EDITORIAL

Improving TB diagnosis in people living with HIV

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Diagnosis of TB remains the weakest link in TB care cascades, and there is an urgent need for better diagnostic tools and strategies to address TB-related morbidity and mortality. HIV-associated TB still accounts for 7% of TB cases, but 15% of TB deaths and 30% of HIV deaths globally, and diagnosis is more challenging with HIV co-infection.¹ In recent years, novel rapid diagnostics such as the Xpert® MTB/RIF assay (Cepheid, Sunnyvale, CA, USA) and urine liparabinomannan (LAM) assays (Alere Determine™ TB-LAM, Abbott, IL, USA) have shown promise for HIV-associated TB. However, better diagnostic accuracy has not necessarily translated to better outcomes for patients in trials.²

Kasaro et al. report the results of a 'before-and-after' implementation study of Xpert and urine LAM as part of the diagnostic algorithm for people living with HIV (PLHIV) with presumed TB in peri-urban outpatient clinics in Zambia.³ They found the addition of sputum Xpert testing increased the proportion of TB culture-positive patients diagnosed and treated for TB within 14 days of attendance (66% vs. 46% in the standard-of-care arm), and reduced median time to TB treatment by 10 days. Sensitivity of the diagnostic algorithm with Xpert was better than standard of care (70% vs. 51%, respectively). They did not find TB treatment outcomes differed between groups, although there was high loss to follow-up and the study was underpowered for these outcomes.

While the accuracy and impact of Xpert in both PLHIV and HIV-negative patients have been well described, there is still much to learn from studies such as these. Implementation of diagnostics pose several challenges within 'real-world' settings, and accuracy and outcomes will differ from trials due to the effect of contextual and health system factors. Sensitivity of Xpert in this pragmatic study was, not surprisingly, lower than that reported from diagnostic accuracy studies.⁴ Furthermore, Kasaro et al.'s findings shed important light on processes that affect impact of diag-

nostics; for example, on-site Xpert reduced time to TB diagnosis more than centralised Xpert placement, although health system delays prevented translation to earlier TB treatment.

This study again showed the utility of the Determine TB-LAM assay for TB diagnosis in PLHIV, especially for those with low CD4 counts, and in identifying those missed by sputum testing. Despite the ease of urine collection, the low cost of urine LAM assays and supportive WHO recommendations, uptake and routine use has been poor. Lack of local piloting and experience using the assay is commonly cited as reasons for poor adoption;⁵ therefore, studies such as Kasaro et al.'s remain important. However, rapid scale-up of urine LAM to improve TB diagnosis in PLHIV is critical, alongside implementation research to identify barriers and anticipate challenges for the next generation of (more sensitive) urine LAM assays.

Improving collection and use of routine data and qualitative research, including process evaluation, can help us understand barriers to uptake and define optimal strategies to implement current and future TB diagnostics. Implementation science allows important evaluation of diagnostics beyond accuracy, but must not delay effective tools reaching patients.

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