

# Xpert MTB/RIF increases timely TB detection among people living with HIV and saves lives

## Information note

People living with HIV (PLHIV) have more than a 20-fold increased risk of TB compared to HIV-uninfected people. (1) Diagnosing TB is a particular challenge among PLHIV who are more likely to have smear-negative pulmonary TB. This results in a delay in the detection of TB and in subsequent start of treatment. As a result, HIV-related TB deaths are a significant public health problem facing HIV-prevalent settings\*.

Compared to sputum smear microscopy, which has limited utility among PLHIV, **Xpert MTB/RIF is able to detect more TB cases regardless of HIV status.** For this reason, WHO recommends **Xpert MTB/RIF as a primary diagnostic test for TB in PLHIV.**

### EARLY EVIDENCE ON USE OF XPERT MTB/RIF FOR DETECTING TB IN PEOPLE LIVING WITH HIV

According to the findings of recent research on the use of Xpert MTB/RIF for detecting TB in people living with HIV:

- Xpert MTB/RIF is **sensitive and specific** for detection of TB when it is used as an initial diagnostic test in patients suspected of having HIV-associated TB. Xpert MTB/RIF detected 80% (95% CI: 67% - 88%) of pulmonary TB cases in people living with HIV. (2)
- Xpert MTB/RIF **increased case detection** of TB by 45% compared with microscopy among people living with HIV enrolling in ART in South Africa. (3)
- Xpert MTB/RIF **improved the quality of rapid TB diagnosis** among PLHIV by increasing significantly the proportion of TB patients with a bacteriologically confirmed diagnosis compared to smear microscopy. In areas of high HIV prevalence, Xpert MTB/RIF confirmed diagnosis in 36 – 75% of pulmonary TB patients who were smear-negative. (4-7)
- Xpert MTB/RIF **facilitated earlier diagnosis and reduced time-to-initiation of TB treatment**, especially for smear-negative pulmonary TB and at the decentralized clinics in areas of high HIV prevalence. (7, 8) Xpert MTB/RIF, therefore, enables decentralization of TB diagnosis from hospitals to peripheral health care facilities in HIV-prevalent settings.
- Xpert MTB/RIF was shown to be **a sensitive and specific test for rapid diagnosis of pulmonary TB in children, including in HIV infected children**, in settings with high HIV and TB prevalence. Xpert MTB/RIF **performed well in two induced sputum samples** for detecting TB in children. (9, 10)

#### Why a new diagnostic test was needed for the detection of TB among people living with HIV

Sputum smear microscopy has a particularly low sensitivity for detecting TB among PLHIV. This is because people in later stages of HIV infection and with compromised immune systems often release fewer organisms into their sputum, at concentrations below the threshold for visual detection under a microscope. For PLHIV with a negative smear microscopy result but who are still presumed to have TB, bacterial culture has been the other option. However, culture can only be undertaken at central level laboratories, and results are normally only available after a number of weeks or months. Culture is therefore not good enough for people living with HIV, who need a speedy TB diagnosis and prompt treatment.

Modeling studies have demonstrated that Xpert MTB/RIF is **cost-effective in reducing mortality and increasing life expectancy** of people living with HIV in HIV-prevalent settings. Modeling has also illustrated an immediate and sustained population health impact by **reducing the burden of TB** in HIV-prevalent settings:

- Inclusion of Xpert MTB/RIF in the TB diagnostic algorithm for people living with HIV was found to be **cost-effective in reducing early mortality** (11) of people with advanced HIV infection in sub-Saharan Africa, and **very cost-effective in increasing life expectancy** of people living with HIV who are initiating ART in South Africa (12). The algorithm using Xpert MTB/RIF averts one additional death among every 100 prevalent TB cases compared to the current practice using symptom screening, sputum smear, and chest radiography. (11)
- In the HIV-prevalent setting of southern Africa, roll-out of Xpert MTB/RIF as the initial TB diagnostic for all individuals with presumptive TB was projected to **reduce the prevalence of TB by 28%** and to **reduce the mortality of TB by 21%** within 10 years, compared with using smear microscopy. Compared with sputum smear, implementation of Xpert MTB/RIF has an estimated cost-effectiveness of US\$959 per disability adjusted life-year (DALY) averted over 10 years in southern Africa setting. (13)

Xpert MTB/RIF improves the sensitivity, timeliness and detection of rifampicin resistance in adults and children living with HIV. Using Xpert MTB/RIF to detect TB among people living with HIV also allows for rifampicin resistance to be simultaneously detected, and facilitates timely drug susceptibility testing (DST) for detection of MDR-TB or XDR-TB. Localized epidemics of MDR-TB and XDR-TB among people with HIV have resulted in extremely high death rates. (14) Diagnosing drug-resistant TB rapidly among people living with HIV can allow for the patient to quickly start the appropriate life-saving treatment.

**IN CONCLUSION: Xpert MTB/RIF should be made widely available in HIV-prevalent settings to improve patient care, as it is a rapid, simple and highly sensitive TB diagnostic tool that can easily be deployed close to the point of patient care.**

\*HIV-prevalent settings: where the adult HIV prevalence rate among pregnant women is  $\geq 1\%$  or HIV prevalence among tuberculosis patients is  $\geq 5\%$ .

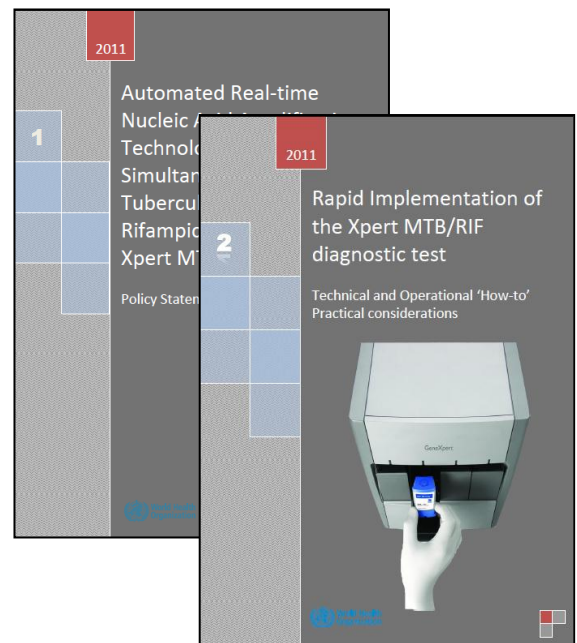
## What is Xpert MTB/RIF?

Xpert MTB/RIF has been recommended by WHO since 2010 for the rapid and simultaneous detection of TB and rifampicin resistance. The fully-automated molecular test has the potential to revolutionize and transform TB care and control. It provides accurate results in less than two hours, has minimal biosafety and training requirements, and can be housed in non-conventional laboratories.

WHO recommends the use of Xpert MTB/RIF as a primary diagnostic test for all people living with HIV who have signs and symptoms of TB, for people with unknown HIV status presenting with strong clinical evidence of HIV infection, for people who are seriously ill and suspected of having TB regardless of HIV status and those at high risk of MDR-TB.

For more information, see:

- [Factsheet on Xpert MTB/RIF](#)
- [WHO Rapid Implementation document](#)
- [WHO Policy Guidance](#)



## People living with HIV should be screened for TB symptoms at each visit to a health facility or each encounter with a health care worker.

- Adults and adolescents living with HIV who report any one of the following: **current cough, fever, weight loss or night sweats** may have active TB and should be evaluated for TB and other diseases.
- Children living with HIV who have any one of the following: **poor weight gain, fever, current cough or contact history with a TB case** may have TB and should be evaluated for TB and other conditions.
- If the evaluation shows no TB, people living with HIV should be offered IPT.

For more information, see:

- [Guidelines for intensified case-finding and isoniazid preventive therapy for PLHIV](#)
- [WHO Policy on collaborative TB/HIV activities](#)

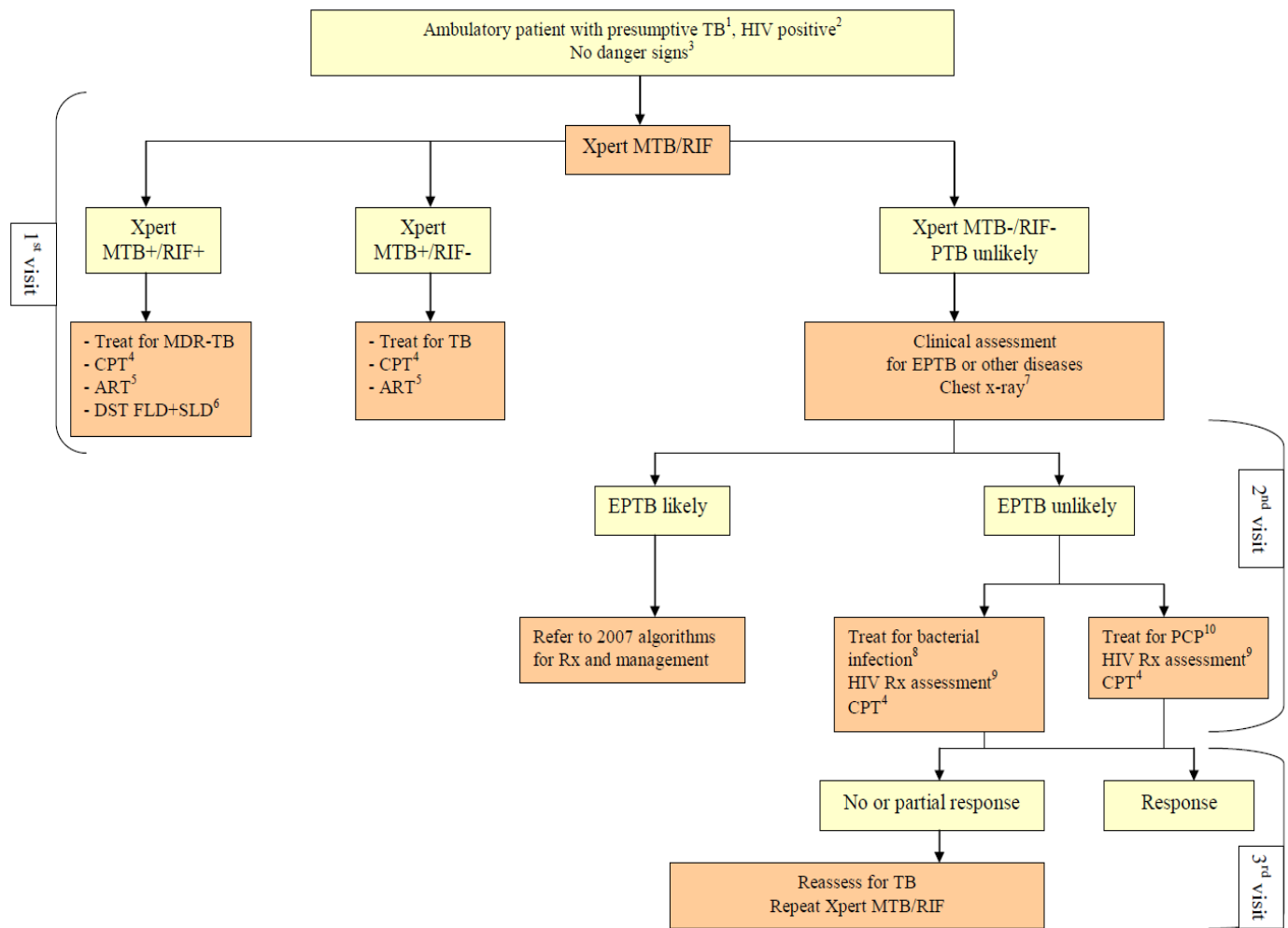
TB is the most common presenting illness and the leading cause of death among people living with HIV. An estimated 1.1 million people living with HIV developed TB in 2011 and 430,000 died as a result. For more information on TB/HIV, visit:

[www.who.int/tb/challenges/hiv/en](http://www.who.int/tb/challenges/hiv/en)

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**Figure 1: Algorithm for ambulatory management of PLHIV and patients with presumptive TB**



<sup>1</sup> Among adults and adolescents living with HIV, a patient with presumptive TB is defined as a person who reports any one of current cough, fever, weight loss or night sweats. Among children living with HIV, a TB suspect is defined as a person who reports one of poor weight gain, fever, current cough, or history of contact with a TB case.

<sup>2</sup> In all persons with unknown HIV status, HIV testing should be performed according to national guidelines. In patients who are HIV negative or remain HIV unknown (e.g. declined testing), a patient with presumptive TB is defined according to national case definitions. A person with unknown HIV status can still be classified as HIV-positive if there is strong clinical evidence of HIV infection.

<sup>3</sup> The danger signs include any one of the following: respiratory rate > 30/min, temperature > 39°C, heart rate > 120/min and unable to walk unaided.

<sup>4</sup> CPT = cotrimoxazole preventive therapy

<sup>5</sup> ART = antiretroviral therapy. All TB patients living with HIV are eligible for ART irrespective of CD4 count. Start TB treatment first, followed by ART as soon as possible within the first 8 weeks of TB treatment. See [WHO Policy on collaborative TB/HIV activities](#).

<sup>6</sup> In low MDR-TB prevalence settings, a confirmatory test for rifampicin resistance should be performed. See MDR-TB Xpert MTB/RIF algorithm.

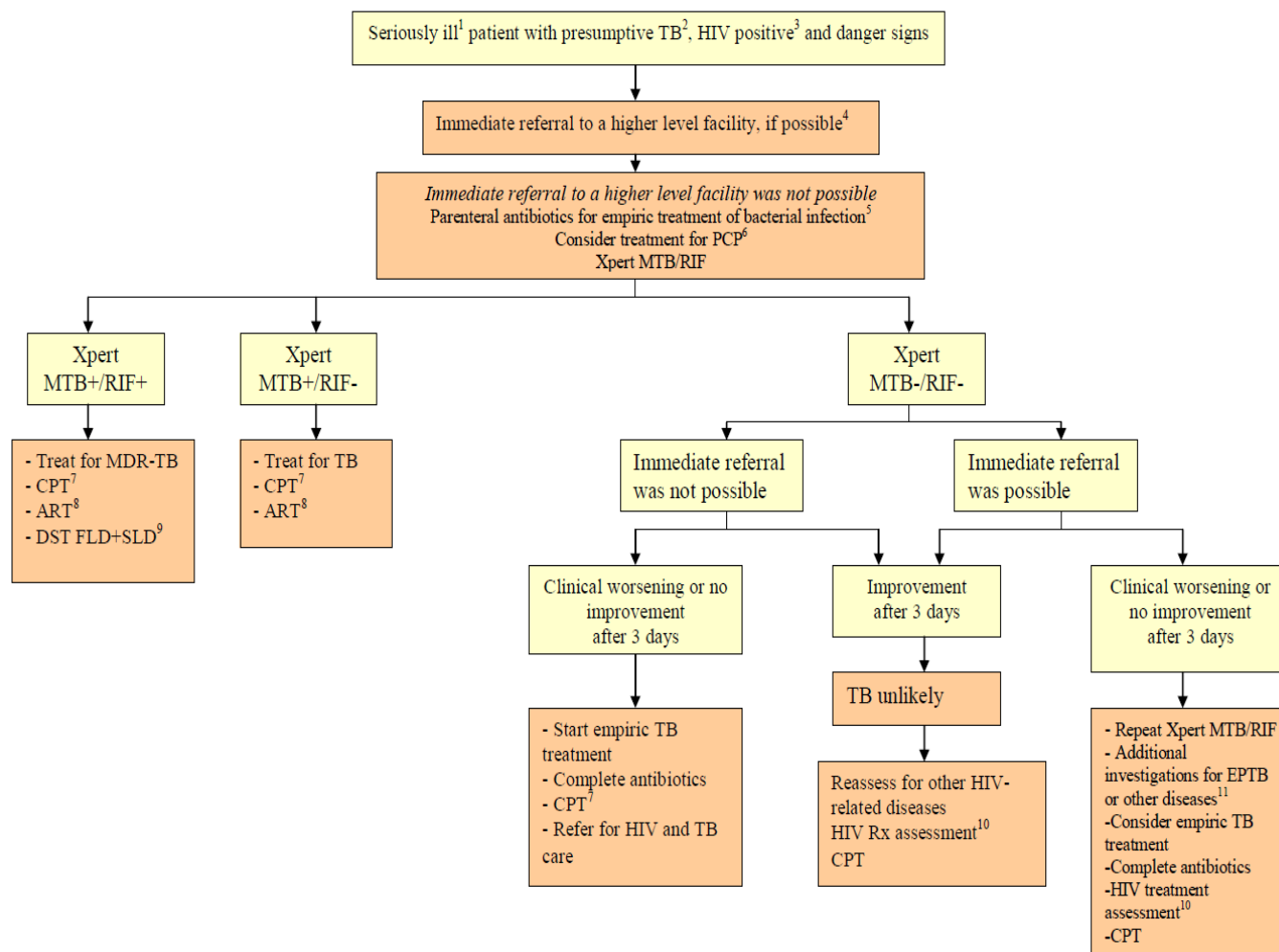
<sup>7</sup> A chest x-ray can assist with the diagnosis of extra-pulmonary TB (e.g., pleural, pericardial) and help assess for other etiologies of respiratory illness. It should only be performed in those settings where the quality of the film and its interpretation are assured.

<sup>8</sup> Antibiotics (except fluoroquinolones) to cover both typical and atypical bacteria should be considered.

<sup>9</sup> An HIV treatment assessment includes WHO clinical staging and/or CD4 count to assess eligibility for antiretroviral therapy. See ART guidelines.

<sup>10</sup> PCP = *Pneumocystis jirovecii* pneumonia

**Figure 2: Algorithm for management of PLHIV and people who are presumed to have TB and are seriously ill**



<sup>1</sup> Seriously ill refers to the presence of danger signs, including: respiratory rate > 30/min, temperature > 39°C, heart rate > 120/min and unable to walk unaided.

<sup>2</sup> Among adults and adolescents living with HIV, a patient with presumptive TB is defined as a person who reports any one of the following: current cough, fever, weight loss or night sweats. Among children living with HIV, a patient with presumptive TB is defined as a person who reports one of poor weight gain, fever, current cough, or history of contact with a TB case.

<sup>3</sup> In all persons with unknown HIV status, HIV testing should be performed according to national guidelines. In high HIV prevalent settings, seriously ill patients should be tested using Xpert MTB/RIF as the primary diagnostic test regardless of HIV status.

<sup>4</sup> The highest priority should be to provide the patient with life-sustaining supportive therapy, such as oxygen and parenteral antibiotics. If life-sustaining therapy is not available at the initial point of care, the patient should be transferred immediately to a higher level facility before further diagnostic testing.

<sup>5</sup> Antibiotics (except fluoroquinolones) to cover both typical and atypical bacteria should be considered.

<sup>6</sup> PCP = *Pneumocystis jirovecii* pneumonia

<sup>7</sup> CPT = cotrimoxazole preventive therapy

<sup>8</sup> ART = antiretroviral therapy. All TB patients living with HIV are eligible for ART irrespective of CD4 count. Start TB treatment first, followed by ART as soon as possible within the first 8 weeks of TB treatment. See [WHO Policy on collaborative TB/HIV activities](#).

<sup>9</sup> In low MDR-TB prevalence setting, a confirmatory test for Rifampicin resistance should be performed. See MDR-TB algorithm.

<sup>10</sup> An HIV treatment assessment includes WHO clinical staging and/or CD4 count to assess eligibility for antiretroviral therapy. See ART guidelines.

<sup>11</sup> Additional investigations for TB may include chest x-ray, liquid culture of sputum, lymph node aspiration for acid-fast bacilli microscopy and culture, abdominal ultrasound. Non-tuberculosis mycobacterial infection should be considered in the differential diagnosis of patients who have a negative Xpert but a sputum or extra-pulmonary specimen with acid-fast bacilli.