Diagnostic evaluation of smear negative tuberculosis in a resource poor setting

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Valorisation
In this section, I consider possible implications, both for the theoretical development of research on quality of TB diagnostic care and the specific public policy implications for professional practice in patients with suspected TB in resource poor setting. The findings in this study suggest a number of avenues for further research. Firstly, I recognize that by situating this research in Ethiopia context, the generalizability of my findings outside the resource constrained setting is limited. Although recent WHO report and others have shown that clinicians often deviate from internationally recommended TB management, our findings add that care offered to smear-negative cases continues to be deviant from the standards, compared to smear-positive TB cases. This then raises the question of the perceived habitual bias by TB healthcare providers, who apparently still consider managing smear-positive cases to be the most effective strategy to curb the TB epidemic. This treatment adherence gap would be significantly closed if strategies that increase compliance to ISTC are identified by programme managers and policymakers in hospitals that best meet the desired standards. Therefore, we suggest that future quality improvement initiatives should focus on the role for real-time, clinic-level monitoring of smear negative TB suspect evaluation practices, in order to capture individual data on clinical measures related to care of smear-negative TB from every patient evaluated.

Less well understood are the determinants of provider adherence to TB treatment guidelines. In particular, there is increasing recognition that guideline implementation is heavily dependent on provider behaviour and in order to improve the quality of diagnostic care, understanding and subsequently changing provider behaviour is required. Our findings indicate that the degree of trust that TB service providers had in the diagnostic test results had a great impact on compliance with the guidelines. Thus, addressing their negative perception of sputum smear microscopy may be just as important as scaling up the diagnostic test. Furthermore, there was dilemma among TB service providers about relying only on sputum microscopy in passive case finding. The underlying conflict was a lack of alternative diagnostic modalities when the initial test result does not correspond with the patient’s clinical presentation. A better strategy to retest those patients whose initial tests are negative in settings where TB is frequently missed may improve compliance with the guideline.

A recent review of the TB guidelines showed that the overall methodological quality of the guideline was low. Several domains of the guidelines, such as applicability to specific local situations, contributed to their poor performance. Our findings offer real-life examples of what is needed to customize TB guidelines to local contexts of healthcare in order to improve compliance. We recommend, more studies in other regions and across a wider health facility spectrum to generalize a whole picture of non-adherence in Ethiopia and develop appropriate strategies that influence their compliance with the guidelines. With the important limitation of this study described above in
mind, further studies are now needed to develop appropriate interventions aimed at addressing the critical factors suggested by this study, and to test these systematically. Consideration should be given to specific sub-groups (smear and culture negative TB suspects) as an important influence on guideline compliance.

Numerous decisions are made by care providers, on the basis of an estimated probability that a specific disease or condition is present in an individual. In the diagnostic setting, the probability estimates are commonly based on combining information from multiple predictors observed or measured from an individual. While application of predictive modelling in patients with clinical suspicion of TB has been described before, these studies usually combined only independent significant predictive variables into the decision models. In addition, information from a single predictor is often insufficient to provide reliable estimates of diagnostic probabilities or risks. However, in this study the critical question is whether patients with smear and culture negative result can be detected and treated early by predictive model. Our finding is in agreement with a previous study that reported that predictive models based on clinical variables may not be useful to discriminate culture-negative TB, because of the variable presentations of symptoms. Therefore, screening for active TB is one of several possible interventions that can improve early detection of all forms of TB, but providing better access to diagnostic tests that are more sensitive than smear microscopy is the first essential step. In addition, sound training in threshold principles and providing tools to correctly assess patients with smear and culture negative results might help in making a better diagnostic decision in resource poor settings.

There is an absolute need to find biomarkers that can distinguish between individuals infected having the highest risk of developing TB (susceptibility) and those who have the highest probability of resisting development of the disease (protection). This would significantly help the control programme to break the chain of transmission of the disease in the long run. We are also in need of validated biomarkers that can be translated as point-of-care assays for early diagnosis and treatment of active TB patients in high-incidence countries. The results of our findings support our hypothesis that, patients unable to respond with an effective production of salivary NO metabolites in response to \textit{Mtb} infection, are more likely to be associated with increased risk of acquiring TB. Our findings and previous studies suggest that the use of NO metabolites as a biomarker may have great value for screening of smear positive TB. Will it be possible to learn from this naturally induced host response and better understand those mechanisms that control infection and exploit their value as potential indicators of protection? There are many studies that suggest that the magnitude of the immune response reflects the magnitude of the bacterial load and two longitudinal studies in untreated contacts suggest that the highest responders are at greatly elevated risk of TB, but these studies are relatively small and lack detailed sequential testing routines. Thus the kinetics and duration of the differences are unknown; however, the fact that the two studies produced similar results in very different populations and environments (Ethio-
pia and Germany) is encouraging. Studies to address the questions of remote versus recent infection, predictive value and optimization of the assays, and their usefulness in HIV infected patients should prove very valuable.