

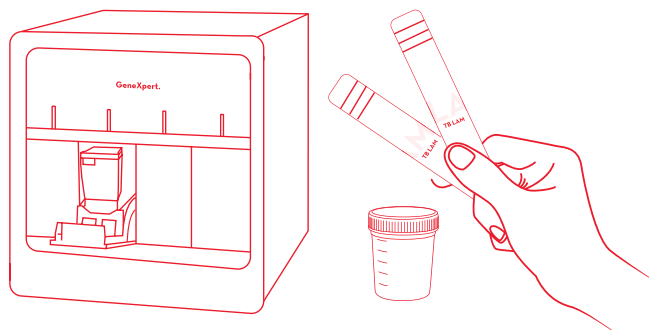
# THE LAM TEST:

## SUPPORTING SCALED-UP, EXPANDED TB LAM TESTING FOR PEOPLE WITH ADVANCED HIV

BY ALBERT MAKONE

Edited by Safiqa Khimani,  
Lindsay McKenna, Erica Lessem,  
and Khairunisa Suleiman

Tuberculosis (TB) is the number one killer of people living with HIV (PLHIV), causing one in three of all AIDS-related deaths.<sup>1</sup> This amounts to 300,000 deaths per year, each of which is preventable.<sup>2</sup> Improving diagnosis will bring us one step closer to achieving the ambitious global targets of reducing the number of deaths from HIV and TB by 90 percent and 75 percent, respectively, and achieving the sustainable development goals.<sup>3,4,5</sup> A simple, inexpensive diagnostic tool, the TB lipoarabinomannan (LAM) test, can catalyze progress toward these targets by allowing for earlier TB diagnosis and treatment to reduce mortality among PLHIV.<sup>6</sup>



**Support from donors for uptake of TB LAM testing in all high TB/HIV burden countries is crucial to stop senseless deaths.**

The World Health Organization (WHO) endorsed TB LAM testing in people with advanced HIV in 2015. Yet this life-

saving test remains vastly underutilized in most high TB/HIV burden countries. The currently marketed TB LAM test, the Determine TB LAM test, is manufactured

by Abbott (formerly Alere); it costs just US\$3.50 and requires no electricity or reagents. As the LAM test is urine-based, it can more easily diagnose TB in PLHIV, who often have difficulties producing sputum or have low amounts of detectable TB in their sputum. Support from donors for uptake of TB LAM testing in all high TB/HIV burden countries is crucial to stop senseless deaths.

### TB LAM TESTING SHOULD BE PRIORITIZED IN HIGH TB/HIV BURDEN COUNTRIES

TB LAM testing is useful in any setting with high rates of TB/HIV coinfection. The following countries have high burdens of TB and HIV, and as such should prioritize implementation of the LAM test<sup>7</sup>:

Angola	Democratic Republic of the Congo	Namibia
Botswana	Djibouti	Nigeria
Brazil	Eswatini	Russia
Burkina Faso	Ethiopia	Rwanda
Burundi	Ghana	Sierra Leone
Cambodia	Haiti	South Africa
Cameroon	India	Sudan
Central African Republic	Indonesia	Thailand
Chad	Kenya	Togo
China	Lesotho	Uganda
Congo	Malawi	Ukraine
Côte d'Ivoire	Mali	Tanzania
	Mozambique	Vietnam
	Myanmar	Zambia
		Zimbabwe

## SCIENTIFIC EVIDENCE & BENEFITS OF URINE LAM TESTING

Evidence strongly suggests the dramatic benefits of using the TB LAM in high TB/HIV burden settings. The test has demonstrated impact in all PLHIV admitted to the hospital, regardless of CD4 count or symptoms, and for all PLHIV with advanced disease or CD4<200 cells/mm<sup>3</sup> presenting to ambulatory care. While the current LAM test has suboptimal sensitivity (a pooled sensitivity of 56% and a pooled specificity of 90% in PLHIV with a CD4 count<100 cells/mm<sup>3</sup> compared with culture or nucleic acid amplification testing<sup>8</sup>), clinical trials have shown that TB LAM testing allows for earlier diagnosis in people with advanced HIV in

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both inpatient and outpatient settings and that it reduces TB mortality. TB LAM is the only TB diagnostic tool to date to show a mortality

benefit in a randomized controlled trial: In a multicenter, multicountry study, adding TB LAM testing to standard TB testing (smear, culture, GeneXpert MTB/RIF, and culture) reduced the time to treatment, thereby reducing mortality in HIV-positive inpatients with symptoms of TB.<sup>9</sup>

Another multicountry, randomized trial, known as the STAMP trial, showed that using TB LAM testing in addition to GeneXpert MTB/RIF in all HIV-positive, hospital-admitted adults resulted in a survival benefit in the most at-risk subpopulations in a pre-specified analysis, and in an increase in TB diagnosis and treatment initiation in the general study population.<sup>10</sup> TB LAM testing was found to increase life expectancy by half a year to 1.2 years and was cost-effective; using TB LAM testing in hospitals in Malawi and South Africa alone for five years would save 122,000 years of life.<sup>11</sup>

These data point to the value of using TB LAM to screen for TB among all hospitalized PLHIV. Further, a prospective observational cohort study of both ambulatory and hospitalized PLHIV in Kenya indicated that adding TB LAM testing to testing algorithms increased diagnostic yield in people with CD4<200 cells/mm<sup>3</sup>.<sup>12</sup> These support the expansion of TB LAM testing to all PLHIV in inpatient settings, and in outpatient facilities for anyone with advanced HIV or, if CD4 count is available, with CD4<200 cells/mm<sup>3</sup>.

## NEXT-GENERATION TESTING

New tests to detect the LAM antigen are in development—tests that may offer improved sensitivity for detecting TB among all PLHIV (not just those with advanced disease). In 2019, the WHO is expected to review evidence for both the existing LAM test manufactured by Abbott, as well as preliminary evidence for a LAM test in development by Fujifilm. This review may result in a broader indication for LAM testing. In the meantime, donors should not wait to support TB and HIV programs in rolling out the existing test, given its potential to save lives and its minimal cost, and to lay the groundwork for rolling out next-generation tests.

## UPTAKE OF TB LAM TESTING

Despite evidence for greater use of the LAM test, few countries have articulated plans to scale up use or availed themselves of donor support to do so. We reviewed Global Fund funding requests for the 2018/19 and 2020/21 cycles, as well as final 2018 President's Emergency Plan for AIDS Relief (PEPFAR) Country Operational Plans (COPs) from 73 countries (WHO high TB/HIV burden countries, Global Fund TB grant-eligible countries, and PEPFAR-eligible countries). Of the 73 countries analyzed, only six COPs and six Global Fund funding requests included the TB LAM test (see Table).

**TABLE: COUNTRIES THAT INCLUDED TB LAM TESTING IN FUNDING APPLICATIONS SUBMITTED TO PEPFAR AND/OR THE GLOBAL FUND**

Country	Donor	Population/setting for use described in Global Fund funding proposal and/or PEPFAR COP
Burundi	Global Fund	PLHIV
Cameroon	Global Fund	PLHIV presenting with symptoms of TB
Côte d'Ivoire	PEPFAR	PLHIV with advanced disease
Democratic Republic of the Congo	PEPFAR	PLHIV with low CD4 counts or those who are seriously ill across selected high-volume antiretroviral therapy (ART) sites in all health zones
Eswatini	PEPFAR	PLHIV who present to care late
	Global Fund	Not specified
Guatemala	Global Fund	PLHIV at integrated care units, before commencing ART
Kenya	PEPFAR	Hospitalized patients
Malawi	PEPFAR	PLHIV at high-volume referral centers
Ukraine	Global Fund	PLHIV
Vietnam	Global Fund	Not specified (mentioned lab equipment to maintain LAM testing)
Zambia	PEPFAR	Not specified

**Countries whose grant documents were reviewed and did not include TB LAM testing:**

**PEPFAR** – Angola, Botswana, Burundi, Cambodia, Cameroon, Dominican Republic, Ethiopia, Ghana, Haiti, India, Indonesia, Lesotho, Mozambique, Namibia, Nigeria, Papua New Guinea, Rwanda, South Africa, South Sudan, Tanzania, Uganda, Ukraine, Vietnam, Zimbabwe

**Global Fund** – Afghanistan, Angola, Bangladesh, Belize, Botswana, Cambodia, Central African Republic, Congo, Costa Rica, Cote D'Ivoire, Democratic Republic of the Congo, Djibouti, Dominican Republic, El Salvador, Ethiopia, Ghana, Guinea-Bissau, Guyana, Haiti, Honduras, India, Indonesia, Jamaica, Kazakhstan, Kenya, Kyrgyzstan, Laos, Lesotho, Liberia, Malawi, Mali, Mozambique, Myanmar, Namibia, Nepal, Nicaragua, Nigeria, Panama, Papua New Guinea, Philippines, Rwanda, Senegal, Sierra Leone, Somalia, South Africa, South Sudan, Suriname, Tajikistan, Thailand, Turkmenistan, Uganda, Tanzania, Uzbekistan, Zambia, Zimbabwe

**Countries without available grant documents (includes ineligible countries / countries that have transitioned):**

**PEPFAR** – Afghanistan, Antigua and Barbuda, Bahamas, Bangladesh, Barbados, Belize, Brazil, Central African Republic, Chad, China, Congo, Costa Rica, Djibouti, Dominica, El Salvador, Grenada, Guatemala, Guinea-Bissau, Guyana, Honduras, Jamaica, Kazakhstan, Kyrgyzstan, Laos, Liberia, Mali, Myanmar, Nepal, Nicaragua, Panama, Philippines, Senegal, Sierra Leone, Somalia, St. Kitts and Nevis, St. Lucia, St. Vincent, Suriname, Tajikistan, Thailand, Trinidad and Tobago, Turkmenistan, Uzbekistan

**Global Fund** – Antigua and Barbuda, Bahamas, Barbados, Brazil, Chad, China, Dominica, Grenada, St. Kitts and Nevis, St. Lucia, St. Vincent, Trinidad and Tobago

## DONORS: TAKE ACTION!

Donors have the opportunity to play a catalytic role in ensuring uptake and expanded use of this important test to improve TB detection and survival among PLHIV. To ensure the rights to health, life, and the benefits of scientific progress of PLHIV, we urge donors to help increase access to TB LAM testing and prevent further needless TB deaths among PLHIV by:

- Ensuring that all grants to high TB/HIV burden countries include support for implementation of the TB LAM test and consumables, including for procurement, training, and nationwide scale-up in both inpatient and outpatient settings;
- Encouraging countries to implement TB LAM testing in line with the latest evidence,

as a hospital-based screening test (along with GeneXpert MTB/RIF Ultra) for all PLHIV regardless of CD4 count or symptoms, and for TB screening in outpatient settings among PLHIV with advanced disease or with CD4 counts < 200 cells/mm<sup>3</sup>;

- Developing TB screening and diagnosis indicators specific to TB LAM to measure implementation and impact on TB diagnosis among PLHIV;
- Funding operational research on TB LAM testing to answer key questions about optimal implementation at different levels of health systems; and
- Supporting research and development for next-generation LAM tests.

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