Author's response to reviews

Title: Current tuberculin reactivity of schoolchildren in the Central African Republic

Authors:

Fanny Minime-Lingoupou (flingoupou@yahoo.fr)
Rock Ouambita-Mabo (ouambita_mr@yahoo.fr)
Aristide-Désiré Komangoya-Nzozo (dkomang@yahoo.fr)
Dominique Senekian (senekian@yahoo.fr)
Lucien Bate (batelucien@yahoo.fr)
François Yango (yangofr@yahoo.fr)
Bachir Nambea (bnambea@yahoo.fr)
Alexandre Manirakiza (amanirak@yahoo.fr)

Version: 2
Date: 26 March 2015

Author's response to reviews: see over
Dear Editor

BMC Public Health

Thank you for sending us the reviews of our manuscript 7934320161225266 “Current tuberculin reactivity in schoolchildren in the Central African Republic”, by Fanny Minime-Lingoupou, Rock Ouambita-Mabo, Aristide-Désiré Komangoya-Nzozo, Dominique Senekian, Lucien Bate, François Yango, Bachir Nambea and Alexandre Manirakiza.

We have taken account of all the comments in revising this manuscript, which is attached.

With best wishes
Alexandre Manirakiza
Reviewer's report

Title: Current tuberculin reactivity in schoolchildren in the Central African Republic

Version: 1

Date: 20 October 2014

Reviewer: Hong Van Tieu

Reviewer’s report:

Major compulsory revisions

This paper examines the prevalence of TST reactivity at different cut-off thresholds in young schoolchildren 6-12 years of age in the Central African Republic to determine prevalence of TB infection. The paper is written in clear English. However, there are several major issues with the paper and analysis.

(1) Page 3, Introduction: What is the TB prevalence in the pediatric population? What are the prophylaxis guidelines for latent TB for children in the country? It would also be good to provide HIV prevalence and HIV/TB coinfection prevalence, as well as prevalence of nontuberculous mycobacterium infection in children in the country? What is the BCG vaccination coverage in children, when do they get vaccinated, is BCG vaccination mandatory? It would also be important to provide reasons why the neighboring region of Ombella M’Poko was selected in addition to Bangui. Is it because it was a convenience sample? Is it a rural region (this was only mentioned much later in the paper), does it have lower HIV prevalence than that of Bangui? Is BCG vaccination coverage different between the 2 regions?

Authors’ response: These questions have been answered.

(2) Page 4, Methods: In the TST and data collection section, it would be good to mention how personal information of the participants (age, BCG history, whether HIV status was asked) was obtained- was it by a counselor-administered questionnaire, questionnaire for parents to complete, what other information of the participants was obtained? Was TB exposure history of the participants obtained? If so, this information should be provided in the manuscript. Was a physical exam done to assess BCG scar? What is the nutritional status of the children, and how was that assessed (ie, exam with weight and height)?

Authors’ response: These questions have been answered.

(3) Page 4, Results section: In the first paragraph, were there any differences in age/demographics between those who completed the TST implant/reading and those who were absent at time of skin reading? Was there a difference between the 2 regions (Bangui and Ombella) in exclusion from the final data set due to being absent, etc.? In the third paragraph: why mention that 26.6% children had a tuberculin reaction induration of >= 1mm; also does this relate to only children with BCG vaccination, or all children in the data set? Was any questionnaire collected or exam performed to assess if any of the children had symptoms or signs
of active TB? Do the positive TST results presented only reflect latent TB without active symptoms/signs?

Authors’ response: These questions have been answered.

(4) Page 5, Discussion section: In the bottom of first paragraph, the authors noted that when prevalence of NTM is high, a threshold value of 10 mm overestimates the prevalence of MTB infection because of cross sensitivities. It would be good to elaborate little bit more here, and why induration of >15 mm was selected to estimate the prevalence of infection and calculation of ARI. Also, it would be good to expand the entire discussion section as it is only 1 paragraph long, with the other paragraph related to limitations. So how does the results differ from previous reports in the country? How do they compare with other countries in Africa? Is it feasible to utilize other techniques such as interferon gamma release assays in the country? Please also add limitation of distinguishing TB and nontuberculous mycobacterium infection in the study, and limiting distinguishing active vs latent TB in the study if these were not assessed.

Authors’ response: These questions have been answered.

Minor Essential Revisions

(1) Page 3, Methods: It would be good to explicitly mention the eligibility criteria here. Also, in the Training section, it would be good to describe what the team consists of. Does it consist of nurses, doctors, or counselors? In the TST and data collection section, it would be good to mention how personal information of the participants (age, BCG history, whether HIV status was asked) was obtained was it by a counselor-administered questionnaire, questionnaire for parents to complete, what other information of the participants was obtained?

Authors’ response: These questions have been answered.

(2) Page 5, Discussion section: In the first sentence, it would be good to specify that it relates to the prevalence of TB infection. It would also be good to specify that it does not distinguish active vs. latent TB infection.

Authors’ response: These questions have been answered.

(3) Table 1: It would be good to put total N=2710 at the end of the title

Authors’ response: The denominators used to calculate the percentages are given in the “Results” section.

(4) Figure 1: the HR7 and HR1 are not highlighted. It is difficult to see where are the 2 regions that are included in the study. HR7 and HR1 should be in a darker shade to differentiate them from the other regions not included in the study.

Authors’ response: These changes have been made.
Discretionary revisions

N/A

**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.
Reviewer’s report

Title: Current tuberculin reactivity in schoolchildren in the Central African Republic

Version: 1

Date: 16 March 2015

Reviewer: Keren Middelkoop

Reviewer’s report:

This paper reports on the prevalence of TB infection and the annual risk of TB infection in two health districts in the Central African Republic, including in the capital city. Since there has not been any TST data published from this country since the 1980’s, this is a timely study. However, I find the reporting of results generally confusing, and this paper requires substantial work before publication.

Major comments

Abstract:

1) Results: Authors should present the prevalence of TST positivity/TB infection for each of the cut-offs assessed.

Authors’ response: This has been added.

Introduction:

1) In the first sentence the authors state that children are the source of spread of TB in a community: given the pauci-bacillary nature of childhood TB disease, this is not accurate. It is generally accepted that adults are mainly responsible for transmission; children are a vulnerable population for infection and disease, and are a good sentinel for TB transmission rates in a community.

Authors’ response: These changes have been made.

2) 2009 DOTS coverage and new TB rates are provided. The authors should use the most up-to-date data available – 2013 data can be obtained from the WHO report. Unless the study was performed in 2009, in which case the authors should state this in the methods.

Authors’ response: We state in the “Methods” that “This survey was conducted in HR1 (Ombella M’Poko) and HR7 (Bangui) in 2011.”

Methods:

1) The sample size calculation information does not say what prevalence the authors were anticipating in the calculation.
Authors’ response: We state in the “Methods” that “A sample size of 1600 children was estimated for each region based on a BCG coverage rate of 75%.”

2) How was BCG vaccination status determined? History from parents/immunisation cards? This is important for understanding potential information biases in this variable.
Authors’ response: This information has been added.

3) Could the authors please provide the formula used for ARI in the format ARI=…..As it currently stands it is not intuitive for the reader to understand.
Authors’ response: This has been added.

Results:
1) Paragraph 1: The numbers given for participants in Bangui (1469) and Ombella M’Poko (1242) do not total the 2710 participants reported. This is true in both the text and Table 1.
Authors’ response: This correction has been made.

2) Paragraph 3: I find the flow/order of the results presented confusing: the authors talk about TST positivity in children with BCG scar, then all vaccinated (I think) and then non-vaccinated. I more logical flow, eg non vaccinated, all vaccinated and then vaccinated with or without BCG scar, would be easier to read.
Authors’ response: The order of presentation of results has been changed.

3) Authors should provide 95% CI around TB infection prevalence estimates.
Authors’ response: These have been added.

4) Table 1: This is a very confusing table – the percentages suggest that the denominator for “not vaccinated” is the total N, but for the “vaccinated with and with BCG scar” the denominator is all those vaccinated (n). Is this correct? And if so, then across what groups was the p-value calculated? Its unclear what groups are being compared statistically.
Authors’ response: The table has been revised.

5) Table 2: Across all 3 cut-off points, the “N” in not vaccinated, vaccinated without BCG scar and BCG scar do not sum to the total provided in the Total column. As with table 1, its not clear which groups are being compared to provide the OR for the BCG effect – this needs to be clarified.
Authors’ response: The table has been revised.
6) Table 3: Similarly, its not clear which groups are being compared to provide the OR for the BCG effect – the legend says “No versus Yes”, but the groups are not labelled as such in the table: is this the effect of BCG scar or having received BCG?

Authors’ response: This table has been deleted.

Discussion:
1) The authors note that their reported TB infection rate is lower than that of the previous study in this country, but they have not attempted to explain why this is.
   a. What cut-off was used in the 1988 study?
   b. What is the confidence interval around this estimate and the 1988 estimate?

Authors’ response: This statement has been deleted.

c. Given the Central African Republic status as a high burdened HIV country, what do the authors estimate may be the HIV prevalence in the study sample? Given the anergy to TST noted in HIV positive patients, may this have contributed to the lower than anticipated TB prevalence rate among the study sample?

Authors’ response: This table has been deleted.

   d. Do the authors think the lower than anticipated TB infection prevalence/ARTI reflect the declining TB rates reported for the country by the WHO? The conclusion is vague and could be strengthened.

Authors’ response: The conclusion has been revised.

Minor comments
Abstract:
1) Introduction (line 3): insert a space between school and children

Authors’ response: According to the Oxford English Dictionary, this is one word.

2) The description of countries bordering the Central African Republic is not necessary (and the information is available on Figure 1). It would be more helpful to have a description of the health regions in which the study was performed, in the methods.

Authors’ response: This change has been made.
3) The last sentence of the first paragraph of the Data Analysis section is very confusing (“The reaction induration size…..”) . Please could the authors re-word this sentence.

Authors’ response: This sentence has been revised.

Methods:
1) A description of the two health districts should be provided – is HR1 a rural district, for example? What are the TB rates in these areas compared to the rest of the country?

Authors’ response: This has been clarified.

Results:
1) Paragraph 3: I would split the first sentence, as BCG coverage and TST induration size are two different concepts

Authors’ response: The sentence has been split.

Discussion:
1) First sentence: the authors should state which cut-off they are using for this final prevalence. I would also explain up front why this cut-off was used for the final prevalence.

Authors’ response: These changes have been made.

2) The authors do pick up on the lack of HIV testing as a limitation to this study, but more information could be provided: what has the PMTCT coverage been like over the birth years of this cohort in these areas; as mentioned above, some estimate of how many of the participants are likely to be infected would be helpful.

Authors’ response: We state that “…. mother-to-children HIV transmission was estimated to be 11% in the Central African Republic in 2012 (Ministry of Public Health, unpublished data). In 2002, a study conducted in antenatal clinics reported a prevalence of HIV infection of 15% among pregnant women.”

Conclusion:
1) Insert a space between school and children

Authors’ response: According to the Oxford English Dictionary, this is one word.

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

Quality of written English: Acceptable
Statistical review: Yes, and I have assessed the statistics in my report.

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