Lots of considerations when evaluating the FujiLAM assay

Author's reply

We thank Alberto Garcia-Basteiro and colleagues for their response to our research Article on the novel FujiLAM assay to detect tuberculosis in HIV-positive ambulatory patients in four African countries.[1]

The evaluation of the inter-lot and intra-lot variability in diagnostic accuracy of an assay is usually not part of late-stage clinical studies but should be assessed during quality control by manufacturers. In this case, we were informed by FIND and the assay manufacturer about inter-lot variability of FujiLAM (Fujifilm, Tokyo, Japan) after our study was completed. Following discussions with our scientific advisory board, we added post-hoc analyses of diagnostic accuracy by test lot. Given the importance of the lot-to-lot variability, we presented pooled and by lot accuracy estimates as part of the main study results. A similar approach presenting pooled and by lot diagnostic accuracy estimates has been used by the FujiLAM study consortium.[2] Regarding the implications of these findings, as stated in the summary and discussion of our Article, this version of the FujiLAM assay cannot be recommended for clinical use until the problem of inter-lot variability is resolved.

We believe that sharing the results from a large and rigorous prospective clinical study is important to inform the scientific community, policy makers, end-users, and programme managers on the performance of an assay that has been considered a promising urine-based point-of-care test.[3] We also hope that these data will be used by the manufacturer to inform root-cause analysis, identify solutions, and communicate these to key stakeholders. We think that providing data in a transparent manner will not damage confidence in the currently recommended Alere Determine TB-LAM Ag test (Abbott, Waltham, MA, USA). Notable reasons for low uptake of this test are related to challenges with access, budget limitations, and difficulties in obtaining regulatory agency approvals.[4] We believe that our conclusion is clear enough to prevent any false hope. We also think that we have an ethical obligation towards the study participants to publish these data.

Notably, the results on inter-lot variability reported by our group and others raise an important question on whether inter-lot and intra-lot variability should be systematically assessed as part of clinical diagnostic studies, and at which stage it is most appropriate to evaluate this. These considerations should be discussed when providing updated guidance for the evaluation of new diagnostics.[5]

Sputum-free point-of-care diagnostic tests for tuberculosis remain urgently needed. Despite these disappointing results for this version of the FujiLAM assay, we hope that research to develop more sensitive LAM-based point-of-care assays will continue.[6]

We declare no competing interests.

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