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10-th Webinar of the mSTR Virtual Medical Concilium

Simultaneous Integrated Diagnostic Testing for COVID-19 and Tuberculosis

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- As the world comes together to fight against the COVID-19 pandemic, it is important to ensure that essential services and operations addressing long-standing health care problems continue to protect lives of people with TB and other diseases or health conditions
- Health services, including national tuberculosis programs, must actively participate in effective and rapid response to COVID-19, while ensuring continuous provision of TB services

Before the COVID-19 pandemic, tuberculosis (TB) had been the leading cause of death from the communicable diseases worldwide. Despite some great progress made by the high TB burden countries over the past few years in TB detection and treatment, there was a sharp decline in TB case notification rate in 2020 due to the COVID-19 pandemic

Tuberculosis and COVID-19
Similarities and Differences

	Tuberculosis	COVID-19
Symptoms	•General •Subfebrile temperature •Weight loss •Night sweats •Lung-specific •Cough •Shortness of breath •Chest pain and hemoptysis	•Fever •Cough (usually dry) •Sore throat •Shortness of breath. •Loss of smell and taste •Shortness of breath (severe acute respiratory distress syndrome, more common in the 2nd week of illness)

Tuberculosis and COVID-19

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REVIEW ARTICLE

Tuberculosis and COVID-19 interaction: A review of biological, clinical and public health effects

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KEYWORDS
COVID-19;
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Rehabilitation

Abstract Evidence is accumulating on the interaction between tuberculosis (TB) and COVID-19.

The aim of the present review is to report the available evidence on the interaction between these two infections. Differences and similarities of TB and COVID-19, their immunological features, diagnostics, epidemiological and clinical characteristics and public health implications are discussed. The key published documents and guidelines on the topic have been reviewed.

Based on the immunological mechanism involved, a shared dysregulation of immune responses in COVID-19 and TB has been found, suggesting a dual risk posed by co-infection worsening COVID-19 severity and favouring TB disease progression.

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Table 1 Differences and similarities between tuberculosis and COVID-19.

Specific aspect	COVID-19	TB
Human exposure	Recent (months)	Ancient (millennia)
Epidemiology	Significant burden	Significant burden
Transmission	Droplet transmission of SARS-CoV-2.	Droplet transmission of *M. tuberculosis* bacterium.
Symptoms	– Fever or chills – Cough, shortness of breath or difficulty breathing – Fatigue and headache – Muscle or body aches New loss of taste or smell – Sore throat, congestion, or runny nose – Nausea, vomiting, or diarrhea	– Coughing with mucus or blood – Coughing that lasts more than 2 months – Chest pain – Loss of appetite – Weight loss Chills, fever, or night sweats – Fatigue
Comorbidities Increasing Vulnerability	– Cancer – Chronic Kidney Disease – Chronic Lung Diseases – Obesity – Heart Conditions – Sickle Cell Disease – Immunocompromised State – Type 2 Diabetes Mellitus	– Cancer – Chronic Lung Diseases – Smoking – Alcohol Use Disorders Depression – HIV – Immunocompromised State – Type 2 Diabetes Mellitus

Table (continuation)

Comorbidities Increasing Vulnerability	– Cancer	– Cancer
	– Chronic Kidney Disease – Chronic Lung Diseases – Obesity – Heart Conditions – Sickle Cell Disease – Immunocompromised State – Type 2 Diabetes Mellitus	– Chronic Lung Diseases – Smoking – Alcohol Use Disorders Depression – HIV – Immunocompromised State – Type 2 Diabetes Mellitus
Availability of rapid diagnostics	Yes	Yes

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Research letter

Active tuberculosis, sequelae and COVID-19 co-infection: first cohort of 49 cases

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- First cohort of patients with TB/COVID-19 (GTN): 49 cases from 8 countries
- Mean age: 48 years
- Males: 82%
- Migrants: 50%
- Vaccinated (BCG): 63%
- HIV +: 12.5%
- TB diagnosed first: 26 (53.0%)
- COVID-19 diagnosed first; 14 (28.5%)
- Both diseases diagnosed at the same time: 9 (18,3%)
- Active TB: 42 (85.7%)
- TB sequelae: 7 (14.3%)

Global TB and COVID-19 study by the Global Tuberculosis Network (GTN)

700 cases from 40 countries were analyzed

- TB was diagnosed before COVID-19 diagnosis in 44.0% (302/686) of patients [median (IQR) 79 (38-141) days];
- COVID-19 was diagnosed before TB diagnosis in 9.7% [67/686 , median (IQR) 28 (15-40) days]
- TB and COVID-19 diagnosed simultaneously in 17.6% [121/686]
- TB sequelae in 28.6% [196/686]

Global TB and COVID-19 Study by the Global Tuberculosis Network (GTN)

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tuberculosis			N(%)
males			508/706
Median(IQR) age, ears at last birthday(n=377)			44(30-58
TB form		New case	560/662(84.6)
		Relapse	56/662(8,5)
		Lost to follow-up	29/662(4.5)
		Failure	17/662(2.6)
Pulmonary TB			600/694(86,5)
TB laboratory confirmed			564/671(84,1)
Solid culture			382/578(66,1)
Liquid culture			306/578(52,9%)
Xpert MTB/RIF			383/578(66,3%)
First line LPA			105/578 (1,8)
Second line LPA			28/578(4,8)
TB drug resistance pattern at TB diagnosis		Pan-susceptible TB	474/561(84.5)
		Drug-resistant TB	85/561(15,5)

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Global TB and COVID-19 Study by the Global Tuberculosis Network (GTN)

Covid-19 signs and symptoms	n(%)	Covid-19 signs and symptoms	n(%)
Abdominal pain	34/498 (6,8%)	Myailgia	74/498(14,9%)
Arthralgia	36/498(7,2%)	Nasal congestion	65/498 (13,1%)
Chest pain	85/498(17,1%)	Olfactory disorders	45/498 (9,0%)
Diarrhoea	47/498 (9,4%)	Shortness of breath	182/493 (36,5%)
Dry cough	293/498 (58,8%)	Sore throat	85/498 (17,1%)
Fever	358/498 (71,9%)	Taste disorders	42/498 (8,4%)
Headache	119/498 (23,9%)	Tiredness	101/498 (20,3%)
Confusion	33/498 (6,6%)	Vomiting/nausea	34/498(6,8%)
Malaise	85/498 (17,1%)	Other symptoms	59/498 (11.85%)

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Global TB and COVID-19 Study by the Global Tuberculosis Network (GTN)

Radiology and COVID-19 diagnosis	n(%)
CT scan	109/601 (18,1)
Chest X-ray	206/601 (34,3)
CT scan and Chest X-ray	156/601 (26,0)
Not done	130/601(21,6)
Unilateral pulmonary cavitary, lesions	39/355 (11,0)
Bilateral pulmonary cavitary, lesions	56/355 (15,8)
Unilateral pulmonary infiltrate, (no cavities)	64/355 (18,0)
Bilateral pulmonary infiltrate, (no cavities)	149/355 (42,0)
Other chest x-ray findings	48/355 (13,5)
No lesion	27/355(7,6)
Typical ground glass opacity, unilateral	40/265 (15,1)
Typical ground glass opacity, bilateral	132/265 (49,8)
Atypical opacity	61/265 (23)
No opacity	38/265(14,3)

Global TB and COVID-19 Study by the Global Tuberculosis Network (GTN)

Radiology at TB diagnosis	N(%)	
Chest X-ray and or CT scan	549/572	(96,0%)
Non done	23/572	(4,0%)
Unilateral pulmonary cavitary lesions	107/549	(19,5%)
Bilateral pulmonary cavitary lesions	119/549	(21,7%)
Unilateral pulmonary infiltrate (no cavities)	110/549	(20,0%)
Bilateral pulmonary infiltrate (no cavities)	130/549	(23,7%)
Other radiological TB form	97/549	(17,7%)
No lesion	38/549	(6,9%)

Tuberculosis is the deadliest communicable disease worldwide (more than HIV/AIDS), causing about 10 million new cases and 1.5 million deaths each year. TB and COVID-19 are infectious diseases that primarily affect lungs. Both diseases have similar symptoms, such as cough, fever, and shortness of breath. However, testing for COVID-19 or TB should be based on clinical characteristics, history, and local burden of TB to ensure that diagnostic needs of TB patients are not ignored when testing for COVID-19.

Patricia Comella-del-Barrio, Maria Luiza De Souza-Galvão, Cristina Prat- Aymerich, José Domínguez˝ mpact of COVID19 on Tuberculosis Control”"

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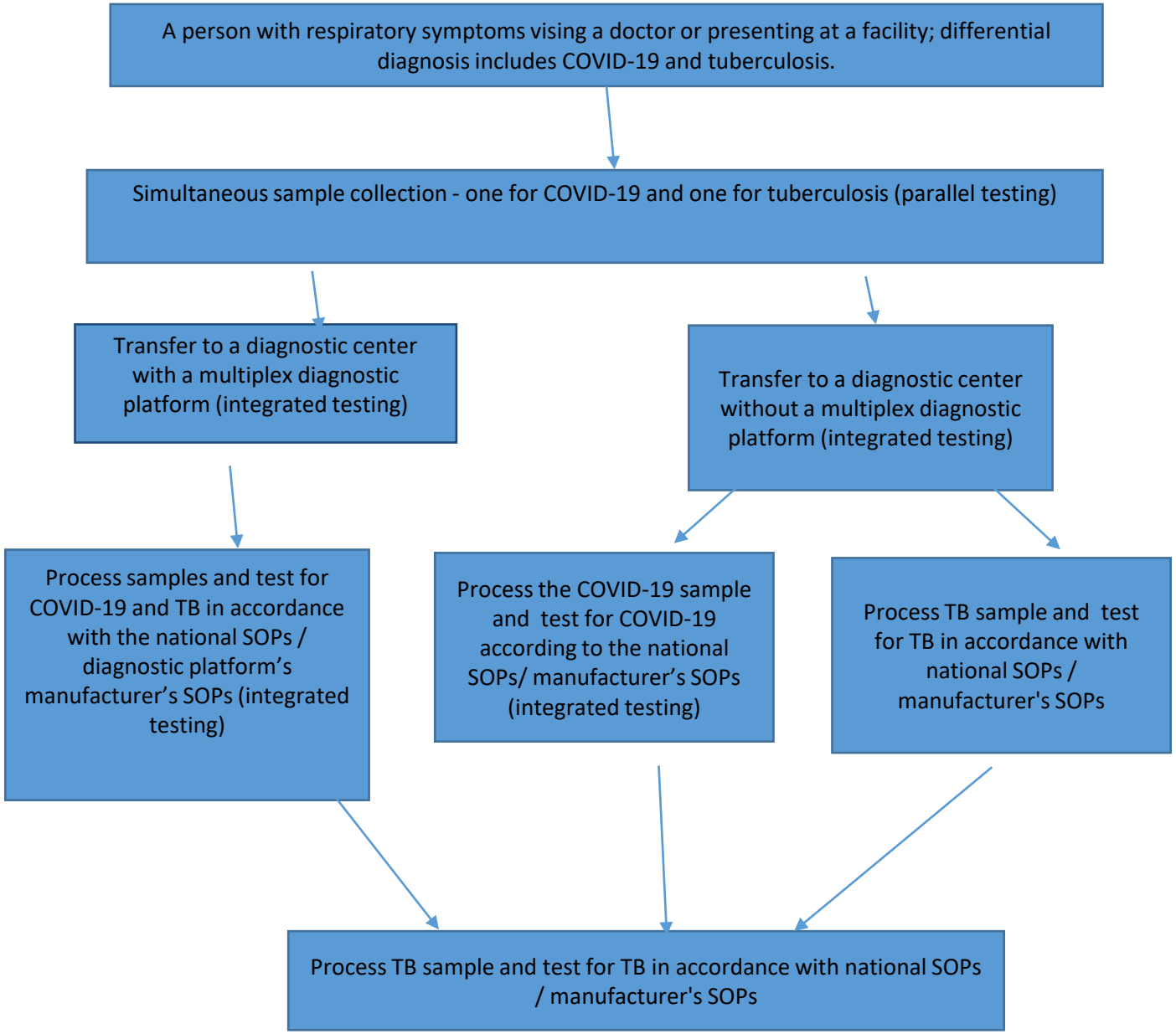
- Diagnostic testing is a critical and necessary step to detect and control pathogens of public health significance, including COVID-19 and tuberculosis
- There is an urgent need to expand access to diagnostic testing for both COVID-19 and tuberculosis. A simultaneous integrated approach to testing for COVID-19 and tuberculosis should be used in high TB burden countries

- For both, TB and COVID-19, there are comorbidities or behavioral factors (malnutrition, diabetes, smoking, chronic obstructive pulmonary disease, HIV, etc.) that increase the risk of both diseases.
- There are multiplex diagnostic testing platforms that can test for both *Mycobacterium tuberculosis* and SARS-CoV-2.
- Both diseases require early detection and treatment to improve patient outcomes.

- When a person presents to a health care facility with respiratory symptoms, including cough and difficulty breathing, diagnostic tests for COVID-19 and tuberculosis should be performed simultaneously according to the national diagnostic algorithms.
- Simultaneous integrated testing is especially important for people at higher risk of developing one or both diseases.

- People with respiratory symptoms who have previously tested negative for COVID-19 and have not been diagnosed with COVID-19 should be tested for tuberculosis.
- People with respiratory symptoms who have previously tested negative for tuberculosis and have not been diagnosed with tuberculosis should be tested for COVID-19.

Simultaneous Integrated Testing for COVID-19 and TB in High TB Burden Countries



Guidance note on Bi-directional TB-COVID screening and screening of TB among ILI/SARI cases (INDIA)

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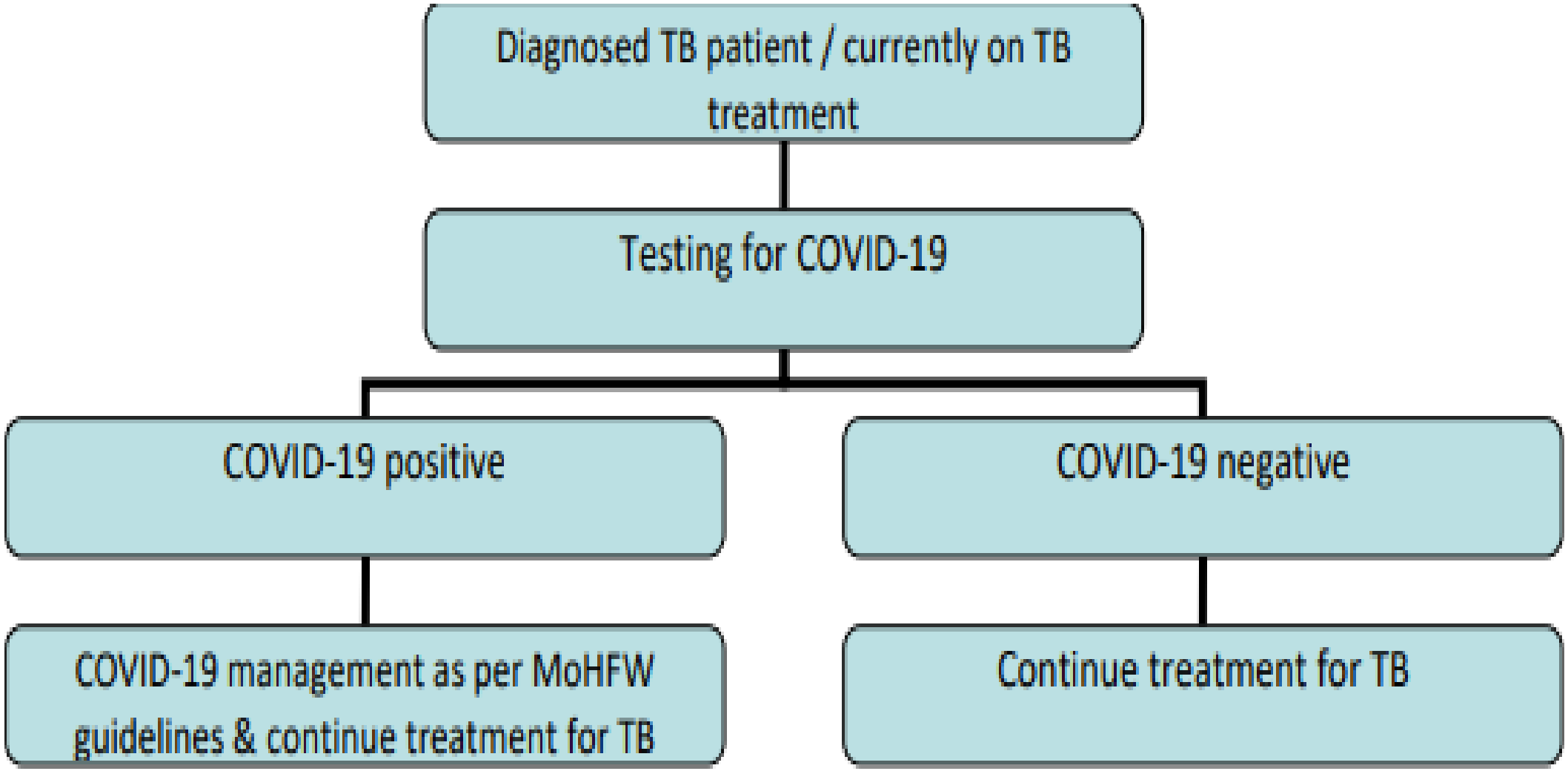
Bi-directional TB-COVID screening



Guidance note on Bi-directional TB-COVID screening and screening of TB among ILI/SARI cases (INDIA)

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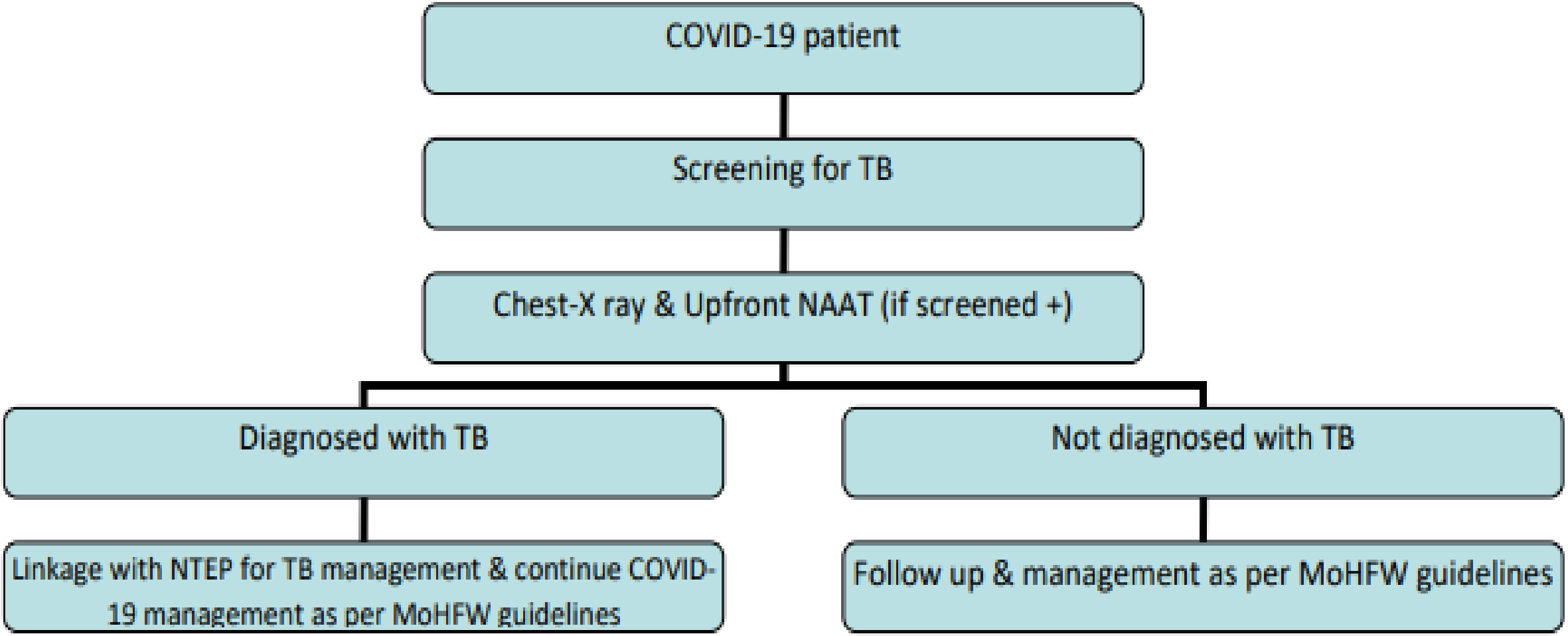
TB screening for COVID positive patients:



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Recommendations for COVID-19 Testing of (TB/RR-TB) Patients [Georgia]

Testing for COVID-19 should be done	
on patients as soon as they are diagnosed with tuberculosis	COVID-19 test should be performed in all patients regardless of whether or not they have typical symptoms and signs of COVID-19;
on TB patients who are on outpatient treatment	•Prior to the start of chemotherapy; •If there has been close contact within the last 14 days with a confirmed or probable case of COVID-19: • If the patient has symptoms characteristic of COVID-19, or if the existing symptoms have worsened

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Recommendations for COVID-19 Testing of TB Patients [Georgia] -continuation

Testing for COVID-19 should be done	
on TB patients who are on inpatient treatment	▪COVID-19 test must be performed on all patients upon admission to the hospital; ▪If the patient develops symptoms characteristic of COVID-19 or if their symptoms have worsened
on patients with LTBI on preventive treatment	•If there has been a close contact within the last 14 days with a confirmed or probable case of COVID-19; •In the presence of symptoms characteristic of COVID-19

Nucleic Acid Amplification Tests (NAAT) for Simultaneous Integrated Testing

- The NAATs available for tuberculosis and COVID-19 testing require different types of specimens: sputum is usually required for detection of pulmonary tuberculosis, and nasopharyngeal or oropharyngeal swabs or lavage samples are required for COVID-19
- Countries can improve testing efficacy by using multiplex NAAT platforms that can test for both diseases

- NAAT platforms that can perform WHO-recommended tests for TB and SARS-CoV-2:

✓Cepheid GeneXpert

✓Abbott Realtime

✓Rochecobas 6800/8800

- GeneXpert system is one of the available NAAT platforms capable of detecting tuberculosis and COVID-19; and using Global Fund resources it can be deployed in health care facilities at the peripheral level improving access to care and reducing diagnostic delays

- The COVID-19 pandemic emphasizes the need to document and report test results in real time through integrated dashboards and mobile apps to facilitate access to inform clinical and programmatic decisions on both diseases.
- National testing algorithms, existing testing infrastructure, and existing specimen referral mechanisms should be taken into account when developing a specimen referral system.
- Other considerations should include a mechanism for transferring high priority results electronically.

- Implementation of simultaneous integrated testing will require a coordinated approach to program management.

This would entail

- coordinated development of diagnostic algorithms with the engagement of multiple stakeholders;
- planning and strengthening laboratory capacity to tackle the burden of both diseases;
- following necessary infection prevention and control measures during specimen collection, packaging, transportation, and testing.

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TB/COVID 19 Coinfections (GEORGIA)

	TYPE OF TB	2020	2021	TOTAL
	DS	34	76	110
	DR	8	22	30
Total		42	98	140

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TB/COVID-19 Coinfections (Georgia)

	2020				2021			
	TB/ COVID	TB	COVID% in TB*	COVID% in TB**	TB/ COVID	TB	COVID% in TB*	COVID% in TB**
DS-TB	34	1608	2.11%	1.9%	76	965	7.88%	6.9%
DR-TB	9	208	4.33%	0.5%	22	131	16.79%	2.0%
TOTAL	43	1816		2.4%	98	1096		8.9%

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Thank you

for

attention!