Mapping of LF-LAM Uptake with Global Fund & PEPFAR Funding

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Presentation Outline

• Importance of LF LAM assay

• How LF LAM fared in GF & PEPFAR Grants

• LF-LAM Availability in Countries

• Let’s Take Action
**BENEFITS OF LATERAL FLOW (LF) URINE LIPOARABBINOMANNAN (LAM) ASSAY TESTING**

- **Saves lives!** - the LAM test is the only TB test shown to reduce deaths. It allows for severely ill people to be started on treatment earlier. (Peter JG, Ziejenah LS, Chanda D, et al, 2016)

- **Aimed at the most vulnerable** - LAM test works best in those sickest with HIV, meaning it targets those most at risk of dying from TB. People with advanced HIV previously lacked other good diagnostic options.

- **Affordable** - LAM test costs just USD 3.50 per test. Unlike other TB tests, LAM requires no special reagents or equipment (only cups for urine collection)

- **Non-invasive** - because the test uses urine, it does not require any uncomfortable procedures as other TB tests can (such as inducing sputum, drawing blood, or taking a biopsy).

- **Simple** - the LAM test is low-tech and requires little training to use. It does not rely on electricity or any special equipment.

- **Fast** - the LAM test provides results in just 25 minutes, making it the fastest TB test.


Peter et al. Lancet 2016. [http://dx.doi.org/10.1016/S0140-6736(15)01092-2](http://dx.doi.org/10.1016/S0140-6736(15)01092-2)

Photo from Alere
EVIDENCE FOR URINE LAM TESTING

• **STAMP** trial results highlighted that expanding urine TB-LAM testing with GeneXpert in all HIV-positive, hospital-admitted adults resulted in a survival benefit in most at-risk subgroups.

• A Cochrane Review assessed 12 studies of LAM and found sensitivity of a combination of LF-LAM + sputum Xpert MTB/RIF (either test positive) was 75%, representing a 13% increase over Xpert alone.
  

• A randomized clinical trial in **South Africa, Tanzania, Zambia, and Zimbabwe** showed that using LAM was associated with a 4% reduction in the number of people who died in the first eight weeks from any cause. LAM reduced the risk of dying by 17%.
  

• Urine LAM positivity predicts higher rates of mortality in **South Africa**.
  

• Study in **Kenya** shows adding LAM increases diagnostic yield from 47.4% to 84.0% when using clinical signs and X-ray; by 19.9%, from 62.2% to 82.1% when using clinical signs and microscopy; and by 13.4%, from 74.4% to 87.8% when using clinical signs and Xpert.
  

• Routine LAM testing in newly admitted HIV-positive adults in **South Africa** is feasible, provides major improvement in diagnostic yield with high specificity, identifies TB in people without respiratory symptoms and/or unable to produce sputum, and can rapidly identify patients at highest risk of death.
  
EVIDENCE-BASED POLICIES FOR LAM USE

WHO Policy Guidance (2015)

**LF-LAM may be used** to assist in the diagnosis of TB in HIV positive adult in-patients with signs and symptoms of TB (pulmonary and/or extrapulmonary) who have a CD4 cell count less than or equal to 100 cells/μL, or HIV positive patients who are seriously ill regardless of CD4.

GLI Model TB Diagnostic Algorithms (2017)

The LF-LAM assay may be used to assist in diagnosing active TB in both in-and out-patients who are seriously ill with danger signs, regardless of CD4 count. Testing with the LF-LAM assay may be especially useful for patients unable to produce a sputum specimen. Whenever possible, a positive LF-LAM should be followed up with other tests such as Xpert MTB/RIF. While awaiting results of other tests, clinicians could consider initiating TB treatment immediately based on the positive LF-LAM and their clinical judgment.

RATIONALE FOR MAPPING

- PEPFAR & Global Fund are two of the main donors to the global TB/HIV response.
- Persistent high rates of undiagnosed TB in people with HIV highlighting the test is underutilized.
- Anecdotal evidence and reports from Alere and the GDF suggest that test procurement remains low.
- UNAIDS set a goal of reducing TB-related deaths in PLHIV by 75 percent by 2020; recent UNAIDS data indicate countries remain wildly off target and that the reduction in annual AIDS deaths has stalled.
- Support from donors for uptake of TB LAM testing in all high TB/HIV burden countries is crucial to stop senseless deaths.

To evaluate scale up of LAM testing through donor funding, we examined PEPFAR & Global Fund grant documents for the inclusion of LAM testing.
METHODOLOGY USED

- Reviewed publicly available grant documents for the grants covering 2018 to 2021 published on the Global Fund website.
- Reviewed final 2018 PEPFAR Country Operational Plans (COPs).
- 55 Global Fund grants and 30 PEPFAR COPs were available from 73 countries total - including 31 WHO-defined high TB/HIV burden countries.
- We searched the grant documents for the following terms: “LAM”; “lipoarabinomannan”; “TB LAM”; “Determine LAM ag”; “LF-LAM”; and “lateral flow.”
- We reviewed and compiled relevant statements including any of the search terms in a spreadsheet and analyzed the findings.
RESULTS OF THE MAPPING

- LAM testing was included in Global Fund grant documents for six countries (Burundi, Cameroon, Eswatini, Guatemala, Ukraine, and Vietnam).
- 2018 PEPFAR COPs for six countries (Cote D’Ivoire, Democratic Republic of Congo, Kenya, Malawi, Eswatini, and Zambia).
- Language on LAM testing was limited.
- 9/11 of grantees stated they would introduce, or support implementation or access to, LAM testing.
- Cameroon and Vietnam specified procurement of LAM tests and consumables.
- Our analysis suggests uptake of LAM testing is indeed limited, even with available donor funding.
<table>
<thead>
<tr>
<th>Country</th>
<th>Donor</th>
<th>Population/setting for use described in Global Fund funding proposal and/or PEPFAR COP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Burundi</td>
<td>Global Fund</td>
<td>PLHIV</td>
</tr>
<tr>
<td>Cameroon</td>
<td>Global Fund</td>
<td>PLHIV presenting with symptoms of TB</td>
</tr>
<tr>
<td>Côte d’Ivoire</td>
<td>PEPFAR</td>
<td>PLHIV with advanced disease</td>
</tr>
<tr>
<td>Democratic Republic of the Congo</td>
<td>PEPFAR</td>
<td>PLHIV with low CD4 counts or those who are seriously ill across selected high-volume antiretroviral therapy (ART) sites in all health zones</td>
</tr>
<tr>
<td>Eswatini</td>
<td>PEPFAR</td>
<td>PLHIV who present to care late</td>
</tr>
<tr>
<td></td>
<td>Global Fund</td>
<td>Not specified</td>
</tr>
<tr>
<td>Guatemala</td>
<td>Global Fund</td>
<td>PLHIV at integrated care units, before commencing ART</td>
</tr>
<tr>
<td>Kenya</td>
<td>PEPFAR</td>
<td>Hospitalized patients</td>
</tr>
<tr>
<td>Malawi</td>
<td>PEPFAR</td>
<td>PLHIV at high-volume referral centers</td>
</tr>
<tr>
<td>Ukraine</td>
<td>Global Fund</td>
<td>PLHIV</td>
</tr>
<tr>
<td>Vietnam</td>
<td>Global Fund</td>
<td>Not specified (mentioned lab equipment to maintain LAM testing)</td>
</tr>
<tr>
<td>Zambia</td>
<td>PEPFAR</td>
<td>Not specified</td>
</tr>
</tbody>
</table>

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

LIMITATIONS OF THE MAPPING

- We acknowledge that national governments may be supporting implementation of the LAM test with other funding sources, including domestic funding. (Though Alere only reports sales in a handful of countries.)

- Other efforts are ongoing to more broadly assess uptake of LAM testing and barriers to it (e.g. survey work by McGill University).
LAM AVAILABILITY IN COUNTRIES

- This life-saving test remains vastly underutilized in most high TB/HIV burden countries; only eSwatini, South Africa, and Uganda have scaled up TB LAM testing nationally as at Dec 2018.

Countries with high burdens of TB and HIV:
The following countries have high burdens of TB and HIV, and as such should be prioritized for implementation of the LAM test:

Angola | Congo | Lesotho | South Africa
Botswana | DR Congo | Liberia | Swaziland
Brazil | Ethiopia | Malawi | Thailand
Cameroon | Ghana | Mozambique | Uganda
Central African Republic | Guinea-Bissau | Myanmar | UR Tanzania
Chad | India | Namibia | Zambia
China | Indonesia | Nigeria | Zimbabwe
       | Kenya | Papua New Guinea |
LETS TAKE ACTION

• No TB diagnostic test is perfect, including the LAM test, but it is an important tool for saving people with advanced HIV from dying of TB.

• Global Fund & PEPFAR can cover purchase of TB LAM.

• Global Fund & PEPFAR can cover training and support for National AIDS Program and National TB Program to update their guidance on diagnostic practices, and implement TB LAM and other diagnostics in line with the latest evidence.

• Advocates should encourage Global Fund & PEPFAR to develop indicators for TB LAM testing and to measure the implementation of TB LAM and impact on TB diagnosis among PLHIV.

• New LAM tests are coming! Implementing LF-LAM now will pave the way for future uptake of next-generation LAM tests with improved sensitivity.

• We plan to examine PEPFAR COP19 for inclusion of TB LAM, and hope to see CCMs advocate for inclusion of TB LAM in future Global Fund funding requests.
For more information

- LAM guide: http://treatmentactiongroup.org/content/activists-guide-tb-lam-test
- TAG Brief for Country Programs:

Acknowledgements

- Treatment Action Group