The impact of COVID-19 on the cascade of care for tuberculosis: A systematic review

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Declaration of Originality

I, Tomiwa T. Fapohunda hereby declare that this manuscript 'The impact of COVID-19 on the cascade of care for tuberculosis: A systematic review' is my original work and it has not been submitted to any academic institution for any examination or degree. All information derived from published literatures and sources were duly referenced and acknowledged in the text.

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Date: 7 September 2022

Abstract

Background

Globally, the effect of the coronavirus pandemic on tuberculosis (TB) cascade of care is not well described.

Objectives

To describe the impact of the 2019 coronavirus disease (COVID-19) pandemic on the TB care cascade, particularly on testing, case notifications and treatment of TB.

Methods

In this systematic review, the Cochrane library, Scopus, CINAHL, Ebscohost, and PubMed databases were comprehensively searched from December 1st, 2019, the onset of the pandemic, till May 5th, 2022, without language restrictions. Eligible studies were observational studies documenting changes in the TB cascade of care one year before and one year during the COVID-19 pandemic. The authors could not conduct a meta-analysis due to the expected differences in the contexts of the included studies, thus, a narrative synthesis was conducted. The Hoy et al.'s (2012) risk of bias tool was used for the quality assessment.

Results

Twenty-seven studies from Asia, North America, Africa, South America, and Europe were included. TB screening suspected cases decreased between 1.3% and 49.5% (n= 5 studies), and multidrug resistance tuberculosis (MDR-TB) screening decreased by 17% in new patients and by 15% in existing patients (1 study). The diagnostic delay increased by11 and 45 days and 25.1% and 60% (2 studies), contact tracing decreased by 36.1% (1 study), case notification decreased between 2.9% and 63.3% (18 studies) and positivity rate increased between 0.1% and 4.5% (4 studies). General and community detection rates decreased by 11.8% and 44.7%, respectively (1 study), clinically diagnosed TB decreased between 10.4% and 46.0% (5 studies), presumptive TB diagnoses decreased between 12.8% and 45.6% (4 studies) and pulmonary TB diagnoses decreased between 20.0% and 50.7% (2 studies). Treatment enrolment decreased between 15.7% and 35.0% (4 studies), the diagnostic and treatment delay increased by 28 and 36 days, respectively, treatment

completion decreased by 8.0% (1 study) and the treatment success rate decreased between 0.1% and 17.0% (7 studies).

Conclusion

These results suggest that the pandemic likely had a detrimental impact on the TB care cascade. In future pandemics, stakeholders and governments must protect the care cascade of infectious diseases like TB and other diseases. The results of this study must be applied with caution since only observational studies, mostly without standardized population data, were included.

Systematic review registration: PROSPERO: CRD42021272456

Key Words

Tuberculosis, case notification, testing, treatment, cascade of care, and COVID-19

Opsomming

Agtergrond

Wêreldwyd word die uitwerking van die koronaviruspandemie op die tuberkulose (TB)-kaskade van sorg nie goed beskryf nie.

Doelwitte

Om die impak van die 2019-koronavirussiekte (COVID-19)-pandemie op die TB-sorgkaskade te beskryf, veral op toetsing, gevallekennisgewings en behandeling van TB.

Metodes

In hierdie sistematiese oorsig is die Cochrane-biblioteek, Scopus, CINAHL, Ebscohost en PubMed-databasisse omvattend deursoek vanaf 1 Desember 2019, die aanvang van die pandemie, tot 5 Mei 2022, sonder taalbeperkings. Kwalifiserende studies was waarnemingstudies wat veranderinge in die TB-kaskade van sorg een jaar voor en een jaar tydens die COVID-19-pandemie gedokumenteer het. Die skrywers kon weens die verwagte verskille in die kontekste van die ingeslote studies nie 'n meta-analise doen nie, en daarom is 'n narratiewe sintese uitgevoer. Die Hoy et al. (2012) se risiko van vooroordeel-instrument is gebruik vir die kwaliteitsbeoordeling.

Resultate

Sewe-en-twintig studies uit Asië, Noord-Amerika, Afrika, Suid-Amerika en Europa is ingesluit. Vermoedelike gevalle van TB-sifting het tussen 1,3% en 49,5% afgeneem (n = 5 studies), en multi-middelweerstandigheid tuberkulose (MDR-TB) sifting het met 17% afgeneem by nuwe pasiënte en met 15% in bestaande pasiënte (1 studie). Die diagnostiese vertraging het met 11 en 45 dae toegeneem en 25,1% en 60% (2 studies), kontakopsporing het met 36,1% afgeneem (1 studie), gevallekennisgewing het tussen 2,9% en 63,3% afgeneem (18 studies) en positiwiteitskoers het tussen 0,1% en 4,5% toegeneem (4 studies). Algemene en gemeenskapsopsporingsyfers het onderskeidelik met 11,8% en 44,7% afgeneem (1 studie), klinies gediagnoseerde TB het tussen 10,4% en 46,0% afgeneem (5 studies), vermoedelike TB-diagnoses het tussen 12,8% en 45,6% afgeneem (4 studies) en pulmonale TB-diagnoses het tussen 20,0% en 50,7% afgeneem (2 studies). Behandelingsinskrywing het tussen 15,7% en

35,0% afgeneem (4 studies), die diagnostiese en behandelingsvertraging het onderskeidelik met 28 en 36 dae toegeneem, die voltooiing van die behandeling het met 8,0% afgeneem (1 studie) en die sukseskoers van die behandeling het tussen 0,1% en 17,0% gedaal (7 studies).

Gevolgtrekking

Hierdie resultate dui daarop dat die pandemie waarskynlik 'n nadelige impak op die TB-sorgkaskade gehad het. In toekomstige pandemies moet belanghebbendes en regerings die versorgingskaskade van aansteeklike siektes soos TB en ander siektes beskerm. Die resultate van hierdie studie moet met omsigtigheid toegepas word, aangesien slegs waarnemingstudies, meestal sonder gestandaardiseerde bevolkingsdata, ingesluit is.

Sleutelwoorde

Tuberkulose, saakkennisgewing, toetsing, behandeling, kaskade van sorg en COVID-19

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I want to thank God for giving me the mental, physical and emotional strength to complete this degree successfully despite all trials and huddles. My testimony on the completion of this study is that 'I can do all things through Christ that strengthens me (Phil.4:13)' and 'With God, all things are possible (Matt.19:26)'. I would like to say a big thank you to my Supervisor (Dr Tawanda Chivese) for his encouragement, guidance and for believing in me all through the trying times.

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1. Introduction

TB remains one of the deadliest infectious diseases in the world, with about 1.8 Billion person infected in the year 2018, and 1.5 million deaths due to TB per annum, most deaths being in the TB high burden countries [1–3]. The countries with the highest burden of TB are Indonesia, India, China, Pakistan, the Philippines, Nigeria, South Africa (SA) and Bangladesh [1]. In 2014, the 67th World Health Assembly endorsed the End TB strategy, which envisions a TB-free society with zero TB disease, suffering, and death by 2035 [4]. It aimed to reduce TB deaths and incidence by 90% and 80%, respectively, and eliminate the catastrophic costs of the affected households by 2030 [4]. Several countries were taking steps to achieve this when the COVID-19 pandemic began. Consequently, this led to many difficulties and changes globally in different countries' health systems [5].

In many countries, the policy responses to the COVID-19, such as restricted movement and lockdowns, disrupted the provision of other healthcare services for both infectious and non-communicable diseases. Hence, this might have negatively impacted the health systems service delivery [6] as several countries shifted policies and priorities to combating the COVID-19 pandemic, and, in many cases, at the expense of other health conditions [2]. The health systems even in developed countries such as Germany, US, Italy, India, and United Kingdom (UK) were overwhelmed with the COVID-19 pandemic management, that their hospital bed space did not accommodate all the affected patients, causing them to turn away of patients with pre-existing diseases(7).

The TB cascade of care was especially vulnerable to disruption as it requires contact between care workers and infected individuals during each of the care stages, from screening to treatment. The TB care cascade is a model of care for the sequential progression of infected individuals from screening, testing and diagnostics, until successful treatment of the disease [7]. The TB care cascade comprises of screening and testing, diagnosis and confirmation of active TB, TB notification, treatment onset, completion and keeping records patient that were free from TB and those who were lost to follow-up [8]. The negative cascade is TB recurrence, MDR and XDR-Tb, incomplete treatment, relapse and re-treatment. TB screening is the process of detecting active Tb which the next step is to inform the patients about their health status (positive or negative active

TB), TB notifications which are subsequently crucial for the treatment initiation, follow-up and contact tracing to prevent TB transmission. Patients' follow-up and monthly hospital visits to assess treatment and complete their treatment till they are free from the disease will aid the achievement of SDG goal 3 which is to promote good health and well-being [9]. Possibly, the COVID-19 pandemic may have disrupted some of these components of the cascade including the follow-up, contact tracing, monthly clinic visits, check-ups and treatment completion processes since most health professionals that were responsible for this were busy with COVID-19 patients.

Additionally, centres for TB management in some countries were changed to COVID-19 testing and treatment centres [10]. Two studies from Ethiopia (Addis Abbaba) and India (South Karnataka) reported a decrease in TB screening and case notification due to the conversion of TB treatment centres into COVID-19 isolation and treatment centres [11,12]. Also, a letter to the editor from South Africa, claimed that TB case notifications were reduced by more than 40% [13]. Yet, the global data remain scarce and uncollated.

Although the effects of the COVID-19 pandemic and the response from countries remain understudied, some evidence suggests that the COVID-19 response might have impeded the TB cascade of care as global priorities had shifted to COVID-19 management. This systematic review investigated the effect of the COVID-19 pandemic on the TB care cascade. Specifically, this study compared TB screening, notification, and treatment before and during the COVID-19 pandemic.

2. Methods

2.1. Study design and eligibility criteria

The design and methods of this descriptive systematic review were based on the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines [14]. The protocol of the systematic review is registered on the International prospective register of systematic reviews (PROSPERO, ref CRD42021272456).

2.2. Information sources

The COCHRANE Library, Scopus, CINAHL, Ebscohost, and PubMed databases were searched, without language restriction, and the references of each included study were also searched manually.

2.3. Search strategy

The database search was from December 1st, 2019, to October 1st, 2021, and an updated search was conducted from September 1st, 2021, to May 5th, 2022. The full search strategy and terms are in Supplementary Table 1.

2.4. Study selection and eligibility

The study records from the searches were exported to Endnote referencing software for duplicate removal and then exported to Rayyan systematic review management website (https://www.rayyan.ai/) for initial screening using the title and abstract screening. Two reviewers conducted the screening independently, any conflicts were addressed via consensus, and a third reviewer resolved discrepancies when consensus was not reached. After the initial selection, full text assessment of eligibility was carried by two independent authors.

Studies were included if they were observational studies such as cohort, cross-sectional, case series, interrupted time series and population-based studies that quantitatively described the number or percentage change of TB screening, case notification, diagnosis, and treatment one year before and one year during the pandemic. Qualitative studies, reviews, case studies, letters to the editor and commentaries were excluded.

2.5. Data extraction

Two reviewers conducted the data extraction independently, and a third reviewer resolved the discrepancies. The extracted data were study title, authors, year of publication and data collection, objectives, country of study, lockdown dates, sample size, settings, study design, data on TB screening, MDR-TB screening in new and existing patients, positivity rate and contact tracing. Other data included detection rate, case notifications, treatment enrolment, diagnostic and treatment delay, clinical diagnosis, presumptive, pulmonary, paediatric, active, latent, and RR/MDR-TB rate, new cases, outpatients, discharged patients and treatment completion, success, and failure. Data on loss to follow-up, re-treated cases, patients not evaluated, sensitive TB, and TB-related deaths before and during the COVID-19 pandemic were also extracted.

2.6. Study outcomes extracted

This study had multiple outcomes of interest based on each level of the cascade of care. These outcomes included TB screening, MDR-TB screening in new and existing patients, positivity rate, diagnostic delay, contact tracing, detection rate, case notifications, treatment delay and clinical diagnosis. Presumptive, pulmonary, paediatric, active, latent, and sensitive TB, TB new cases, outpatients and discharged inpatients, treatment enrolment, completion, success, and failure, RR/MDR-TB rate, loss to follow-up, re-treated cases, patients not evaluated and TB death. For each study, the percentage change in the number of events was calculated by subtracting the pre and during COVID-19 events and expressing it as a percentage of the pre-COVD19 period. Most studies did not report the populations during the two intervals, so the results could not be standardized.

2.7. Assessment of risk of bias in included studies

The Hoy risk of bias tool was used to assess the risk of bias of the 27 included studies. Two reviewers independently assessed the risk of bias in the included studies using the Hoy et al. (2012) risk of bias tool [15]. They resolved conflicts through consensus, and the third reviewer resolved the outstanding discrepancies. The tool by Hoy et al. has 10 questions assessing the studies' external and internal validity. Items 1 to 4 assess a study's external validity; items 5 to 9 assess internal validity and item 10 assesses biases related to the analysis. Each of these items were assessed for the included studies and used to assess the quality of the studies, with “Yes” represented by a “1” and “No” by a “0”.

2.8. Synthesis methods

The characteristics of included studies and the risk of bias were described in a narrative approach. For the main outcomes, we could not conduct the meta-analysis due to the expected differences in the contexts of the included studies, including different lockdown dates and restriction levels, health systems, policies and pre-existing TB burden and policies. Findings were summarized using tables and grouping together similar outcomes across studies A narrative descriptive synthesis of the percentage change in the number of events was therefore conducted. Tableau software [16]

was used to create the map of the countries included and the number of studies embedded in each country.

2.9. Ethics approval

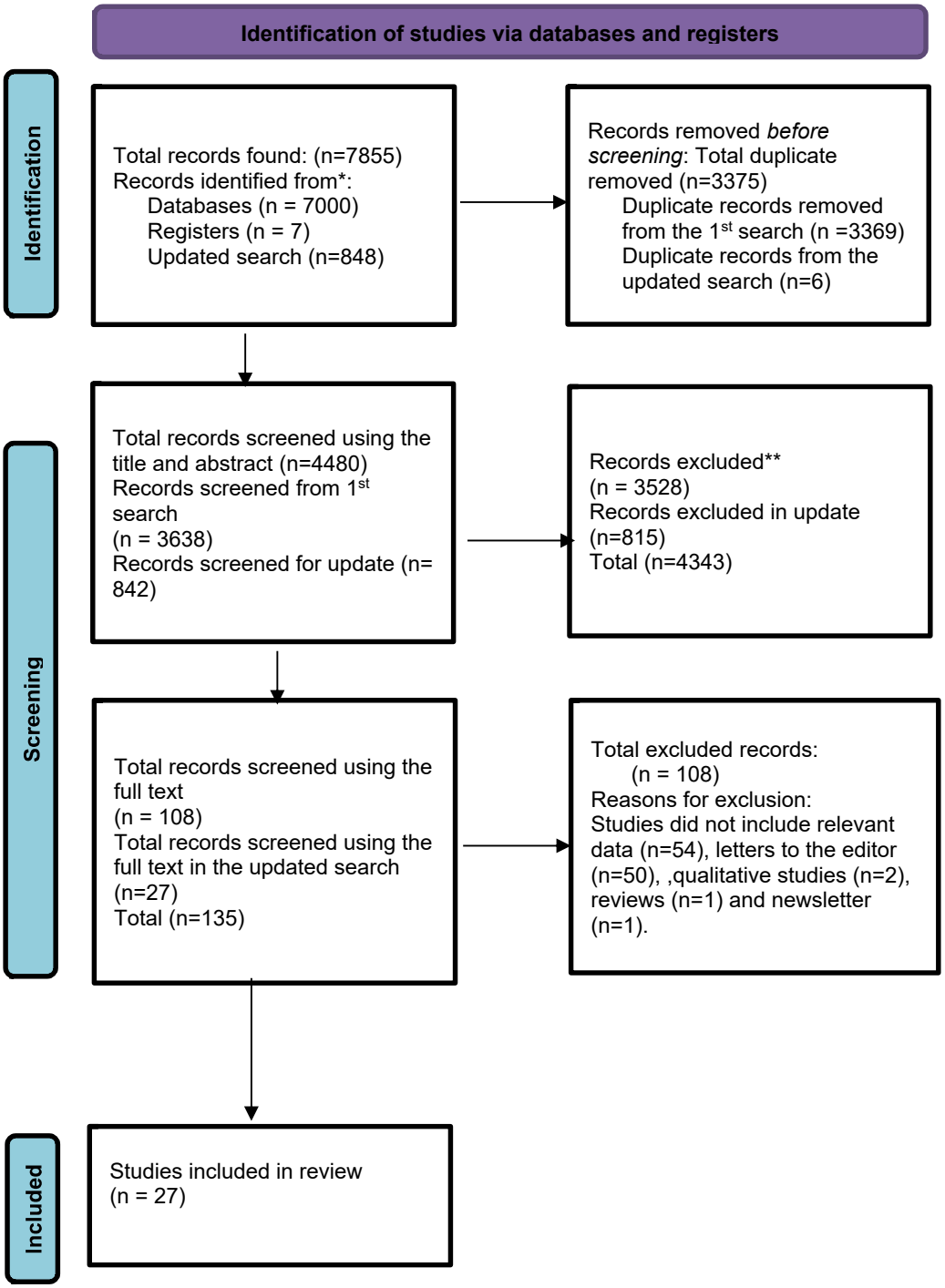
This systematic review used data from published studies and aggregated data; thus, ethics approval was not required.

3. Results

3.1. Study selection

Overall, 7855 records were found from the electronic database and other citation searches, and subsequently 3375 duplicates were removed. Out of the 4480 records, 4343 records were excluded using the title and abstract only. The remaining 135 records were screened using the full text and 109 excluded, resulting in 27 included studies [11,12,17–41] (Figure 1). The reasons for excluding some studies were because studies were, that some studies did not include relevant data required for this systematic review (n=54), letters to the editor (n=50), qualitative (n=2), newsletters (n=1) and review (n=1) (Figure 1).

Figure 1:Flowchart of the search and inclusion

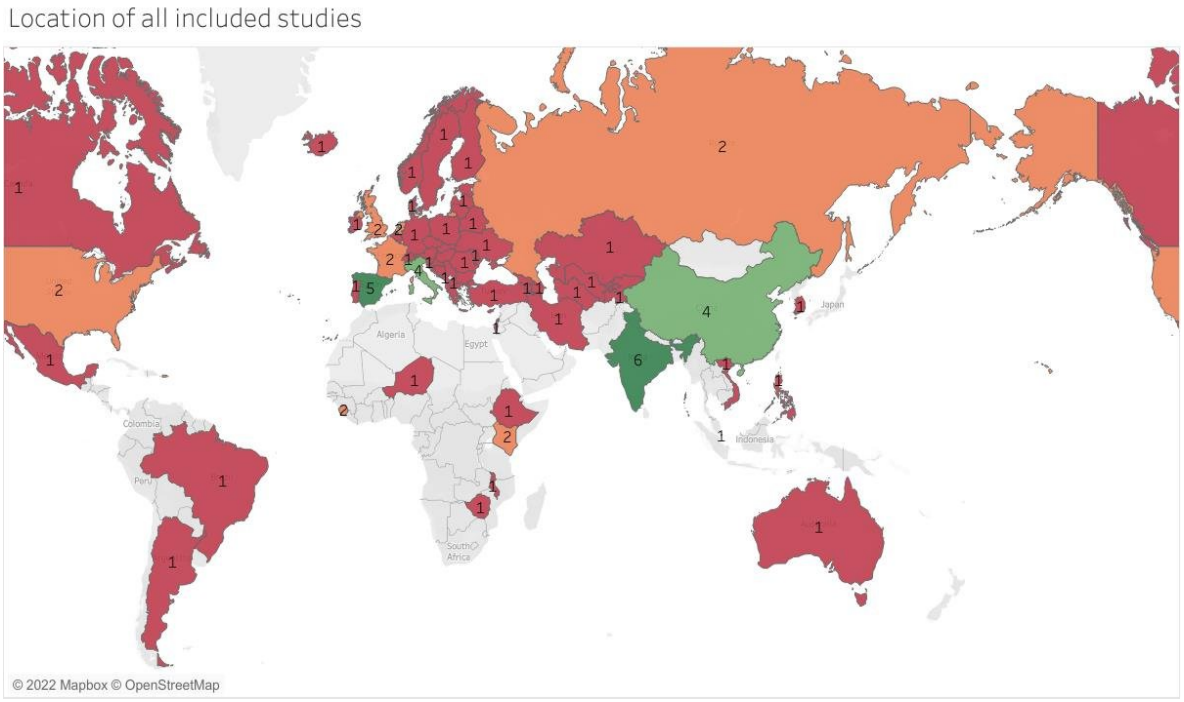


3.2. Study characteristics

The included studies were from all regions, as shown on the map in Figure 2. The studies were from the following countries in Africa; Ethiopia, Sierra Leone, Niger, Kenya, Zimbabwe, Malawi, in Asia; Vietnam, India, Singapore, Philippines, China, Iran, Korea, Azerbaijan, South Korea, Israel, Kazakhstan, Kyrgyzstan, Tajikistan, Turkmenistan and Uzbekistan, Australia, South American countries of Brazil and Argentina, North America countries of the USA, Canada and Mexico. There were also studies from Europe countries, names; Spain, United Kingdom, Russia, Netherlands, Italy, France, Armenia, Georgia, Portugal, Moldova, Turkey, Ukraine, Albania, Austria, Belarus, Belgium, Bosnia and Herzegovina, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Montenegro, Norway, Poland, Romania, Serbia, Slovakia, Slovenia, Spain, Sweden, Switzerland, The former Yugoslav and Republic of Macedonia.

The study designs of the included studies were surveillance report (n=1 study) [9], longitudinal before and after time series (n=12 studies) [12,17,22,27–29,31–33,35–37], cohort (n=12 studies) [11,18–20,25,26,30,34,38–40] and cross-sectional studies (n=3 studies) [21,23,41]. Ten studies [11,17,23,24,27,29,31,33,34,36] had national representation while others were provincial, and community based. About six studies reported some summary measures of age [28,30–32,35,37], but the other twenty studies did not state the age of included participants. The characteristics of the included studies are shown in study Supplementary Table 2.

Figure 2: Location of all included studies- the numbers indicate the total number of included studies from each country



3.3. Risk of bias in studies

Twenty-five studies had acceptable scores on the Hoy risk of bias tool, between 6 to 9, and 2 studies had moderate scores of 4 to 5. The risk of bias assessment is shown in Supplementary Table 3.

Most of the studies scored well on items that measured internal validity with most studies having no issues with selection bias (selection was from an appropriate sampling frame and the response rate was good but a deficiency noted here is that most studies did not use random selection), or information bias (data were measured directly and not by proxy, the same data collection methods were used for all participants, case and outcome definitions were clear). However, some of the studies had deficiencies in external validity. For item 1, 9 studies [11,23,24,27,29,31,33,34,36] had a close representation of the country's national population while the remaining studies did not have a close representation of their countries since they were conducted in provinces and communities. For item 2, the sampling frame in 22 of the 27 studies [11,12,17,19–21,23–25,27–

34,36–40] closely represented the target population. For item 3, only 5 out of the 27 studies [17,27,29,33,34] randomly selected their samples.

3.4. Impact of COVID-19 on TB and MDR screening and testing

3.4.1 Changes in screening

Three studies stated decrease between 1.3% and 49.5% in China [28] and India [12,35] while one study reported an increase of 14.1% in Ethiopia [11]. One study from China reported a 15.0% decrease in MDR-TB screening in existing patients and a 17% decrease in newly diagnosed TB cases, respectively [28] (Table 1).

Table 1: Change in TB and MDR-TB screening, case notification, clinically diagnosed and presumptive TB.

Study	Country	TB screening	Case notifications	Clinically diagnosed TB	Presumptive TB
Soko 2021 [17]	Malawi (All provinces)	Not reported	35.9% reduction in TB notifications in April 2020 as compared to the pre-pandemic numbers in April 2016 to March 2020 and April 2020.	Not reported	Not reported
Liu 2020[28]	China (Jiangsu Province)	15.0% decrease in MDR-TB screening in existing TB cases and a 17.0% decrease in MDR TB between January 2015 to December 2019 and January to May 2020.	36.5% decrease between January 2015 to December 2019 and January to May 2020.	Not reported	Not reported
Srivastava 2021[35]	India (Gurgaon)	24.9% reduction from March 2019 to December 2019 and January 2020 to October 2020.	15.9% increase between March 2019and October 2020.	Not reported	Not reported

Hazra 2021 [12]	India (South Karnataka)	49.5% decrease between January 2019 and December 2020.	49.1% decrease between January 2019 and December 2020.	Not reported	Not reported
Geng 2021[22]	China (Henan province)	44.5% decrease between January to December 2019 and January to December 2020.	Not reported	Not reported	Not reported
Arega 2022 [11]	Ethiopia (Addis Ababa)	14.1% increase between April 2019 to March 2020 and April 2020 to March 2021.	11% decrease between April 2019 to March 2020 and April 2020 to March 2021.	10.4% decrease between April 2019 to March 2021.	Not reported
Hasan 2022 [34]	Vietnam (all provinces)	1.3% decrease between January 2019 to December 2019 and January 2020 to December 2020.	8.2% decrease between January 2019 to December 2019 and January 2020 to December 2020.	Not reported	Not reported
Kwak 2020 [36]	South Korea (all provinces)	Not reported	28.9% decrease between the first 18 weeks of 2015 to 2019 and the first 18 weeks of 2020.	Not reported	Not reported
Thekkur 2021 [39]	Malawi (Lilongwe)	Not reported	19.1% decrease between March 2019 and February 2020 to March 2020 and February 2021.	17.1% decrease between March 2019 and February 2020 to March 2020 and February 2021.	45.6% decrease between March 2019 and February 2020 to March 2020 and February 2021.
Dara 2021 [41]	48 European countries	Not reported	35.5% decrease between January to June 2019 and January to June 2020.	Not reported	Not reported
Lakoh 2021 [18]	Sierra Leone (Free Town)	Not reported	2.9% decrease between January 2019 to September 2019 and January 2020 to September 2020.	20.6% decrease between January 2019 to September 2019 and January 2020 to September 2020.	12.8% decrease between January 2019 to September 2019 and January 2020 to September 2020.
Min 2020 [20]	Korea (all provinces)	Not reported	19.3% decrease between July 2019 to June 2020.	Not reported	Not reported
Thekkur 2021 [40]	Zimbabwe (Harare)	Not reported	33.7% decrease between March 2019-February	46.0% decrease between March 2019 -	40.6% decrease between March 2019 -

			2020 to March 2020- February 2021.	February 2020 to March 2020 -February 2021.	February 2020 to March 2020 -February 2021.
Fei 2020 [23]	China	Not reported	24.6% decrease between January – December 2017 to 2019 and January - December 2020.	Not reported	Not reported
Feldman 2021 [9]	United States of America (USA) (all States)	Not reported	19.6% decrease from January - December 2019 and January - December 2020.	Not reported	Not reported
Kamakoli 2021 [25]	Iran (Tehran)	Not reported	32.1% decrease between Feb-June 2016- 2019 to Feb-June 2020.	Not reported	Not reported
Arentz 2022 [27]	India (all provinces)	Not reported	63.3% decrease between January 2017 to April 2021.	Not reported	Not reported
Filardo 2022 [29]	USA (US 50 states and the District of Columbia)	Not reported	8.7% increase between January 2011- December 2011 to January 2021- December 2021.	Not reported	Not reported
Golandaj 2021 [33]	India (all provinces)	Not reported	14.1% decrease between January to September 2019 and January to September 2020.	Not reported	Not reported
Mbithi 2021 [38]	Kenya (Nairobi)	Not reported	Not reported	22.1% decrease between March 2019 to February 2020 and March 2020 to February 2021.	31.2% decrease between March 2019 to February 2020 and March 2020 to February 2021.

3.4.2 Changes in diagnostic delay and contact tracing

Two studies, each from Italy [37] and India [30], reported 11 to 45 days and a 25.1% to 60.0% increase in TB diagnostic delay (Supplementary Table 4). One study from Spain [32] reported a 36.1% decrease in TB contact tracing (Supplementary Table 4).

3.5. Impact of COVID-19 on TB detection rates, diagnosis, and case notifications

3.5.1 Changes in detection rate and case notifications

Sixteen studies from China [22,28] , India [12,27,33], South Korea [36], Malawi [17,39], 48 European countries [41], Sierra Leone [18], Korea [20], Zimbabwe [40], USA [24], Iran [25], Ethiopia [11] and Vietnam [34] reported between 2.9% and 63.3% decrease in TB case notification (Table 1). Two studies from the USA [29]and India [35] reported an 8.7% and 15.9% increase in TB case notifications, respectively. A study from India [35] reported 24.9% decrease in TB positivity rate [35], while 3 studies from Kenya [38], Malawi [39], and Zimbabwe [40] reported between 0.1% and 4.5% increase in positivity rates. Additionally, a study from Ethiopia [11] reported 44.7% and 11.8% decrease in community and general detection rates, respectively (Supplementary Table 4).

3.5.2 Changes in clinical diagnosis and presumptive TB

Five studies from Kenya [38], Malawi [39], Sierra Leone [18], Zimbabwe [40] and Ethiopia [11] reported between 10.4% and 46.0% decrease in clinically diagnosed TB. Four studies from Kenya [38], Malawi [39], Sierra Leone [18], and Zimbabwe [40] reported between 12.8% and 45.6% decrease in presumptive TB (Table 1).

3.5.3 Changes in latent, active and pulmonary TB

Two studies from India [30] and Spain [32] reported between 20.0% and 50.7% decrease in pulmonary TB, respectively. One study from India [33] (Table 2) reported 14.1% decrease in pediatric TB [33] (Table 2). Two studies from Spain [21] and Canada [31] reported between 12.2% and 29.0% decrease in active TB cases (Table 2). Two studies from Canada [31] and Spain [21] reported 30.0 to 66.0% increases in latent TB (Table 2).

Table 2: Change in pulmonary, active, latent and paediatric TB

Study	Country	Pulmonary TB	Active TB	Latent TB	Paediatric TB
Gandhi 2022 [30]	India (Northern India)	20.0% decrease between January 1st, 2020 to June 30th, 2020.	Not reported	Not reported	Not reported
Godoy 2022 [32]	Spain (Catalonia)	50.7% decrease between January 2019 to February 2020 and March 2020 to April 2021.	Not reported	3.9% increase between January 2019 to February 2020 and March 2020 to April 2021.	Not reported
Golandaj 2021 [33]	India (all provinces)	Not reported	Not reported	Not reported	14.1% decrease between January to September 2019 and January to September 2020.
Aznar 2021[21]	Spain (Catalonia)	Not reported	12.2% decrease between March 15th - June 30th2019, and March 15th – June 30th 2020.	3.9% decrease from March 15th -June 30th 2019, and March 15th – June 30th 2020.	Not reported
Geric 2021 [31]	Canada (Montreal and Toronto)	Not reported	16.0 to 29.0% increase between January to December 2005 and January to December 2020.	30.0% to 66.0% increase between January to December 2005 and January to December 2020.	Not reported

3.5.5 Changes in TB new cases

A multinational study [26] from Australia, the Philippines and UK and a study from China [19] reported between 6.3% and 75.6% increase in TB new cases. Other countries in the multinational study [26], such as Singapore, France, Italy, Netherlands, Russia, Spain, Mexico, Argentina, Brazil, Kenya, Niger and Sierra Leone, reported between 2.6% and 48.4% decrease in new TB cases (Supplementary Table 5).

3.5.6 Changes in outpatients

A multinational study [26] for Australia, Singapore, France and Spain reported between 1.0% and 40.1% increase in TB outpatients. However, other countries in the study, such as India, Philippines, Italy, Russia, UK, Mexico, Argentina, Brazil, Niger and Sierra Leone, reported between 0.5% and 71.6% decrease in TB outpatients [26] (Supplementary Table 5).

3.6. Impact of COVID-19 on TB treatment

3.6.1 Changes in treatment enrolment and treatment delay

About 4 studies in Kenya [38], Malawi [39], Zimbabwe [40], and 48 European countries [41] reported between 15.7% and 35.0% decrease in TB treatment enrollment and RR/MDR-TB treatment enrollment (Table 3). A study from China [28] reported 8.0% decrease in treatment completion (Table 3). Two studies from India [30] and Italy [37] reported between 1 and 4 days and 1% and 6.2% increase in TB treatment delay. The latter study also reported between 28 and 36 days and 52.0% increase in diagnostic and treatment delay [30] (Supplementary Table 4).

Table 3: Change in TB treatment enrolment and completion

Study	Country	TB Treatment enrolment	Treatment success rate	Treatment completion
Mbithi 2021[38]	Kenya (Nairobi)	35.0% decrease between March 2019 to February 2020 and March 2020 to February 2021.	2.0% increase between March 2019 to February 2020 and March 2020 to February 2021.	Not reported
Thekkur 2021[39]	Malawi (Lilongwe)	15.7% decrease between March 2019 - February 2020 to March 2020 -February 2021.	0.1% decrease between March 2019 - February 2020 to March 2020 -February 2021.	Not reported
Dara 2021[41]	48 European countries	33.5% decrease between April to June 2020.	Not reported	Not reported
Thekkur 2021[40]	Zimbabwe (Harare)	19.1% decrease between March 2019 - February 2020 to March 2020 -February 2021.	11.6% decrease between March 2019 - February 2020 to March 2020 -February 2021.	Not reported

Liu 2020[28]	China (Jiangsu province)	Not reported	Not reported	8.0% decrease between January 2015 to December 2019 and January to May 2020.
Lakoh 2021 [18]	Sierra Leone (Free Town)	Not reported	15.7% increase between January 2019 to September 2019 and January 2020 to September 2020.	Not reported
Min 2020 [20]	Korea (all administrative provinces)	Not reported	5.9% decrease between July 2019 to June 2020.	Not reported
Arega 2022 [11]	Ethiopia (Addis Abba)	Not reported	17.0% decrease between April 2019 to March 2020 and April 2020 to March 2021.	Not reported
Hasan 2022 [34]	Vietnam (all provinces)	Not reported	0.3% decrease between January 2019 to December 2019 and January 2020 to December 2020.	Not reported

3.7. Impact of COVID-19 on TB treatment outcomes

3.7.1 Changes in TB treatment success rate

Two studies from Kenya [38] and Sierra Leone [18] reported between 2.0% and 15.7% increase in TB success rate, respectively. Five studies from Malawi [39], Korea [20], Zimbabwe [40], Ethiopia[11] and Vietnam [34] (Table 3) reported between 0.1% and 17.0% decrease in treatment success rate before and during the COVID-19 pandemic.

3.7.2 Changes in discharged inpatients

Two studies reported data on this outcome [26,35]. A multinational study [26] reported between 6.1% and 63.0% decrease in discharged patients in Australia, India, the Philippines, France, Italy, Russia, Spain, UK and Brazil. In the same study [26] other countries such as Singapore, Netherlands and Mexico reported between 12.1% and 90.8% increase in discharged inpatients

during the COVID-19 pandemic compared to the period before the pandemic. The second study, from India, [35] reported a 15.0% increase in discharged TB inpatients [35] (Supplementary Table 5).

3.7.3 Changes in treatment failure and re-treated cases

Four studies, each from Kenya [38], Sierra Leone [18], Zimbabwe [40] and Vietnam [34] reported 0.2% and 64.2% decrease in TB treatment failure. China [19] reported 76.2% decrease in re-treated cases (Table 4).

3.7.4 Changes in loss to follow-up and patients that were not evaluated

Four studies, each from Kenya [38], Sierra Leone [18], Vietnam (all provinces) [34] and Zimbabwe [40] reported between 0.3% and 77.0% decrease and 0.3% increase in loss to follow-up (Table 4). Three studies from Malawi [39], Sierra Leone [18], and Zimbabwe [40] (Table 4) reported between 0.3% and 32.5% increase in TB patients that were not evaluated. Two studies from Kenya [38] and Vietnam [34] reported a 2.2% and 70.8% decrease in TB patients that were not evaluated (Table 4).

Table 4 Change in TB loss to follow-up, failed treatment, re-treated cases and patients not evaluated.

Study	Country	TB loss to follow-up	Failed treatment	Patients that were not evaluated	Re-treated cases
Mbithi 2021[38]	Kenya (Nairobi)	0.3% decrease between March 2019 to February 2020 and March 2020 to February 2021.	0.3% decrease between March 2019 to February 2020 and March 2020 to February 2021.	2.2% decrease between March 2019 to February 2020 and March 2020 to February 2021.	Not reported
Thekkur 2021 [40]	Zimbabwe (Harare)	0.3% increase between March 2019-February 2020 to March 2020- February 2021.	0.2% decrease between March 2019-February 2020 to March 2020- February 2021.	12.1% decrease between March 2019-February 2020 to March 2020- February 2021.	Not reported

Lakoh 2021 [18]	Sierra Leone (Free Town)	25.4% decrease between January 2019 to September 2019 and January 2020 to September 2020.	20% decrease between January 2019 to September 2019 and January 2020 to September 2020.	32.5% increase between January 2019 to September 2019 and January 2020 to September 2020.	Not reported
Hasan 2022 [34]	Vietnam (all provinces)	77% decrease between 2018 and 2020.	64.2% decrease between January 2019 to December 2019 and January 2020 to December 2020.	70.8% decrease between January 2019 to December 2019 and January 2020 to December 2020.	Not reported
Wang 2021 [19]	China	Not reported	Not reported	Not reported	76.2% decrease between 2018-2020.
Thekkur 2021[39]	Malawi (Lilongwe)	Not reported	Not reported	0.3% increase between March 2019-February 2020 to March 2020- February 2021.	Not reported

3.7.5 Changes in drug resistance (DR) occurrence

Three studies, each from India [35], 48 European countries [41] and Vietnam [34] reported between 9.9% and 33.5% decrease in RR-TB/MDR-TB (Supplementary Table 6). One study from Ethiopia [11] reported a 27.7% increase in the RR/MDR-TB rate. A study from China [22] reported a 5.1% increase in the MDR-TB rate, and a study from India [35] reported a 12.3% increase in sensitive TB (Supplementary Table 6).

3.7.6 Changes in death due to TB

Three studies from China [28], India [35] and Kenya [38] reported between 0.8% and 18.8% increase in TB-related deaths. Four studies from Malawi [39], Sierra Leone [18], Zimbabwe [40],

and Vietnam [34] reported between 0.6% and 67.0% decrease in TB deaths (Supplementary Table 6).

4. Discussion

This review which included 27 studies from various countries globally showed that COVID-19 appeared to have affected the cascade of care for TB. Findings from included studies, COVID-19 caused a decrease in TB screening and MDR-TB screening, although findings varied from about 1% to 50% decrease in screening. Findings from this review could not be compared to other reviews, as there was no other review on the effect of COVID-19 on TB screening, to the best of our knowledge. It is worth noting that decrease in TB and MDR TB screening could have multiple adverse effects on the health system due to lengthened case detection gap, diagnostic delay, and decreased linkage to care. Therefore, increasing TB prevalence, community transmission and incidence. [42–44]. Furthermore, decrease in screening may trigger a resurgence of the disease in countries were on the road to achieving suppression of the diseases. It is therefore important that care is taken, in future health emergencies, to protect key components of the cascade of care of infectious diseases such as TB.

Also, based on findings from included studies, it was discovered that COVID-19 caused a decrease in TB detection rates, diagnosis, and case notifications, although with varying findings from about 11.8% to 44.7%, 10.4% to 46.0% and 2.9% to 63.3% decrease in detection rate, diagnosis and case notifications, respectively. These findings could not be compared to other reviews since no other review on the effects of COVID-19 on TB detection rate, diagnosis and case notification has been conducted. Consequently, a decrease in detection rate, diagnosis and case notifications can have multiple side effects on the health system such as increasing TB prevalence, community transmission and incidence [45,46]. It is therefore important to take caution in future health emergencies to protect and maintain the key component of the care cascade of infectious diseases such as TB.

Additionally, findings from the included studies revealed that COVID-19 caused a decrease in treatment success rate, drug resistance rate and death due to TB, although findings varied from about 0.1% to 17.0%, 9.9% to 33.5% and 0.6% to 67.0%. These results might not be the true reflection of the situation as the death due to TB might have been unknowingly attributed to death

causes due to the reduction in screening and diagnosis. Likewise, the results of the drug resistance rate might have been reduced due to the restrictions and decrease in screening and diagnosis rates. These findings could not be compared to other reviews since no other review on the effects of COVID-19 on TB treatment success rate, drug resistance and deaths due to TB has been conducted.

The decreases in treatment success, drug resistance and death rate could have multiple adverse effects on the health system due to lengthened diagnostic and treatment delay, case notification and detection rate. Therefore, leading to an increase in incidence and community transmission and consequently an increase in clinical severity and death [46–48]. A key consideration is that these deficiencies in treatment success, drug resistance and death rate may trigger a resurgence of drug resistance and deaths in countries that were on the road to achieving the suppression of the disease before the pandemic. It is therefore crucial that care is taken, in future health emergencies, to protect key components of the care cascade of infectious diseases such as TB.

These results suggest that there was a reduction in TB case notifications, testing, diagnosis, and treatment, which could later cause worsening of TB cases, MDR-TB, XDR-TB and deaths due to the pandemic restrictions, especially in countries with a high prevalence of TB. The COVID-19 pandemic disrupted the TB care cascade, thus, delaying the achievement of the End TB strategy and the SDG goal 3 which could lead to an upsurge in the number of people living with TB, MDR-TB, XDR-TB and mortality. These results imply that the health workers were overwhelmed with COVID-19 cases and could not attend to TB screening and care. There is a need to integrate the TB care cascade into universal health coverage as this can be used to manage and identify missing TB patients [48]. Additionally, there is a great need to prioritize TB treatment and management amid pandemics to reduce the adverse after-effects, especially in countries with a high prevalence of TB.

The study limitations were that the included studies were observational, requiring cautious interpretation. Another limitation was the presence some confounding variables such as comorbidities and age in the studies. Also, the sample size, mean age and representativeness were not explicitly stated in most of the included studies. The authors could not conduct meta-analysis as anticipated due to the contextual differences of the included studies; thus, a narrative descriptive

synthesis was conducted. Also, some of the studies had small sample sizes, which would affect the percentage difference significantly. Comorbidities, age and other factors might have affected the results of the included studies. Another limitation was that many studies did not report population sizes at each point and therefore the analysis could not use standardized results. Due to the lack of data, we could not conduct the subgroup analysis on some of these probable confounders. The strength of this study includes using PRISMA guidelines for its conduct, a comprehensive search strategy to ensure the inclusion of every relevant study and the risk of bias assessment of each included study with Hoy et al. (2012) risk of bias tool.

5. Conclusion

Our findings indicate that TB screening, case notification, contact tracing and treatment enrolment all decreased during the COVID-19 era. These results are important as they can inform necessary preparations and decision-making for future pandemic preparedness. However, the results of this study must be applied with caution since only observational studies, mostly without standardized population data, were included. Therefore, it is advised that public health stakeholders and governments must protect the care cascade of infectious diseases in future pandemics to prevent the surge of diseases in health emergencies.

6. Other information

6.1. Registration and protocol

This systematic review protocol was registered on PROSPERO CRD42021272456.

6.2. Support

This study was not funded.

6.3. Competing interests

The authors of this study had no conflicts of interest.

6.4. Availability of data, code and other materials

Other study tables, data extraction sheets and lists of excluded studies are attached to this article as study supplementary documents and excel sheets.

6.5. Author's contributions

TF- conceptualization, formal analysis, data curation, visualization, investigation, project administration, methodology, software, original draft writing, editing and reviewing.

LM- conceptualization, formal analysis, risk bias assessment data curation, validation, investigation, visualization and review.

RT- formal analysis, data extraction, risk bias assessment and data curation.

TC- conceptualization, formal analysis, data curation, validation, investigation, project administration, methodology, supervision, visualization and review.

6.6. Abbreviations

COVID-19- 2019 Coronavirus disease

DR- Drug resistance

MDR- Multidrug resistance

n= Number of studies

PRISMA- Preferred Reporting Items for Systematic Reviews and Meta-Analysis

SA- South Africa

TB – Tuberculosis

UK- United Kingdom

USA- United States of America

WHO- World Health Organisation

XDR- Extensively Drug-Resistance

HIV- Human Immunodeficiency Virus

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Addendum A

Supplementary Table 1: Search terms

S/N	Search
#1 TB	Tuberculosis OR tuberculosis OR "Mycobacterium tuberculosis Infection" OR TB OR "active TB" OR "symptomatic TB" OR "asymptomatic TB" OR "latent TB" OR "MDR tuberculosis" OR "multidrug resistance TB" OR "XDR tuberculosis" OR "Extensive drug resistance TB" OR "MDR-TB" OR "multidrug resistance tuberculosis" OR "XDR-TB" OR "Extensive drug resistance tuberculosis" OR "tuberculosis infection" OR "TB infection" OR "Pulmonary tuberculosis" OR "Mycobacterium tuberculosis" Filters: from 2018-2021
#2 COVID-19	COVID19 OR covid19 OR coronavirus OR SARS OR sars OR severe acute respiratory syndrome OR covid19 OR cov2 OR COV2 OR "2019-nCoV" OR "SARS-CoV-2" OR "Severe Acute Respiratory Coronavirus 2" OR "coronavirus infections" OR "bat coronavirus" OR "betacoronavirus 1" OR "betacoronavirus" OR "coronavirus disease 2019" OR "Coronavirus Infection" OR Coronaviruses OR "nCoV" OR "Coronavirus Infection Disease 2019" OR "Novel Coronavirus Pneumonia" OR "2019-nCoV Infections" OR "2019 novel coronavirus" OR "2019 novel coronavirus infection" Filters: from 2018 – 2021
#3 TB AND COVID-19	(#1) AND (#2)

Supplementary Table 2- Characteristics of the included studies

Study	Study design	Country	Setting	Outcomes	Lockdown period	Number of participants	Study period	Findings
Liu 2020	Longitudinal (before and after) time series study	China (Jiangsu Province)	Hospital (Urban and rural)	TB case notification, MDR TB screening and treatment completion.	January 23rd, 2020	143,250	January 2015 to December 2019 and January to May 2020.	Our analysis suggests a substantial reduction between 36%–52% in tuberculosis notifications in 2020 compared to 2015–2019.
Srivastava 2021	Longitudinal (before and after) time series study	India (Gurgaon)	Hospital (Urban and rural)	TB diagnosis, case notifications, positivity rate, RR and sensitive TB rate,	March 24th, 2020	For testing samples: 484 in 2020, 644 in 2019 For	March 2019 to December 2019 and January 2020 to	Our study reported an increase in confirmed TB cases in 2020 as compared to 2019.

				discharge inpatients and deaths.		notification samples 146 in 2020, 127 in 2019	October 2020.	
Hazra 2021	Longitudinal (before and after) time series study	India (South Karnataka)	Hospital (Rural)	TB diagnosis and case notifications.	March 24th, 2020	Not Stated	January 2019 to December 2020.	Our study reported a significant decrease in TB diagnosis and active TB case detection.
Kwak 2020	Longitudinal (before and after) time series study	South Korea (all provinces)	Community (Urban and rural)	TB case notification	February 23rd, 2020	Not Stated	First 18 weeks of 2015 to 2019 and the first 18 weeks of 2020.	Our study reported a significant decrease in TB diagnosis and notification as the surge of COVID-19 infection in South Korea.
Gennaro 2021	Longitudinal (before and after) time series study	Italy (Rome)	Hospital (Urban)	TB diagnostic and treatment delay.	March 10th, 2020	201 patients in 2019 115patients in 2020	March 2019 to August 2020.	Our study reported higher TB diagnostic delay, a reduction in hospitalization and greater severity of clinical presentations during the COVID-19 pandemic.
Mbithi 2021	Cohort study	Kenya (Nairobi)	Hospital (Urban)	TB treatment enrolment, failure and success rate, loss to follow-up, patients not evaluated and deaths.	March 20th, 2020	Not Stated	March 2019 to February 2020 and March 2020 to February 2021.	Our study reported that the programmatic interventions implemented during the COVID-19 period were associated with improved case detection and treatment outcomes during the COVID-19 period, suggesting that monthly real-time surveillance is useful during unprecedented events.
Thekkur 2021	Cohort study	Malawi (Lilongwe)	Hospital (Urban and rural)	TB case notification, treatment enrolment, clinical diagnosis, positivity rate, presumptive TB, treatment success and failure rate, patients that were not	April 18th, 2020 17 January 2021	Not Stated	March 2019 and February 2020 to March 2020 and February 2021.	Our study reported a decline in TB case detection and treatment outcomes for TB during the COVID-19 pandemic.

				evaluated and deaths.				
Dara 2021	Cross-sectional survey	48 European countries	Community (Urban and rural)	TB case notifications, TB treatment	The lockdown period varied in countries.	Not stated	January to June 2019 and January to June 2020.	Our study reported a substantial decrease in TB notifications in Q2 2020 in the WHO European Region. This delay or lack of diagnosis can lead to ongoing transmission of the disease to close contacts, increased severity of TB disease and a potential increase in case fatality.
Lakoh 2021	Cohort study (Retrospective)	Sierra Leone (Free Town)	Hospital (Urban)	TB notification TB treatment	April 1st, 2020	Not Stated	January 2019 to September 2019 and January 2020 to September 2020.	Our study reported COVID-19 negative impacts on TB care at the largest treatment centre in Sierra Leone.
Wang 2021	Cohort study	China (Ningxia Hui)	Hospital (Urban)	TB case notification TB treatment TB Patient delay	January 23rd, 2020	Not stated	2018-2020	Our study reported a reduction in cases of TB notification in Ningxia due to the COVID-19 pandemic.
Min 2020	Cohort study	Korea (all provinces)	Hospital (Urban)	TB case notification TB treatment success rate	February 23rd, 2020	Not stated	July 2019 to June 2020	Our study reported the COVID-19 pandemic's enormous potential to hinder the efforts of TB services in prevention, case detection, and management, particularly in resource-limited settings.
Aznar 2021	Cross-sectional survey	Spain (all provinces)	Hospital (Urban)	TB case notification	March 14th, 2020	Not stated	March 15-June 30, 2019 and March 15- June 30, 2020.	Our study reported an increase in LTBI infection and active TB in children whose household had contact with patients. This reflects increased household transmission due to the anti-COVID-19 measures.
Thekkur 2021	Cohort study	Zimbabwe (Harare)	Hospital (Urban)	TB case notification, treatment enrolment, clinical diagnosis, positivity	March 30th, 2020	Not stated	March 2019 and February 2020 to March 2020 and	Our study reported a declining trend in TB case detection and treatment outcomes.

				rate, presumptive TB, treatment success and failure rate and patients that were not evaluated.			February 2021.	
Geng 2021	Longitudinal (before and after) time series study	China (Henan province)	Hospital (Urban and rural)	TB diagnosis and MTB cumulative rate.	January 23rd, 2020	Not stated	January to December 2019 and January to December 2020.	Our study reported less effect of a non-pharmaceutical public health intervention on MTB transmission in 2020.
Fei 2020	Cross-sectional survey	China (all provinces)	Hospital (Urban and rural)	TB case notifications	January 23rd, 2020	Not stated	January – December 2017 to 2019 and January - December 2020	Our study reported reductions in TB notifications and follow-up examinations in China during the COVID-19 pandemic and this may cause an upsurge in TB cases in the nearest future.
Feldman 2021	Surveillance report	USA (all states)	Community (Urban and rural)	TB case notifications	Days between March 19th to April 7th, 2020 (it varies with the area).	Not stated	January - December 2019 and January - December 2020.	Our study reported incidence a 20% TB incidence decrease in 2020 as compared to 2019 cases.
Kamakoli 2021	Longitudinal (before and after) time series study	Iran (Tehran)	Research Institute (Urban and rural)	TB case notifications	March 13th, 2020	Not stated	February -June 2016-2019 to February -June 2020	Our study reported a significant decrease in TB case identification in Tehran, in 2020.
Migliori 2020	Cohort study	16 countries	Hospital (Urban)	TB new cases discharged inpatients and outpatients.	The lockdown period varied in countries.	Not Stated	January-April 2019 and January-April 2020.	Our study reported reductions in TB-related hospital discharges, newly diagnosed cases of active TB, total active TB outpatient visits and new LTBI and LTBI outpatient visits in the first 4 months of 2020.
Arega 2022	Cohort study	Ethiopia (Addis Ababa)	Research Institute (Urban)	TB screening, case	April 8th, 2020	Not Stated	April 2019 to March	Our study reported a negative impact of the COVID-19 pandemic

				notification, detection rate, clinical diagnosis, treatment success and MDR-RR rate.			2020 and April 2020 to March 2021.	on TB service indicators in Addis Ababa, Ethiopia.
Arentz 2022	Longitudinal (before and after) time series study	India (all provinces)	Research Institute (Urban and rural)	TB case notification	March 24th, 2020	Not Stated	January 2017 to April 2021.	Our study a large difference between reported TB cases in India and those expected in the absence of the pandemic.
Filardo 2022	Longitudinal (before and after) time series study	USA (US 50 states and the District of Columbia)	Community (Urban and rural)	TB case notification	March 19th to April 7th 2020	Not Stated	January 2011-December 2011 to January 2021-December 2021.	Our study reported a significant decrease in TB case notifications in the USA.
Gandhi 2022	Retrospective cohort study	India (Northern India)	Community (Rural)	TB diagnostic delay, treatment delay and pulmonary TB.	March 24th, 2020	103	January 1st, 2020 to June 30th, 2020.	Our study reported a significant decrease in pulmonary TB notification and an increase in diagnostic delay in Northern India.
Geric 2021	Longitudinal (before and after) time series study	Canada (Montreal and Toronto)	Hospital (Urban)	Active and latent TB.	March 14 and 17 2020 in the Quebec and Ontario provinces respectively.	10833	January to December 2005 and January to December 2020	Our study reported a significant decrease in active and latent TB treatment in Ontario and Quebec provinces. The enactment of public health emergency measures against COVID-19 in Canada weakened the measures for tuberculosis control and treatment.
Godoy 2022	Longitudinal (before and after) time series study	Spain (Catalonia)	1 Hospital in Catalonia (Northern Spain) (Urban)	TB contact tracing, pulmonary and latent TB.	March 14th, 2020	6363	January 2019 to February 2020 and March 2020 to April 2021.	Our study reported less exhaustive TB and LTBI case detection, though an increase in LTBI was observed during the pandemic.
Golandaj 2021	Longitudinal (before and after) time series study	India (all provinces)	Research Institute (Urban and rural).	Case notifications and paediatric TB.	March 24th, 2020	Not Stated	January to September 2019 and 2020.	Our study reported a significant decrease in paediatric TB during the COVID-19 pandemic.

Hasan 2022	Retrospective cohort study	Vietnam (all provinces)	Vietnam's 63 provinces (Community, Urban and rural)	TB screening, notification, treatment success and failure rate, loss to follow-up, patients that were not evaluated, RR MDRTB and deaths.	April 1st, 2020	Not Stated	January 2019 to December 2019 and January 2020 to December 2020.	Our study reported a limited decrease in TB notifications in Vietnam during the first year of the COVID-19 pandemic.
Soko 2020	Interrupted time series study	Malawi	Hospital (Urban and rural)	TB notifications	April 18th, 2020 17 January 2021	Not stated	April 2016 to March 2020 and April 2020.	Our study reported a 35.9% reduction in TB notifications in April 2020 as compared to the pre-pandemic numbers from April 2016 to March 2020 and April 2020.

Supplementary Table 3: Hoy risk of bias assessment

Studies	I	II	III	IV	V	VI	VII	VIII	IX	X	Summary of the overall Risk of bias for each study (XI)
Liu 2021	0	1	0	1	1	1	1	0	1	1	7
Srivastava 2021	0	0	0	0	1	1	1	1	1	1	6
Hazra 2021	0	1	0	1	1	1	1	1	1	1	8
Kwak 2020	1	1	0	1	1	0	1	1	1	1	8
Gennaro 2021	0	1	0	0	1	0	1	1	1	1	6
Mbithi 2021	0	1	0	1	1	1	1	1	1	1	8
Thekkur 2021 Malawi	0	1	0	1	1	1	1	1	1	1	8
Dara 2020	0	0	0	1	1	1	1	1	1	1	7
Lakoh 2021	0	0	0	1	0	1	1	1	1	1	6
Wang 2021	0	1	0	1	0	1	1	1	1	1	7
Min 2020	0	1	0	0	0	0	1	1	1	1	5
Aznar 2021	0	1	0	0	1	1	0	1	1	1	6
Thekkur 2021 Zimbabwe	0	1	0	1	1	1	1	1	1	1	8
Geng 2021	0	0	0	1	0	1	1	1	1	1	6
Fei 2020	1	1	0	0	1	1	1	1	1	1	8
Feldman 2020	1	1	0	0	1	0	1	1	1	1	7

Kamakoli 2021	0	1	0	1	1	0	1	1	1	1	7
Migliori 2020	0	0	0	0	0	0	1	1	1	1	4
Arega 2022	1	1	0	1	0	1	1	0	1	1	7
Arentz 2022	1	1	1	1	0	1	1	0	1	1	8
Filardo 2022	1	1	1	1	0	1	1	1	1	1	9
Gandhi 2022	0	1	0	1	1	1	1	1	1	1	8
Geric 2021	1	1	0	1	0	1	1	1	1	1	8
Godoy 2022	0	1	0	1	0	1	1	0	1	1	6
Golandaj 2022	1	1	1	1	0	1	1	0	1	1	8
Hasan 2022	1	1	1	1	0	1	1	0	1	1	8
Soko 2020	0	1	1	1	1	1	0	1	1	1	8
Summary total for each question.	9	22	5	20	15	21	25	21	27	27	

NB

I. Was the study's target population a close representation of the national population's relevant variables, e.g. age, sex and occupation?

I. Was the sampling frame a true or close representation of the target population?

II. Was some form of random selection used to select the sample, OR, was a census undertaken?

III. Was the likelihood of non-response, or is bias minimal?

IV. Were data collected directly from the subjects (as opposed to a proxy)?

V. Was an acceptable case definition used in the study?

VI. Was the study an instrument that measured the parameter of interest (e.g. prevalence of low back pain) shown to have reliability and validity (if necessary)?

VII. Was the same mode of data collection used for all subjects?

VIII. Was the length of the shortest prevalence period for the parameter of interest appropriate?

IX. Were the numerator(s) and denominator(s) for the parameter of interest appropriate?

X. Summary of the overall Risk of bias for each study

Yes=1

No=0

Supplementary Table 4: Changes in TB diagnostic and treatment delay contact tracing, positivity and detection rate.

Study	Countries	Diagnostic delay	Treatment delay	Detection rate	Positivity rate	Contact tracing
Gennaro 2021	Italy (Rome)	45days and a 60.0% increase between March 2019 to August 2020. There was a 52% and 28-36 days increase in diagnostic and treatment delays between	1 to 4 days and a 1.0% increase between March 2019 to August 2020.	Not reported	Not reported	Not reported
Gandhi 2022	India (Northern India)	11 to 17days and a 25.1% increase between January to June 2020.	3 days and 1.0% to 6.2% increase between January to June 2020.	Not reported	Not reported	Not reported
Godoy 2022	Spain (Catalonia)	Not reported	Not reported	Not reported	Not reported	36.1% decrease in contact tracing between January 2019 to February 2020 and March 2020 to April 2021.
Mbithi 2021	Kenya (Nairobi)	Not reported	Not reported	Not reported	0.1% increase between March 2019 to February 2020 and March 2020 to	Not reported

					February 2021.	
Srivastava	India (Gurgaon)	Not reported	Not reported	Not reported	24.9% decrease between March 2019 to December 2019 and January 2020 to October 2020.	Not reported
Thekkur 2021	Malawi (Lilongwe)	Not reported	Not reported	Not reported	4.5% increase between March 2019 and February 2020 to March 2020 and February 2021.	Not reported
Thekkur 2021	Zimbabwe (Harare)	Not reported	Not reported	Not reported	2.4% increase between March 2019 and February 2020 to March 2020 and February 2021.	Not reported
Arega 2022	Ethiopia (Addis Ababa)	Not reported	Not reported	11.8% and 44.7% decrease between April 2019 to March 2020 and April 2020 to March 2021.	Not reported	Not reported

Supplementary Table 5: Changes in TB outpatients, new cases and discharged inpatients

Study	Country	TB outpatients	TB new cases	TB discharged inpatients
Migliori 2020	Australia	22.1% increase between January-April 2019 and January-April 2020.	48.6% increase between January-April 2019 and January-April 2020.	20.7% decrease between January-April 2019 and January-April 2020.
Migliori 2020	India	71.6% decrease between January-April 2019 and January-April 2020.	Not reported	63% decrease between January-April 2019 and January-April 2020.
Migliori 2020	Philippines	66.7% decrease between January-April 2019 and January-April 2020.	71.4% increase between January-April 2019 and January-April 2020.	6.1% decrease between January-April 2019 and January-April 2020.
Migliori 2020	Singapore	17.5% increase between January-April 2019 and January-April 2020.	48.4% decrease between January-April 2019 and January-April 2020.	12.1% increase between January-April 2019 and January-April 2020.
Migliori 2020	France	40.1% increase between January-April 2019 and January-April 2020.	31.4% decrease between January-April 2019 and January-April 2020.	12.9% decrease between January-April 2019 and January-April 2020.
Migliori 2020	Italy	17.1% decrease between January-April 2019 and January-April 2020.	4.8% decrease between January-April 2019 and January-April 2020.	13.3% decrease between January-April 2019 and January-April 2020.
Migliori 2020	Netherlands	Not reported	46.0% decrease between January-April 2019 and January-April 2020.	5.4% decrease between January-April 2019 and January-April 2020.
Migliori 2020	Russia	10.3% decrease between January-April 2019 and January-April 2020.	11.1% decrease between January-April 2019 and January-April 2020.	31.3% decrease between January-April 2019 and January-April 2020.
Migliori 2020	Spain	1.0% increase between January-April 2019 and January-April 2020.	31.3% decrease between January-April 2019 and January-April 2020.	41.7% decrease between January-April 2019 and January-April 2020.
Migliori 2020	UK	1.1% decrease in TB outpatients between January-April 2019 and January-April 2020.	6.3% increase between January-April 2019 and January-April 2020.	42.9% decrease between January-April 2019 and January-April 2020.

Migliori 2020	Mexico	43.2% decrease between January-April 2019 and January-April 2020.	47.5% decrease between January-April 2019 and January-April 2020.	90.8% decrease between January-April 2019 and January-April 2020.
Migliori 2020	Argentina	3.9% decrease between January-April 2019 and January-April 2020.	2.6% decrease between January-April 2019 and January-April 2020.	Not reported
Migliori 2020	Brazil	0.5% decrease between January-April 2019 and January-April 2020.	20.5% decrease between January-April 2019 and January-April 2020.	24.0% decrease between January-April 2019 and January-April 2020.
Migliori 2020	Kenya (Nairobi)	Not reported	There was a 12.6% decrease in TB new cases between January to April 2019 and 2020.	Not reported
Migliori 2020	Niger	15.6% decrease between January-April 2019 and January-April 2020.	15.6% decrease between January-April 2019 and January-April 2020.	Not reported
Migliori 2020	Sierra Leone (Free Town)	30.1% decrease between January-April 2019 and January-April 2020.	26.5% decrease between January-April 2019 and January-April 2020.	Not reported
Srivastava 2021	India (Gurgaon)	Not reported	Not reported	15.4% increase between March 2019 to October 2020.

Supplementary Table 6: Changes in sensitive TB, RR/MDR TB rate and TB Deaths

Study	Country	Sensitive TB	RR/MDR rate	TB deaths
Srivastava 2021	India (Gurgaon)	12.3% increase between March 2019 to October 2020.	9.9% decrease between March 2019 to December 2019 and January 2020 to October 2020.	2.6% increase between March 2019 to October 2020.
Dara 2021	48 European countries	Not reported	33.5% decrease between January to June 2019 and January to June 2020.	Not reported
Arega 2022	Ethiopia (Addis Ababa)	Not reported	27.7% increase between April 2019 to March 2020 and April 2020 to March 2021.	Not reported

Geng 2021	China (Henan province)	Not reported	5.1% increase in the MTB cumulative rate between January to December 2019 and January to December 2020.	Not reported
Mbithi 2021	Kenya (Nairobi)	Not reported	Not reported	0.8% increase between March 2019 to February 2020 and March 2020 to February 2021.
Thekkur 2021	Malawi (Lilongwe)	Not reported	Not reported	0.6% decrease between March 2019 and February 2020 to March 2020 and February 2021.
Lakoh 2021	Sierra Leone (Free Town)	Not reported	Not reported	51.4% decrease between January 2019 to September 2019 and January 2020 to September 2020.
Hasan 2022	Vietnam (all provinces)	Not reported	1.3% decrease between 2018 and 2020.	67% decrease between January 2019 to December 2019 and January 2020 to December 2020.

Addendum B

BMJ Open Author guidelines

Original research author guidelines

Research submissions should have a clear, justified research question. We strongly encourage you to register your study. Prospective registration is mandatory for any clinical trials. Acceptable registries for trials include clinicaltrials.gov. We recommend Prospero for registration of systematic reviews. All articles should include the following:

- **The article title should include the research question and the study design**. Titles should not declare the results of the study.
- **A structured abstract** (max. 300 words) including all the following where appropriate (please note that for RCTs there is a specific CONSORT extension for abstracts):
    - **objectives:** clear statement of main study aim and major hypothesis/research question
    - **design:** e.g. prospective, randomised, blinded, case control
    - **setting:** level of care e.g. primary, secondary; number of participating centres. Generalise; don't use the name of a specific centre, but give geographical location if important
    - **participants:** numbers entering and completing the study; sex and ethnic group if appropriate. Clear definitions of selection, entry and exclusion criteria
    - **interventions:** what, how, when and how long (this can be deleted if there were no interventions)
    - **primary and secondary outcome measures:** planned (i.e. in the protocol) and those finally measured (if different, explain why) - for quantitative studies only
    - **results:** main results with (for quantitative studies) 95% confidence intervals and, where appropriate, the exact level of statistical significance and the number need to treat/harm. Whenever possible, state absolute rather than relative risks
    - **conclusions:** primary conclusions and their implications, suggest areas for further research if appropriate. Do not go beyond the data in the article
    - **where applicable, trial registration:** registry and number (for clinical trials and, if available, for observational studies and systematic reviews)
- **Please include a 'Strengths and limitations of this study' section after the abstract.** This section should be no more than 5 bullet points relating specifically to the methods - not the results of the study. This will be published as a summary box after the abstract in the final published article.
- **The original protocol for the study**, as a supplementary file.
- **A funding statement,** preferably worded as follows. Either: 'This work was supported by [name of funder] grant number [xxx]' or 'This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors'. You must ensure that the full, correct details of your funder(s) and any relevant grant numbers are included.
- **A competing interests statement**. See the BMJ Author Hub for details on what to include as competing interests.

- **Articles should list each author's contribution individually at the end**; this section may also include contributors who do not qualify as authors. Please visit the ICMJE website for more information on authorship.
- **Any checklist and flow diagram for the appropriate reporting statement**, e.g. STROBE (see below).
- **A patient consent form:** any article that contains personal medical information about an identifiable living individual requires the patient's explicit consent before we can publish it. We will need the patient to sign our consent form, which requires the patient to have read the article. This form is available in multiple languages.
- **A data sharing statement**, such as: "Technical appendix, statistical code, and dataset available from the Dryad repository, DOI: [include DOI for dataset here].
- **Word count,** we recommend your article does not exceed 4000 words, with up to five figures and tables. This is flexible, but exceeding this will impact upon the paper's 'readability'. Authors are encouraged to submit figures and images in colour - there are no colour charges. We require that you upload your figures as separate files rather than embedding them in the manuscript.
- **Supplementary and raw data** can be placed online alongside the article although we prefer raw data to be made publicly available and linked to in a suitable repository (e.g. Dryad, FigShare). We may request that you separate out some material into supplementary data files to make the main manuscript clearer for readers.

We also recommend, but do not insist, that the discussion section is no longer than five paragraphs and follows this overall structure (you do not need to use these as subheadings): a statement of the principal findings; strengths and weaknesses of the study; strengths and weaknesses in relation to other studies, discussing important differences in results; the meaning of the study: possible explanations and implications for clinicians and policymakers; and unanswered questions and future research. At upload you will be asked to choose one general subject area that applies to your article - it will be published under this banner on the main table of contents. You will also be asked to select further subject headings to be used for the 'Browse by topic' section, and specific keywords for help with identifying reviewers. Following the lead of The BMJ and its patient partnership strategy, *BMJ Open* is encouraging active patient involvement in setting the research agenda. As such, we require authors of Research Articles to add a Patient and Public Involvement statement in the Methods section. Please see more details above.

Pilot studies

Articles reporting pilot studies should explain the work's wider context and explain why the term 'pilot study' applies. The term 'pilot study' should not be applied to justify reporting a small-scale study. Justifications for a pilot study include:

- trialling a new procedure intended for use in a larger programme of research
- establishing power calculations required for a full-scale study
- establishing how many patients and/or healthcare professionals can be recruited
- evaluating the financial, technical, administrative or logistic feasibility of a full-scale study, including issues of data collection, protocol adherence, and questionnaire design.

The sample/patient size should still be justified. The article should explain the impact that the pilot study had on decisions regarding future research.

Reporting guidelines

The guidelines listed below should be followed where appropriate. Please use these guidelines to structure your article. Completed applicable checklists, structured abstracts and flow diagrams should be uploaded with your submission; these will be published alongside the final version of your paper.

CONSORT Statement
For reporting of randomised controlled trials: please use the appropriate extension to the CONSORT statement, including the extension for writing abstracts

SRQR
For reporting qualitative research

COREQ
For reporting qualitative research

STARD
For reporting of diagnostic accuracy studies

STROBE
For reporting of observational studies in epidemiology Checklist for cohort, case-control, and cross-sectional studies (combined) Checklist for cohort studies Checklist for case-control studies Checklist for cross-sectional studies

PRISMA
For reporting of systematic reviews

PRISMA-P
For reporting of systematic review and meta-analysis protocols

PRISMA-ScR
For reporting of scoping reviews

MOOSE
For reporting of meta-analyses of observational studies

SPIRIT
For reporting protocols for RCTs

STREGA
For reporting of gene-disease association studies

TRIPOD
For reporting of studies developing, validating, or updating a prediction model, whether for diagnostic or prognostic purposes.

CHEERS
For reporting of health economic evaluations The Equator Network (Enhancing the Quality and Transparency Of Health Research) provides a comprehensive list of reporting guidelines.

Protocol

Protocol manuscripts should report planned or ongoing research studies. If data collection is complete, we will not consider the manuscript. We encourage the submission of protocol manuscripts at an early stage of the study. Protocols nearing completion of data collection will be treated on a case by case basis and the final decision on whether to consider a protocol for publication will rest with the Editor. Publishing study protocols enables researchers and funding bodies to stay up to date in their fields by providing exposure to research activity that may not

otherwise be widely publicised. This can help prevent unnecessary duplication of work and will hopefully enable collaboration. Publishing protocols in full also makes available more information than is currently required by trial registries and increases transparency, making it easier for others (editors, reviewers and readers) to see and understand any deviations from the protocol that occur during the conduct of the study. The SPIRIT (Standard Protocol Items for Randomized Trials) statement has now been published. It is an evidence-based tool developed through systematic review of a wide range of resources and consensus. It closely mirrors the CONSORT statement and also reflects important ethics considerations. We encourage investigators to adhere to the SPIRIT recommendations when drafting their protocols and include a completed SPIRIT checklist with their trial protocol submission. The PRISMA-P (Preferred reporting items for systematic review and meta-analysis protocols) is a new reporting guideline. An article stating the guideline checklist has now been published. The PRISMA-P checklist contains 17 items considered to be essential and minimum components of a systematic review or meta-analysis protocol. Systematic review authors and assessors are strongly encouraged to make use of PRISMA-P when drafting and appraising review protocols and authors should include a completed PRISMA-P checklist with their protocol submission. Various other resources exist that list the ingredients of an authoritative trial protocol, e.g. the UK Dept of Health/Medical Research Council Clinical Trials Toolkit and the US National Institutes for Health provide advice on how to structure a trial protocol. *BMJ Open* will consider for publication protocols for any study design, including observational studies and systematic reviews. We strongly encourage you to register your study. Prospective registration is mandatory for any clinical trials. Acceptable registries for trials include clinicaltrials.gov. We recommend Prospero for registration of systematic reviews.
Following the lead of The BMJ and its patient partnership strategy, *BMJ Open* is encouraging active patient involvement in setting the research agenda. As such, we require authors of Study Protocols to add a Patient and Public Involvement statement in the Methods section. please see more details above. General BMJ policies apply (see above) on manuscript formatting, editorial policies, licence forms and patient consent (where applicable to study designs). Protocols should include, as a minimum, the following items.

- **Protocol papers should report planned or ongoing studies.** Manuscripts that report work already carried out will not be considered as protocols. The dates of the study must be included in the manuscript and cover letter.
- **Protocols for studies that will require ethical approval**, such as trials, are unlikely to be considered without having received that approval
- **Title:** this should include the specific study type, e.g. randomised controlled trial.
- **Abstract:** this should be structured with the following sections. Introduction; Methods and analysis; Ethics and dissemination. Registration details should be included as a final section, if appropriate.
- **Please include a 'Strengths and limitations of this study' section after the abstract.** This section should be no more than 5 bullet points relating specifically to the methods - not the results of the study. This will be published as a summary box after the abstract in the final published article.
- **Introduction:** explain the rationale for the study and what evidence gap it may fill. Appropriate previous literature should be referenced, including relevant systematic reviews.

- **Methods and analysis:** provide a full description of the study design, including the following. How the sample will be selected; interventions to be measured; the sample size calculation (drawing on previous literature) with an estimate of how many participants will be needed for the primary outcome to be statistically, clinically and/or politically significant; what outcomes will be measured, when and how; a data analysis plan.
- **Ethics and dissemination:** ethical and safety considerations and any dissemination plan (publications, data deposition and curation) should be covered here.
- **Full references.**
- **Authors' contributions:** state how each author was involved in writing the protocol.
- **Funding statement:** preferably worded as follows. Either: 'This work was supported by [name of funder] grant number [xxx]' or 'This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors'.
- **Competing interests statement.**
- **Word Count:** 4,000 words. Should the word count exceed this number, please state this in the cover letter upon submission.

Cohort profile

The cohort profile is an article type set up in *BMJ Open* to fill the space between a study protocol and a results paper. Cohort profiles should describe the rationale for a cohort's creation, its methods, baseline data and its future plans. Cohorts described should be long-term, prospective projects and not time-limited cohorts established to answer a small number of specific research questions. If a cohort has yet to complete recruitment or baseline data collection, it should be submitted as a study protocol. Papers addressing a specific research question using cohort data should be submitted as a Research paper. Following the lead of The BMJ and its patient partnership strategy, *BMJ Open* is encouraging active patient involvement in setting the research agenda. As such, we require authors of Cohort Profiles to add a Patient and Public Involvement statement in the Methods section. please see more details above.
Title Should begin 'Cohort profile: …'. It should include the full name and any commonly used abbreviation of the cohort, plus its location or whether it is international. Include the type of cohort. **Abstract** Use these headings to provide brief descriptions of the following:

- **Purpose:** describe why the cohort was set up
- **Participants:** describe who is in the cohort
- **Findings to date:** what data has been collected so far and any major results
- **Future plans:** how will the cohort be used in future, including any date for completion of data collection
- **Registration:** if your Cohort Profile is linked to a clinical trial, we require the registry and trial registration number to be included. In line with the recommendations of the International Committee of Medical Journal Editors, we require prospective registration of all clinical trials. For Cohort Profiles not linked to a clinical trial, registration is not required.

Introduction Describe the rationale for the study, including any specific research questions that motivated the project. **Cohort description** Describe the setting, locations and relevant dates, including periods of recruitment, exposure, follow-up and data collection. Give the eligibility

criteria and how participants were recruited. Report numbers of individuals at each stage of the study, e.g. how many were approached, included in the study and have been retained. Reasons for non-participation should be reported. A flow diagram is recommended to illustrate this. Describe methods of data collection and follow-up, and any external data sources used. Give characteristics of study participants (e.g. demographic, clinical, social) and information on exposures and potential confounders. Indicate number of participants with missing data for each variable of interest. Detailed statistical plans should not be reported.
Findings to date Include a short explanation of the most notable results from the cohort so far, with references to relevant publications. This section should summarise rather than present results. **Strengths and limitations** Please include a 'Strengths and limitations of this study' section after the abstract. This section should be no more than 5 bullet points relating specifically to the methods - not the results of the study. This will be published as a summary box after the abstract in the final published article. **Collaboration** Authors should include a section on what data will be available, to whom, how it can be accessed and what restrictions to reuse may apply. (This should be in the text, not the data sharing statement.) Please also state what kind of collaboration you are encouraging. **Further details** Our standard inclusions – Strengths and limitations of this study, a data sharing statement, funding declaration, contributorship statement, etc., should also be included.

Communication

If you are interested in submitting a communication article to *BMJ Open*, we ask that you send us a presubmission enquiry via our online submission system. You will be asked to provide a title, an abstract, and a cover letter explaining why you think your work is appropriate as a communication article for *BMJ Open*. Communication articles will be considered at the discretion of the editorial team at *BMJ Open* based on the relevance of the topic and the quality of a presubmission enquiry. If your presubmission enquiry is accepted, the editorial team will invite you to submit a full manuscript. The communication article will cover content that does not fit within our existing article types, but is of interest to *BMJ Open*'s readership. Rather than presenting primary research, it is an opportunity to present ideas, examples, and innovations relating to the conduct of clinical research. As with all content in *BMJ Open*, communication articles will relate to key research issues in clinical medicine, public health, and epidemiology. Examples of topics of relevance to *BMJ Open* include:

- Encouraging patient and public involvement
- Improving research transparency and reproducibility
- Reducing research waste through collaboration
- Improving best practice in publishing and peer review

All communication articles will undergo external open peer review. As with our other content, the peer reviewer reports and previous versions of the manuscript will be posted alongside the final article. We also encourage readers to participate in the discussion by posting comments on the articles.
The communication article should include, as a minimum, the following items:

- **Title:** a clear, concise description of the article's content.

- **Abstract:** we recommend a structured abstract that states the objective of the piece along with a summary of the key data or arguments and an overall conclusion.
- **Full References**
- **Authors' Contributions:** state how each author was involved in writing the article.
- **Funding statement:** preferably worded as follows. Either: 'This work was supported by [name of funder] grant number [xxx]' or 'This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors'.
- **Competing Interests statement.** see the BMJ Author Hub for details.

The structure and format of the article is at the discretion of the author. However, it should follow a logical form and be divided into subsections. Communication articles should be kept as brief as possible. We recommend a word count of approximately 2,500 words (not including references). If you expect that your word count will exceed our recommendations, please mention this in the cover letter of your presubmission enquiry along with a justification.

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BMJ Journals are willing to consider publishing supplements to regular issues. Supplement proposals may be made at the request of:

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- The journal editor, editorial board member or learned society may wish to commission a supplement on a particular theme or topic. Again, sponsorship may be sought.
- BMJ itself may have proposals for supplements where sponsorship may be necessary.
- A sponsoring organisation, often a pharmaceutical company or a charitable foundation, that wishes to arrange a meeting, the proceedings of which will be published as a supplement.

In all cases, it is vital that the journal's integrity, independence and academic reputation is not compromised in any way.
For further information on criteria that must be fulfilled, download the supplements guidelines.
When contacting us regarding a potential supplement, please include as much of the information below as possible.

- Journal in which you would like the supplement published
- Title of supplement and/or meeting on which it is based
- Date of meeting on which it is based
- Proposed table of contents with provisional article titles and proposed authors
- An indication of whether authors have agreed to participate
- Sponsor information including any relevant deadlines
- An indication of the expected length of each paper Guest Editor proposals if appropriate

Addendum C

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Title page
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	Completed
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Introduction
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Last part of introduction
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	2.1
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	2.2
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	2.3
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	2.4
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	2.5
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	2.6
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	2.7
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	Data items, 2.6
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	2.8
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	2.8
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	2.8
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	N/A
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	2.8
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	N/A

Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	N/A
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	N/A

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Figure 1 and 3.1
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	3.1
Study characteristics	17	Cite each included study and present its characteristics.	3.2 and study supplementary table 3.
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	3.3
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	3.4 to 3.6 and study supplementary Table 4 to 6.
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	3.3
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	N/A
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	3.4 to 3.7 and study supplementary Table 4 to 6.
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	N/A
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	N/A
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	N/A
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	4
	23b	Discuss any limitations of the evidence included in the review.	4
	23c	Discuss any limitations of the review processes used.	4
	23d	Discuss implications of the results for practice, policy, and future research.	4
OTHER INFORMATION			
Registration and	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	6.1

protocol	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	6.1
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	6.1
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	6.2
Competing interests	26	Declare any competing interests of review authors.	6.3
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	6.4

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

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