Reviewer's report

Title: Intensified specimen collection to improve tuberculosis diagnosis in children from rural South Africa, an observational study.

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Reviewer: Annelies Van Rie

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In the manuscript “Intensified specimen collection to improve tuberculosis diagnosis in children from rural South Africa, an observational study”, the authors aim to determine the diagnostic yield of routine sputum, gastric aspirates, blood and urine cultures in children presenting with symptoms and signs of active TB. Knowledge of pediatric TB remains limited and this study describes findings when intensified sampling is integrated within routine care at a rural government hospital. It is unfortunate that samples were not stored so that they could be tested by LAM and Xpert MTB/RIF. Despite this limitation, the findings are still relevant and contribute to the limited knowledge on this subject.

Comments:

Title: explicitly state that the study took place in a hospital setting

Abstract: The fact that “MDR-TB was detected by urine culture alone in one child” and “urine … provided one additional TB diagnosis” is misleading, as gastric aspirates were not collected in this child. I believe that the statement in the discussion “accurate diagnosis of MDR-TB and XDR-TB in children has great potential to save lives and reduce transmission but the low yield from current diagnostic tests remains a challenge” provides a better summary of the data.

Introduction: It is not the prevalence of TB but the prevalence of MDR-TB that may make one consider whether TB treatment can be initiated without the need for culture confirmation in a child.

Materials and methods:
- This is an observational study, not an efficacy trial
- Children were classified as having possible, probable or confirmed TB based on WHO guidelines (reference?). There is a strong consensus in the field that the consensus clinical case definitions should be used in any evaluation of TB diagnostics in children. It is thus strongly recommended that for this manuscript, children are classified according to these definitions (ref 31).

Results:
- According to figure 1, sputum was only collected in 66.7% of outpatient and GA in 70% of inpatient children. The reasons for not collecting specimens should be stated in the manuscript. If it is because parents refused or procedures failed,
then this needs to be discussed as this would change the findings of feasibility of these procedures.
- Table 1: Given the small sample size, it is unlikely that any differences between groups will be statistically significant. It may be more informative to have the data presented by three groups (probable, possible and confirmed TB) instead of presenting the data in probable and confirmed together.
- Table 2: please add information on age

Discussion:
- In the discussion on CXR, the low (21%) specificity should be highlighted as a limitation of using CXR in the diagnosis of childhood TB

**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 I have no competing interests