Author's response to reviews

Title: Survival and health status of a cohort of tuberculosis patients in rural Lao PDR

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Version: 3 Date: 9 September 2009

Author's response to reviews:

Minor revision, 9 Sept 2009
Dear Editor
Lastly we found minor editing and typographic mistakes on our last submission performed on Monday 7 September.
We also add p signification when missing
So, we replaced the files and submitted a revised version called:
hb9septpostPOcorrectionsTB_attapeu.doc
We also revised the figure 1 and 2 (Two words), the new version is:
9septlaosfigure1 and 9septlaosfigure2
we hope you do no mind
I attached the new main manuscript,
Below our cover letter sent on 7 september with a point to point reply
To the Editor,
Sir,
We thank the reviewers for their very useful comments.
Please find enclose the revised manuscript entitle :
Survival and health status of a cohort of tuberculosis patients in rural Lao PDR
We have revised the manuscript and references. Last revision of the manuscript was made by a native English speaker, (not this letter). We have corrected all the errors listed, and made all the requested clarifications by reviewers.
Some paragraphs have been modified.
You will find below a point by point reply, and details of these changes, according
to the reviewers comments.
We hope that the paper may now be acceptable to the BMC Journal. Please let us know if any aspects need further clarification.
We wish you good reception
Sincerely yours,
H Barennes

Associate Editor:

A. This MS requires through reading by a native English reader for the correction of English and typographic mistakes.

Dr C John and Dr A Gray revised the final manuscript

B. Abstract, page 2; method section: Authors must mention specific month of study (month of 2002 and month of 2004).

We enrolled all TB patients who started DOTS treatment at Attapeu Provincial Hospital from January 2002 until December 2004.

C. Main text Method, page 4, para 1: Author must cite some reference of sero-prevalence of HIV at the end of the para.

HIV prevalence in incident TB cases is 2% in Laos[6].

Results: Page 6, para 2: the authors must mention the time of death after diagnosis in addition to death during hospitalization.

Twenty-six patients (15.1%) died (mean time to death after diagnosis: 271±59.9 days).

Was added accordingly

Discussion: Page 10, para 1: Paragonomiasis is irreverent and should be deleted from this MS.

This point was justified in the text

A systematic search of paragonimiasis was performed in this subgroup of 10 villages since there has been some evidence of paragonimiasis foci in Laos and since it is often misdiagnosed as TB[10].

Systematic sputum examination was performed only in a sub-sample of villages, and etiology of persistent symptoms could not be followed-up in detail; i.e. the role of drug resistance, treatment failure, advanced and complicated TB, associated lung injuries due to heavy smoking, or paragonimiasis, or both. Paragonimiasis is endemic in Laos and is frequently overlooked [10,16].
Reviewer: KM Kam
Reviewer’s report:
General comments:
(1) Reviewing hospital based records is a well-known biased sample of more serious cases that may present late and thus require hospitalization; the authors should state this limitation clearly.

We agree, this comment was added in discussion section as follows

Our patients were drawn out of the hospital records and might have been more serious cases. This may overestimate the low health status of our sample. However, in Laos all TB patients are hospitalised for a DOTS regardless their physical status.

(2) Diagnosis is based only on clinical findings and AFB smear microscopy. Were chest X-rays routinely done? was there any external quality assessment (EQA) in place in Attapeu hospital laboratory?

In 1995-1996, the National Tuberculosis Program (NTP) started a stepwise introduction of directly observed treatment short-course (DOTS) with diagnosis (microscopic for acid-fast bacilli (AFB)) and treatment at the district level. Chest X-rays are not done routinely [5].

And in methodology section

NTP with the help of Service Fraternel d’Entraide, a non governmental organisation was responsible of the training and regular quality assessment of the laboratory

This was clarified in the text

Specific comments:
(3) Abstract, lines 18- 19: what does "still symptomatic" mean? after treatment started, or after certain hospitalization period?

This was clarified in the text as follows:
Survivors had persistently poor health status. They were underweight (54.7%), and still had clinical symptoms (53.5%), including dyspnoea (28.8%) and haemoptysis (9.5%).

(4) Background: the first 3 lines are irrelevant and can be deleted. The first 10 lines in under Methods should be moved to Background.

Changes were made accordingly

(5) Background, line 10: "acid fast".
Thank you, we corrected

(6) Methods: the authors should concentrate on how the diagnosis of TB was made i.e. what clinical/ chest X-ray/ laboratory criteria (smear gradings vs positivity, length of stay/ treatment) rather than on how height and body weight were measured. If really want to be vigorous: were the measurement tapes calibrated with a standard? i.e it may be precise, but were the measurements accurate?

We agree, the diagnosis method was clarified in this section

This was clarified in the text:

Patients were enrolled if they had a positive AFB examination at Attapeu Hospital (following the 3 sputum sample collection and grading according to NTP criteria). For sputum negative patients diagnosis was based on a chest radiograph read by a trained radiologist or, if not available, on the NTP diagnostic algorithm[7].

(7) How were other causes, e.g. COPD, of the same symptoms excluded?

This was added in discussion section:

We conducted our study with limited resources. Our results rely largely on interviews and basic physical examinations. Systematic sputum examination was performed only in a sub-sample of villages, and etiology of persistent symptoms could not be followed-up in detail; i.e. the role of drug resistance, treatment failure, advanced and complicated TB, associated lung injuries due to heavy smoking, or paragonimiasis, or both. Paragonimiasis is endemic in Laos and is frequently overlooked [10,16].

(8) Discussion, line 7: why was paragonimiasis suddenly mentioned, with references 17, 18? There was no such component in the whole study. It might be relevant as a remote cause of hemoptysis in Laos, but the authors should justify this.

You are right, the reason were clarified in method section as follows:

As a sub study conducted on a sub-sample of 10 villages, we screened people with a chronic cough of more than 3 weeks (and/or haemoptysis) using a questionnaire approach [9]. We collected two sputum samples, one immediately and one the following morning according to standard procedures of the NTP[7]. Samples were collected each day and sent to the district hospital where a Ziehl-Neelsen stained slide was examined for the presence of acid-fast bacilli. Positive patients were referred to the provincial hospital for treatment. A systematic search of paragonimiasis was performed in this subgroup of 10 villages since there has been some evidence of paragonimiasis foci in Laos and since it is often misdiagnosed as TB[10].
And in discussion section:
Systematic sputum examination was performed only in a sub-sample of villages, and etiology of persistent symptoms could not be followed-up in detail; i.e. the role of drug resistance, treatment failure, advanced and complicated TB, associated lung injuries due to heavy smoking, or paragonimiasis, or both. Paragonimiasis is endemic in Laos and is frequently overlooked [10,16].

(9) Page 8 last 2 lines: why is latent TB mentioned? This does not seem to be part of this study at all.
We agree, this is not part of the study. However this work report the risk for close contact in Laos. It is an positive argument to improve the case detection in the field and decrease the TB transmission in Laos

(10) Page 9 line 22: should be "GDP"?
you are right, this was revised : ..gross domestic product (GDP) of 500 USD/year..

(11) Figure 2: it seemed that only about 30% had sputum examination at month 5. Since this is a critical period to assess treatment success/failure, it is unacceptable to have such a low percentage, even more so if these were all hospitalized patients. Was there any specific reasons for this? The authors should explain.
This is an important point
The result section was revised:
At the time of DOTS enrolment, 166 (96.5%) sputum tests were performed. At months 2, 5, and 8 after enrolment the rates of sputum testing fell to 73.9% (n=108), 63.0% (n=92), and 55.4% (n=81) respectively. After 2 months, 5 of 142 (3.5%) sputum follow-up examinations remained positive. Three of these were negative at 5 months, and one not checked after 5 months was reported negative at 8 months of treatment. Data of one patient is not available. No sputum was reported positive after 5 and 8 months treatment (Figure 2).

This was added in the discussion section
The proportion of sputum controls at 2, 5, 8 months was low. Health workers who deliver the drugs monthly should also carefully check whether the scheduled control sputum examinations have been completed. Treatment of TB patients in Attapeu would have also improved with this support.
Reviewer: Shampa Anupurba
Reviewer's report:
The article titled “Survival and health status of a cohort of tuberculosis patients in
rural Lao PDR” may be accepted after essential minor revisions.

Thank you for your comments,

Each comment (1 to 20) was revised in the text, accordingly

Comment 1. Background section; Para 1, Line 2: were to be inserted after which.
This was revised in the text, accordingly
Comment 2. Background section; Para 2, Line 2: Started in place of starts.
Comment 3. Background section; Para 2, Line 4: Acid fast in place of acrid fast.
Comment 4. Methods section; Para 2, Line 2: The line “The large part……………….” May be replaced with The population was predominantly poor, illiterate and belongs to ethnic minority.
Comment 5. Methods section; Para 2, Line 3: as to be inserted after estimated.
Comment 6. Methods section; Para 2, Line 5: statement may be restructured as fifth most frequent cause of hospitalization.
Comment 7. Methods section; Para 2, Line 9: visit to the district hospital.
Comment 8. Lab and field procedure section; Para 1, Line 6: Sent instead of send. And delete established and.
Comment 9. Results section; Para 1, Line 1: patients were included, of whom 159 were cases of pulmonary TB.
Comment 10. Results section; Para 1, Line 5: Delete of and were in place of are.
Comment 11. Results section; Para 2, Line 4: delete a after lower.
Comment 12. Results section; Para 3, Line 3: than instead of that.
Comment 13. Results section; Para 7, Line 1: of to be inserted after observance.
Comment 14. Discussion section; Para 1, Line 6-7: “……………village visits in ten of the 80 villages fascilitated in diagnosing 5 new TB…………..”
Comment 15. Discussion section; Para 2, Line 7-8: Last sentence of the para may be ommited.
The sentence was ommited, accordingly
Comment 16. Discussion section; Para 5, Line 3: …the survey gives insight to the……………twice than that of …………”
Comment 17. Discussion section; Para 7, Line 9: .. future investigation……..
Comment 18 : Figure legends: Figure 1-2: Legend mentioned in the end of MS is not the same as given along with the figures.

Thank you, we agree, This was revised in the text, accordingly
Comment 19 : Figure legends: Figure 1: chart may be inserted after Flow.
This was revised in the text, accordingly

Comment 20. Figure 1. BK may be explained as a foot note.

We agree, BK was replaced by MTB (mycobacterium tuberculosis) and a foot note was added