Reviewer's report

Title: Malaria prevention reduces in-hospital mortality among severely ill Tuberculosis patients: a three step intervention in Bissau, Guine-Bissau

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Reviewer: elizabeth ashley

Reviewer's report:

This is an interesting manuscript on an important topic. However the interpretation is limited significantly by

1. Presenting data as summarised statistics
2. The fact that no malaria incidence data were collected
3. Absence of any data on cause of death

Without these, presenting the intervention as a package of anti-malarial prevention and control strategies is potentially misleading since numbers studied per year were moderate and, as other studies have shown, a significant part of any impact on mortality in 2007 could have been as a result of prevention of bacterial infections by cotrimoxazole. Reduction of malaria has been shown to be a useful by-product of cotrimoxazole prophylaxis in patients with HIV but it is not the only indication for its use.

Major Compulsory Revisions:

1. Please clarify if the study was designed prospectively, why this design was chosen and include a statement on sample size calculation if performed
2. The objective of the study was stated as reducing mortality. Was there any evidence that malaria was an important cause of death in the rainy season?
3. Some more explanation and justification for the choice of the death/discharge ratio as the outcome for comparison rather than mortality rates would be welcome. Please include raw data for deaths and discharges as well as the ratios to aid data interpretation. Can it be assumed that all patients who did not die were discharged? Can a comparison of mortality rates with 95% confidence intervals each year as well as the ratios be presented?
4. Outcomes: ideally malaria would have been a secondary outcome. If this was not possible please explain why. Was malaria diagnosis clinical or laboratory confirmed?
5. More discussion on the limitations of the design would be worthwhile

Minor Essential Revisions:

1. Results- is it possible to compare outcomes stratified by HIV status?
2. Please clarify how patients admitted towards the end of a year were dealt with in the analysis and whether admission rates across the months of the 3 years were broadly comparable.

3. Can the relative benefits of cotrimoxazole versus the other interventions be explored in more detail?

4. It is likely that most malaria in G-B at the time of the study was sensitive to sulfadoxine-pyrimethamine (SP). The findings may not be generalisable to other African countries with high rates of antifol/sulfa drug resistance in bacteria and malarial parasites. The rapid evolution of antifol resistance observed in malaria elsewhere also raises questions about the durability of this strategy. This could be mentioned.

Discretionary Revisions:

1. Introduction- possible interactions between TB & malaria are mentioned and referenced but with no details given. It would be interesting and highly relevant to have any hypotheses summarised.

2. Introduction mentions ‘TB seronegative’ patients twice. Presumably this means seronegative for HIV? Should be stated.

3. Did the same proportion of patients receive antiretroviral therapy each year? These data would be of interest if available.

4. It is likely that the efficacy of chloroquine, even though national policy, was poor. This raises the possibility that patients may have died partly as a result of ineffective treatment for their malaria. Are there data on chloroquine efficacy in Guinea Bissau? I believe national policy has changed to artemether-lumefantrine? This could be added.

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