Briefing Note
Testing for both Tuberculosis and SARS-CoV-2

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1. Purpose

This document has been developed by the Global Fund with inputs from the World Health Organization’s Global TB Programme and the Health Emergencies Programme, the United States Agency for International Development, and the Stop TB Partnership. It is aimed at supporting implementation of relevant Global Fund grants.

2. Summary

The COVID-19 pandemic continues to pose both direct and indirect diagnostic challenges.\textsuperscript{1,2} In many countries, COVID-19 testing rates are lower than WHO targets and TB case notification rates have dropped, reflecting serious disruptions in access to TB diagnostic services. Understanding the indications for testing for both conditions via, for example, integrated service delivery models, will assist in developing and implementing screening and diagnostic strategies supporting both diseases. These are intended to optimize public health by ensuring rapid turnaround of results to enhance clinical and public health actions and effective use of resources.
3. Clinical Features of TB and COVID-19

Even if both TB and COVID-19 commonly affect the lungs and have similar symptoms such as cough, fever and difficulty in breathing, clinical features differ in certain respects (Table 1).

Table 1: Common clinical features of COVID-19 and TB

<table>
<thead>
<tr>
<th>Common features</th>
<th>COVID-19*</th>
<th>TB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cough type</td>
<td>dry</td>
<td>productive</td>
</tr>
<tr>
<td>Cough duration</td>
<td>&lt;2 weeks</td>
<td>&gt;2 weeks**</td>
</tr>
<tr>
<td>Shortness of breath</td>
<td>early</td>
<td>late</td>
</tr>
<tr>
<td>Haemoptysis</td>
<td>+/-</td>
<td>Yes</td>
</tr>
<tr>
<td>Fever</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Unexplained weight loss</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Night sweats</td>
<td>+/-</td>
<td>Yes</td>
</tr>
<tr>
<td>Sore throat</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Loss of smell/taste</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Headache</td>
<td>+/-</td>
<td>+/-</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>+/-</td>
<td>No</td>
</tr>
<tr>
<td>Malaise</td>
<td>Yes</td>
<td>+/-</td>
</tr>
</tbody>
</table>

* For more details see reference (4)
** This time limit is in common use but may need to be adjusted (e.g., in people of all ages with HIV, cough of any duration to be considered)

Existing WHO algorithms for screening people at risk of TB (e.g., contacts, people living with HIV, prison inmates), as well as algorithms for diagnostic testing in people with presumptive TB, remain valid during the COVID-19 pandemic.²³ These algorithms support active TB case-finding in people who may otherwise not seek care early and who may therefore be at greater risk of poor outcomes during restrictions in health care delivery and utilization induced by the COVID-19 pandemic.

As is true for TB, indications for testing for SARS-CoV-2 infection should be based on clinical features, medical history and local epidemiology.⁴ Testing for SARS-CoV-2 in people with presumed or confirmed TB should not be different from testing in other individuals. WHO has produced guidance on diagnostic testing for SARS-CoV-2 and specifically on the use of antigen detection rapid diagnostic tests (Ag-RDTs).⁵⁶ When employed, only approved assays*** should be used, and testing should be conducted by trained operators following manufacturer’s instructions.

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***For updates to the WHO Emergency Use Listing Procedure (EUL) for SARS-CoV-2 see:
4. When to Test Individuals for Both Pathogens

On this note, we review when to test individuals for both TB and SARS-CoV-2, indications for testing confirmed TB cases for SARS-CoV-2 infection, and testing COVID-19-diagnosed patients for TB.

a) Indications for testing individuals for both TB and SARS-CoV-2

Testing an individual for both TB and SARS-CoV-2 should be considered when clinical signs and symptoms meet the case definitions for both diseases and these are prevalent in the patient’s community. In addition, individuals meeting the following criteria may be prioritized for testing:

- There are risk factors for both diseases (e.g., exposures to known contacts);
- There are risk factors for poorer outcomes from both diseases (e.g., diabetes, advanced age).

Figure 1: Algorithm for testing for both TB and SARS-CoV-2*

* simplified algorithm showing main decision points. Other tests may be considered (e.g., screening for TB using chest X-ray with or without computer aided detection software).

Individuals are assessed to see if the above criteria apply and if their clinical features match the TB or COVID-19 case definitions. In people who meet case definitions for both TB and COVID-19, systematic testing for both pathogens is recommended. Testing for both pathogens will require obtaining two separate specimens from each patient (usually sputum for TB, and nasopharyngeal or oropharyngeal swabbing for SARS-CoV2) (Figure 1). Sample processing for TB and SARS-CoV2 test may involve testing on the same or on different platforms, depending on availability of commodities, equipment, and staff training.
In clinical settings faced with surges of SARS-CoV-2 infection, patient triage becomes an essential component of effective infection control and prevention. People being evaluated for TB or SARS-CoV-2 infection must be rapidly sampled and tested ensuring adequate infection, prevention control measures are in place. Those who test positive being counselled for immediate self-isolation, and receiving clinical care as needed.

WHO-approved molecular rapid diagnostics for TB (mWRD), such as Xpert MTB/RIF, Xpert MTB/RIF Ultra, Truenat MTB/RIF and other automated NAATs (such as Roche Abbott, BD Max and Hain test) are strongly recommended for the initial diagnosis of TB.

**b) Indications for testing people with confirmed TB for SARS-CoV-2 infection**

As the pandemic advances in a population, more people with TB will be exposed to SARS-CoV-2. Under such conditions a diagnosis of TB may not exclude concomitant SARS-CoV-2 infection. Pulmonary disease, including TB, is a risk factor for severe COVID-19 and adverse clinical outcomes. Testing people with TB for SARS-CoV-2 infection is indicated if they meet the COVID-19 case definition or when there is persistence or worsening of their condition despite appropriate treatment for the specific form of TB (e.g., drug-resistant TB) (Figure 2). People with TB who are contacts of confirmed or probable cases of COVID-19 should be prioritized for SARS-CoV-2 testing.

**Figure 2. Indications for testing people with confirmed TB for SARS-CoV-2**

![Diagram showing indications for testing people with confirmed TB for SARS-CoV-2](image-url)
c) **Indications for testing people diagnosed with COVID-19 for TB disease**

A positive SARS-CoV-2 test result does not exclude concurrent TB, particularly in high TB burden settings (Figure 3). Consider TB in a person with COVID-19 if:

- Respiratory symptoms don’t abate e.g., prolonged cough (2 weeks or more), progression to haemoptysis, night sweats or weight loss;
- There is a previous history of TB in the same person or if they are a close contact with another person with confirmed TB; and
- Chest radiography or imagery suggests TB.

These criteria for testing may also apply to people with COVID-19 whose symptoms persist even after their SARS-CoV-2 test converts to negative.

**Figure 3. Indications for testing people with COVID-19 for TB disease****

**** prolonged cough usually defined as >2 weeks but this may be shorter (e.g., people with HIV).
5. Types of Tests

Molecular-based tests are recommended methods for the identification of both SARS-CoV-2 and TB. The most sensitive and specific tests for SARS-CoV-2 are nucleic acid amplification tests (NAATs), and several WHO prequalified NAAT assays are available. However, there are many situations where SARS-CoV-2 molecular testing may not be available, or when it is associated with prolonged turnaround times (>48-72hrs) that makes rapid triaging impossible (e.g., community-based testing).

The use of Ag-RDTs helps address the need for rapid turnaround times (results available within 15 minutes), which greatly facilitates patient triage and early implementation of isolation procedures. Ag-RDTs perform best during the early phase of disease, in the days just before the onset of symptoms and the first 5–7 days after symptom onset, when viral loads are highest. WHO recommends that Ag-RDTs meeting minimum performance requirements can be used for primary case detection, contact tracing, during outbreak investigations and to monitor trends of disease incidence in communities. The need to confirm Ag-RDT positive or negative results with molecular assays depends on several considerations including the SARS-CoV-2 prevalence, degree of clinical suspicion, and accessibility to NAATs.

6. Conclusion

Control of COVID-19 and sustained progress towards TB elimination requires intensified, dual program management aimed at identifying all those with TB and COVID-19 and achievement of country testing targets. It is critical that governments and partners design their testing strategies to optimize the use of available laboratory resources, such as by selecting and balancing testing modalities and capacities to achieve effective and efficient lab diagnostic services in order to achieve national testing targets for both diseases, enable robust disease surveillance, and maximize the impact of investments on both diseases. As part of our efforts to integrate services, it is important to address barriers in accessing testing services, including stigma and discrimination which have increased in light of the COVID-19 epidemic.
7. References


