



## The Effects of the Coronavirus Pandemic on the Indicators of the End Tuberculosis Strategy: A Literature Review

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### **Abstract**

The Coronavirus disease 2019 (COVID-19) has severely taken a toll on the health system in all nations from the wealthiest to the poorest countries. The disruption to the health system was not only due to the direct effects of the COVID-19 pandemic but also the pressure it caused to stretch the health systems beyond their capability indirectly. The purpose of this review was to explore the effects of the COVID-19 pandemic on the indicators of the end tuberculosis strategy. Methods: Articles were searched from scientific search engines such as CINAHL Plus (EBSCO), PubMed, Google Scholar, Medline, ProQuest, APA Psych and INFO as well as manual searches through Google and Google Scholar search engines. Both quantitative and qualitative studies that showed the impact or effects of the COVID-19 pandemic on TB diagnosis, TB patient management, treatment initiation, treatment adherence, and patients' loss to follow up were included. A total of 375 articles were screened, and 12 full-text articles were ultimately included in the review. Findings: The extracted impact was synthesised thematically into three indicators of the end TB strategy: impact on TB incidence rate; impact on TB deaths; and impact on catastrophic costs due to TB. Conclusion: The COVID-19 pandemic has affected the three indicators of the end TB strategy and has significantly reversed the global TB progress in the fight to end the TB epidemic. This has increased the risk of TB incidence, deaths, and the severity of the economic impact on TB-affected households. Therefore, there is a need for countries to take a step forward and develop intervention strategies that will help them resolve the damage caused by the pandemic to achieve the targets to end TB. This study could improve strategies implementation regarding the management of TB disease.

**Keywords:** *Coronavirus Pandemic; End Tuberculosis Strategy; Indicators*

## 1. Introduction

Despite the implementation of global plans to end tuberculosis (TB), this disease has for many years been the leading cause of death from a single pathogen; however, it is the second leading cause of infectious killers after severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and the 13th leading cause of death worldwide. It was also the leading killer of people living with HIV and a major cause of deaths related to antimicrobial resistance (World Health Organisation, 2020). Global progress was noticed in 2019 when TB illness developed in an estimated 10 million persons, representing a decline in incidence of 2.3% from 2018 and 9% since 2015 (World Health Organisation, 2020). Although progress has been made, the world is not yet on track to achieve the global end TB strategy, and there is a need to expand and amplify access to TB curative and preventive treatment. The Coronavirus disease 2019 (COVID-19) pandemic has hampered global health systems and has made it worse and potentially altered the road map toward the end of TB (Fukunaga et al., 2019). The impact of the COVID-19 pandemic on healthcare delivery systems has been overwhelming globally, with an unexpected number of cases that have mobilised hospital teams and resources, and 'non-essential' care of non-COVID patients was cancelled or postponed, creating a challenge in providing adequate care for patients with other chronic illnesses (Haghdoost et al., 2021).

The target for 2020 of accelerating TB service provision was not possible in most countries because of the COVID-19 pandemic. Lockdown orders, movement restrictions, and the prioritisation of COVID-19 services in healthcare facilities have affected TB services through restricted service provision, diverted human resources, and disrupted supply chains (World Health Organization, 2020). Different studies used different methods and assumptions about the future of the pandemic, as well as modelling for a variety of settings, such as India, China, South Africa, Kenya, Ukraine and Brazil; these analyses reached approximately similar conclusions. Specifically, TB incidence, and especially TB mortality, are expected to increase by about 5–15% over the next five years, which will lead to hundreds of thousands of additional TB deaths globally (McQuaid et al., 2021).

Different studies have studied the impact of the COVID-19 pandemic on the health system, including the TB programme; however, none of them have studied the comprehensive impact of COVID-19 on the end TB strategies. This literature review synthesises both qualitative and quantitative studies to thematically present the comprehensive impact that has been identified on the end TB strategies. This includes all types of disruptions caused by the TB programme, such as case finding, diagnosis, treatment initiation and treatment adherence, including treatment support and counselling. Therefore, this review could help nations to take steps to design and implement intervention strategies that will help them move forward to reach the end TB strategies by 2035.

## 2. Methodology

Research articles were searched for from CINAHL Plus (EBSCO), PubMed, Google Scholar, Medline, ProQuest, APA Psych and INFO as well as manual searches through Google and Google Scholar search engines. Search expressions were developed for the impact or effects of the COVID-19 pandemic on TB diagnosis, TB management, treatment adherence, TB care and patient outcome that were published in English from December 2019 to September 2022 (see Table 1). The same expression of search strategy was used for all databases and search engines. Article searching was undertaken from September 2022 to October 2022.

Table 1. Searching strategy

<b>AND (COVI-19) OR (Coronavirus)</b>
<b>AND (TB diagnosis) OR (case notification)</b>
<b>AND (TB treatment initiation) OR (TB treatment adherence) OR</b>
<b>AND TB treatment disruption" OR "patients' loss to follow up</b>

Both qualitative and quantitative research articles were included, and articles that did not report original research were excluded. Articles that did not assess the impact or effects of the COVID-19 pandemic on TB diagnosis, TB patient management, treatment initiation, treatment adherence, and patients' loss to follow up were excluded, following the protocol of Figure 1. Data were extracted and captured in Microsoft Excel, then sorted and arranged alphabetically by the first author's name, with all duplicates removed. To ensure quality, scoring based on the quality of the study was agreed on, any studies with 5 scores or fewer points were excluded from the review. Each record was screened independently by both reviewers. Selection was performed based on the specified inclusion and exclusion criteria of the study. During the abstract-level screening, records were included for full-text review if in doubt. Both reviewers had to agree through consensus on the document that one was having a doubt.

To synthesise the full-text studies that met the quality assessment criteria of 5 or more scores, thematic data analysis was used. To develop themes, data were coded and categorised. The synthesis process was checked by an experienced researcher to ensure quality and compliance with the inclusion criteria. Prior to synthesising the data, the included papers underwent meticulous quality assessments, while a formal risk-of-bias evaluation was also conducted to ascertain the validity and reliability of the findings.

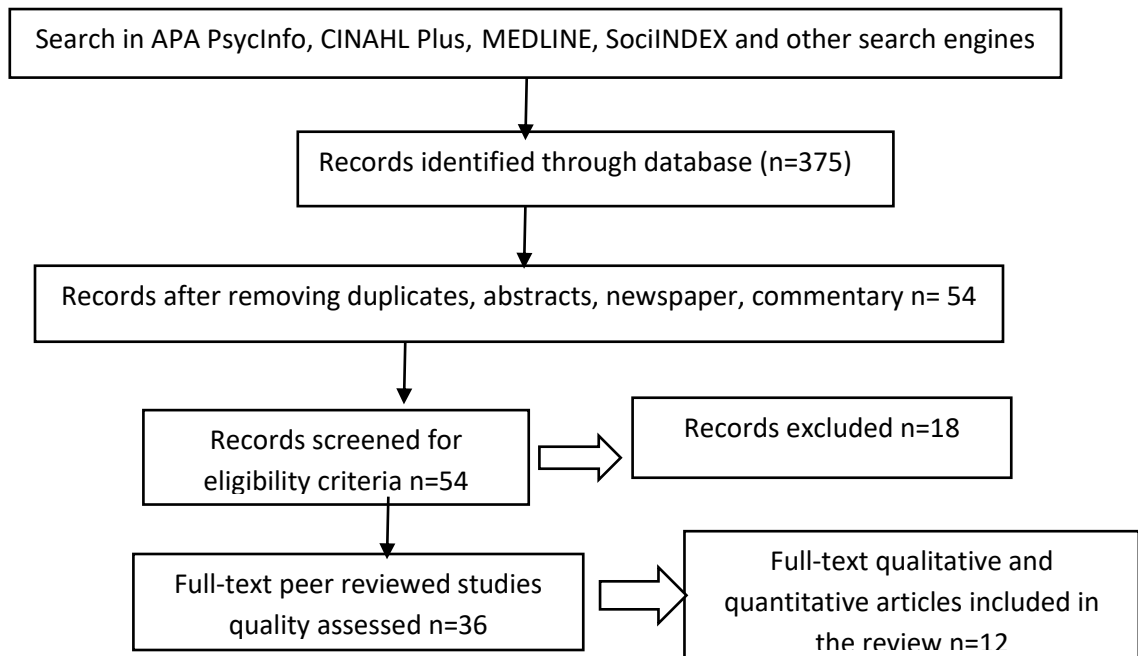


Figure 1. Flow chart for selection of reviewed

## 2.1 Ethical approval

This review did not require ethical approval because all the information gathered was freely available in the public domain.

## 3. Findings

Twelve peer-reviewed research papers that were published between 2021 and 2022 were found to meet the inclusion criteria. Of these 12 papers, about seven focused on exploring the impact of the COVID-19 pandemic on TB diagnosis, TB management, treatment adherence, TB care and patient outcome. Only one was a data review focusing on the impact of COVID-19 on TB, another one focused

on the impact of the COVID-19 pandemic on tuberculosis testing and treatment, and another one focused on the impact of the COVID-19 pandemic on contact tracing of patients with pulmonary tuberculosis.

The majority (eight) of studies were published in 2022, three were published in 2021, and only one was published in 2020. The synthesised findings from both quantitative and qualitative studies are presented below, and they are grouped into specific effects identified in this review. The researcher further looked at how the findings show the effects on the end TB strategies' indicators. The individual studies that showed the impact of COVID-19 on end TB strategy are presented in Appendix A Table A1.

### **3.1 Increase the rate of undetected TB cases**

The literature revealed that new case detection and notification had decreased during the COVID-19 pandemic, as the pandemic adversely impacted the TB diagnostic services, resulting in a significant increase in the rate of undetected TB cases. A cross-sectional study that was conducted in the Malatya region in Turkey showed that in the previous three years, the rate of clinical TB diagnosis ranged between 13.4% (in 2017) and 18.3% (in 2019), but it dropped insignificantly to 7.7% during the COVID-19 pandemic year (2020) (Yakupogullari et al., 2022). According to the Central TB Nikshay portal of the Government of India, a 62% drop in TB case detection was recorded during the COVID-19 lockdown for eight weeks (Hazra et al., 2021).

### **3.2 Prolong diagnostic delays**

Studies revealed that there was a delay in TB diagnosis during the COVID-19 pandemic due to widespread disruptions in healthcare services. The prolonged lockdown has adversely affected TB diagnostics since the priority was given to COVID-19 patients, and there was a shift in resources. A study by Rodrigues et al., (2022) shows that the delays in active TB diagnosis were a result of multiple factors, such as patient's fear of seeking care, referral delays from the healthcare centre, the insufficient response of health and diagnostic units, and incorrect diagnoses.

The literature further shows that there was a postponement of healthcare seeking due to COVID-19 as there was a hindrance to accessing service TB services. A study by Zhang et al., (2022) that was conducted in China, shows that, among 358 participants who were diagnosed with pulmonary TB during the COVID-19 response, 61 (17%) postponed seeking TB diagnosis due to COVID-19.

Rodrigues et al., (2022) show that delays in TB diagnosis were caused by difficulty in TB diagnosis as TB patients were presenting symptoms like COVID-19, and there was a need for healthcare workers to differentiate diagnosis among COVID-19 suspected cases and active TB patients, to maximise diagnosis of TB amidst the COVID-19 pandemic.

### **3.3 Poor access to TB healthcare service due to lockdown restrictions**

A study conducted by Rosser et al., (2023) in Zambia at a tertiary hospital shows that during the COVID-19 pandemic, there was a significant decrease in the number of prescriptions dispensed for TB treatment compared to the previous years.

There was postponement of healthcare services among TB patients, which affected their treatment initiation and treatment adherence. A delay in TB treatment initiation from the onset of TB symptoms was seen as patients were afraid to visit the healthcare centres due to fear of COVID-19. One study shows that fear of contracting COVID-19 during clinic visits was a major barrier to patients receiving TB services and caused patients to postpone healthcare services (Rosser et al., (2023). A study by Zhang et al., (2022) shows that a total of 57 patients (11%) postponed a regular visit to the TB clinic during treatment due to COVID-19, including 25 (44%) who postponed for  $\geq 30$  days, 13 (23%) for 14–29 days, and 19 (33.3 %) for <14 days due to the fear of COVID-19.

TB treatment initiation and treatment adherence were found to be impacted greatly during the COVID-19 lockdown as TB patients did not have access to healthcare services since the COVID-19 pandemic disrupted the treatment services and care for tuberculosis. One study shows that in 2020, the nationwide imposition of lockdown to control the spread of COVID-19 adversely impacted TB diagnosis, as well as treatment services (Hazra et al., 2021).

### **3.4 Lack of treatment supervision and DOT support**

The findings of this review show that TB patients, during the COVID-19 pandemic, lacked treatment supervision or DOT support as they were taking their treatment and that might have influenced poor treatment adherence and treatment interruption. One study conducted in China shows that 175 (34%) received no treatment supervision, and 32 (6%) experienced treatment interruption (Zhang et al, 2022). The challenge with patient supervision might relate to the shortage of healthcare staff when they were reallocated to COVID-19 control. A study by Rodrigues et al., (2022) shows that about 70% of healthcare workers and programme and policy officers reported a reduction in TB patients receiving DOT support since the beginning of the COVID-19 pandemic, due to the lack of material and human resources.

### **3.5 Increased vulnerability of TB transmission among household contacts**

Literature shows that delays in active TB case detection and notification as well as treatment initiation might have impacted the progress that was made to end TB by 2035 as it has promoted TB transmission and increased the TB death rate in the communities. Active TB cases might act as a new source of infections and increase the transmission among the household and community. Delays in TB treatment initiation will increase the disease severity and under-detection of TB cases might lead to a surge in deaths. A study carried out in Spain compared data from March-June in 2019 and 2020 and described an increase in latent and active TB in children of patient households (5.3% vs 7.7% in 2019 and 2020, respectively,  $p < 0.001$ ); additionally, patients with the active disease diagnosed during the pandemic showed more severe manifestations (Aznar et al., 2021).

Postponement of healthcare seeking caused a delay in TB diagnosis, not only exacerbated symptomology and clinical disease but also increased the risk of transmission. On the other hand, delays in TB diagnosis and treatment initiation were estimated to be the greatest concern leading to an increase in deaths (Millones et al., 2022). In Brescia, Italy, during the early two months of the COVID-19 epidemic, the proportion of patients with TB lost to follow up was significantly higher compared to the previous year (10.8 vs. 2.6%,  $P = 0.03$ ), and more TB deaths occurred (4.6 vs. 0%,  $P = 0.04$ ). Globally, 1.6 million people died from TB (including 187 000 among HIV-positive people). TB deaths increased in 2020 compared to 2019 because of reduced access to TB diagnosis and treatment in the face of the COVID-19 pandemic (Zhang et al., 2022).

Literature shows that there was also difficulty in accessing healthcare assistance among TB patients as the TB services were affected by the pandemic and have additionally delayed TB diagnosis and missed diagnoses, which have increased TB transmission in the community. The similarities in TB and COVID-19 symptoms have also influenced misdiagnosis among TB patients, which may have an impact on community transmission. Delays in TB diagnosis have also increased household transmission in the communities. According to Amimo et al., (2020), delayed diagnosis may have negatively impacted vulnerable populations and have increased household TB transmission.

## **4. Discussion of Study Findings**

This review has revealed that the COVID-19 pandemic has affected TB services and has increased the rate of undetected TB cases, prolonged diagnostic delays, poor access to TB healthcare service due to lockdown restrictions, lack of treatment supervision and DOT support, increased vulnerability of TB transmission among household contacts. The current review found that the identified

impact of the COVID-19 pandemic on the TB service disruption has had severe effects on the indicators of the end TB strategy and has reversed the progress that has already been made in fighting the TB epidemic. The first end TB strategy indicator aims at a 95% reduction of TB deaths by 2035. This review shows that the first indicator of the end TB strategy has been impacted by the disruption caused by the COVID-19 pandemic on TB service. The study by Bhargava and Shewade (2020) indicated that a prolonged lag for TB diagnosis and treatment initiation will increase the disease severity and undetected TB cases might lead to a surge of TB incidence, TB transmission and even deaths.

A delay in diagnosis and treatment for TB was estimated to be the greatest concern leading to an increase in deaths (Hogan et al., 2020). The World Health Organisation (2021) showed that during their study period, an increase in the death rate of 43% was observed among TB patients compared to the control period. The global TB report of 2020 shows that disruptions of TB services globally are estimated to have caused an increase of about 100 000 in the global number of TB deaths between 2019 and 2020, which has impacted the target for end TB strategy (WHO, 2021). Similarly, TB incidence and TB mortality are projected to increase by around 5– 15% over the next five years, amounting to hundreds of thousands of additional TB deaths worldwide.

Indicator 2, which aims at a 90% reduction in the TB incidence rate by 2035 was also impacted. The current review shows that during the pandemic, countries imposed lockdowns to control the spread of COVID-19, where people were forced to stay indoors, and those who tested positive for COVID-19 were forced to quarantine (Bhargava & Shewade, 2020). The similarity of the symptoms between TB and COVID-19 has probably resulted in a delay in suspecting TB, as most people could have attributed similar symptoms to COVID-19 and preferred to quarantine, which might have caused TB might act as a new source of infections and increases the transmission among the household and community (Hazra et al., 2021). Those who were sick and wished to seek medical advice were discouraged from doing so, as the diagnosis of novel TB was delayed and TB services were ignored, as most nonemergency services were suspended and access to private sector healthcare was also reduced.

It is evident from this review that there was an overall high disruption of TB testing, diagnoses and case finding for TB patients in India, Nepal, Tajikistan, Tanzania, Thailand, Uganda, Ukraine, Uzbekistan, Vietnam, Zambia and Zimbabwe (McQuaid et al., 2021; Yakupogullari et al, 2022; Hazra et al., 2021). The government of Nepal reported a 67.3% reduction in the mean number of sputum samples collected, a 45.5% reduction in the mean number of active TB cases enrolled on treatment, and a 41.7% decline in the mean number of follow-up appointments of TB patients during the COVID-19 lockdown as compared to 2019 (Amimo et al., 2020). A study conducted in the WHO European Region reported a decrease of more than one-third in TB case notifications in the second quarter of 2020 compared to the same period in 2019 and suggested that the deterioration in TB services due to the COVID-19 response may impede the region's ability to meet the TB targets of the 2030 Sustainable Development Goals (Yakupogullari et al, 2022).

The TB notification rate in India and Indonesia was reduced by approximately 25% from January 2020 to June 2020 as compared to January 2019 to June 2019 (Alene, et al., 2020). This has a huge impact on the progress that was already made on end TB strategy launched by WHO along with the World Health Assembly that aims to end the global tuberculosis epidemic by 2030, by reducing TB death by 95%, cutting new cases of TB by 90% and to eliminate the high costs for TB-affected households (Nepal Ministry of Health, 2021). Reduced TB diagnosis has a huge impact on TB transmission and TB death within the communities and this will cause a major global TB burden which is a setback on the progress that is already made so far to combat TB burden.

Bhargava and Shewade (2020) indicated that a prolonged lag for TB diagnosis and treatment initiation will increase the disease severity and undetected TB cases might lead to a surge in TB incidence, TB transmission and even deaths. Delays in diagnosis and treatment for TB were estimated to be the greatest concern leading to an increase in death (Hogan et al., 2020). The World Health

Organisation (2021) showed that during their study period, an increase in the death rate of 43% was observed among TB patients compared to the control period. This has a major impact on the progress that has been made to try and reach the end TB targets to ensure that zero TB-affected families face catastrophic costs due to TB by 2035.

### **5. Implications of the Study**

The study findings may contribute to the adaptation and adjustment of TB policies and protocols in the management of TB disease to meet the end TB targets. This may help to ensure the TB burden is managed appropriately with a clear goal to reduce the TB burden globally. It may also contribute to the public health body of knowledge by providing insight into the impact of COVID-19 on the management of TB disease.

### **6. Limitations of the Study**

The study only focused on full-text, peer-reviewed studies conducted and published in English; other sources were excluded as they did not comply with the inclusion criteria.

### **Conclusion**

To reach the end TB strategy in 2035, the annual global TB incidence rates should decline by 10%, and the proportion of TB deaths should decline from a projected 15% in 2015 to 6.5% by 2025. The review shows that the COVID-19 pandemic has hampered and disrupted health services globally and has affected the end TB strategy indicators. The researcher identified evidence of significant disruption to the TB diagnoses, treatment initiation and adherence, and poor patient management as well as TB counselling. The healthcare system failed to protect the most vulnerable TB patients and ensure continuous testing for TB and continuity of care for those grappling with ongoing TB epidemics. Since the end TB strategy has suffered during the COVID-19 pandemic, countries and governments should take steps and develop intervention strategies that will help them move forward to achieve the target for the end TB strategy. TB epidemic must be tackled the same way COVID-19 was tackled to reach the end TB goals by 2035.

**AUTHORS' CONTRIBUTIONS:** H Matakanye conceptualised, designed and conducted data collection through a literature search where the librarian from the University of South Africa was requested to assist in doing the literature search. The researcher then requested a skilled academic to assist with data analyses and selecting quality articles. The researcher then wrote the manuscript and submitted it to the journal.

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**Informed Consent Statement:** Not applicable as the study was a systematic literature review.

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Appendix A

**Table A1. Summary of reviewed articles showing the impact of the COVID-19 pandemic on the end TB strategy**

First Author (Year)	Region	Purpose	Population and sample size	Methodology	Impact of Covid 19 on end TB strategy.	QARI Score
<b>Hazra et al., 2021</b>	India	The aftermath of the COVID-19 pandemic on the diagnosis of TB at a tertiary care hospital in India. 1770	1770 TB samples.	Ambispective observational study.	The COVID-19 pandemic adversely impacted TB diagnostic services, resulting in a reduction of active TB case detection.	8
<b>Yakupogullari et al., 2022</b>	Turkey	To assess the impact of the COVID-19 pandemic on pulmonary tuberculosis (PTB) diagnosis, treatment, and patient outcomes, using the WHO definitions.	2970 Patient who was tested for and diagnosed with pulmonary TB	cross-sectional study.	The study shows notable deterioration of TB case detection, TB tests, TB relapse, and treatment failure increased significantly and poor outcomes of TB due primarily to patients' reluctance to visit a health care facility.	6
<b>McQuaid et al., 2021</b>	WHO high TB burden countries	The impact of COVID-19 on TB: a review of the data	48 studies were included	Systematic literature review	TB health services appear to have decreased significantly in most settings due to COVID-19. The number of patients, as well as testing and prevention coverage, have decreased more noticeably than treatment outcomes.	7
<b>do Rosário Souza et al., 2022</b>	Brazil	To assess the impact of the COVID-19 pandemic on the diagnosis of TB in Brazil.	Lesson learned during the COVID-19 pandemic on TB diagnosis.	Ecological and population-based study.	Findings show a reduction in TB diagnosis after the irruption of the COVID-19 pandemic in Brazil.	7
<b>Jamwal et al., 2022</b>	India	To provide a true insight into the disruption of TB care during the pandemic period at a tertiary care hospital in India.	6491 patients who accessed the TB diagnostics	A retrospective observational cohort analysis	The study observed a decline in TB notification, a reduction of 44% in treatment accession, patients' loss to follow up increased, the death rate also increased.	6
<b>Rodrigues et al., 2022</b>	Portugal	To understand how infection control norms and standards	Thirty-two Outpatient TB Centres coordinators	cross-sectional study.	Findings show that TB diagnosis was delayed and Directly Observed Therapy	6



		were applied and how these centres responded during the pandemic.			(DOT) appliance was the most affected.	
<b>Millones et al., 2022</b>	Peru	To assess the impact of the COVID-19 pandemic on patients' experiences obtaining a tuberculosis diagnosis in Peru.	100 adults who had recently enrolled for TB treatment.	Sequential explanatory mixed methods.	TB patients could not access diagnostic services and suffered from misdiagnoses. Patients who were already receiving treatment for TB have reported difficulty accessing health services for treatment monitoring.	8
<b>Zhang et al., 2022</b>	China	To understand the influence of the COVID-19 pandemic on the proportion of patients with TB who delayed seeking the diagnosis and care for TB and explore the reasons for their postponement.	518 pulmonary TB patients participated in the anonymous survey	Cross-sectional study.	Patients postponed seeking TB diagnosis due to fear of COVID-19. Participants receiving antituberculosis treatment postponed their regular healthcare visits due to COVID-19, some received no treatment supervision, and others experienced treatment interruption.	8
<b>Yang et al., 2020</b>	Korea	Investigate the impact of the COVID-19 pandemic on TB diagnosis and management in the Republic of Korea.	98 346 data on TB cases were included.	Retrospective cross-sectional study.	TB diagnoses during the COVID-19 pandemic in the ROK were delayed nationwide, especially for patients notified by public-private mixed TB control hospitals. TB individual case investigations were delayed in regional COVID-19 outbreak areas (Daegu and Gyeongbuk province), especially in public health centres.	7
<b>Aznar et al., 2021</b>	Spain	Assess the impact of COVID-19 on the diagnosis and management of tuberculosis (TB) patients.	90 TB centres were invited and included in the study.	Quantitative design	The COVID-19 pandemic has caused substantial changes in TB care. The increase in latent TB infection and active TB in children of patient households	7

					could reflect increased household transmissions due to anti-COVID-19 measures.	
<b>Rosser et al., 2022</b>	Zambia	Impact of the COVID-19 Pandemic on Tuberculosis Testing and Treatment at a Tertiary Hospital in Zambia	Compared the number of tests, prescriptions, and visits between the pre-pandemic and pandemic periods.	Retrospective study.	The COVID-19 pandemic significantly disrupted TB care in Zambia, which could have long-lasting impacts on TB transmission and mortality.	8
<b>Godoy et al., 2022</b>	Spain	Impact of the COVID-19 pandemic on contact tracing of patients with pulmonary tuberculosis.	6363 Contact tracing of pulmonary TB cases in the pre-pandemic and pandemic periods.	Epidemiological study.	COVID-19 is affecting TB control due to less exhaustive TB and LTBI case detection.	8

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