. However, in our study we tried to increase the number of variables more related to the system (high volume of DOTS centers, density of inhabitants/health care workers, waiting time at the center), and therefore not limiting the measure of the system delay to socio-demographic and clinical characteristic of the patients). The following phrase which underling this limit in the
Finally, although for the health centres we have tried to analyse several factors focused more on system delay other than the socio-demographic characteristics of patients, part of the factors analysed are related to socio-demographic and clinical characteristics of patients. As already observed by Finnie et al. [16], these would be considered predisposing factors for system delay in the sense that they may be related to the aspect of system delay in which patient return for diagnosis is required; they also may indicate health care workers’ perceptions of patients that may cause them to be less likely to test and diagnose TB [16]. Anyhow, in future research factors more pertinent to the health system have to be studied in a better way [16,18].

Discussion:
12. The discussion is generally poor and should be rewritten (please see examples):
   a. Line 1-3 will not add to the quality of your discussion. If there is no standard definition of “patients” or health systems delay”, how did you choose your own definition?
   b. Page 8, paragraph 2, line 6-13 should clearly state how education influences delay in Angola and elsewhere;
   c. Page 9, paragraph 2, lines should be clearly discussed or removed;
   d. System delay, paragraph 2 is not relevant to delay and should be removed/replaced

The Discussion section has been deeply revised (page 9-14). The points a, b, c, d, highlighted by the reviewers have been restructured/revised. A new section (Total delay) has been added. Nine new bibliographic references have been added.

Conclusion: What has been described as conclusion is limitation of the study. The two should be given separately and clearly
The comments related to the limitation of the study are now opportunely reported at the end of the Discussion section.

References: Check references (e.g. is reference no 19 Yemane T or Yemani T?)
The reference at page 5 (line 13) was correctly changed.

Figures and tables: Tables 3, 4, and 5 should be removed and results can be summarized in the text.
Previous table 3 was removed and the content was inserted in the Result section (pages 6 and 7). Previous tables 4 and 5 were merged into a single table (now Table 3) and the columns reporting the multivariate analysis were removed. Now the results of the multivariate analysis compare only in the text.

Reviewer #III: Pieter Uys

Conclusion section: Although the authors briefly summaries the important factors it might be helpful to the reader if these were listed in point form, in descending order of importance. Possibly they could suggest ways to address these factors.
A new phrase was added in the Conclusion (page 14): Moreover, collaboration with hospitals, health care providers and private health workers is important to reduce enrolment delays in DOTS programmes in Luanda.

Minor revisions
Following the suggestions of the referee, corrections have been done in the revised manuscript.

**EDITORIAL REQUESTS**

Title page: Please include a title page at the front of your manuscript file. It should contain, at minimum, the names, institutions, countries and email addresses of all authors, and the full postal address of the submitting author.

A new title page at the front of the manuscript has been included (page 1).

Authors' contributions: Please include an Authors' contributions section before the Acknowledgements and Reference list.

An Authors' contributions section before the Acknowledgements and Reference list has been inserted (page 14).

Acknowledgements: We strongly encourage you to include an Acknowledgements section between the Authors Contributions section and Reference list.

The Acknowledgements section is in the right position (page 14).

Please list the source(s) of funding for the study, for each author, and for the manuscript preparation in the acknowledgements section. Authors must describe the role of the funding body, if any, in study design; in the collection, analysis, and interpretation of data; in the writing of the manuscript; and in the decision to submit the manuscript for publication.

The role as funding body of the NGO Doctors with Africa CUAMM, has been described (page 14).