
Urine LAM tests: A golden opportunity to end TB deaths among people with advanced HIV

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The World Health Organization (WHO) and Treatment Action Group (TAG) convened a satellite event at the 10th International AIDS Society Conference (IAS 2019) entitled *Urine LAM tests: A golden opportunity to end TB deaths among people with advanced HIV*, in Mexico on 22nd July 2019. The session shared the latest evidence on diagnostic tests, provided a broad overview of the update to the WHO guidelines for the use of the lateral flow urine lipoarabinomannan (LF-LAM) assay, reviewed the reasons behind poor policy uptake by countries and shared best practice and advocacy efforts by civil society to promote urine LF-LAM uptake. The event was chaired by Mark Harrington of Treatment Action Group and Gabriella Magnabosco of the Ministry of Health, Brazil.

Global Health Advocate, Albert Makone presented on [Mapping of LF-LAM Uptake with Global Fund & PEPFAR Funding](#). Makone cited the latest evidence supporting the use of LF-LAM, and highlighted its importance as a simple, fast, very affordable, non-invasive TB diagnostic test that saves lives and performs best among hospitalized people with the most advanced HIV disease. Results from a mapping exercise found that only eleven of the 73 countries whose grants were evaluated had included LF-LAM in their grants. Makone stressed that whilst countries might be purchasing tests through domestic funding or

using other means, the manufacturer, Abbott, reports sales in only a handful of countries, highlighting untapped opportunity for countries to use PEPFAR and Global Fund grants to expand access to LF-LAM.

Ankur Gupta-Wright of the London School of Tropical Hygiene and Medicine presented on [Urine LAM in the inpatient setting: Lessons learnt from the STAMP trial](#), a pragmatic, multi-country randomized controlled trial that compared sputum Xpert MTB/RIF in the standard of care arm with sputum Xpert MTB/RIF, and urine LF-LAM and Xpert TB/RIF in the intervention arm for diagnosing TB in 2,600 adults living with HIV. Findings from the trial support the use of LF-LAM to test patients living with HIV in inpatient settings, as it resulted in increased TB diagnosis, timely initiation of treatment with a reduction in mortality. Modelling further showed that LF-LAM led to an increased life expectancy of 0.5 to 1.2 years, that it was cost-effective and that over five years it would be expected to save 51,000 years of life in Malawi and 171,000 years of life in South Africa. Dr Gupta-Wright also highlighted LF-LAM's prognostic benefits for detecting those at higher risk of mortality. Challenges that he highlighted in implementation of LF-LAM included CD4 threshold as a criterion for LF-LAM, since CD4 testing has been deprioritised by many countries in favour of viral load monitoring; procurement issues; and the need for training in reading and interpreting results. To support the latter, the STAMP trial developed an app to assist with reading the Alere LAM assays for use on a low-cost Android smart phone. The app correctly read 202/204 LAM strips, compared to two blinded human readers. Gupta-Wright concluded that whilst there are new diagnostic platforms on the horizon, scale-up of LF-LAM in the short-term will save lives and lead to quicker adoption of newer assays once they are available.

Tom Ellman of Médecins Sans Frontières (MSF) presented on the [Challenges in implementing LF-LAM in outpatient settings: Experiences from MSF field programmes](#). Dr Ellman provided an overview of a study conducted in 8 health facilities in Malawi, Mozambique and the Democratic Republic of Congo, that looked at the effectiveness and feasibility of LF-LAM in primary health clinics, in outpatient departments and in inpatient settings. The study found that among patients with self-reported TB symptoms, irrespective of their CD4 cell count, 17% were LAM positive, and among patients with no self-reported TB symptoms and low CD4, 12% were LAM positive. The study also found that only a third of patients could produce sputum, whilst almost all could produce urine. Ellman highlighted the ease and speed of turnaround time of LF-LAM, compared with microscopy and Xpert MTB/RIF. Challenges raised included the additional burden on already overstretched health staff to conduct a considerable number of tests as part of the advanced HIV disease package, readability of the test, poor access to CD4 cell counts, and mistrust of a positive LAM result. He concluded that LF-LAM is feasible in outpatient settings but there is need to focus on ensuring access and human resource capacity, including through task sharing and through community awareness and activism.

Chris Gilpin of the World Health Organization presented initial findings from a survey on LF-LAM uptake in 30 high burden countries together with a preliminary update of the revised guidelines on the use of LF-LAM to assist TB diagnosis among people living with HIV. Findings from the survey revealed low uptake and scale-up by countries of LF-LAM policy. The evidence reviewed during the revision of the guidelines confirmed that highest sensitivity of LF-LAM for the diagnosis of TB was among the sickest patients, notably in-patients with low CD4 counts, but also confirmed that LF-LAM has utility among select populations in out-patient settings. Evidence from two randomized controlled trials [1, 2] showed that LF-LAM remains the only TB test proven to reduce mortality among seriously ill PLHIV. The updated policy guidelines are expected to be released in October 2019.

During the panel discussion, with Sean Cavanaugh of the Office of the Global AIDS Coordinator (OGAC); Ezio Távora dos Santos Filho representing civil society from Brazil and Stella Zawedde-Muyanja, Makerere University, Uganda the following key points were raised:

- Political will is a critical enabler of scale-up.
- Skepticism among senior healthcare workers needs to be addressed. We need to garner buy-in from key opinion leaders, advocate more and remove doubts about this test, in order to increase uptake.
- For seriously ill patients in need of urgent treatment, non-availability of CD4 cell count can create a delay in conducting a LAM test. The tendency to de-prioritize CD4 cell-count measurement, which represents a significant barrier to use of LF-LAM, was reiterated.
- PEPFAR does not support routine use of CD4 cell count testing; rather, it has been waiting for the launch of the latest point-of-care Vitect CD4 qualitative test that can detect people whose cells/mm³ are lower or higher than 200 – and thus detect those eligible for the advanced HIV disease package.
- Optimal placement of the test within healthcare facilities is critical – to ensure immediate initiation of TB treatment as indicated (e.g., bedside rather than laboratory).
- Health management information systems should be aligned to track scale-up – consider introducing an indicator for LF-LAM, as well as linkage to treatment.
- Ministries of health, donors, partners and diagnostic providers should collaborate to align procurement processes to ensure LF-LAM procurement does not slip through the net.
- National pilot studies should not stand in the way of implementation and scale-up; however, close monitoring and evaluation is essential for fine-tuning strategies for assuring linkage to care and quality service delivery.

To conclude, there is now ample evidence to support the use of LF-LAM to assist in the diagnosis of TB among seriously ill people living with HIV. Policy uptake by countries has been inadequate. Barriers to implementation and scale-up persist. However, these barriers are not insurmountable and international and national stakeholders, including civil society, need to advocate to ensure this life-saving point-of-care test is taken to scale to prevent TB deaths among people living with HIV.

References

1. Peter JG, Zijenah LS, Chanda D, Clowes P, Lesosky M, Gina P, et al. Effect on mortality of point-of-care, urine-based lipoarabinomannan testing to guide tuberculosis treatment initiation in HIV-positive hospital inpatients: a pragmatic, parallel-group, multicountry, open-label, randomised controlled trial, *The Lancet*, Volume 387, Issue 10024, 19 March 2016, p1187-1197
2. Gupta-Wright A, Corbett EL, van Oosterhout JJ, Wilson D, Grint D, Alufandika-Moyo M, et al, Rapid urine-based screening for tuberculosis in HIV-positive patients admitted to hospital in Africa (STAMP): a pragmatic, multicenter, parallel-group, double-blind, randomized controlled trial, *The Lancet*, Volume 392, Issue 10144, 28 July 2018, p292–30