

World Health Organization (WHO) Information Note

Tuberculosis and COVID-19

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COVID-19: Considerations for tuberculosis (TB) care

As the world comes together to tackle the COVID-19 pandemic, it is important to ensure that essential services and operations for dealing with long-standing health problems continue to protect the lives of people with TB and other diseases or health conditions. Health services, including national programmes to combat TB, need to be actively engaged in ensuring an effective and rapid response to COVID-19 while ensuring that TB services are maintained.

Substantial reductions in TB notification sustained over successive months have been observed in 2020 in several high TB burden countries as measures to respond to the pandemic were introduced (1). Modelling work suggests that if the COVID-19 pandemic led to a global reduction of 25% in expected TB detection for 6 months then we could expect a 26% increase in TB deaths, bringing us back to the levels of TB mortality that we had in 2012 (2). Between 2020 and 2025 an additional 1.4 million TB deaths could be registered as direct consequence of the COVID-19 pandemic (3). These are likely to be conservative estimates as they do not factor in other possible impacts of the pandemic on TB transmission, treatment interruptions, impact on comorbidities and poorer outcomes in people with TB and COVID-19 infection.

The World Health Organization (WHO) is advising Member States that are leading the response to the unfolding COVID-19 pandemic (4),(5). The WHO Global TB Programme, along with WHO regional and country offices, has developed an information note, in collaboration with stakeholders. This note is intended to assist national TB programmes and health personnel to **urgently maintain continuity of essential services for people affected with TB during the COVID-19 pandemic**, driven by innovative people-centred approaches, as well as maximizing joint support to tackle both diseases. It is important that the progress made in TB prevention and care is not reversed by the COVID-19 pandemic. Finding and treating people with TB remain the fundamental pillars of TB prevention and care and those would require maintained attention.

The COVID-19 pandemic has provoked social stigma and discriminatory behaviours against people of certain ethnic backgrounds as well as anyone perceived to have been in contact with the virus. Stigma can undermine social cohesion and prompt social isolation of groups, which might contribute to a situation where the virus and TB are more likely to spread. This can:

- Drive people to hide the illness to avoid discrimination
- Prevent people from seeking health care immediately
- Discourage them from adopting healthy behaviours.

Stigma and fear around communicable diseases like TB hamper the public health response. What works is building trust in reliable health services and advice, showing empathy with those affected, understanding the disease itself, and adopting effective, practical measures so people can help keep themselves and their loved ones safe (6). Governments, citizens, media and communities have an important role to play in preventing and stopping stigma. We all need to be intentional and thoughtful when communicating on social media and other communication platforms, showing supportive behaviours around COVID-19, as well as older diseases like TB.

1. Are people with TB likely to be at increased risk of COVID-19 infection, illness and death?

While experience on COVID-19 infection in TB patients remains limited, it is anticipated that people ill with both TB and COVID-19 may have poorer treatment outcomes, especially if TB treatment is interrupted(7).

TB patients should take precautions as advised by health authorities to be protected from COVID-19 and continue their TB treatment as prescribed.

People ill with COVID-19 and TB show similar symptoms such as cough, fever and difficulty breathing. Both diseases attack primarily the lungs and although both biological agents transmit mainly via close contact, the incubation period from exposure to disease in TB is longer, often with a slow onset.

2. What should health authorities do to provide sustainability of essential TB services during the COVID-19 pandemic? What services can be leveraged across both diseases?

All **measures should be taken to ensure continuity of services** for people who need preventive and curative treatment for TB. Health authorities should maintain support to essential TB services, including during emergencies such as COVID-19. People-centred delivery of TB prevention, diagnosis, treatment and care services should be ensured in tandem with the COVID-19 response.

Prevention: Measures must be put in place to limit transmission of TB and COVID-19 in congregate settings and health care facilities, as per WHO guidelines (8),(9). Although modes of transmission of the two diseases are slightly different, administrative, environmental and personal protection measures apply to both (e.g. basic infection prevention and control, cough etiquette, patient triage). Provision of TB preventive treatment should be maintained as much as possible.

Diagnosis: Accurate diagnostic tests are essential for both TB and COVID-19. Tests for the two conditions are different and both should be made available for individuals with respiratory symptoms, which may be similar for the two diseases. TB laboratory networks have been established in countries with the support of WHO and international partners. These networks as well as specimen transportation mechanisms could also be used for COVID 19 diagnosis and surveillance.

Treatment and care: TB programme staff with their experience and capacity, including in active case finding and contact tracing, are well placed to share knowledge, expertise, and to provide technical and logistical support.

People-centred outpatient and community-based care should be strongly preferred over hospital treatment for TB patients (unless serious conditions are requiring hospitalisation) to reduce opportunities for transmission.

Provision of anti-tuberculosis treatment, in line with the latest WHO guidelines, must be ensured for all TB patients, including those in COVID-19 quarantine and those with confirmed COVID-19 disease. Adequate stocks of TB medicines should be provided to all patients to take home to ensure treatment completion without having to visit treatment centres unnecessarily to collect medicines.

Use of digital technologies should be intensified to support patients and programmes through improved communication, counselling, care, and information management, among other benefits. In line with WHO recommendations, technologies like electronic medication monitors and video-supported therapy can help patients complete their TB treatment. The replacement of paper records with electronic systems will help improve the timeliness of TB data but needs to be matched with adequate human resources, infrastructure, funding, political commitment and visionary leadership.

Proactive planning, procurement, supply and risk management: Appropriate planning and monitoring are essential to ensure that procurement and supply of TB medicines and diagnostics are not interrupted. Mobilization of additional funding by donors, with a more equitable allocation for TB, will be critical in a near future to support countries to catch up on their TB activities from now unto the post-COVID-19 recovery stages. In this way they can keep progressing towards the targets of the End TB Strategy and the 2018 UN High Level Meeting on TB and review the operationalization of their national TB strategic plans in order to be able to achieve the expected objectives in a shorter space of time.

WHO is monitoring medicine supply at the global level, while The Global Fund, the Stop TB Partnership Global Drug Facility (GDF), USAID, UNITAID and other donors play an essential role in supporting countries to secure adequate and sustainable supplies of TB medicines and diagnostic tests. Countries are advised to place their orders for 2021 delivery as soon as possible given anticipated delays in transport and delivery mechanisms.

Human resources: Respiratory physicians, pulmonology staff of all grades, TB specialists and health workers at the primary health care level may be points of reference for patients with pulmonary complications of COVID-19. They should familiarize themselves with the most current WHO recommendations for the supportive treatment and containment of COVID-19 (9),(10). Detection and effective supportive treatment may reduce morbidity and mortality from both COVID-19 and most forms of TB.

Capacity building: The response to COVID-19 can benefit from the capacity building efforts developed for TB over many years of investment by national authorities and donors. These include infection prevention and control, contact tracing, house-hold and community-based care, and surveillance and monitoring systems. Countries

need to invest in robust systems to monitor COVID-19 related disruptions to TB services and activities to mitigate them now and into the post-pandemic phase. For this purpose, WHO has been collecting monthly TB notification data from high TB burden countries since January 2020 and will continue this into 2021.

3. What measures should be in place to protect staff working in TB laboratories and healthcare facilities, and community health workers, from COVID-19 infection?

Health care facilities, including those that diagnose and care for TB and lung diseases, are bound to receive patients with COVID-19, many of whom may be undiagnosed. Additional measures may be needed to avoid that staff in these centres are exposed to COVID-19 infection.

Staff should familiarize themselves with WHO recommendations for the containment of COVID-19 (9). The networks of TB laboratories that countries have established in recent years are one of the important assets that should be leveraged in the response to COVID-19. Lessons learnt over many years of TB infection prevention and control, contact tracing, investigation and management can benefit efforts to stop the spread of COVID-19. Existing WHO recommendations for infection prevention and control for TB and for COVID-19 (8),(9),(11),(12) should be strictly implemented, including personal protection equipment. The following additional, temporary measures should be considered during the COVID-19 pandemic to minimize risks of infecting the staff and vice versa:

- Subject to local circumstances, alternative arrangements should be made to reduce visits for TB follow-up, e.g. spreading appointments on specific days or times to avoid exposure to other clinic attendees; using innovative communication technologies to maintain treatment support; limiting to when follow-up testing is needed
- Enough TB medicines will need to be dispensed to the patient or caregiver to last until the next visit - or the end of treatment if no other visit is planned. This will limit interruption or unnecessary visits to the clinic to collect medicines.
- Special precautions are needed when collecting and transporting sputum samples and bronchoalveolar lavage fluid, as well as reception and unpacking in the laboratory, to avoid exposure of staff, patients and other individuals to both COVID-19 and TB (13),(14). Sputum collection for TB at home should be encouraged with specific instructions (e.g., to be done in open area outside the home and away from others). If this is not possible, sputum should be collected in an open, well-ventilated space – preferably outside of the health facility - and staff should not stand near the patient during collection.
- When testing for TB, it is essential that all WHO-recommended infection prevention and control measures are observed and followed by operators when handling sputum and any other infectious specimens, including the use of biosafety cabinets (where available), consistent use of the N95 respirator, handwashing, use of gloves, goggles or protection shield, waterproof aprons, regular decontamination of surfaces, staff distancing in the laboratories, ventilated workplaces and safe transportation. The staff responsible for transport of samples to the site of testing and operators of the machines should also follow existing requirements to process COVID-19 samples.

There is an ethical obligation for healthcare workers to deliver care to patients. The rights and responsibilities of healthcare workers in the context of COVID-19 are listed elsewhere (15). Governments and people responsible of organizations delivering health care have the ethical obligation to ensure that health care workers can operate under the recommended safety standards that are provided. Healthcare workers should follow all recommendations to protect themselves, other health care workers, patients and other caregivers (16).

4. How can we protect people seeking TB care during the COVID-19 pandemic?

The sudden surge in demand for care of COVID-19 patients is presenting a challenge for health services worldwide. During this exceptional period it is important that TB prevention and care continue uninterrupted (5). Past emergencies, like influenza and Ebola, have impinged negatively upon TB care by, for example, requiring a reassignment of staff and inpatient facilities for patients with serious respiratory complications. Similar measures are already being taken by several countries during this pandemic. Prolonged disruptions in the production of consumables in countries under lock-down and of international and local transportation are expected to impact upon the stocks of medicines and laboratory supplies in many places.

In many countries restriction of movement has been imposed for much of the population in response to the pandemic. Isolation of individuals with presumptive or confirmed COVID-19 exposure or disease is also commonplace. Advice on quarantine for people with COVID-19 have been published by WHO (17). Communication with the healthcare services should be maintained so that TB patients, especially those most vulnerable, get essential services in case of need, such as management of adverse drug reactions and co-morbidities, nutritional and mental health support, and restocking of the supplies of medicines. Mechanisms to deliver medicines at home and even to collect specimens for follow-up testing of TB - as well as COVID - may become expedient. As visits to health centres will be minimised, home-based TB treatment is bound to become the norm. Community health workers become more critical as treatment, including for drug-resistant TB, is more decentralised. More TB patients will probably start their treatment at home and therefore limiting the risk of household transmission of TB during the first few weeks are important. Under such circumstances it is important that vulnerable and marginalised populations who have poor access to healthcare services do not get further disadvantaged as a result of this episode.

Despite differences in the modes of TB and COVID-19 transmission (Box), certain measures are relevant to both diseases. Infection control measures for healthcare facilities highlighted under Question 3 above may also limit transmission to patients. Usual precautions to protect from TB must continue along with additional action to protect workers from COVID-19. A number of these precautions apply also to TB care in institutions like prisons and long-term care facilities where reduction in outside visitors, special arrangements for treatment and follow up and other measures may be necessary to avoid explosive spread of COVID-19 (18),(19).

Box: Transmission of TB and COVID-19

While both TB and COVID-19 spread by close contact between people the exact mode of transmission differs, explaining some differences in infection control measures to mitigate the two conditions. TB bacilli remain suspended in the air in droplet nuclei for several hours after a TB patient coughs, sneezes, shouts, or sings, and people who inhale them can get infected. The size of these droplet nuclei is a key factor determining their infectiousness. Their concentration decreases with ventilation and exposure to direct sunlight. Current evidence suggests that the main way that the COVID-19 virus spreads is by respiratory droplets among people who are in close contact with each other. Aerosol transmission can occur in specific settings, particularly in indoor, crowded and inadequately ventilated spaces, where infected person(s) spend long periods of time with others (people may be infectious before clinical features become apparent) (20). Droplets produced by coughing, sneezing, exhaling and speaking may land on objects and surfaces, and contacts can get infected with COVID-19 by touching them and then touching their eyes, nose or mouth¹. Physical distancing, wearing a mask, keeping rooms well ventilated, avoiding crowds, hand hygiene, and respiratory precautions are thus important in the control of COVID-19 (22),(23). Hospital procedures that generate aerosols predispose to infection of both conditions and should only be conducted within recommended safeguards.

Under the current circumstances the rapid roll-out of measures that reduce the need for daily encounters with healthcare staff becomes more critical. These include WHO recommended, all-oral TB treatments for multidrug-resistant TB and extensively drug-resistant TB; TB preventive treatment with recommended shorter regimens and increased testing to find more of the 'missing' or undiagnosed TB cases. More experience will be acquired in the effective use of digital technologies for patient support, such as adverse event reporting. Nonetheless, any redeployment of staff treating TB and drug-resistant TB to work on COVID-19 should consider the long-term consequences that this may have on the wellbeing of TB patients and programmes.

5. Should all people being evaluated for TB also be tested for COVID-19 and vice-versa?

Simultaneous testing of the same patient for both TB and COVID-19 could reduce diagnostic delays and would generally be indicated for three main reasons, subject to the specific setting in the country:

1. clinical features that are common to both diseases; or
2. simultaneous exposure to both diseases; or
3. presence of a risk factor for poor outcomes to either disease.

Even if both TB and COVID-19 commonly involve the lungs and have similar symptoms such as cough, fever and difficulty breathing, clinical features differ in certain respects. While fever and cough in COVID-19 have a rapid onset and an incubation period of about one to two weeks, the clinical manifestations of TB typically develop

¹ Human coronaviruses in general are known to persist on inanimate surfaces such as metal, glass or plastic for up to a maximum of 9 days (21)

over a much longer period. The coughing in TB is usually productive of sputum and even blood, while in uncomplicated COVID-19 it is more commonly a dry cough at presentation. When shortness of breath occurs in COVID-19 it develops early after onset; in TB this usually happens at a much later stage or as a long-term sequela. Outbreaks of COVID-19 in the same household or in a congregate setting usually become apparent within a week or two while in TB the progression is rarely abrupt and may only become apparent after several months.

As the pandemic advances, more people and TB patients of all ages will have been exposed to COVID-19 when they first present for diagnosis. A positive result for COVID-19 infection does not exclude the possibility of concomitant TB, particularly in high TB burden settings. Healthcare workers need to consider the possibility of TB in a patient with COVID-19 if the course of the illness after the first weeks suggests so, e.g. progression to haemoptysis, persistent fever, night sweats or weight loss. A careful history of exposure to TB or even a past episode of TB in the same patient or in the family may clinch the diagnosis. Chest radiography or imagery may help differentiate TB from other pathologies.

An early diagnosis of both TB and COVID-19 is important in the care of people who are vulnerable to unfavourable outcomes, including death. Older age and certain comorbidities like diabetes mellitus and chronic obstructive pulmonary disease increase the likelihood of severe COVID-19 and the necessity for intensive care and mechanical ventilation. These risk factors are also poor prognostic factors in TB. TB patients who have lung damage from past tuberculosis sequelae or chronic obstructive pulmonary disease may suffer from more severe illness if they are infected with COVID-19 (7). There is thus a stronger case for concurrent testing for both conditions in these individuals even if the clinical picture is atypical. The understanding of how COVID-19 impacts on TB outcomes of people with other risk factors - such as malnutrition, renal failure and liver disease - is still developing. While untreated HIV is an important risk factor for progression to TB or for poor outcomes in TB patients, its influence on the prognosis of COVID-19 patients is unclear. Nonetheless additional precautions for all people with advanced HIV or poorly controlled HIV are recommended by WHO (8). Updates will be released by WHO as evidence accrues on these interactions.

Countries are advised to adopt diagnostic algorithms that adhere to WHO recommendations for testing for TB or COVID-19 based on the clinical features and history of a patient and local TB burden (24),(25). Programmes need to be wary that the diagnostic needs of TB patients are not neglected while COVID-19 testing is rolled out.

6. Can TB and COVID-19 be tested on the same type of specimen?

The diagnostic methods for TB and COVID-19 are quite distinct and individuals being evaluated for both conditions require specimens which are commonly different.²

Sputum, as well as many other biological specimens, can be used to diagnose TB using culture or molecular techniques (26).

Tests for COVID-19 are done most commonly by nasopharyngeal or oropharyngeal swab or wash in ambulatory patients, but sputum or endotracheal aspirate or bronchoalveolar lavage may be used in patients with severe respiratory disease.

Molecular testing is the mainstay recommended method for the rapid identification of infectious COVID-19 (24),(27)as for TB (28).

The pipeline for COVID-19 diagnostics flourished impressively over 2020 (tests that are commercially available or in development are compiled by FIND, a WHO Collaborating Centres for Diagnostics (29)). By 1 December 2020, 21 nucleic acid amplification tests were eligible for procurement on the WHO Emergency Use Listing for SARS-CoV-2 in vitro diagnostic products(30). Amongst these is the Xpert® Xpress SARS-CoV-2 cartridge for use on GeneXpert machines (31).

Instructions on how to procure critical supplies for pandemic response are now available via the COVID-19 Partners Platform (32),(33). More details on the use of existing equipment for SARS-CoV-2 testing and potential multiplexing is also available from the Stop TB Partnership's Global Drug Facility (34).

Additional resources to roll-out COVID-19 testing should be mobilised during this episode, rather than relying only on existing resources that are used for TB, to ensure that the diagnostic coverage for TB is maintained as necessary.

7. Is TB treatment different in people who have both TB and COVID-19?

In most cases TB treatment is not different in people with or without COVID-19 infection. Experience on joint management of both COVID-19 infection and TB remains limited. However, suspension of TB treatment in COVID-19 patients should be exceptional. TB preventive treatment, treatment for drug-susceptible or drug-resistant TB disease should continue uninterrupted as it is important to safeguard the patient's health.

Effective treatments to prevent TB and to treat active TB have been scaled up and are in use worldwide. It is critical that people who need treatment continue taking it during the pandemic, even if they acquire COVID-19, to increase chances of cure and reduce transmission and the development of drug-resistance. The risk of death in

² Testing sites are likely to be different as well, and tests for COVID-19 may be less decentralised than for TB early on until capacity increases.

TB patients approaches 50% if left untreated and may be higher in the elderly or in the presence of comorbidity.

Support for uninterrupted TB preventive treatment and treatment of TB disease should be ensured alongside the COVID-19 response (5). **It is critical that TB services are not disrupted during the COVID19 response.**

While treatment trials for COVID-19 are ongoing, no potential drug-drug interactions with TB medicines are cautioned at present (35). TB patients on treatment should nonetheless be asked if they are taking any medicines, including traditional cures, that may interact with their medication (e.g. risk of additive cardiotoxicity).

Gathering evidence as this pandemic unfolds will be very important, while upholding the norms of professional conduct and patient confidentiality when handling clinical details.

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