TECHNICAL REPORT

The cascade-of-care for tuberculosis infection in low-incidence countries – a scoping review protocol

Introduction

Ending tuberculosis (TB) by 2030 is one of the targets outlined in the Sustainable Development Goals [1]. To achieve this goal it is necessary to implement a comprehensive strategy, including several interventions to prevent, diagnose and treat TB in a timely and effective manner [2]. Among these interventions, management of TB infection is considered essential [3].

TB infection, also known as latent TB infection (LTBI), is defined as 'a state of persistent immune response to stimulation by *Mycobacterium tuberculosis* antigens with no evidence of clinically manifest active TB' [4]. People with TB infection have no signs or symptoms of TB and are considered to be at risk of progressing to TB disease. TB preventive treatment should be offered to those who have been exposed to TB or who are infected with TB to avoid progression to active TB disease [5].

Approximately one-fourth of the world's population is infected with TB [6]. In Europe alone, the prevalence of TB infection has been estimated at between 11 and 15% [7]. Delivering systematic screening of TB infection in at-risk populations and provision of TB preventive treatment are key components of the global TB elimination strategy, particularly in countries with low TB incidence (i.e. with a notification rate <10 TB cases per 100 000 population) [3,8]. A majority of the Member States of the European Union (EU) and European Economic Area (EEA) have a low TB incidence [3].

Rationale

The management of TB infection involves the sequential implementation of key interventions, a process that has been labelled as cascade-of-care [9]. The concept cascade-of-care (or continuum of care), is also an analytical framework used to evaluate public health interventions by constructing models of the proportion of people completing sequential steps of care for a given condition or disease [10].

Cascade-of-care analyses have been applied to both TB disease and TB infection [9,11-13]. For the latter, systematic and scoping reviews have focussed on specific at-risk populations and/or settings with high-TB burden [14-16]. So far, information on data sources and analytical decisions on how to conduct cascade-of-care analyses for TB infection have not been mapped in sufficient detail, as has been done for other diseases [17-19]. In an exploratory search conducted in August 2023 there were no ongoing systematic or scoping reviews identified on this topic in three open-access repositories (PROSPERO [20], OSF Registries [21] and Figshare [22]).

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The purpose of this scoping review will therefore be to describe and summarise the rationale behind and methodological approaches used to conduct cascade-of-care analyses for TB infection in low-TB incidence countries. Knowledge users, defined as 'those who have a vested interest in the research, its outcomes and impacts' [23], will be involved throughout the review process, including the identification of relevant publications and the discussion of findings to inform surveillance and monitoring strategies for TB infection at national and regional levels in the EU/EEA.

Review questions

Table 1 below presents the questions for the scoping review.

Table 1. Review questions

Type of question	Review question
Main question	Why and how have cascade-of-care analyses for TB infection been implemented in low-TB incidence countries?
Secondary questions	• What was the purpose of the cascade-of-care analysis? • Which key populations have been monitored? • What data sources have been used for constructing cascade-of-care analyses? • Which steps of the cascade-of-care are commonly reported? • Which methods have been used to construct cascade-of-care analyses? • Which and what type of indicators have been used in cascade-of-care analyses for TB infection? • What challenges and/or lessons learned have been identified?

This protocol has been developed based on the best practice guidance proposed by Peters et al [24], as presented in Annex 1, and will be available on the European Centre for Disease Prevention and Control (ECDC) website.

The scoping review will be conducted according the JBI scoping review methodology [25,26] and reported following the Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) [27] and the Guidance for Reporting Involvement of Patients and the Public (GRIPP 2) [28].

Methods

Eligibility criteria

Sources of evidence will be eligible for inclusion in the scoping review if they fulfil the criteria below. These criteria were defined using the PCC framework (i.e. participants, concepts and context) [25].

Participants

Publications that will be considered for inclusion in the scoping review are those reporting on people (i.e. adults, adolescents and children) assessed for eligibility for TB preventive treatment (i.e. with or without a screening test for TB infection), irrespective of concomitant risk factors and/or comorbidities, where at least two consecutive steps of the cascade-of-care process for TB infection (as defined below) are described.

Publications reporting on people with confirmed TB disease (also referred to as active TB), including any drug-resistant form of the disease, will be excluded from this review.

Concepts

The concepts to be explored relate to the methodological approaches used to estimate and report care cascade analyses for TB infection.

For the purposes of this scoping review, the steps of the TB infection care cascade have been pre-defined, based on existing models [5,9,14,29], as set out below.

1. Initially identified for assessment of TB preventive treatment eligibility, either by using:
    a. Screening tests for TB infection, in which case two additional steps will be considered, namely:
        – tested for TB infection (irrespective of the diagnostic test used);
        – received positive test results.
    b. Clinical assessment of risk factors (i.e. people at higher risk of progressing to active TB if infected).

2. Referred for medical evaluation (to rule out active TB).
3. Completed medical evaluation.
4. Offered TB preventive treatment (irrespective of treatment regimen indicated).
5. Started TB preventive treatment.
6. Completed TB preventive treatment.

Cascade-of-care models will be characterised in terms of their breadth (i.e. range of staging from the initial to the final event of the cascade) and depth (i.e. number of steps within a given breadth) [30].

Analytical approaches to estimating the care cascade will be described based on the type of data linkage, population and time horizon. Data linkage will be defined as denominator-denominator (i.e. if the same group of people can be assessed across all the steps, using individually linked data) or denominator-numerator (i.e. all those eligible for inclusion in the numerator in a given step are included in the denominator of the same step by using 'linked' individual data or 'unlinked' aggregated data) [30]. The population will be defined as single (i.e. same underlying population across all the steps) or multiple (i.e. data are drawn from different populations) [30]. The time horizon will be defined as longitudinal, (if people are followed over time) or cross-sectional (if observations are made at one point in time) [30].

Depending on the aim of the cascade-of-care analysis, public health indicators could focus on patient outcomes to monitor programme performance or (i.e. outcome indicators) or processes to better understand the quality of care (i.e. process indicators) [5,11].

Narrative comments on challenges and/or lessons learned, as reported by the authors, will be collected (if applicable).

Context

The scoping review will focus on the epidemiological context of low-TB incidence countries, from the perspective of surveillance and monitoring programmes for TB infection. Therefore, only publications reporting primary data from countries with a TB notification rate <10 cases per 100 000 population (as per latest surveillance data from ECDC and/or the World Health Organization) will be considered for inclusion.

Type of evidence source

Primary studies –both peer-reviewed and grey literature – with any of the following study designs will be considered for inclusion: observational studies (cohort and cross-sectional), randomised control trials, qualitative studies, systematic reviews and scoping reviews.

Editorials, commentaries and case reports will be excluded, as well as earlier versions of a publication (e.g. pre-prints or conference abstracts of a final peer-reviewed article).

Publications focussing only on the diagnostic accuracy of screening tests for TB infection, assessing the efficacy of TB preventive treatment regimens or analysing cost-effectiveness will be excluded.

No language restriction will be applied in the eligibility assessment.

Search strategy

Four databases – PubMed, Embase, Scopus and Cochrane Database of Systematic Reviews – will be searched to identify data sources published after 1 January 1990. This cut-off date is used based on the findings of the first systematic review reporting on care cascade for TB infection [9], which identified relevant studies on the topic from 1990 onwards. The search strategy will be informed by search terms used in previously published systematic and scoping reviews on TB infection and further developed with the assistance of an information specialist. No study design or language limits will be applied for the search.

The final search strategy will be defined using an iterative process of preliminary searches for identification of relevant search terms. Annex 2 includes the draft of the search strategy for three databases.

A second information specialist, (not involved in this project) will peer-review the final search strategy using the Peer Review of Electronic Search Strategies (PRESS) checklist [31].

In addition, backwards and forwards citation chasing[1] [32] of all selected publications will be performed, and email search alerts will be established for the above-listed databases to keep the review team informed of any new studies published after the search is conducted. Knowledge users will also be consulted (more details in the section 'Knowledge user engagement').

[1] A process that uses connections between similar publications to identify additional relevant records.

Selection process

The selection process will consist of the following steps:

1. **De-duplication:** all publications identified in the selected databases will be collated and imported into EndNote (Clarivate Analytics, Philadelphia, US) and duplicates will be removed from the dataset.
2. **Abstract and title screening supported by artificial intelligence (AI):** unique references (i.e. the de-duplicated dataset) will be uploaded to ASReview, an open-source AI tool [33] which uses active machine learning to rank publications according to relevance. Two independent reviewers will assess the title and abstract against the eligibility criteria, using a researcher-in-the-loop pipeline supported by ASReview. In this pipeline, all inclusion decisions are made by the reviewer and a stop criterion (e.g. pre-defined parameters to decide when to stop screening) is required [34]. After pilot testing ASReview for the purpose of this scoping review, the stop criterion was defined as follows: each reviewer will continue screening until reaching 100 consecutive title/abstracts labelled as 'irrelevant' after screening at least 30% of the dataset. All citations labelled as 'relevant' by both reviewers will undergo full-text screening. Any disagreement will be discussed by the reviewers until an inclusion or exclusion decision is reached.
3. **Full-text screening:** publications labelled as 'relevant' will be uploaded to Covidence (Veritas Health Innovation, Melbourne, Australia), a web-based application for collaborative screening and data extraction. Two independent reviewers will assess the full text of pre-selected publications against the eligibility criteria. Any discrepancies between the two reviewers will be resolved by consensus. If consensus cannot be reached, a third reviewer will be consulted until final decision is reached.
4. **Screening additional results from other sources:** unique citations (i.e. new to the dataset) identified through backwards and forwards citation chasing, or email alerts, or suggested by knowledge users will undergo a two-step screening (e.g. title/abstract and full text) by two independent reviewers using Covidence.

Check lists for the title/abstract and full text screening will be developed to ensure that a consistent approach is applied by all reviewers (Annex 3). The review team will pilot test the inclusion/exclusion criteria before initiating the screening and discuss any challenges encountered during the screening process on a weekly basis. If necessary, the screening procedures will be adapted during the review process. Any deviation from the protocol will be described in the final report.

The results of the search and selection process will be summarised in a PRISMA-ScR flowchart [27].

Data extraction

Data extraction will be performed in Covidence, using pre-defined categories described in Annex 4. The data extraction form will be pilot tested using at least five publications, and adapted as necessary.

One reviewer will independently extract data from selected publications and a second reviewer will screen 20% of the data extracted.

Analysis of the evidence

The review team will apply an iterative and deductive process to assess a priori categories (e.g. scope, type of data linkage, population and time horizon of the care cascade) and an inductive approach for post hoc considerations (e.g. reported study objectives and key findings).

Basic characteristics of the evidence found will be summarised descriptively – e.g. distribution of the number and type of publications, year of publication, study designs and country of origin.

A critical appraisal of the publications included (i.e. assessment of methodological considerations or risk of bias) will not be performed as this is a scoping review.

Presentation of the results

Results will be summarised in tables and diagrams aligned with the review questions. Narrative summaries will further describe the main findings.

Knowledge user engagement

For the purposes of the proposed scoping review, members of the EU/EEA TB Disease Network [35] were identified as the main knowledge users. The TB Disease Coordination Committee (an advisory group elected from members of the EU/EEA TB Disease Network) was consulted in the early stages of conceptualisation.

After an initial list has been drawn up of the publications to be included TB Disease Network members will be involved in the identification of additional sources of evidence. In addition, they will be consulted about the relevance of preliminary results and dissemination channels for key findings. This collaborative process will be documented and included in the final report.

Timeline

The anticipated completion date of the scoping review is 1 December 2024.

Table 2. Stages of the scoping review and timing

Stage	Time	Started	Completed
Conceptualisation and initial design	November 2022	Yes	Yes
Explorative searches and definition of review questions	April – May 2023	Yes	Yes
Development of scoping review protocol	August 2023 – January 2024	Yes	Yes
Development of search strategy	September – November 2023	Yes	Yes
Running of literature searches	January 2024	Yes	Yes
Pilot testing of data extraction forms	December 2023 – January 2024	Yes	No
Assessment of eligibility	February – March 2024	No	No
Data extraction	April – July 2024	No	No
Data analysis	August – September 2024	No	No
Preparation of final report	October – November 2024	No	No

Review team

Table 3. Review team members and their roles

Members	Contributions				
	Conceptualisation	Design of search strategy	Overall study design	Drafting the protocol	Approved final version
Senia Rosales-Klintz*	X	X	X	X	X
Ana-Belen Escriva		X			X
Veronica Cristea	X		X		X
Csaba Ködmön	X		X		X

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Annex 1. Checklist of recommended items to address in a scoping review protocol

Section	Item	Checklist item	Reported on page #
Title			
Identification	1a	Identify the report as a protocol of a scoping review.	1
Update	1b	If the protocol is for an update of a previous scoping review, identify it as such.	Not applicable
Registration	2	If registered, provide the name of the registry and registration number.	Not applicable
Authors			
Contact	3a	Provide name, institutional affiliation, email address of all protocol authors; provide physical mailing address of corresponding author.	5
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review.	5
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes. Otherwise, state plan for documenting important protocol amendments.	Not applicable
Support			
Sources	5a	Indicate the sources of financial or other support for the review.	5
Sponsor	5b	Provide name of the review funder and/or sponsor.	5
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol.	5
Introduction			
Rationale	6	Describe the rationale for the review in the context of what is already known. (Note: consider providing a rationale for the decision to conduct a scoping review rather than other evidence synthesis approaches).	1
Objectives	7	Provide an explicit statement of the question(s) that the review will address, with reference to the inclusion and exclusion criteria.	2
Methods			
Eligibility criteria	8	Specify characteristics of the sources of evidence to be used as eligibility criteria (e.g. years considered, language, and publication status).	2-3 and 13-14 (Annex 3)
Information sources*	9	Describe all intended information sources (e.g. databases, contact with authors, trial registers or other grey literature sources) with planned dates of coverage.	3
Search strategy	10	Present draft of search strategy to be used for at least one database, including any limits used, so that it could be repeated.	3 and 10-12 (Annex 2)
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review.	4
Selection process	11b	State the process that will be used for selecting sources of evidence† (such as two independent reviewers) through each phase of the review (i.e. screening, eligibility, and inclusion).	4
Data collection process	11c	Describe the planned methods for extracting data from reports (such as piloting forms, completed independently, in duplicate), and any processes for obtaining and confirming data from investigators.	4
Data items	12	List and define all variables for which data will be sought, any preplanned data assumptions and simplifications made.	15 (Annex 4)
Outcomes and prioritisation	13	List and define all outcomes for which data will be sought, including prioritisation of main and additional outcomes, with rationale (Note: scoping reviews may not extract outcome data, so this can refer to whichever data items are extracted).	Not applicable

Section	Item	Checklist item	Reported on page #
Risk of bias in individual studies	14	If this is to occur, describe anticipated methods for assessing the risk of bias of individual studies, including whether this will be done at the outcome, study level, or both. State how this information will be used in data synthesis (Note: scoping reviews typically do not include risk of bias assessment, but this information should be described if there will be a risk).	Not applicable
Data synthesis	15a	Describe criteria under which study data will be presented (Note: scoping reviews do not typically include quantitative synthesis of study data, but should still describe in advance how it is anticipated that extracted data will be presented in the resulting review).	4
	15b	Describe the planned approach to how extracted data will be presented (such as figures, tables, evidence gap maps).	4
	15c	Describe any proposed additional analyses (such as thematic analyses). (Note: the JBI methodological guidance does not recommend undertaking thematic analysis as the data synthesis should ideally occur following methodological appraisal of the included sources).	Not applicable
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned.	Not applicable
Meta-bias (es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies). (Note: scoping reviews typically do not include assessment of meta-bias, but if there will be bias, this information should be described).	Not applicable
Confidence in cumulative evidence	20	Describe how the strength of the body of evidence will be assessed (such as GRADE).	Not applicable

** Where 'sources of evidence' (see second footnote) are compiled from, such as bibliographic databases, social media platforms, and websites.*

† A more inclusive/heterogeneous term used to account for the different types of evidence or data sources (e.g. quantitative and/or qualitative research, expert opinion, and policy documents) that may be eligible in a scoping review, as opposed to only studies. This should not be confused with information sources (see first footnote).

Adapted from [24, 27].

Annex 2. Draft search strategy

No.	PubMed search string
1	"latent tuberculosis"[MeSH] OR latent tuberculosis[TW] OR latent TB[TW] OR LTBI[TW] OR "latent tuberculosis"[Title/Abstract:~5] OR "latent TB"[Title/Abstract:~5] OR tuberculosis infect*[TW] OR TB infect*[TW] OR "TB infection"[Title/Abstract:~1] OR "TB infections"[Title/Abstract:~1] OR "TB infected"[Title/Abstract:~1] OR "TB infecting"[Title/Abstract:~1] OR "TB infectious"[Title/Abstract:~1] OR "TB infectiousness"[Title/Abstract:~1] OR "tuberculosis infection"[Title/Abstract:~1] OR "tuberculosis infections"[Title/Abstract:~1] OR "tuberculosis infected"[Title/Abstract:~1] OR "tuberculosis infecting"[Title/Abstract:~1] OR "tuberculosis infectious"[Title/Abstract:~1] OR "tuberculosis infectiousness"[Title/Abstract:~1]
2	"Tuberculin Test"[Title/Abstract:~1] OR "Tuberculin Tests"[Title/Abstract:~1] OR "Tuberculin Testing"[Title/Abstract:~1] OR "Tuberculin Tested"[Title/Abstract:~1]
3	#1 AND #2
4	"interferon-gamma release tests"[Mesh] OR "interferon gamma release test*"[TW] OR "interferon gamma release assay*"[TW] OR igra[TW]
5	#1 AND #4
6	Treatment adheren*[TW] OR treatment complian*[TW] OR treatment complet*[TW] OR "treatment comply"[Title/Abstract:~3] OR "treatment adhere"[Title/Abstract:~3] OR "treatment adherence"[Title/Abstract:~3] OR "treatment compliance"[Title/Abstract:~3] OR "treatment compliant"[Title/Abstract:~3] OR "treatment completion"[Title/Abstract:~3] OR "treatment complete"[Title/Abstract:~3] OR "treatment completed"[Title/Abstract:~3]
7	#1 AND #6
8	"Contact Tracing"[Mesh] OR contact trac*[TW] OR "contact tracing"[Title/abstract:~3] OR "contact trace"[Title/abstract:~3] OR "contact traces"[Title/abstract:~3] OR "contact tracers"[Title/abstract:~3] OR "contact tracking"[Title/abstract:~3] OR contact investigat*[TW] OR "contact investigation"[Title/abstract:~3] OR "contact investigators"[Title/abstract:~3]
9	#1 AND #8
10	preventive treat*[TW] OR "preventive treatment"[Title/abstract:~3] OR "preventive treatments"[Title/abstract:~3] OR preventive therap*[TW] OR "preventive therapy"[Title/abstract:~3] OR "preventive therapeutic"[Title/abstract:~3] OR "preventive therapeutics"[Title/abstract:~3]
11	#1 AND #10
12	#3 OR #5 OR #7 OR #9 OR #11
13	"latent tuberculosis"[MeSH] OR latent tuberculosis[TW] OR latent TB[TW] OR LTBI[TW] OR "latent tuberculosis"[Title/Abstract:~10] OR "latent TB"[Title/Abstract:~10] OR tuberculosis infect*[TW] OR TB infect*[TW] OR "TB infection"[Title/Abstract:~10] OR "TB infections"[Title/Abstract:~10] OR "TB infected"[Title/Abstract:~10] OR "TB infecting"[Title/Abstract:~10] OR "TB infectious"[Title/Abstract:~10] OR "TB infectiousness"[Title/Abstract:~10] OR "TB infections"[Title/Abstract:~10] OR "tuberculosis infection"[Title/Abstract:~10] OR "tuberculosis infections"[Title/Abstract:~10] OR "tuberculosis infected"[Title/Abstract:~10] OR "tuberculosis infecting"[Title/Abstract:~10] OR "tuberculosis infectious"[Title/Abstract:~10] OR "tuberculosis infectiousness"[Title/Abstract:~10] OR "tuberculosis infections"[Title/Abstract:~10]
14	"treatment cascade"[Title/Abstract:~10] OR "care cascade"[Title/Abstract:~10] OR "diagnostic cascade"[Title/Abstract:~10] OR "treatment cascades"[Title/Abstract:~10] OR "care cascades"[Title/Abstract:~10] OR "diagnostic cascades"[Title/Abstract:~10] OR "treatment cascading"[Title/Abstract:~10] OR "care cascading"[Title/Abstract:~10] OR "diagnostic cascading"[Title/Abstract:~10] OR "treatment cascaded"[Title/Abstract:~10] OR "care cascaded"[Title/Abstract:~10] OR "diagnostic cascaded"[Title/Abstract:~10] OR "continuum care"[Title/Abstract:~10] OR "linkage care"[Title/Abstract:~10] OR "care continuity"[Title/Abstract:~10] OR "care continuation"[Title/Abstract:~10] OR "care continuous"[Title/Abstract:~10] OR "care continua"[Title/Abstract:~10] OR "care continuums"[Title/Abstract:~10] OR care cascad*[TW] OR "cascades of care"[TW] OR "cascade of care"[TW] OR continuum of care*[TW] OR continuum care*[TW] OR linkage to care*[TW] OR care continu*[TW] OR "Continuity of Patient Care"[Mesh]
15	((cascad*[TI] OR continu*[TI] OR linkag*[TI]) AND care*[TI])
16	(treat*[TI] OR diagnos*[TI]) AND cascad*[TI]
17	#14 OR #15 OR #16
18	#13 AND #17
19	#12 OR #18
20	#19 AND 1990:2024[dp]

No.	Embase search string
#1	ltbi:ab,ti,kw
#2	(latent NEAR/5 (tuberculosis OR tb)):ab,ti,kw
#3	(infect* NEAR/1 (tuberculosis OR tb)):ab,ti,kw
#4	#1 OR #2 OR #3
#5	(tuberculin NEAR/1 test*):ab,ti,kw
#6	#4 AND #5
#7	'interferon gamma release test*':ab,ti,kw OR 'interferon gamma release assay*':ab,ti,kw OR igra:ab,ti,kw
#8	#4 AND #7
#9	(treatment* NEAR/3 (adhere OR comply OR adheren* OR complian* OR complet*)):ab,ti,kw
#10	#4 AND #9
#11	(contact NEAR/3 (trac* OR investigat*)):ab,ti,kw
#12	#4 AND #11
#13	(prevent* NEAR/3 (treat* OR therap*)):ab,ti,kw
#14	#4 AND #13
#15	#6 OR #8 OR #10 OR #12 OR #14
#16	(latent NEAR/10 (tuberculosis OR tb)):ab,ti,kw
#17	(infect* NEAR/10 (tuberculosis OR tb)):ab,ti,kw
#18	#1 OR #16 OR #17
#19	'cascade of care'/syn
#20	((treat* OR diagnos* OR care*) NEAR/10 cascad*):ab,ti,kw
#21	((continu* OR linkag*) NEAR/10 care*):ab,ti,kw
#22	(cascad*:ti OR continu*:ti OR linkag*:ti) AND care*:ti
#23	(treat*:ti OR diagnos*:ti) AND cascad*:ti
#24	#19 OR #20 OR #21 OR #22 OR #23
#25	#18 AND #24
#26	#15 OR #25
#27	#26 AND [1990-2024]/py

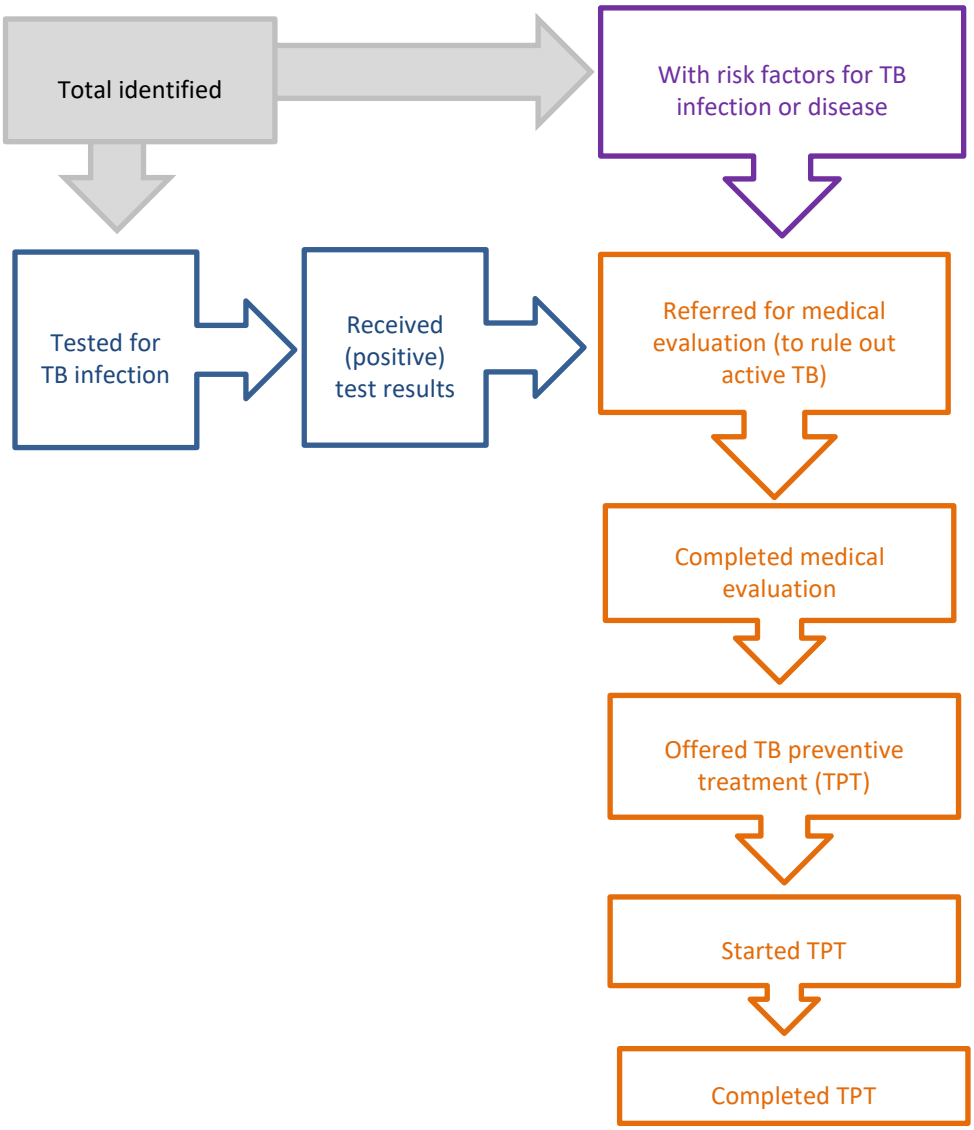
No.	Scopus search string
#1	TITLE-ABS(ltbi)
#2	TITLE-ABS(latent W/5 (tuberculosis OR tb))
#3	TITLE-ABS(infect* W/1 (tuberculosis OR tb))
#4	#1 OR #2 OR #3
#5	TITLE-ABS(tuberculin W/1 test*)
#6	#4 AND #5
#7	TITLE-ABS("interferon gamma release test*" OR "interferon gamma release assay*" OR igra)
#8	#4 AND #7
#9	TITLE-ABS(treatment* W/3 (adhere OR comply OR adheren* OR complian* OR complet*))
#10	#4 AND #9
#11	TITLE-ABS(contact W/3 (trac* OR investigat*))
#12	#4 AND #11
#13	TITLE-ABS(prevent* W/3 (treat* OR therap*))
#14	#4 AND #13
#15	#6 OR #8 OR #10 OR #12 OR #14
#16	TITLE-ABS(latent W/10 (tuberculosis OR tb))
#17	TITLE-ABS(infect* W/10 (tuberculosis OR tb))
#18	#1 OR #16 OR #17
#19	TITLE-ABS((treat* OR diagnos* OR care*) W/10 cascad*)
#20	TITLE-ABS((continu* OR linkag*) W/10 care*)
#21	TITLE(cascad* OR continu* OR linkag*) AND TITLE(care*)
#22	TITLE(treat* OR diagnos*) AND TITLE(cascad*)
#23	#19 OR #20 OR #21 OR #22
#24	#18 AND #23
#25	#15 OR #24
#26	#25 AND PUBYEAR AFT 1989

Annex 3. Checklists for inclusion and exclusion criteria

Title/abstract screening	
Criteria for inclusion (all must be present)	**Yes /No**
1. The publication relates to TB infection.	
2. The publication reports on human populations (irrespective of age).	
3. The publication reports primary data from a low-TB incidence country/countries.	

Full text screening	
Criteria for inclusion (all must be present)	**Yes/No**
1. The publication reports on at least two consecutive steps of the cascade-of-care for TB infection (described in Figure A below).	
2. The publication reports on primary data from one (or more) low-TB incidence country.	
3. Primary studies (both peer-reviewed and grey literature) with any of the following study designs: observational studies (cohort and cross-sectional), randomised control trials, qualitative studies, systematic reviews and scoping reviews.	
Criteria for exclusion (any of these justify exclusion)	
1. Editorials, commentaries, case reports and earlier versions of a publication (e.g. pre-prints or conference abstracts of a final peer-reviewed article).	
2. The publication focuses on diagnostic accuracy of screening tests for TB infection.	
3. The publication focuses on efficacy of TB preventive treatment regimens.	
4. The publication focuses on cost-effectiveness analyses.	
5. Full-text not available for screening.	

Figure 1. TB infection cascade-of-care process



Annex 4. Data extraction variables

Concept	Variables
General information	• Reference ID number • Author • Year of publication • Publication status (published/unpublished) • Country • Aim of the study • Study design • Period of data collection (if applicable).
Population	• Number of study participants • Type of population (by age) • Type of population (by risk factors/comorbidities).
Cascade-of-care	• Data sources used (as reported by the authors) • Steps of the cascade-of care reported by the authors • Definition of numerator and denominator used in each step, as reported by the authors. • Methods used for constructing the cascade-of-care analysis (as reported by the authors) • Type of data linkage • Type of population base (single or multiple) • Time horizon (longitudinal or cross-sectional) • Type of indicators used (as reported by the authors, if any).
TB infection	• Screening methods used for diagnosing TB infection (if any).
TB preventive treatment	• Criteria used for assessing eligibility (e.g. positive test result or risk factor) • TB preventive treatment regimen indicated (as reported by the authors) • Adherence support approaches (as reported by the authors, if any) • Monitoring of adverse events (as reported by the authors, if any).
Context	• Type of healthcare setting (primary, secondary or tertiary level) • Jurisdiction (local, regional or national).
Key findings	• Key findings or main conclusion(s) (as reported by the authors) • Challenges, if applicable (as reported by the authors) • Lessons learned, if applicable (as reported by the authors).