My friends call me **Intensified Case Finding (ICF)**

I undertake regularly screening all people with, or at high risk of HIV, for symptoms of TB in health care facilities, communities as well as in homes. This is an important task because once we identity people who present with these signs and/or symptoms, these friends are promptly diagnosed and immediately initiated on treatment.

How do I go about my investigations… keep reading and learn more!
Intensified Case Finding (ICF) for TB means regularly screening all people with, or at high risk of HIV, for the symptoms of TB, followed promptly with diagnosis and treatment, and then doing the same for household contacts.

Active case finding and the provision of treatment to infected individuals is beneficial because:

- Active TB disease, if left untreated kills more than 50% of people infected.
- TB treatment also reduces the spread of infection; a person on TB treatment for at least 2 weeks can no longer spread TB to others.
- Screening for TB should be taking place both in health facilities, when people first seek HIV services and in other congregate settings (mines, prisons, schools, churches, and the home); in particular amongst people living with HIV.

How often should people living with HIV be screened for TB?

People living with HIV should be screened for TB at every clinic or home visit, regardless of whether they have received or are receiving IPT or ART.

What is the WHO recommended screening algorithm for ruling out active TB, including extrapulmonary TB in people living with HIV?

As recommended by the WHO, all people living with HIV should be regularly screened for TB at every visit using a clinical algorithm whenever they are receiving care. At the minimum PHIV should be screened for common TB signs and symptoms for all types of TB disease. The WHO recommended screening algorithm for adults and adolescents living with HIV include a set of four symptoms:

- Current cough
- Fever
- Night sweats
- Weight loss

The WHO recommends that adults and adolescents living with HIV who do not have any of these four symptoms are unlikely to have active TB and should be offered IPT. However, if any of these four symptoms are present, it may indicate the presence of active tuberculosis and the patient should be further evaluated for TB and other diseases.

DAI-Orainey IO. Diagnosis of latent tuberculosis: Can we do better? Ann Thorac Med, 2009; 4:5-9
What diagnostic tests exist to detect latent tuberculosis infection and confirm active TB disease?\(^\text{19}\)

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| **Tuberculin Skin Test (TST)** | Small amount of TB protein injected into the skin. If a person is infected with TB then a firm red bump will develop on the skin within 48-72 hours. An induration of 5 or more millimeters is considered positive in:  
- HIV-infected persons  
- A recent contact of a person with TB disease  

An induration of 15 or more millimeters is considered positive in any person, including persons with no known risk factors for TB. However, targeted skin testing programs should only be conducted among high-risk groups.\(^\text{20}\) | Allows detection of latent TB. | • Inaccurate positive results for patients who received BCG vaccine or exposed to a different mycobacteria  
• Inaccurate negative results in people living with HIV, people with poor nutrition and those with disseminated TB.  
• Difficult to administer and interpret, costly, and has to be stored in cool temperatures. Patient has to return after 2 days to interpret results, which causes loss to follow up. |
| **Chest X-rays** | TB creates cavities in the lungs that may be visible through x-rays. | | • Increased cost and work load  
• Requires qualified staff  
• Only useful for detecting pulmonary TB, which is less common in PLHIV |

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Smear microscopy

Biological samples (normally sputum) are dyed, placed on a glass slide and looked at under a microscope. The dye makes mycobacteria easier to see, allowing for a diagnosis to be made.\(^{21}\)

Cost-effective test.\(^{22}\) Improvements in automated smear testing and light-emitting diodes (LED)\(^{23}\) microscopy have the potential to greatly improve testing due to improved accuracy in testing TB in PLHIV and less workload.\(^{24}\)

- Poor results in identifying TB if co-infected with HIV since 24%-61% of PLHIV with TB are smear negative
- Further developments are needed regarding capitalising on smear microscopy. The process remains “relatively unchanged”\(^ {25}\)

LED: Fluorescent Light Emitting Diode. LED microscope lamp is inexpensive when compared to the mercury vapor or halogen lamp used in regular fluorescent microscopy and has a life span of more than 10,000-50,000 hours (http://www.finddiagnostics.org/programs/tb/find_activities/led_microscopy.html)


## ADVANTAGES

Compared to conventional mercury fluorescence microscopes, LED microscopes are less expensive and have lower maintenance requirements. The diodes are very durable, do not require warm-up time, and do not contain toxic products. Importantly, they are reported to perform equally well without a darkroom. These qualities make them attractive for use in low- and middle-income countries.\(^{27}\)

## HOW DOES IT WORK

### Line Probe Assay

Is a molecular diagnostic (LPA) test which amplifies the DNA of TB. If TB is present in a sample, it will amplify the TB DNA and yield a positive result. The test detects both TB bacteria and TB strains that are resistant to Isoniazid and Rifampicin. Hence the test diagnoses MDR-TB.\(^{28}\)

### Xpert MTB/RIF

Xpert is a molecular diagnostic test, which amplifies the TB DNA within a sample. Sample (unprocessed sputum or sediment from concentrated specimen) is incubated for 15 minutes in a tube. Diluted sample is put into cartridge with a pipette, which is then inserted for the test. It is used for the diagnosis of pulmonary TB, by use of sputum samples. The sputum samples require minimal manipulation and results are available in 2 hours. There are ongoing studies showing varying sensitivities for diagnosis of EPTB.

The test detects TB and TB strains with rifampicin resistance. Suitable for individuals at risk for MDR-TB and smear negative specimen from PLHIV as it has better sensitivity than smear microscopy to detect TB in PLHIV. Xpert is the fastest molecular TB diagnostic test.

## ADVANTAGES

### LPA testing can be used with sputum samples and culture isolates, and when used with sputum samples, LPA can deliver results within 2 days, rather than 6 weeks. Both INH and Rif resistance can be detected by this test. A new version can be used for all samples irrespective of smear result (both smear positive and smear negative). A 2nd-line line probe assay also in development.\(^{29}\)

## DISADVANTAGES

Instrument requires specialised facilities and access to a stable electricity supply, and are best utilised on smear positive TB cases. However, the new version of this diagnostic test is expensive.

Not cost effective – cannot be used in all types of facilities (e.g. stable electricity and air conditioning are needed). Costs $10 per cartridge test yet studies in South Africa show costs such as shipping etc increase this to $25.\(^{30}\)

Only detects Rif-resistance and not INH resistance, and hence confirmatory testing is needed. Staff training required to ensure treatment initiation and testing is on same day. Sample processing of at least 15 minutes is required; although there is minimal handling of sample.

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\(^{27}\) Smart, T. Determine LAM urine antigen TB test is highly cost-effective for use in hospitalised people living with HIV.


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<td>Determine TB-LAM assay</td>
<td>Urine antigen is tested from the urine cell wall. LAM is a protein found in the outer cell wall of TB. The test requires no processing and is preferred for high burden setting in combination with other tests. It is used as 'rule in' test to detect active TB. It is a molecular diagnostic (LPA) test which amplifies the DNA of TB. If TB is present in a sample, it will amplify the TB DNA and yield a positive result. The test detects both TB bacteria and TBs.</td>
<td>Relatively cost-effective at $2.50-3.50/test. Easy sample processing required. Easy storage conditions for diagnostic kit. Easy readability of results. Handling urine decreases the risk of infection that can occur with blood and sputum. Urine is easier to “obtain” than sputum; which is especially useful for people coinfected with HIV and extrapulmonary TB who have difficulty producing sputum. Rapid diagnostic test; only takes 25 minutes. This is a point of care test which is suitable for basic health facilities (in limited resource settings).</td>
<td>Test is not sensitive. It is most sensitive (57%) in PLHIV with CD4 counts below 100, used in combination with other tests for confirmation. WHO has not yet endorsed this test although there is much evidence on accuracy of the test.</td>
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13 **Should a positive skin test result be a requirement for administering IPT to people living with HIV?**

The WHO recommends that TST is not a requirement for administering IPT to people living with HIV. Symptom screening to exclude those with active TB should be the method used to administer IPT.

14 **Do the 2011 WHO IPT ICF Guidelines recommend Interferon Gamma Release Assay (IGRA) for the screening of people living with HIV for IPT?**

IGRA is a test used which diagnoses latent TB in BCG vaccinated individuals, using blood samples. It is a more sensitive test than TST to diagnose latent TB in BCG vaccinated people. The TB specific antigens in the test activate the release of Interferon Gamma from the blood of a person who is infected with TB. IGRA tests cannot distinguish between latent infection and active TB disease and should not be used for diagnosis of active TB, as was the case in India, until the Government banned it for use for the false diagnosis of active TB. IGRA tests are not recommended by WHO for the screening of children and adults living with HIV for IPT, since “IGRAs cannot accurately predict the risk of infected individuals developing active TB disease. IGRAs are more costly and technically complex to do than the TST.” Significantly higher rates (11.5% vs 4.3%) of indeterminate test results were found in persons with HIV compared to persons without HIV, and in persons with low CD4 cell counts compared to persons with higher CD4 cell counts.

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35 Also marketed as QuantiFERON Gold—“TB Gold” or TB platinum