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Coronavirus Pandemic

Impact of the COVID-19 pandemic on the temporal trend of indicators for access to tuberculosis diagnosis: A systematic review

Mariana Gaspar Botelho Funari de Faria[1], Rubia Laine de Paula Andrade Gonçalves[1], Livia Maria Lopes[2], Elisangela Fransiscon Naves[1], Rafaele Oliveira Bonfim[1], Diogo Henrique Mendes da Silva[1], Ana Beatriz Marques Valença[1], Valdes Roberto Bollela[3], Maria Josefa Perón Rujula[4], Ricardo Alexandre Arcêncio[1], Ione Carvalho Pinto[1], Pedro Fredemir Palha[1], Jaqueline Garcia de Almeida Balestero[1], Dulce Gomes[5], Zhiting Guo[6,7], Jason Farley[6], Nancy Reynolds[6], Aline Aparecida Monroe[1]

[1] Ribeirão Preto College of Nursing, University of São Paulo, Ribeirão Preto, São Paulo, Brazil
[2] Municipal University Centre of Franca (Uni-FACEF), Franca, São Paulo, Brazil
[3] Ribeirão Preto School of Medicine, University of São Paulo, Ribeirão Preto, São Paulo, Brazil
[4] Centro de Vigilância Epidemiológica (CVE) da Secretaria Estadual de Saúde de São Paulo, São Paulo, São Paulo, Brazil
[5] School of Science and Technology, Universidade de Évora, Évora, Alentejo, Portugal
[6] School of Nursing, Johns Hopkins University, Baltimore, MD, United States
[7] School of Nursing, Zhejiang University, China

Abstract

Introduction: The COVID-19 pandemic influenced the behaviour of numerous diseases, overloading health systems and weakening public health infrastructure and access.

Methodology: This study aimed to analyse the repercussions of the COVID-19 pandemic on tuberculosis diagnosis indicators. A systematic review was conducted, examining studies published between 2020 and 2024 in Portuguese, English, or Spanish across five databases and Google Scholar. The search, performed in March 2024, led to the identification of 6,378 studies, of which 23 were included after an independent review of titles, abstracts, and full texts. Data were extracted and narratively synthesized following a methodological quality assessment.

Results: The review revealed significant declines in TB incidence, detection, notification, and diagnosis during the pandemic, alongside reduced etiological confirmation of cases.

Conclusions: The findings highlight a need to reorganize and enhance health service responses to address the disruptions caused by the pandemic. Strengthening these services is crucial to recover missed TB cases and improve indicators, supporting the goal of eliminating TB by 2030.

Key words: COVID-19; tuberculosis; diagnosis; time series analysis.

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Introduction

Tuberculosis (TB) remains a serious public health problem and one of the main causes of death from infectious diseases worldwide [1]. However, as of December 2019, the SARS-CoV-2 virus, which causes COVID-19, had surpassed TB in the number of deaths per day, so that COVID-19 became the deadliest infectious disease in recent times [2].

The COVID-19 pandemic influenced epidemiologic indicators of numerous diseases due to its rapid spread and its potential for lethality, overloading health systems and weakening public health infrastructure and access [3]. Among the diseases with an altered epidemiological pattern, global TB programs documented losses in prevention, control, and monitoring actions, which were weakened due to the required actions to face the pandemic, representing a major obstacle on the path towards the end of TB in many countries [4].

Societal impact was reflected in the difficulty of accessing the health system, social isolation, rising unemployment, worsening poverty and social inequality, with these realities being faced by several countries, including language barriers and other cultural aspects when considering care production for migrants and refugees [5]. Furthermore, the similarities between the symptoms of the two infections focussed greater attention on COVID, with less testing for TB,

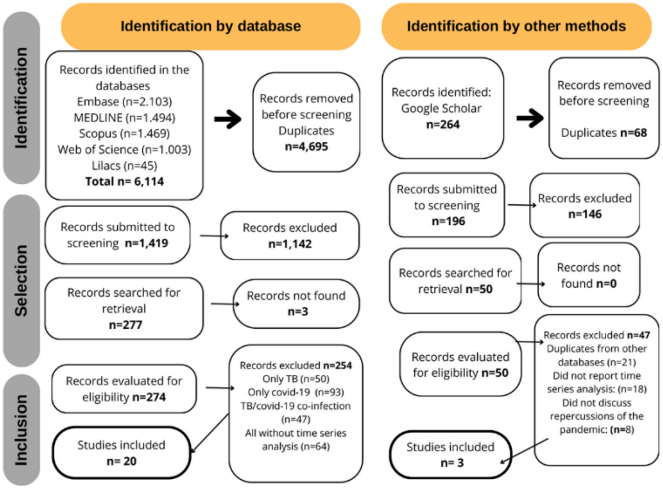
contributing to the increase and spread of the disease, intensifying transmission, pulmonary sequelae, as well as social stigma [6,7]. The interconnection of both infections has not only exacerbated the health crisis, but also the economic, social, and even humanitarian crises.

TB control remains a significant challenge for health systems, particularly in developing countries where the burden is higher. It is essential to develop and implement strategies that ensure timely access to diagnosis and treatment, especially as the availability of medicines, food, and nutritional support has become increasingly limited due to the prioritization of COVID-19 funding [8].

Given the fragility of health services in detecting and monitoring TB cases which has been aggravated by the pandemic, an investigation to understand this impact is essential to assess how actions and services have been affected, as well as to support reflections and strategies capable of increasing response capacity in different contexts and scenarios in the post-pandemic period. Therefore, this study aimed to examine the scientific evidence on the repercussions of the COVID-19 pandemic on the temporal trend of indicators for access to TB diagnosis.

In a preliminary search in the International Prospective Register of Systematic Reviews (PROSPERO) and Medical Literature Analysis and Retrieval System Online (MEDLINE), it is worth noting that no literature review with the same characteristics as this review was found, thus reinforcing its originality and relevance. The protocol for this review was registered with PROSPERO under number CRD-42024511315.

Figure 1. Study selection flowchart for the studies included in the systematic review on the repercussions of the COVID-19 pandemic on the temporal trend of indicators for access to tuberculosis diagnosis, Brazil, 2024.



Methodology

This is a systematic review study conducted in accordance with the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) recommendations, involving three main steps: identification, screening, and eligibility. We chose to conduct a systematic review due to its potential to gather and evaluate data from the literature with scientific rigor and transparency to produce an unbiased portrait of the knowledge produced on the topic [9], through specific methodological steps to gather evidence capable of collaborating in decision-making processes.

This systematic review included the following steps: elaboration of the guiding question; establishment of eligibility criteria for primary studies; survey and selection of publications; identification of articles in the different databases using specific keywords; and finally, assessment of the methodological quality and synthesis of the main results.

The PECO acronym was used to formulate the question that guided this review, considering: P (population or problem to be addressed) – temporal trend of indicators for access to TB diagnosis; E (exposure) – the COVID-19 pandemic period and/or after; C (comparator) – period before the COVID-19 pandemic; O (outcome) – repercussions (changes), resulting in the following question "What are the repercussions of the COVID-19 pandemic on the temporal trend of indicators for access to tuberculosis diagnosis?".

The article screening process considered the following inclusion criteria: ecological time series studies, regardless of the country of origin, and studies that address all clinical forms of TB. Studies were excluded if they: were published before 2020; did not focus on the COVID-19 pandemic periods and after it; or did not address indicators for access to TB diagnosis, which include: TB incidence/notification; bacteriological confirmation rate of TB; TB discovery rate during hospitalizations; TB discovery rate after death; GeneXpert Rapid Molecular Test (RMT) coverage among TB cases; rate of new TB cases diagnosed by GeneXpert RMT; sputum culture coverage rate among TB cases; sensitivity test coverage rate among TB cases; drug-resistant TB rate; HIV test coverage rate among TB cases; or others that were eventually found.

The databases selected for the bibliographic survey covered the following: Pubmed (National Library of Medicine), Embase (Excerpta Medica Database),

Scopus (SciVerse Scopus), LILACS (*Literatura Latino-Americana e do Caribe em Ciências da Saúde*) and Web of Science, while Google Scholar was chosen to search for gray literature. The descriptors and keywords were identified in the Science and Health Descriptors (DeCS), Medical Subject Headings (MeSH), and Emtree, in addition to preliminary searches in the literature, aiming to identify the free vocabulary used in writing the publications. The Boolean operators OR and AND were considered for the search, adapting them for each database [9], according to the search strategies described in Table 1. No language limit was defined for the searches. The search in the databases took place on March 15, 2024.

The studies retrieved from the databases were exported to an application designed for conducting systematic reviews, Rayyan QCRI from the Qatar Computing Research Institute. Duplicate publications were excluded, and then the studies were selected by two independent reviewers (MGBFF; LML) by reading the title and abstract. The studies retrieved from Google Scholar were exported to a Microsoft® Word file (.doc), which was duplicated to also conduct the selection by two independent reviewers (MGBFF; ROB). This selection was performed only by reading the titles of the materials. A third reviewer was called in in case of doubt or disagreement about the inclusion of the materials (RLPA). All articles that met the eligibility criteria were read in full to ensure that they answered the study question. In addition, a flow diagram was prepared to illustrate the steps for selecting the materials considered in the review, as proposed by PRISMA. Three trained reviewers (MGBFF; LML; EFN) each extracted the data from a fraction of the studies each, and a fourth reviewer with expertise checked them. The extraction was conducted using a structured form, prepared by the reviewers themselves, containing the following variables: authors, journal name, year of publication, study objective, study type, study period, study location, population and characteristics of the study sample, indicators analysed, main results of the study and elements for discussion.

The methodological quality assessment (MQA) of the included articles was performed using the JBI (Joanna Briggs Institute) Checklist for quasi-experimental studies. At this stage, it was possible to identify the number of items that should be considered in the study and that were met according to those

Table 1. Search strategies used in the systematic review on the repercussions of the Covid-19 pandemic on indicators for access to tuberculosis diagnosis, Ribeirão Preto, SP, Brazil, 2024.

Database	Controlled vocabulary / free vocabulary
PUBMED	(("Covid-19" [All Fields] OR "Covid-19" [All Fields] OR ("Covid-19" [MeSH Terms] OR "Covid-19" [All Fields] OR "covid19" [All Fields]) OR ("coronavirus" [MeSH Terms] OR "coronavirus" [All Fields] OR "coronaviruses" [All Fields]) OR "sars cov 2" [All Fields] OR "sars cov 2" [All Fields] OR "sars cov 2" [All Fields] OR "sars cov 2" [All Fields] OR "sars-cov2" [All Fields] OR "sars-cov2" [All Fields] OR "2019-ncov" [All Fields] OR "2019-ncov" [All Fields]) AND ("effect" [All Fields] OR "effects" [All Fields] OR "repercussion" [All Fields] OR "repercussions" [All Fields] OR "impact" [All Fields] OR "impacts" [All Fields] OR "time series" [All Fields] OR "time trend" [All Fields] OR "temporal trend" [All Fields] OR "temporal series" [All Fields]) AND ("tuberculosi" [All Fields] OR "tuberculosis" [MeSH Terms] OR "tuberculosis" [All Fields] OR "tuberculoses" [All Fields] OR "tuberculosis s" [All Fields] OR "tb" [All Fields])) AND (2020:2024 [pdat])
LILACS	("covid 19 " OR "Covid-19" OR covid19 OR coronavirus OR "sars cov 2" OR "sars cov-2" OR "sars-cov-2" OR "sars-cov 2" OR "sars-cov2" OR "sars cov2" OR "2019-ncov" OR "2019 ncov") AND ("effect" OR "effects" OR "repercussion" OR "repercussions" OR "impact" OR "impacts" OR "time series" OR "time trend" OR "temporal trend" OR "temporal series" OR efeito OR efeitos OR repercussão OR repercussões OR impacto OR impactos OR "séries temporais" OR "tendência tempora"l OR efecto OR efectos OR repercusión OR repercusiones OR impacto OR impactos OR "series de tiempo" OR "tendencia en el tiempo") AND (tuberculosis OR tb OR tuberculose) AND (db:("LILACS")) AND (year_cluster: [2020 TO 2024])
Embase	#1 'covid 19'/exp OR 'covid 19' OR 'Covid-19'/exp OR 'Covid-19' OR 'covid19'/exp OR covid19 OR 'coronavirus'/exp OR coronavirus OR 'sars cov 2'/exp OR 'sars cov 2' OR 'sars cov-2'/exp OR 'sars cov-2' OR 'sars-cov-2'/exp OR 'sars-cov-2' OR 'sars-cov 2'/exp OR 'sars-cov 2' OR 'sars-cov2' OR 'sars cov2' OR '2019-ncov'/exp OR '2019-ncov' OR '2019 ncov'/exp OR '2019 ncov' #2 'effect' OR 'effects' OR 'repercussion'/exp OR 'repercussion' OR 'repercussions' OR 'impact'/exp OR 'impact' OR 'impacts' OR 'time series'/exp OR 'time series' OR 'time trend'/exp OR 'time trend' OR 'temporal trend'/exp OR 'temporal trend' OR 'temporal series' #3 'tuberculosis'/exp OR tuberculosis OR 'tb'/exp OR tb #4 #1 AND #2 AND #3 #5 #4 AND (2020:py OR 2021:py OR 2022:py OR 2023:py OR 2024:py) AND [embase]/lim
Scopus	TITLE-ABS-KEY ("covid 19 " OR "Covid-19" OR covid19 OR coronavirus OR "sars cov 2" OR "sars cov-2" OR "sars-cov-2" OR "sars-cov 2" OR "sars-cov2" OR "sars cov2" OR "2019-ncov" OR "2019 ncov") AND TITLE-ABS-KEY ("effect" OR "effects" OR "repercussion" OR "repercussions" OR "impact" OR "impacts" OR "time series" OR "time trend" OR "temporal trend" OR "temporal series") AND TITLE-ABS-KEY (tuberculosis OR tb) AND PUBYEAR > 2019 AND PUBYEAR < 2025
Web of Science	"covid 19 " OR "Covid-19" OR covid19 OR coronavirus OR "sars cov 2" OR "sars cov-2" OR "sars-cov-2" OR "sars-cov 2" OR "sars-cov2" OR "sars cov2" OR "2019-ncov" OR "2019 ncov" (Topic) and "effect" OR "effects" OR "repercussion" OR "repercussions" OR "impact" OR "impacts" OR "time series" OR "time trend" OR "temporal trend" OR "temporal series" (Topic) and tuberculosis OR tb (Topic) and 2020 or 2021 or 2022 or 2023 or 2024 (Publication Years)
Google Scholar (Three strategies were used)	Covid-19 tuberculose "séries temporais" Covid-19 tuberculosis "time series" Covid-19 tuberculosis "series de tiempo"

Table 2. Search strategies used in the systematic review on the repercussions of the Covid-19 pandemic on indicators for access to tuberculosis diagnosis, Ribeirão Preto, SP, Brazil, 2024.

Impact	Characteristics
Reduction in TB suspicion	Andom *et al.*, 2023 [10]; Kamakoli *et al.*, 2021 [30]
Reduction in investigations	Dlangalala *et al.*, 2023 [11]
Reduction in diagnosis/detection	Andom *et al.*, 2023 [10]; Hentringer *et al.*, 2023 [12]; Osei *et al.*, 2023 [15]; Singh *et al.*, 2023 [16]; Souza *et al.*, 2023 [17]; Souza *et al.*, 2022 [26]
Late diagnosis	Osei *et al.*, 2023 [15]
Reduction in case confirmation	Dlangalala *et al.*, 2023 [11]; Heunis *et al.*, 2023 [13]; Souza *et al.*, 2022 [26]; Kamakoli *et al.*, 2021 [30]
Reduction in notifications	Osei *et al.*, 2023 [15]; Berra *et al.*, 2022 [18]; Chen *et al.*, 2022 [19]; Hasan *et al.*, 2022 [20]; Lungu *et al.*, 2022 [21]; Manhiça *et al.*, 2022 [22]; Masina *et al.*, 2022 [23]; Ranasinghe *et al.*, 2022 [25]; Souza *et al.*, 2022 [26]; Souza, 2022 [27]; Ding *et al.*, 2021 [28]; Crowder *et al.*, 2021 [29]; Oliveira *et al.*, 2021 [31]; Soko *et al.*, 2021 [32]
Increase in notifications	Malik *et al.*, 2022 [24]
Reduction in incidence	Lee, Chun, 2023 [14]; Souza *et al.*, 2023 [17]; Manhiça *et al.*, 2022 [22]; Souza, 2022 [27], Ding *et al.*, 2021 [28]

recommended in the instrument. The data were then narratively synthesized.

Results

A total of 6,378 studies were identified and evaluated, and 1,615 articles remained after removing duplicates. The titles and abstracts were then read, resulting in 327 articles being selected for full reading, of which three were not available in full and 301 were excluded, making a total of 23 articles included in this review (Figure 1).

Among the 23 articles that comprised this review, eight were published in 2023 [10-17], 10 in 2022 [18-27] and five in 2021 [28-32]; 21 were published in English [10-23,25,26,28-30,32] and two in Portuguese [27,31]; six were from the Americas, more specifically from Brazil [12,17,26,27,31], eight were from Africa [10,13,15,21-23,32], eight from Asia [14,16,19,20,24,28-30] and one study was conducted at a global level [25]. The characteristics and results of the 23 studies included in the review are summarized in Table 2, and Supplementary Table 1.

Table 3. Assessment of the methodological quality of studies included in the systematic review on the impacts of the Covid-19 pandemic on the temporal trend of indicators for access to tuberculosis diagnosis.

	1. Is it clear in the study what is the cause and what is the effect?	2. Was there a control group?	3. Were participants included in any similar comparisons?	4. Were the participants included in any comparisons receiving similar treatment/care, other than the exposure or intervention of interest?	5. Were there multiple measurements of the outcome, both pre and post the intervention / exposure?	6. Were the outcomes of participants included in any comparisons measured in the same way?	7. Were outcomes measured in a reliable way?	8. Was follow-up complete and if not, were differences between groups in terms of their follow-up adequately described and analyzed?	9. Was appropriate statistical analysis used?
Andom *et al.*, 2023 [10]	S	NA	NA	NA	S	S	N	S	N
Dlangalala *et al.*, 2023 [11]	S	NA	NA	NA	S	S	N	S	S
Hentringer *et al.*, 2023 [12]	S	NA	NA	NA	S	S	N	S	N
Heunis *et al.*, 2023 [13]	S	NA	NA	NA	S	S	N	S	S
Lee, Chun 2023 [14]	S	NA	NA	NA	S	S	N	S	S
Osei *et al.*, 2023 [15]	S	NA	NA	NA	S	S	N	S	S
Singh *et al.*, 2023 [16]	S	NA	NA	NA	N	S	N	S	S
Souza *et al.*, 2023 [17]	S	NA	NA	NA	N	S	N	S	S
Berra *et al.*, 2022 [18]	S	NA	NA	NA	S	S	N	S	S
Chen *et al.*, 2022 [19]	S	NA	NA	NA	S	S	N	S	N
Hasan *et al.*, 2022 [20]	S	NA	NA	NA	S	S	N	S	S
Lungu *et al.*, 2022 [21]	S	NA	NA	NA	S	S	N	S	S
Manhiça *et al.*, 2022 [22]	S	NA	NA	NA	S	S	N	S	S
Masina *et al.*, 2022 [23]	S	NA	NA	NA	S	S	N	S	S
Malik *et al.*, 2022 [24]	S	NA	NA	NA	S	S	N	S	N
Ranasinghe *et al.*, 2022 [25]	S	NA	NA	NA	N	S	N	S	S
Souza *et al.*, 2022 [26]	S	NA	NA	NA	S	S	N	S	S
Souza, 2022 [27]	S	NA	NA	NA	S	S	N	S	S
Ding *et al.*, 2021 [28]	S	NA	NA	NA	S	S	N	S	S
Crowder *et al.*, 2021 [29]	S	NA	NA	NA	S	S	N	S	S
Kamakoli *et al.*, 2021 [30]	S	NA	NA	NA	S	S	N	S	S
Oliveira *et al.*, 2021 [31]	S	NA	NA	NA	S	S	N	S	N
Soko *et al.*, 2021 [32]	S	NA	NA	NA	S	S	N	S	S

In assessing the methodological quality of the publications included in the review, the reliability of the measures was not considered by any study. The studies [16,27,25] presented fewer than three measures of the outcomes studied in the period after the beginning of the pandemic, and another five studies [10,19,20,24,31] presented weaknesses in the statistical analysis procedures (Table 3).

Discussion

The emergence of the COVID-19 pandemic has significantly disrupted the management of various diseases, with a particularly detrimental effect on efforts to eradicate TB [20]. The United Nations estimated that the pandemic would push approximately 100 million people into poverty in 2020. Additionally, developing countries—represented in all the studies reviewed—were projected to face economic losses of around $12 trillion by 2025 due to the pandemic [36], further intensifying the challenges to TB control efforts.

Responses to the COVID-19 pandemic have required intense concentration of public health actions through emergency measures, leading to disruptions in a variety of services in different contexts [33]. Interference in key indicators was observed when analyzing the economic impacts, including increased unemployment, worsening poverty, and growing social inequality. These impacts had repercussions on the difficulty of accessing health services, as well as on the intensification and spread of diseases, such as TB.

There was an upward trend when observing the suspicion of TB cases in the years before the pandemic, and a 55.6% reduction in suspicions was identified when compared with the period from March to June 2020 [30]. This drop was also identified in another study [10], indicating that other respiratory diseases, in addition to COVID-19, were also neglected during the pandemic, since the diagnostic hypothesis raised by professionals was based on SARS-CoV-2 infection in any person with respiratory symptoms [32].

The number of people tested for TB was drastically reduced due to focusing research on COVID-19, given the global emergency scenario [11]. Furthermore, the production of responses to confront the pandemic led to discontinued TB detection programs [34], including reallocating the use of diagnostic equipment intended for TB to perform tests for COVID-19 [35].

The health crisis caused a significant drop in global TB diagnoses, with a decline of 1.55 million cases in 2020 and an additional 1.28 million in 2021 [1]. This reduction in diagnosed cases was evident across several studies included in the review [10,15-17,20,26], highlighting the challenges faced by developing countries, particularly in maintaining healthcare services and addressing health demands that extended beyond COVID-19. Some COVID-19 mitigation measures may have contributed to the reduction in TB diagnoses by approximately 40 % [1], with emphasis on compliance with isolation/staying at home, reallocation of health resources to combat COVID-19, reduction in health unit opening hours, as well as reduced financial capacity to pay for services [37].

The pandemic context not only impacted the detection of TB cases, but also caused significant delays in the diagnosis of suspected cases [15]; this was both the result of the aforementioned social isolation and health service contingency measures, and due to people's fear of seeking health services and being diagnosed with COVID-19, thus fearing its possible consequences, such as isolation, hospitalization and death.

A reduction in the number of positive cultures for TB was also identified when comparing pandemic periods and previous years. This test is considered the gold standard for TB diagnosis and can increase the diagnosis of the disease by 30% in cases where bacilloscopy was negative [38]. Findings indicate a reduction in laboratory confirmation of approximately 76.5% [30] during the pandemic, and a reduction through culture was also observed in other studies [11,13,26].

The same scenario is also observed in Brazil regarding the increasing trend of confirmed cases in all regions of the country before the pandemic [27], reflecting efforts made to offer adequate and timely treatment, with actions focused on preventing general antimicrobial resistance [39].

Most studies have shown a decrease in the number of notifications [15,18-23,25-29,31,32], with the overall reduction being around 18 % in 2020 [40], representing around 5.83 million notifications of TB cases, the lowest number recorded since 2013 [1]. The study showed that the immediate decline in TB notifications was greater for clinically diagnosed cases compared to those confirmed bacteriologically [29]. The explanation for this may be related to possibly ruling out suspicion of the disease when a negative test result is found.

In contrast, a study mentioned an increase in the notification of TB cases during the pandemic period in the capital of Pakistan due to local initiatives to integrate activities developed for TB control with actions to combat COVID-19 [24]. However, this study has certain limitations in the statistical analyses

undertaken, as discussed later.

The incidence also followed this dynamic in view of the negative repercussions of COVID-19 in relation to indicators for access to TB diagnosis, resulting in a decreasing trend during the pandemic period reported by several studies [14,17,22,27,28]. TB notifications increased again in response to the various post-pandemic measures [21], as did the incidence rate.

There is an urgent need to recognize the setbacks caused by COVID-19 for TB diagnosis, as well as the successful initiatives undertaken to reflect on achieving the goals of eliminating the disease based on actions and strategies with the potential to mitigate the repercussions imposed by the disease on health programs and services. To effectively address TB in developing countries, particularly those more vulnerable to the impacts of COVID-19 mitigation measures, several strategies could be implemented. One key approach would be the creation of TB monitoring dashboards, similar to those used for COVID-19. These dashboards would make disease data more accessible, empowering civil society to demand greater government accountability and advocate for the continuation of essential disease control measures. Another critical strategy is the integration of testing for both TB and COVID-19 within healthcare services, given the overlapping symptoms of the two diseases. Furthermore, leveraging digital applications for case monitoring and contact tracing could play a pivotal role in reducing transmission and identifying undiagnosed cases, thereby reinforcing TB control efforts.

Regarding the MQA of the studies included in the review, homogeneity was observed between the groups compared in all studies; however, one aspect not addressed concerns the reliability of the measurements, since secondary data were collected in all studies, meaning possible information biases. Regarding the other items, three studies [16,17,25] presented less than three measurements of the outcomes studied in the period after the beginning of the pandemic, which can be considered a limitation for the trend assessment of the indicators analysed. Furthermore, five studies [10,19,20,24,31] presented limitations in the statistical analyses undertaken, since they did not use interrupted time series or did not test whether the changes in trends were significant. However, despite these limitations, other studies in this review contributed to providing support and sustainability for their conclusions.

Regarding the implications of this review for advancing knowledge and health practices, the findings reinforce the need for visibility and appreciation of health actions and services that permeate TB diagnosis from the perspective of integration and coordination, as well as practices aligned with guidelines based on person-centred care. This, in turn, requires robust public policies capable of strengthening the response capacity of health systems to address TB as a socially determined disease to achieve internationally agreed-upon goals and commitments, with emphasis on the Sustainable Development Goals.

As a limitation of the study, we highlight the limited number of databases used in the bibliographic search, which may have reduced the total number of studies included in the review, in addition to the impossibility of conducting a meta-analysis, as it does not apply to time series studies.

Conclusions

The study identified a reduction in suspicion, investigation, diagnosis/detection, confirmation, and reporting of TB cases during the pandemic period, with significant setbacks in disease control actions. There is an urgent need to strengthen and integrate health actions and services to increase the response capacity of health systems, improve the quality of care provided, and consequently increase these indicators that express access to TB diagnosis. Revitalizing and redirecting TB control actions requires the commitment of public authorities to eliminate the disease, as established in international agreements.

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Author's Contribution

Conception (MGBFF; RLPAG; AAM; ROB; EFN; ABMV; DHMS), method (MGBFF: RLPAG; DG; VRB; AAM), Discussion and Corrections (MGBFF; MJPR; RAA; ICP; PFP; JGAB; ZG; JF; NR; AAM).

Corresponding author

Mariana Gaspar Botelho Funari
Bandeirantes, 3900. Campus Universitário
Ribeirão Preto – SP, Brazil
CEP 14040-902
Tel: +55(16)3315-3407
Email: rimagod@usp.br

Conflict of interests

No conflict of interests is declared.

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Annex – Supplementary Items

Supplementary Table 1. Description of articles included in the systematic review on the repercussions of the Covid-19 pandemic on the temporal trend of indicators for access to tuberculosis diagnosis.

Authors, Year / Journal / Country	Study design	Objective(s)	Sample size and characteristics	Indicator analyzed	Study results
Andom *et al.*, 2023 [10]/ Tropical Medicine and Infectious Disease/ Lesotho	Study with time series modeling	To assess the magnitude of disruption in the TB care cascade related to COVID-19, including care seeking, diagnosis, treatment initiation and completion of TB treatment.	Monthly average of 53,748 outpatient consultations, 2,357 suspected TB cases and 249 TB cases.	TB suspicion rate, TB diagnosis rate and TB/HIV co-infection diagnosis rate.	The number of presumed cases was as expected in March 2020, but fell during the rest of the pandemic, with a cumulative decline of -46.1% (95% PI -52.2%, -39.0%) compared to expectations. The number of diagnosed cases was below expectations in all months of the pandemic except November 2020, with a cumulative decline of -38.7% (95% PI -47.2%, -28.4%). The number of TB diagnoses in HIV-coinfected individuals was as expected in March 2020, but fell during the rest of the pandemic, with a cumulative decline of -67.0% (95% PI -72.6%, -60.0%) compared to expectations.
Dlangalala *et al.*, 2023 [11]/ Scientific Reports/ South Africa	Study with analysis of interrupted time series	To assess the impact of the pandemic on TB diagnosis in primary healthcare (PHC) clinics during different phases of COVID-19 in the Thekwini district, South Africa.	28,281 TB investigations between January 2018 and March 2020 and 41,173 from April 2020 to June 2022; 2,565 TB confirmations between January 2018 and March 2020 and 2,801 from April 2020 to June 2022.	Number of TB investigations and number of confirmed cases.	The initial lockdown resulted in immediate declines of -45% (95% CI -55 to -31) and -40% (95% CI -59 to -28) in TB investigations and confirmed cases, respectively. At the end of the study period, the number of investigations reached higher levels than the pre-pandemic period, however the reduction in the number of confirmed cases persisted until the end of the period.
Hentringer *et al.*, 2023 [12]/ Revista O mundo da saúde/ Brazil	Ecological study, with spatial analysis and temporal trend	To analyze the effect of the COVID-19 pandemic on the detection of new TB cases in Brazil through spatial and temporal patterns.	5,570 Brazilian municipalities - 92,089 new cases annually in the pre-pandemic period (2016 to 2019) and 86,166 cases detected in the pandemic period (2020).	Average detection rate of new TB cases.	There was a reduction in the tuberculosis detection rate in all Brazilian regions and in 81.5% of the states between the two study periods. Approximately 60.0% of the municipalities showed stabilization or decrease in detection rates due to the pandemic. A reduction in the detection rate was observed in 2020, from 44.2 cases/100,000 inhabitants to 40.7 new cases/100,000 inhabitants. The temporal analysis revealed that all regions showed an increasing trend in the case detection rate from January 2016 until the beginning of 2020, and that a strong trend towards a reduction in said rate was identified, especially in the first half of 2020.
Heunis *et al.*, 2023 [13]/ BMC Health Services Research/ South Africa	Interrupted time series analysis	To measure the effects of the COVID-19 pandemic on essential public health services related to Primary Healthcare utilization and outpatient care seeking, antiretroviral treatment, confirmation of drug-sensitive tuberculosis and initiation of treatment, and BCG vaccine coverage.	Did not provide the number.	TB confirmation rate.	The drug-sensitive TB confirmation rate (≥ 5 years) decreased by 5.24% (p= 0.297). The COVID-19 pandemic reinforced a downward trend in this rate, which was occurring even before the pandemic.
Lee, Chun 2023 [14]/ Open Forum Infect Dis/ South Korea	Study with interrupted time series analysis	To investigate how tuberculosis incidence and mortality levels and trends changed before and after the	204,190 TB cases.	TB Incidence	The results showed that the incidence had a significant decreasing trend before the COVID-19 pandemic (b=-0.024, p<0.01) and an even more significant decrease after the pandemic (b=-0.72, p<0.01). The decreasing trend in TB incidence was not statistically significant after the pandemic.

Authors, Year / Journal / Country	Study design	Objective(s)	Sample size and characteristics	Indicator analyzed	Study results
		COVID-19 pandemic in Korea.			
Osei *et al.*, 2023 [15]/ Plos One/ Ghana	Study with interrupted time series analysis	To evaluate the impact of COVID-19 on disease control programs, particularly TB and HIV control.	Not cited.	Reported cases, missed diagnosis or late diagnosis	In the 39 months before COVID-19 (January 2016 to March 2020), a median of 1163 TB cases were reported per month (Interquarterly Range [IQR]: 680), compared with 932 cases per month (IQR: 351) in the 9 months of the COVID-19 pandemic (April to December 2020). The results showed that COVID-19 led to a steep 20.5% decline in reporting in April, which declined to 32.7% the following month. Overall, a median of 21.4% (95%CI: 16.4%, 30.6%) of TB cases were missed or diagnosed late per month during the COVID-19 period. A cumulative loss of 2,128 or 20% (15.3%, 24.2%) notifications was observed nationwide in December 2020 due to the Covid-19 pandemic.
Singh *et al.*, 2023 [16]/ Indian Journal of Community Medicine/ India	Study based on retrospective data with time series analysis	To study the temporal trend of TB cases and assess the impact of lockdown on TB detection.	Records of 1,010 cases of TB from April 2018 to May 2019 and 1,074 from April 2019 to March 2020.	Number of cases relative to expected.	The time series analysis showed that the projected TB cases for April and May 2020 were 67 and 86, respectively, while the number of cases in these months were 35 and 76.
Souza *et al.*, 2023 [17]/ Tropical Medicine Infectious Disease/ Brazil	Ecological study of time series and spatial distribution	To analyze the temporal evolution, spatial distribution, and impact of the COVID-19 pandemic on tuberculosis records in a state in Northeastern Brazil.	91,225 new cases of TB between 2001 and 2019; the number of cases diagnosed during the pandemic was not reported.	Diagnostic missed diagnosis and incidence rate.	They observed an 8.5% reduction in the number of new TB cases in 2020, representing a diagnostic loss of 392 patients and an 8.73% reduction in the incidence rate. In the pre-pandemic period, 10.8% of municipalities had a TB incidence rate below 10 cases/100,000 inhabitants. The percentage of municipalities was 27.0% in 2020, and 17.8% in 2021.
Berra *et al.*, 2022 [18]/ Tropical Medicine and Infectious Disease/ Brazil	Ecological study of time series	To visualize and classify the time series of Covid-19, tuberculosis (TB) notification and TB outcomes (cure, treatment abandonment and death), verify the impact of the novel coronavirus pandemic on these indices in Brazil and verify the presence of spatial autocorrelation between Covid-19 and TB.	1,054,793 cases of TB between 2010 and 2021	Notification rates.	Brazil and its macroregions showed an increasing temporal trend for TB notification in the pre-pandemic period. According to the interrupted time series analysis, Covid-19 caused a decline in TB notification rates. The five Brazilian regions recorded a decline in the number of notifications due to the Covid-19 pandemic.
Chen *et al.*, 2022 [19]/ Infection and Drug Resistance/ China	Study with time series modeling	To predict the incidence of pulmonary TB by establishing the autoregressive integrated moving average (ARIMA) model and provide support for TB prevention and control during the Covid-19 pandemic.	255,656 cases of TB.	TB notification rate.	There were 34,580 cases reported in 2013, while only 25,493 were reported in 2020. This equates to a decline of 26.3% in eight years.
Hasan *et al.*, 2022 [20]/ Emerging Infectious Diseases/ Vietnam	Retrospective cohort study with interrupted time series analysis	To evaluate the effect of the Covid-19 pandemic on TB case notifications and treatment outcomes during the first year of the	102,676 reported cases of TB in 2015, 106,627 in 2017, 105,733 in 2017, 102,171 in 2018, 105,680 in 2019 and 96,998 in 2020.	TB notification rate and drug/multidrug-resistant TB notification rate.	National TB case notifications decreased by 8% during 2020 compared with 2019. We observed a 29% decrease in TB notifications in April 2020 during the first COVID-19 outbreak in Vietnam compared with April 2019. We also observed a decrease during January 2020 compared with January 2019. TB notifications during the second major COVID-19 outbreak in August 2020 decreased by 19% nationally and by 71% in the most affected provinces, compared with August 2019. TB

Authors, Year / Journal / Country	Study design	Objective(s)	Sample size and characteristics	Indicator analyzed	Study results
		pandemic, comparing programmatic data from 2020 with data from the previous 5 years.	2,130 cases of drug-resistant or multidrug-resistant TB in 2015, 2,450 in 2016, 2,965 in 2017, 2,807 in 2018, 2,889 in 2019 and 2,851 in 2020.		notifications decreased by 364 notifications per quarter (95% CI -1,236 to 508) during the year after the onset of COVID-19 compared with the previous 5 years. Notifications for MDR-TB decreased by 27% in April 2020 compared to notifications in April 2019.
Lungu *et al.*, 2022 [21]/ Bulletin of the World Health Organization / Zambia	Study with interrupted time series	To evaluate the impact of the coronavirus (COVID-19) pandemic and the subsequent implementation of tuberculosis response measures on tuberculosis notifications in Zambia.	3,979 cases before the pandemic (January 2019 to February 2020) and 4,107 cases during the pandemic period (April to June 2020) and during the period of implementation of tuberculosis response actions (August 2020 to September 2021).	Number of TB notifications per month.	TB notifications before the onset of the pandemic were slowly increasing by approximately 32 reported cases/month, from 2,890 cases in January 2019 to 3,337 cases in February 2020. Although trends in monthly TB notifications varied across subgroups and provinces, notifications did not decrease in any subgroup or province before COVID-19 cases were diagnosed. After mitigation measures were implemented, the total number of TB notifications decreased from an anticipated 3,400 cases to an observed 2,668 cases (95%CI: 2,628 to 2,707), an immediate decline of 733 cases. In response to TB response measures implemented from August 2020 to September 2021, national TB notifications immediately increased from an anticipated 2,700 cases (95%CI: 2,603–2,796) to an observed 3,906 cases (95%CI: 3,761–4,051), an increase of 1,206 (45%) cases. The total number of TB notifications in 2021 was 4,107 cases (95%CI: 3,923–4,292), a value not significantly different from the estimated number of notifications, assuming a continuation of pre-pandemic trends.
Manhiça *et al.*, 2022 [22]/ BMJ Global Health/ Mozambique	Study with segmented time series analysis	To understand the effects of Covid-19 on TB diagnostic services in Mozambique, estimating the effects of state of emergency measures on the total number of new cases of all forms of TB at district level and the variability between districts.	154 administrative districts did not report the number (2017 to 2019) and n = 96,182 cases (2020).	Notification rate ("incidence").	Until the onset of the COVID-19 pandemic, national TB notifications in Mozambique (all forms) had been gradually increasing since the first quarter of 2017. The average incidence of 283 (95%CI 200–406) cases per 100,000 of population was increasing annually by 5.0% by the end of 2019. Had this trend continued, 113,329 cases should have been diagnosed in 2020. However, only 96,182 cases were reported in 2020. Therefore, 17,147 new cases of all forms of TB were potentially missed in the 9-month period following the onset of COVID-19, representing a statistically significant relative loss of 15.1% (95% CI 5.9–24.0). The pattern of new cases of pulmonary TB is similar to that of new cases of all forms of TB, and the incidence of pulmonary TB had been increasing at an average rate of approximately 6.6% annually; however, a sharp decline (15%) was also observed immediately after the onset of COVID-19 in March 2020.
Masina *et al.*, 2022 [23]/ International Journal of Public Health/ Eswatini	Retrospective cohort study with interrupted time series analysis	To investigate the impact of the Covid-19 pandemic on tuberculosis (TB) case reporting and treatment outcomes.	1,560 TB cases between December 2018 and February 2020 and 840 cases between March 2020 and May 2021.	TB notifications.	There was a significant decrease in TB case reporting (IIR 0.71, 95%CI: 0.60–0.83) among those reported during the pandemic compared to pre-pandemic. A sudden drop in the number of TB cases was observed at the onset of the pandemic.
Malik *et al.*, 2022 [24]/ Tropical Medicine and Infectious Disease/ Pakistan	Study with temporal trend analysis	To understand the impact of adaptations made during the Covid-19 period on TB case reporting.	Not cited.	Case notifications	Case notifications between January 2020 and March 2021 were above 80% of expected in all districts studied, with three districts exceeding 90%. There was an initial decline in TB case notifications in all districts in the second quarter of 2020, but as TB activities were integrated into COVID-19 work, there was a sustained increase throughout the study period. The average notification of pediatric cases was 94% of expected notifications, and in four districts it exceeded 100%. The percentage of notifications in the private sector averaged 65% between 2020 and 2021, compared with 60% between 2018 and 2019.
Ranasinghe *et al.*, 2022 [25]/ The Lancet/ 215 countries	Time series modeling analysis	To assess the impact of Covid-19 on childhood tuberculosis reporting.	5,464,855 notifications in 2014; 5,748,193 in 2015; 6,220,884 in 2016; 6,182,575 in 2017; 6,775,506 in 2018; 6,912,330 in	Notifications of TB cases in people aged zero to four years, five to 14 years and over 14 years.	The annual TB notification count increased across all age groups and high-TB burden countries from 2014 to 2019. Global notifications in 2020 were 35.4% lower than expected for children aged zero to four years, 27.7% lower among children aged five to 14 years, and 18.8% lower among people aged 15 years and older. Among 28 high-TB burden countries, no association was observed between the stringency of COVID-19

Authors, Year / Journal / Country	Study design	Objective(s)	Sample size and characteristics	Indicator analyzed	Study results
			2019; 5,790,676 in 2020.		restrictions and the relative difference in observed versus expected notifications.
Souza *et al.*, 2022 [26]/ Frontiers in Pharmacology/ Brazil	Population-based ecological study, with spatial and temporal analysis techniques	To assess the impact of the Covid-19 pandemic on TB diagnosis in Brazil during 2020.	91,225 TB cases annually between 2015 and 2019; 83,678 cases in 2020.	Percentage change in new cases observed in relation to the number of expected cases; Percentage change in new cases of pulmonary TB observed in relation to the expected; Percentage change in cases positive for smear microscopy in relation to the expected.	A total of 83,678 cases of TB were reported in Brazil in 2020. However, based on the average number of cases between 2015–2019, approximately 91,225 cases were expected in 2020, representing a reduction of 7,547 cases (% variation: −8.3%). After analyzing all Brazilian states, 22 showed a reduction in TB diagnoses. Regarding pulmonary tuberculosis, 70,855 cases were reported in 2020, in contrast to the 77,090 cases estimated for this period (reduction of 6,235 cases of PTB; −8.1%). From March to December 2020, the % variation curve showed a progressive reduction in monthly notifications of new TB cases in all Brazilian regions after the onset of the pandemic in the country. Likewise, there was a reduction in the number of smear-positive cases. The decrease in positive cases was more pronounced from March onwards after the first confirmed case of COVID-19, both nationally and regionally, with the largest reductions observed in December. The TB and PTB detection rate (per 100,000 population) increased from 2015 to 2019 in all regions. Impressively, all rates in 2020 were lower than those reported in 2015. Furthermore, analyses of time trends in the years preceding the COVID-19 pandemic (2015–2019) confirmed increasing trends in TB and PTB diagnosis (AIC: 3.8% and 3.7%, respectively) in all regions. We observed a non-stationary and decreasing trend in TB diagnosis (p-value = 0.06), after establishment of the pandemic in March 2020. Similarly, there was a non-stationary and decreasing trend in PTB diagnosis (p-value = 0.066)
Souza, 2022 [27]/ Master's dissertation/ Brazil	Time series analysis	To analyze the behavior of the TB incidence rate from 2010 to 2019 in the five Brazilian states with the largest population and highest TB incidence rates in each region in 2019, in addition to the impact of the pandemic on TB notification in 2020 in the country.	Not cited.	TB notifications and incidence rates.	The incidence rate of TB in the country generally decreased, but began to increase again around 2016. No federative unit predicted a downward trend in the rate. It was possible to observe that the impact occurred mainly in the first months after the arrival of the coronavirus, when the symptoms were still unknown; health services were focused on Covid-19 actions and social isolation made it difficult to diagnose and report new cases of TB.
Ding *et al.*, 2021 [28]/ Infection and Drug Resistance/ China	Study with Bayesian structural time series analysis	To analyze the impacts of anti-Covid-19 measures on the reductions in TB case notifications and estimate whether the TB epidemic is on track to achieve the 2030 and 2035 goals of achieving a world free of the disease.	20,549,724 cases reported between 2005 and 2020 (94,807 cases/100,000 inhabitants annually).	Reporting rate ("incidence").	TB incidence was declining during 2005–2020, with a mean annual percentage change of -3.186 (95%CI -4.083 to -2.281), showing a peak in March–April and a minimum in January–February each year. We also assessed a mean monthly reduction of 14% (95%CI 3.8% to 24%) in case notifications from January to December 2020 due to Covid-19 (causal effect probability = 99.684%, P = 0.003). There was a peak number of case notifications of 153,347 (115,764 per 100,000 population) in 2008 and a minimum number of notifications of 914,265 (65,030 per 100,000 population) in 2020. The expected numbers indicated an average monthly reduction in TB case notifications of 29% (95%CI 11% to 48%) from January to March 2020, 15% (95%CI 1.6% to 31%) from January to June 2020 and 14% (95%CI 3.8% to 24%) from January to December 2020 as a consequence of the COVID-19 outbreak.
Crowder *et al.*, 2021 [29]/ Journal of Clinical Tuberculosis and Other Mycobacterial Diseases/ The Philippines	Study with interrupted time series analysis	To evaluate the effect of community quarantine policies due to Covid-19 on notifications of drug-susceptible tuberculosis (DS-	72,966 cases reported before quarantine; 1,156 cases reported on the day quarantine was implemented and 118,796 after implementation.	TB case notifications.	There was a statistically significant decline in daily TB notifications during the 49 days prior to implementation of community quarantine (0.3% decline per day, 95%CI 0.1–0.4); after quarantine, there was a significant drop and a steeper decline in daily TB notifications, resulting in 44.6% (95%CI 38.3–50.1) fewer daily notifications in the 60 days following quarantine. DS-TB case notifications never returned to pre-quarantine levels during 2020. In the 18 days following implementation of quarantine, TB notifications decreased by

Authors, Year / Journal / Country	Study design	Objective(s)	Sample size and characteristics	Indicator analyzed	Study results
		TB) cases in the Philippines.			74.8% from pre-quarantine levels. The immediate decline in TB case notifications was greater for clinically diagnosed cases (48.9%, 95%CI 43.6–53.7) than for bacteriologically confirmed cases (38.2%, 95%CI 30.7–44.9), but the difference was not statistically significant (p = 0.12).
Kamakoli *et al.*, 2021 [30]/ mSphere/ Iran	Study that analyzed temporal trends	To investigate the short-term effects of lockdowns due to the Covid-19 pandemic on tracking and detection of tuberculosis (TB) patients in Tehran, Iran.	897 suspected cases of TB in 2016; 746 in 2017; 724 in 2018; 617 in 2019 and 419 in 2020 - between February and June of those years.	Number of patients with suspected TB and positive culture.	The number of suspected TB patients between March and April 2020 (concurrent with the outbreak of the COVID-19 epidemic in Iran) had a sharp decrease compared to previous years (65.9% and 71.4% decrease, respectively). The trend of suspected TB patients in 2020 was -4.18 (95%CI = -6.37, -1.77; P-value = 0.001). Furthermore, there was an increase in the number of suspected TB patients in March compared to February in 2016, 2018, and 2019, but in 2020 we saw a sharp decrease in the number of suspected TB patients in the same previous period. The lowest number of patients with suspected TB was recorded (55.6% reduction) on all months of the Covid-19 outbreak (March to June 2020) compared to previous years (2016 to 2020). Furthermore, the number of positive TB cultures in March 2020 was the lowest compared to the same month in all previous years (76.5% reduction).
Oliveira *et al.*, 2021 [31]/ Revista Interdisciplinar de Pesquisa e Inovação/ Brazil	Ecological study with temporal trend analysis	To compare the number of reported tuberculosis cases in the State of Sergipe during the Covid-19 pandemic and in the period from 2010 to 2019 through a time series.	8,469 cases between 2010 and 2019 and 1,166 cases between March 2019 and August 2020.	TB case notifications.	Prior to the Covid-19 pandemic, there were peaks in TB in 2013 and the series was showing signs of growth. However, a decreasing trend was observed in the number of reported cases in two regions studied, but the notifications were stationary in five of them.
Soko *et al.*, 2021 [32]/ Emerging Infectious Diseases/ Malawi	Study with interrupted time series analysis	To estimate the number of missed TB case reports; determine whether missed reports were affected by sex, health facility or HIV status; and investigate and explain the underlying causes of TB underreporting.	10,274 cases reported in Blantyre-Malawi between June 2016 and December 2020, with 9,199 people reported in the pre-Covid-19 period (June 2016 to December 2020).	TB case notification rates.	Trends in Blantyre's annual TB notification rates declined by approximately 1% per month during June 2016 to March 2020 (pre-Covid-19), peaking at 405 cases/100,000 people in November 2016 and declining to 137 cases/100,000 people in October 2019. A total of 9,199 TB cases were reported in Blantyre during the pre-Covid-19 period (June 2016 to December 2020). The declaration of a national COVID-19 disaster led to a steep 35.9% (95%CI 22.1%–47.3%) decline in TB notifications in April 2020. During April–December 2020, a total of 1075 TB cases were notified (196 cases/100,000 people-year). However, in the absence of COVID-19, we would have expected 1,408 (95%CI 1366–1451) TB cases to have been notified, equivalent to a rate of 221 cases/100,000 people-year. Therefore, we estimate that COVID-19 led directly and indirectly to a loss of 333 (95%CI 291–376) notifications, representing a 23.7% (95%CI 21.4%–26.0%) reduction in TB notifications.