Equitable access to diagnostic resources means one Xpert-Ultra cartridge for all inpatients with HIV being investigated for tuberculosis

Tuberculosis (TB) remains the leading cause of death among people with advanced HIV disease (AHD).[1] Early and accurate diagnosis is crucial for reducing mortality, yet standard diagnostic methods often fail, owing to the challenges faced by patients with AHD. The GeneXpert platform (Xpert, USA) and in particular the Xpert MTB/RIF Ultra (Xpert-Ultra) test is accurate in diagnosing TB in those who can produce sputum,[2] but ~50% of patients admitted to hospital with AHD and TB are unable to produce sputum due to severe illness, mental status changes, or extrapulmonary TB.[3] Sputum induction greatly increases the diagnostic yield,[4] but is not widely available. The diagnostic gap is partially filled by the urine Determine TB LAM Ag assay (AlereLAM Abbott, USA), which is available in most South African (SA) hospitals. This assay has a sensitivity of ~52% in inpatients, which is higher than in outpatients, but this is accompanied by a suboptimal specificity of around 87%.[5] AlereLAM does not provide rifampicin resistance results. Consequently, ~30% of inpatients with HIV are not diagnosed with TB with a combination of sputum Xpert-Ultra and AlereLAM.[6] This leads to missed diagnoses and delayed treatment, with negative impact on morbidity, mortality and cost.

Current policy in SA is to perform Xpert-Ultra testing on sputum, pus, cerebrospinal fluid (CSF) and selected other extrapulmonary samples, but not on urine. Since this policy was written, the World Health Organization (WHO) has recommended using Xpert-Ultra tests on urine samples for extrapulmonary TB diagnosis in high-burden settings.[7] Urine Xpert-Ultra offers several advantages. It can detect TB in patients unable to produce sputum, can diagnose rifampicin resistance and provides results within a few hours, crucial for initiating timely treatment.[8] It has a similar sensitivity to AlereLAM (and in some studies superior sensitivity), with a greater specificity and positive predictive value, and can confirm *Mycobacterium tuberculosis* v. nontuberculous mycobacteria. A multi-country study demonstrated that combining an Xpert-Ultra on concentrated urine with sputum Xpert-Ultra and AlereLAM increased diagnostic yield to >80%, particularly in patients with CD4 counts ≤200 cells/μL.[9] Importantly, the diagnostic yield included patients who were only diagnosed on one of urine Xpert-Ultra, AlereLAM, or sputum Xpert-Ultra. In *post-hoc* analyses, participants with urine Xpert-Ultra positive results were also more likely to die within 10 weeks than were those with negative results, demonstrating the test's potential value in earlier diagnosis and initiation of TB treatment to reduce TB deaths. By integrating urine Xpert-Ultra into standard protocols, healthcare providers can enhance diagnostic accuracy, potentially reduce TB-related mortality and support the global effort to improve outcomes for people living with HIV.[10]

The main reason for exclusion of urine Xpert-Ultra from guidelines in SA is cost, as well as concerns that healthcare providers may flood the system with large numbers of samples if proper training is not first undertaken. There are also logistical concerns with regard to concentration steps, although the National Health Laboratory Service standard operating procedures already include centrifuging CSF for Xpert-Ultra if >3 mL are received, so this should not be a barrier. One modelling study has suggested that implementing urine-based tests for inpatients with HIV will increase life expectancy, be cost-effective and should be prioritised.[11]

We are encouraged that the SA TB Think Tank recently endorsed the use of Urine Xpert-Ultra for hospitalised adults with HIV, particularly in those who cannot produce sputum. Given the need for novel TB diagnostics in patients with AHD, we further advocate for the formal adoption into policy of Xpert-Ultra of urine for inpatients being investigated for TB, but who are unable to produce sputum. This represents equity for patients, as everyone is allocated at least one Xpert-Ultra cartridge for the diagnosis of TB and rifampicin resistance, and those who are unable to produce sputum are not unduly disadvantaged.

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