



Treatment Action Group

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LAM TESTING IN 2020 PEPFAR COPS

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TREATMENT ACTION GROUP

GOOD COPS OR BAD COPS WEBINAR

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Why we need better TB tests for PLWHA

- **TB is the number one killer of people living with HIV/AIDS (PLWHA), causing one in three AIDS-related deaths - 251,000 people in 2018.**
- **TB is preventable and curable, but most TB in PLWHA is diagnosed late or not at all.**
- **PLWHA who are seriously ill can have difficulty producing sputum, so sputum-based tests are not ideal.**
- **PLWHA have less TB bacteria, so rapid molecular tests (GeneXpert, Truenat) are less sensitive.**
- **Rapid molecular tests also rely on sputum or samples from other parts of the body that can be difficult to obtain.**

What is the LAM test?

- **The LAM test is the only test that can rapidly and easily diagnose TB in PLWHA.**
- **It is a simple, urine-based test that provides results in just 25 minutes, and costs just US\$3.50 per test (Abbott Determine TB LAM Ag).**
- **The test detects LAM, a component of the outer cell wall of TB bacteria that is discarded in the body.**
- **The LAM test is more sensitive among people with advanced HIV disease.**
- **In 2019, WHO recommended the LAM test for PLWHA:**
 - **with signs and symptoms of TB,**
 - **who are seriously ill, OR**
 - **who have advanced HIV disease**
 - (with less than 200 CD4 cells/mm³ for inpatients, and less than 100 CD4 cells/mm³ for outpatients)



<https://www.alere.com/en/home/product-details/determine-tb-lam.html>

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Key benefits of LAM testing








































































- **SAVES LIVES: the LAM test is the only TB test shown to reduce deaths**
 - It does this by identifying PLWHA with TB earlier, allowing them to start treatment earlier.
 - The LAM test works best among those sickest with HIV, and most at risk of dying.
 - One study showed that using LAM reduced the risk of dying by 17 percent (Peter et al, Lancet, March 2016).
- **Improves rates of TB diagnosis among PLWHA when used in combination with GeneXpert or Truenat**
 - When used together, the combined sensitivity of the tests is higher than when used separately, providing the best chance of diagnosing TB.
 - WHO recommends that both tests should be used in combination.

LAM in 2018 + 2019 PEPFAR COPs

	LAM in 2018 COPs?	Language included in 2018 COPs	LAM in 2019 COPs?	Language included in 2019 COPs
Cote d'Ivoire	Y	People living with HIV (PLHIV) with advanced disease	Y	Introducing LAM to address co-infections of PLWHA with advanced HIV disease; plans to implement at 10 reference sites; aims to reduce mortality
Democratic Republic of the Congo	Y	PLHIV with low CD4 counts or those who are seriously ill across selected high-volume antiretroviral therapy (ART) sites in all health zones	Y	Package for advanced disease includes CD4 and LAM testing for acutely ill PLWHA in Kinshasa; will introduce LAM in select ART sites for PLWHA with low CD4 cell counts or seriously ill
Eswatini	Y	PLHIV who present to care late	Y	Scale up LAM for seriously ill PLWHA with CD4 counts less than 100 cells/mm ³ ; training of clinicians and lab technicians in the use of LAM
Kenya	Y	Hospitalized patients	Y	Kenya will prioritize TB prevention and treatment through... improved diagnosis using GeneXpert and TB-LAM; (TB-LAM) test will be availed for severely sick hospitalized patients; The Ministry of Health will procure (TB-LAM)
Lesotho	N		Y	Support the roll-out of LAM for patients with CD4 counts less than 200 cells/mm ³
Malawi	Y	PLHIV at high-volume referral centers	Y	Implement national guidelines to implement LAM among PLWHA with CD4 counts less than 200 cells/mm ³ , WHO Stage III/IV, or "seriously ill"; will procure and scale up the use of LAM
Namibia	N		Y	Introduce LAM; include procurement of 1,000 LAM assays
South Africa	N		Y	Support efforts to make LAM available to PLWHA hospitalized with advanced disease
Tanzania	N		Y	Support scale up of LAM for PLWHA with advanced disease; targeting those with CD4 counts less than 200 cells/mm ³ or those seriously ill
Uganda	N		Y	Using LAM as part of screening and management of PLWHA with advanced disease; committed to introducing LAM testing
Ukraine	N		Y	Provision of LAM testing for PLWHA with advanced disease
Zambia	Y	Not specified	Y	Introducing the LAM test
	6		12	

AVAILABILITY OF LAM IN PEPFAR COUNTRIES WITH HIGH BURDENS OF TB AND HIV

 YES
 PENDING*
 PLANNING
 NO
 NO DATA

	LAM in National Guidelines/ Algorithm ^{1,2}	LAM registered with National Regulatory Authority ³	LAM procured by National Program in 2018 ⁴	LAM in routine use in National Program ^{5,6}
Angola				
Botswana				
Cameroon				
DR Congo				
Eswatini				
Ethiopia				
Ghana				
India				
Indonesia				
Kenya				
Lesotho				
Liberia				
Malawi				
Mozambique				
Namibia				
Nigeria				
Papua New Guinea				
South Africa				
Tanzania				
Thailand				
Uganda				
Zambia				
Zimbabwe				

* Countries procuring LAM with registration pending utilized temporary import permits or waivers.

¹ World Health Organization. Global Tuberculosis Report. Geneva: World Health Organization, 2019.

² O'Shea, Rachel (Abbott Rapid Diagnostics, Galway, Ireland). Personal communication with: David Branigan (Treatment Action Group, New York, USA). 2020 January 27.

³ Ibid.

⁴ Ibid.

⁵ Pai, Madhukar. Country adoption and uptake of urine LAM test: current landscape and barriers. Presentation at the 50th World Conference on Lung Health of the International Union Against Tuberculosis and Lung Disease (The Union). 2019 November 1. Unpublished.

⁶ Pai, Madhukar (McGill International TB Centre, Montreal, Canada). Personal communication with: David Branigan (Treatment Action Group, New York, USA). 2020 January 20.

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Papua New Guinea				
South Africa				
Tanzania				
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LAM in 2020 PEPFAR COPs Guidance

- **What's good?**
 - **6.5.2 Identification and Treatment of Advanced Disease**
 - “Both tests—Xpert MTB/RIF Ultra and LF-LAM—should be implemented, in order to ensure optimal diagnostic results.” p283
 - “Urinary LAM is indicated in screen-positive individuals who are seriously ill or who have advanced disease and in all hospitalized PLHIV who are ill, regardless of CD4 cell count or TB symptoms.” p283
 - **6.5.2.1 Advanced Disease: Algorithms for Treatment**
 - “TB signs and symptoms present: Perform Xpert MTB/RIF Ultra and LF-LAM on all” p284
 - “TB signs and symptoms absent: If seriously ill (any setting) OR an inpatient with advanced disease OR an outpatient with CD4<100... or WHO Stage 3/4 disease: Perform Xpert MTB/RIF Ultra and LF-LAM” p284

LAM in 2020 PEPFAR COPs Guidance

- **What's good?**

- **6.5.3.1 Effective TB Case-Finding among PLHIV and Integration of TB and HIV Case-Finding Efforts**

- “The LF-LAM assay is the only TB diagnostic test currently available that has demonstrated a mortality reduction in a randomized controlled trial.” p288
 - “[T]eams should make the test available in all in-patient settings that admit PLHIV with advanced disease as well as outpatient settings where PLHIV are evaluated for TB symptoms or may present with advanced disease.” p290
 - “PEPFAR implementing partners should ensure development of training materials as well as roll-out of trainings on use of LF-LAM for facility personnel, in coordination with national TB programs.” p290
 - “A newer, more sensitive version of the test may become commercially available in the next few years; however, teams should not wait for this newer assay to be available and should procure the available LF-LAM assay immediately.” p290

LAM in 2020 PEPFAR COPs Guidance

- **What's bad?**

- **6.5.3.1 Effective TB Case-Finding among PLHIV and Integration of TB and HIV Case-Finding Efforts**

- “PEPFAR implementing partners should ensure that sensitive molecular testing, such as Xpert MTB/RIF Ultra, [in combination with LF-LAM] are used as the initial diagnostic test for TB in all PLHIV with TB symptoms...” p288
- “LF-LAM is not intended to replace GeneXpert MTB/RIF testing in any setting - it should be used in combination with GeneXpert, when available, for adults, adolescents, and children living with HIV.” p289
- **No procurement targets set!** Countries should set procurement targets for LF-LAM that at minimum match procurement estimates for other interventions intended for people presenting with advanced HIV disease.

LAM in 2020 PEPFAR COPs

- **COPs should say that LAM...**
 - has a proven mortality benefit
 - is most sensitive in PLWHA with advanced HIV disease (those most at risk of dying of TB)
 - does not depend on CD4 cell count testing
 - should be used in combination with rapid molecular tests such as GeneXpert or Truenat
 - should be used in both inpatient and outpatient settings
- **COPs should include...**
 - training for health care workers in the use of LAM
 - concrete procurement targets for LAM (including urine kits) that at minimum match those of other interventions for advanced HIV disease
 - concrete plans for LAM introduction, roll out, and scale up
 - inclusion of LAM as part of a comprehensive HIV/TB package

PEPFAR Point, Counterpoint

- **There isn't sufficient budget for LAM.**
 - The LAM test can be procured through PEPFAR funding—it costs just US\$3.50 per test, does not require electricity or reagents, and it **SAVES LIVES!**
- **The LAM test is just for a small population.**
 - LAM testing improves diagnosis and saves the lives of those most at risk of dying from TB—it is the only TB test with a proven mortality benefit. It is well worth the investment!
- **The sensitivity of the LAM test is too low.**
 - LAM is most sensitive in PLWHA with advanced HIV disease—those most at risk of dying from TB. The LAM test should be used together with GeneXpert or Truenat to improve the overall sensitivity of the tests.
- **LAM is reliant on CD4 cell count testing.**
 - In 2019, the WHO expanded its recommendations for LAM to include all PLWHA with signs and symptoms of TB, serious illness, OR advanced HIV disease, in both inpatient settings (<200 CD4 cells/mm³) and outpatient settings (<100 CD4 cells/mm³)—Note: advanced HIV disease can be determined without CD4 cell count testing, based on presence of WHO clinical stage 3 or 4 events.

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Activist Guide to the LAM Test



THE LAM TEST: VITAL FOR DIAGNOSING TB IN PEOPLE WITH ADVANCED HIV

Written by Adam Almeida

August 2017

Edited by Erica Lessem, Khairunisa Suleiman, Timur Abdullaev, Lynette Mabote, Bruce Tushabe, Albert Makone, Dorothy Namutamba, and Luckyboy Mkhondwane

WHY DIAGNOSING TB MATTERS

Tuberculosis (TB) is caused by bacteria called *Mycobacteria tuberculosis*. TB is the number one killer of people with HIV, causing one in three of all AIDS-related deaths.¹ Yet, unlike HIV, TB is curable: each one of these 400,000 deaths annually is preventable.² All people with HIV should be screened for TB, yet many countries do not report screening for TB in people with HIV.^{3,4}

Advocating for better TB diagnosis is essential to ending suffering for those living with HIV. In 2015, 1.2 million people with HIV fell ill with TB.⁵ People living with HIV are at increased risk of developing TB, and of dying from it—especially when they have low CD4 counts.⁶

Most TB in people with HIV is diagnosed very late, or not at all. Studies from Sub-Saharan Africa show about half (45.8%) of the people with HIV who died of TB remained undiagnosed at death,⁷ meaning people do not get the treatment they need. This is in part because diagnosing TB in people with HIV, especially those with low CD4 counts who are most at risk of dying from TB, has been challenging, until now, with the development of LAM testing (see text box).

WHY WE NEED NEW TB DIAGNOSTICS FOR PEOPLE WITH ADVANCED HIV

The most common TB test, sputum smear microscopy, does not work well in people with advanced HIV, for three reasons. First, it relies on sputum (mucus coughed up from the lungs). But people with HIV are more likely than HIV-negative people to develop TB outside the lungs (40–80% versus 10–20%), so sputum-based TB tests do not work as well in people with HIV.⁸ Most adults (87.9%) with advanced HIV* who died of TB had disseminated TB (TB throughout the body, rather than in the lungs).⁷

Second, people with HIV also tend to have fewer TB bacteria in their bodies even when they are sick. This makes it harder for the test, which is not very sensitive, to detect the TB bug. Third, the physical act of coughing up sputum for the test can be difficult and unpleasant for someone who is very ill.

Tests like GeneXpert MTB/RIF can better detect TB, including TB outside the lungs, in people with HIV. GeneXpert MTB/RIF is an important tool for diagnosing TB in people with advanced HIV, but it still relies on sputum or other samples from the body that are hard to obtain. GeneXpert is not as simple, fast, or inexpensive as the LAM test. **GeneXpert MTB/RIF and LAM should be used together for the best chance of diagnosing TB.**

* For adults, adolescents, and children over five years, advanced HIV disease is defined as a CD4 cell count <200 cells/mm³ or a clinical stage 3 or 4 event at presentation for care.

- **A 2020 version of TAG's Activist Guide to the LAM test is coming soon!**
- **It will be available online, and printed copies will be distributed at the regional PEPFAR planning meetings in Johannesburg in February!**



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