Missed opportunities for diagnosis and treatment in patients with tuberculosis symptoms: a systematic review

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Research article

Keywords: tuberculosis, symptoms, identification, underdiagnosis

Posted Date: August 8th, 2020

DOI: https://doi.org/10.21203/rs.2.22742/v2

Abstract

Background Identification of symptomatic patients followed by prompt on-site investigation form the foundation of facility-based tuberculosis (TB) screening and diagnosis. However, underdiagnosis is common, contributing to ongoing transmission and adverse health outcomes. We conducted this systematic review with the hypothesis that underdiagnosis is largely secondary to patient drop out from presentation, through the diagnostic and care pathway, to treatment initiation.

Methods We searched (to 22 January 2019) MEDLINE, Embase, and Cinahl for studies investigating the pathway of care for patients (and standardised patients) presenting to health facilities or pharmacies with TB symptoms. We used QUADAS-2 to assess risk of bias. We reported the proportions of symptomatic patients at each stage of the diagnostic and care pathway from symptom screening to treatment initiation.

Results After screening 3,184 titles and abstracts, we identified 14 eligible studies. None provided data addressing the full cascade of care from clinical presentation to treatment initiation in the same patient population. Symptom-screening, the critical entry point for diagnosis of TB, was not done for 40%, 50%, and 96% of symptomatic participants in the three studies that reported this outcome. The proportion of symptomatic attendees offered a diagnostic investigation (data available for 13 studies), was very low with a study level median of 38% (IQR: 22% to 45%, range 5% to 84%).

Conclusions Inefficiencies of the TB symptom screen-based patient pathway are a major contributor to underdiagnosis of TB in health facilities, and reflect inconsistent implementation of longstanding guidelines to ask all patients attending health facilities about respiratory symptoms and to offer diagnostic tests to all patients promptly once TB symptoms are identified. Better screening tools and interventions to improve the efficiency of TB screening and diagnosis pathways in health facilities are urgently needed.

Background

Every year, the fate of 3 million of the 10 million people who develop active tuberculosis (TB) remains unclear.[1] This large case-notification gap is comprised of both patients who are diagnosed but unreported (especially in countries with large private sectors), and people with active but undiagnosed TB.[1] Underdiagnosis is most common in low-income settings, where geographical and financial barriers impede access to care.[1-3] These and other delays in the pathway to effective treatment[4] are major contributors to the high case fatality of TB[5] – with 1.6 million deaths estimated in 2017[1] – and to onward TB transmission.[2, 3, 6]

The diagnosis and care pathway for adult presumptive TB patients starts with presentation to healthcare services, followed by the need for healthcare workers to elicit symptoms, initiate and complete TB diagnostic investigations by interpreting results and communicating to patients, before commencing and supporting completion of effective anti-tuberculosis treatment.[7] Progress along this pathway can be analysed using a TB “cascade of care” model (Figure 1). Key indicators of cascade progress include: percentage of facility attenders in whom TB symptoms are elicited; percentage of TB symptomatic individuals who are offered and complete TB diagnostic testing; percentage of patients with TB disease (identified either by diagnostic test or clinical diagnosis) who initiate TB treatment; and percentage of patients who start treatment, are retained to treatment completion and achieve recurrence-free survival for at least a year.[4, 7]

The International Standards for Tuberculosis Care recommend that all patients attending a health facility with unexplained cough of two weeks or more should be investigated for TB.[8] However, symptoms of TB are often missed by healthcare workers,[9] leading to diagnostic and care delay.[10] The scale of missed TB symptoms is poorly defined, but thought to make a considerable contribution to TB underdiagnosis at the global level. International infection control guidelines recommend systematic enquiry for cough for all patients attending acute care services.[11] Since 2013 International TB guidelines have also recommended systematic enquiry of all patients in high TB burden countries for cough duration, and additional TB symptoms according to the national prevalence of TB and HIV, aiming to support early diagnosis.[12]

This systematic review aimed to collate evidence relating to how effectively TB symptoms are recognized and acted upon under routine programmatic conditions in WHO-defined high-TB burden countries (HBCs).

Methods

Protocol registration and adherence to international standards

We registered the systematic review protocol with the International Prospective Register of Systematic Reviews (PROSPERO, registration number CRD42018106284). We prepared our study protocol, performed the systematic review and wrote the report following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) recommendations.[13]

Definitions

We aimed to provide summary estimates of: the proportion of patients seeking health care at different levels of the health system who had symptoms consistent with TB; the proportion of those who were offered TB symptom screening; the proportion who were offered and received diagnostic testing for TB (including patient receipt of results); and the proportion found to have microbiologically confirmed TB who were subsequently initiated on anti-tuberculosis treatment.

We defined “TB symptom screening” as any enquiry into symptoms consistent with TB. We defined “investigation for TB” as any screening/diagnostic test for tuberculosis defined by primary studies including (but not limiting to) microbiologic (including, but not limited to smear of sputum or other body fluid, culture or Xpert), or radiological (including but not limited to chest x-ray or ultrasound), or referral to another health facility with the intent to diagnose TB. “investigation” was defined as undergoing a TB investigation. “Receipt of result” was defined as receiving outcome after undergoing a TB investigation. We defined “initiation of TB therapy” as commencement of any course of therapy with intent to treat active TB. We defined “recruitment period” as the time during which a patient with symptoms consistent with TB attended any healthcare setting. For participant follow-up time, we adopted the definitions provided by individual studies.

Eligibility Criteria

We included studies published in any language in or after 2000, that recruited adult participants from WHO’s Published List of 30 High TB Burden Countries, attending any healthcare setting for any reason with symptoms consistent with TB. To be eligible, a study needed to report data allowing extraction of at least one of the following proportions of the population of interest that enter into any step of the TB cascade of care: offered TB symptom screening; offered TB investigation for TB; received investigation for TB; and initiated TB therapy.

Eligible study designs were cross-sectional studies, standardised patient studies, exit interview studies, and cohort studies (prospective and retrospective). Standardised (simulated) patient were studies that involved a covert member of the research team (the standardised patient) who presented to a healthcare facility or pharmacy and, when questioned by health workers, would give a history of TB symptoms that should prompt further clinical questions, examinations and tests for TB. Exit interview studies are typically done at the point of clinic exit shown in Fig. 1, where a sample of patients leaving the health facility are asked about the screening and diagnostic tests received during their clinic visit. We excluded studies that reported on clinical trials, register linkage studies, autopsy studies, prevalence surveys, and community-based studies because participants in these studies would not be representative of patients in routine care. Studies starting with diagnosed TB patients were excluded as being unable to provide unbiased numbers for stages earlier in the TB care cascade.

Information Sources And Data Extraction

We systematically searched for studies meeting our eligibility criteria in Medline (Pubmed), Embase (OVID), and CINAHL (EBSCOHost) using the search strategies shown in Appendix 1. We included studies published between 01 Jan 2000 and 22 January 2019, when we ran the search.

Two reviewers (THD and JL) independently screened titles and abstracts of the articles identified through the electronic searches against the eligibility criteria. THD and JL independently assessed full texts of the included papers, extracted data from eligible studies using a standardised electronic form (Google Forms, Google, United States), and documented reasons for non-inclusion. A third reviewer, PM, resolved disagreements in eligibility.

We extracted the following data from the eligible articles: first author; year of publication; facility and country of data collection; dates of study; level of healthcare facility (primary care, hospital); study definitions of review outcomes (TB symptoms, TB symptom screening, TB investigation); management options available on site (e.g. smear, chest X-ray, Xpert, TB treatment); study design; study eligibility criteria; study population characteristics (HIV status, sex, age); number of patients recruited; number of patients with TB symptoms; number of patients symptom-screened; number of patients with symptoms tested for TB; number of patients with microbiologically confirmed TB; number of patients started on TB treatment; and factors associated with an individual being screened based on quantitative analysis. We excluded studies that did not report information on any of the study outcomes.

Assessment Of Methodological Quality

For a meta-analysis of exit-interview and standardised patient studies, no accepted risk of bias tool exists. We therefore adapted the QUADAS-2 tool[14] to our specific question (see Appendix 2) to assess risk of bias, at the level of the study, across three domains: patient selection, classifying TB symptoms, and diagnosing TB. For each domain, we reported the level of risk or concern as being either high, low or unclear.

Statistical analysis

For each included study, we reported on the following proportions (and corresponding 95% exact binomial confidence intervals, either as reported in respective articles or, if not available, as calculated by us): a) patients attending a health care facility for any reason who were offered symptom screening for TB; b) patients with TB symptoms who were offered further investigation for TB; c) patients who were offered further investigation for TB who receive results of TB testing; d) patients who receive results of TB testing who were initiated on TB therapy; and e) missed TB: the proportion of patients with TB who were not initiated on TB therapy. We performed descriptive analysis producing forest plots of these proportions. We estimated the pooled weighted proportion of participants (and 95% confidence interval) who were offered a diagnostic test for TB using the double arcsine transformation. All statistical analysis was carried out in R V3.6.0 (R Foundation for Statistical Computing, Vienna).

Results

Selection of studies

We identified 5,062 articles from the electronic searches, which reduced to 3,184 after removing duplicates (Fig. 2), and to 26 after title and abstract screening. After full text review against eligibility criteria, 14 articles remained and were included in the systematic review. We excluded 12 articles: two because the data applicable to the review was already included in the authors' other included publication,[15, 16] two because data were not original to research manuscripts (one commentary and one systematic review),[7, 17] seven studies because they did not report data that could be mapped to our pre-defined patient categories, and one because it was a community-based study.[18–24]

Description Of Studies

The 14 eligible studies were published between 2000 and 2018 and reported data from India,[25–29] South Africa,[9, 30–32] Kenya,[33] Thailand,[34] China,[35] Vietnam[36] and Ghana[37] (Table 1). Nine studies employed the standardised patient design, three were exit interview studies, and the remaining two were cross-sectional studies. All studies included adults only; most studies defined TB symptoms as “having chronic cough”; and available TB tests included smear microscopy, chest X-ray, or referral to the next level of care. All three cohort studies[9, 30, 32] were from South African primary health care settings. The two included cross-sectional studies were: a rural hospital study from Ghana;[37] and a hospital based study from India.[29] Four of the seven standardised patient studies were done at pharmacies in India,[27, 28] Thailand,[34] and Vietnam;[36] one was in a South African primary health care setting;[31] one involved facilities at various levels of care in Kenya;[33] and another two involved various levels of Indian health care system.[25, 26]

Table 1
Characteristics of the included studies (n = 14)

Study	Country	Study design	Setting	Participants eligibility	TB symptom definition	TB test available at study site	Number (%) with TB symptoms[1]	Number (%) with TB symptoms screened[1]	Number (%) offered TB test[1]	Nu (% re TE
Amenuvegbe 2016	Ghana	Cross-sectional	Two rural hospitals	Outpatient presentation during study period with cough of ≥ 2 weeks	≥ 2 weeks of cough	Smear	Not reported	Not reported	Not reported	23
Chihota 2015	South Africa	Exit interview	PHC	≥ 18yrs exiting PHC	Any of cough ≥ 24hr or fever of night sweats or weight loss	Xpert	4098/8104 (51%)	2130/3604 (60%)	818/2130 (38%)	No rep
Claassens 2013[2]	South Africa	Exit interview	PHC	≥ 18yrs exiting PHC not on TB Rx or collecting TB results	Any cough, productive cough, haemoptysis, fever, night sweats, chest pain or weight loss.	Smear and culture	3564/4686 (71%)	16/423 (4%)	4/16 (25%)	2/ (5
Kweza 2018[3]	South Africa	Exit interview	PHC	≥ 18yrs exiting PHC not on TB Rx	any duration of cough, loss of weight, fever or night sweats	Xpert	Not reported	622/1255 (50%)	134/622 (22%)	61 (4
Christian 2018	South Africa	Standardised patient	PHC	SP, presumptive TB	Cough ≥ 2/52	Sputum test and HIV test	143/143 (100%)	143/143 (100%)	119/143 (83%)	No rep
Daniels 2017	Kenya	Standardised patient	Various	SP, presumptive TB	2 to 3 weeks of cough and fever	Sputum testing	42/42 (100%)	42/42 (100%)	21/42 (50%)	No rep
Das 2015	India	Standardised patient	Various	SP, presumptive TB	2 to 3 weeks of cough and fever	Sputum test, CXR or referral	150/150 (100%)	Not reported	22/150 (15%)	No rep
Kwan 2018	India	Standardised patient	Various	SP, presumptive TB	2 to 3 weeks of cough and fever	Sputum test, CXR or referral	1762/1762 (100%)	1762/1762 (100%)	807/1762 (46%)	No rep
Miller 2017	India	Standardised patient	Pharmacies	SP, presumptive TB	3 to 4 weeks of cough and fever	Refer	333/333 (100%)	333/333 (100%)	150/333 (45%)	No rep
Rojpibulstit 2007	Thailand	Standardised patient	Pharmacies	SP, presumptive TB	1 month of cough and fever	Refer	70/70 (100%)	70/70 (100%)	3/70 (4%)	No rep
Satyanarayana 2016	India	Standardised patient	Pharmacies	SP, presumptive TB	2 to 3 weeks of cough and fever	Refer	599/599 (100%)	599/599 (100%)	96/599 (16%)	No rep
Sylvia 2017	China	Standardised patient	Various (hospital, health centre)	SP, presumptive TB	2 to 3 weeks of cough and fever	Sputum test, CXR or refer	274/274 (100%)	274/274 (100%)	112/274 (41%)	No rep
Vu 2012	Vietnam	Standardised patient	Pharmacies	SP, presumptive TB	4 weeks of cough and fever	Refer	138/138 (100%)	138/138 (100%)	59/138 (43%)	No rep
Singh 2014	India	Cross-sectional	Hospital	cough more than 2 weeks or HIV pos and cough any duration	Cough ≥ 2 weeks or HIV + and cough any duration	Smear or CXR or “serological test”	242/242 (100%)	Not reported	93/242 (39%)	No rep

Study	Country	Study design	Setting	Participants eligibility	TB symptom definition	TB test available at study site	Number (%) with TB symptoms[1]	Number (%) with TB symptoms screened[1]	Number (%) offered TB test[1]	Nu (% re TE

1. Outcome (definitions): TB symptoms (as reported in studies); TB symptoms screen (any enquiry into symptoms consistent with TB); TB test (any screening for tuberculosis or referral to another health facility for the same); receiving TB test (undergoing a TB investigation); receiving TB result (receiving outcome af TB investigation)
2. Classens 2013: collected spot sputum from 423 TB symptomatic participants individuals exiting a health facility regardless of reason for presentation or c management. 21 of the 406 (5%) with available smear and/or culture result were positive. None of the 21 presented because of their respiratory symptoms, n symptoms screen, and none were offered TB test during their visit
3. Kweza 2018: collected spot sputum from 779 TB symptomatic participants missed by clinic staff and performed Xpert/MTB/RIF and 39 (5%) tested positi
PHC = primary health care; SP = Simulated patient study; CXR = chest x-ray.

The TB Diagnostic And Care Pathway

None of the included studies provided data addressing the full cascade of care from clinical presentation to treatment initiation in the same patient population. Exit interview studies reported proportion of participants systematically screened for symptoms, while the remainder of the studies mostly reported the proportion that were offered or received a diagnostic investigation.

The proportions of participants who reported having been screened for TB symptoms in the three exit interview studies were 60% (2130/3604),[30] 50% (622/1255),[15] and 4% (16/423)[9] respectively (Fig. 3A). The proportion of symptomatic attendees offered a diagnostic investigation (data available for 13 studies), was highly variable, ranging from 5–84% (pooled weighted percentage 38% [IQR: 26–51%]) (Fig. 3B). Of note is that nine of these 13 studies were standardised patient studies[25–28, 31, 33–36] in which, despite reporting classical TB symptoms to attending care givers, up to 96% of the participants were not offered a TB diagnostic investigation (Table 1). The three studies that assessed receipt of TB investigation reported the following proportions: 50% (2/4),[9] 46% (61/134),[32] and 24% (230/932).[37] One study[32] that collected sputum, at point of exit, from 779 individuals not tested by clinic staff, detected 39 cases (5%). Out of the 39, twenty-four were symptom screened by clinic staff, but not offered a TB test.

Predictors Of Correct Management

Six studies reported factors associated with correct patient management. Interaction with holders of a medical degree was assessed and found to be associated with correct patient management in two studies.[25, 26] One study assessed hospital, health centre and village clinic management of symptomatic patients and reported that management improved with increasing level of facility.[35] Private facilities were less likely to prescribe sputum diagnostics to symptomatic patients in one study reporting this outcome (OR 7.26 4.04–13.08).[29] Two studies examined patient characteristics associated with receipt of a TB investigation. Male patients were more likely than women to be offered TB investigations in the Chihota study,[30] while Kweza et. al[32] reported that women were more likely to receive “good management”. Additionally, Chihota et al [30] reported that HIV-positive patients were more likely than other patient groups to receive appropriate management, while Kweza et. al[32] identified better management of older (≥ 55 years) patients.

Assessment Of Risk Of Bias

We evaluated the identified studies using the pre-adapted QUADAS 2 tool for assessment of risk of bias and found that all included studies conducted their patient selection and classification of TB symptoms according to the expectation of the systematic review question. In the five studies that involved diagnosing TB, one exhibited a high risk of bias because not all patients utilised the same diagnostic strategy (Table 2).[29]

Table 2
Assessment of the included studies for Risk of Bias using the QUADAs 2 tool

	Risk of Bias in each of the assessed domains		
Author and Year	Patient Selection	Classification of TB symptoms	Diagnosing TB
Amenuvegbe	High	High	High
Chihota 2015	Low	Low	Low
Claassens 2013	Low	Low	Low
Kweza 2018	Unclear	Low	High
Christian 2018	Low	Unclear	Not applicable
Daniels 2017	Low	Low	Not applicable
Das 2015	Low	Low	Not applicable
Kwan 2018	Low	Low	Not applicable
Miller 2017	Low	Low	Not applicable
Rojpibulstit 2007	Low	Low	Not applicable
Satyanarayana 2016	Low	Low	Not applicable
Sylvia 2017	Low	Low	Not applicable
Singh 2014	Low	High	High
Vu 2012	Low	Low	Not applicable
Not applicable: risk of bias in the “diagnosing TB” domain for studies that involved standardised patients was reported as not applicable			

Discussion

The main finding of this systematic review was that in 13 studies across high-TB burden countries, a study-level median of only 39% (IQR 22–45%) of patients with TB symptoms were offered a TB test. TB symptom-screening, the critical entry point for diagnosis of TB, was reportedly not done for 40–96% of symptomatic participants in the three studies that reported this outcome. There was substantial heterogeneity between studies. Nevertheless, this review suggests that a failure to identify TB symptoms in those seeking health care and a failure to test those that present with TB symptoms may be a key driver of missed TB diagnosis in high TB settings. If so, this should be amenable to interventions that aim to reduce the TB diagnosis and treatment gap but also highlights existing gaps for screening and diagnostic tools that can be employed at the point of care.

Our results are consistent with long-standing concerns about the quality of TB care provided at primary care level facilities, with high levels of missed identification of symptoms and suboptimal management once symptoms are identified, and contributing to inefficiency in the TB diagnostic pathway.[38] Optimising facility-based management of self-presenting patients with TB symptoms should be a priority for national TB programmes because it addresses the targeting of the “missing millions,” infection control, and complements community-based active case finding.[6] Failure to promptly identify symptomatic patients will also reduce the likely patient and public health impact of new TB diagnostics because most of the target population would simply not be offered the testing they should receive.[39]

Better management of symptomatic self-presenting primary care-level patients is an urgent priority that all countries should be focused on. However, we also recognise the limitations of a symptom-based approach. The inherent subjectivity with symptom-screening leads to variations in the way questions are asked or responded to,[40] and different responses to the same question when asked at different times or by different individuals.[40] In population-level TB prevalence surveys, the sensitivity of cough≥2 weeks for active TB disease is only 35% (95% CI 24%; 46%) compared to microbiological reference standards.[41] This highlights the need for screening tools that are more accurate, less subjective and easier to monitor than symptom screening, while ideally staying as accessible and low-cost.

A key principle of TB screening is that it must be directed towards populations with higher prevalence of disease where individual benefits are likely to outweigh risks, and delivered with patient convenience as a key priority.[42] Amongst populations attending health centres, alternatives to symptom-based approaches for facility-based TB screening include TB triage tests such as digital chest radiography and computer-aided diagnosis or point-of care host biomarkers performed prior to confirmatory testing. Triage tests aim to rule-out TB, allowing health workers to prioritise patients with a higher prior probability of TB for more expensive, slower confirmatory tests such as Xpert or culture.[40]

Individual and public health consequences of inefficiencies in establishing a diagnosis and providing prompt and effective treatment of TB include premature death, as patients with undiagnosed TB have a high mortality rate especially if also living with HIV,[5] and more severe post-tuberculous lung disease and other permanent sequelae of TB.[43] Increasingly severe illness tends to prompt multiple healthcare visits, with patients incurring pre-diagnosis “catastrophic costs” and repeated courses of non-specific treatments including broad-spectrum antibiotics until their TB is finally diagnosed.[38, 44, 45] Cost-savings from timely diagnosis of TB averting visits, from both health-system and patient-perspective need to be factored into economic decision-making when TB diagnostic investments are considered. Public health consequences of delayed diagnosis include onward transmission, including nosocomial transmission

while attending health facilities for diagnosis, with patients potentially becoming more infectious as the severity of their underlying TB and symptoms progress.[46–48] Early diagnosis and treatment therefore are key tools if national TB programs are to arrest transmission.

The key programmatic implication of our findings is that front line health workers in the TB diagnostic pathway either are unaware of expectations of national programs or are unable to adhere to current TB case finding guidelines. Results from two included studies done in India[25, 26] suggest that TB diagnosis can be improved in that setting by having better qualified personnel at the entry point of the diagnostic pathway. On the other hand, Silvia et. al found that management at a higher level facility (hospital) was more likely to include TB diagnosis that health centre or village clinic management.[35] Finally, Singh et.al, who compared management of symptomatic patients in public and private facilities, found that public facilities performed better.[29] There are three likely underlying problems issues that need to be addressed. First is general health system weakness, which can be amenable to investments in health sector strengthening programs (particularly in universal health coverage)[49] and in public private partnerships.[50] Second is the lack of good screening tools beyond symptom-screening which – if faithfully adhered to – would overburden the already limited capacity for confirmatory testing. Third is the very lack of simple, quick and low-cost confirmatory diagnostic test with the ability to provide same-day, same-clinic results.

Our review has several limitations. The first limitation is paucity of data; only 14 studies were identified with relevant data, and the number of participants per study also limited our analytical scope. Secondly, our focus on a single clinical episode, may have limited our ability to fully interrogate the TB diagnostic pathway, which often includes multiple clinical encounters. Thirdly, our case definitions for TB investigation which included referral for TB assessment, as well as more sensitive diagnostics such as Xpert/MTB/RIF in one category, may have limited specificity.

Conclusions

In conclusion, this study demonstrates that the substantial gaps within the TB diagnosis and care pathway are likely making substantial contributions to the so-called “missing millions” of TB cases. Failure to complete TB symptom screening and offering TB tests to all those screening positive is a critical breakpoint in this cascade at which patients with TB may be missed. Acknowledging the limitations of symptom screening and the need for better tools, there is urgent need to identify and implement interventions and health systems strengthening approaches that recognise local TB epidemiology and can improve the quality of clinical encounters in favour of TB recognition, diagnosis and treatment.

Abbreviations

TB	Tuberculosis
PROSPERO	Prospective Register of Systematic Reviews
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
WHO	World Health Organisation
PHC	Primary Health Care
SP	Simulated patient study
CXR	Chest X-ray
OR	Odds Ratio

Declarations

Ethics approval and consent to participate

This work did not involve direct contact with human subjects or participant identifiable data. Ethical approval was therefore not required.

Consent to publish

Not applicable.

Availability of data and materials

We have included all data and analysis code in Appendix 3.

Competing interests

The authors declare that they have no competing interests.

Funding

THD is funded by the Commonwealth Scholarship Commission and the Helse Nord RHF. PM and ELC are funded by Wellcome Fellowships in Clinical Science (WT206575 and WT200901, respectively). The funding agencies had no role in the systematic review, preparation or decision to submit this manuscript.

Acknowledgements

Not applicable.

Authors' Contributions

All authors substantially contributed to the conception and design of the study and reviewed all documents and materials. PM, SGS, and ELC designed the study. VL developed and implemented the search strategy. THD screened articles, extracted data, interpreted results, and developed the first draft of the manuscript. JL screened articles, extracted data, analysed data, interpreted results, and reviewed manuscript. PM screened articles, interpreted results, and reviewed manuscript. SGS, MAB, VL and ELC critically reviewed results, and manuscript. All authors read and approved the final manuscript. TD is the guarantor for this work.

Ethics approval and consent to participate

This work did not involve direct contact with human subjects or participant identifiable data. Ethical approval was therefore not required.

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Figures

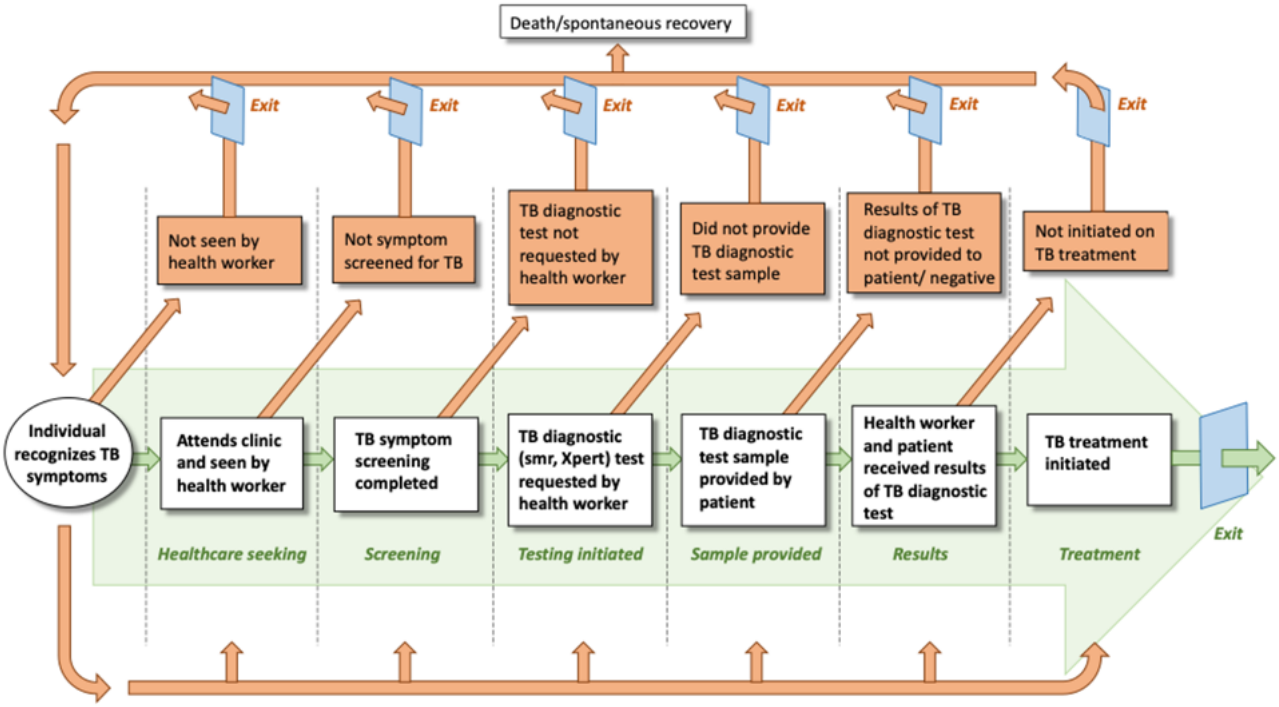

Figure 1

The diagnostic and care pathway for tuberculosis at health facility level, outlining opportunities for tuberculosis diagnosis and treatment in a symptomatic individual.

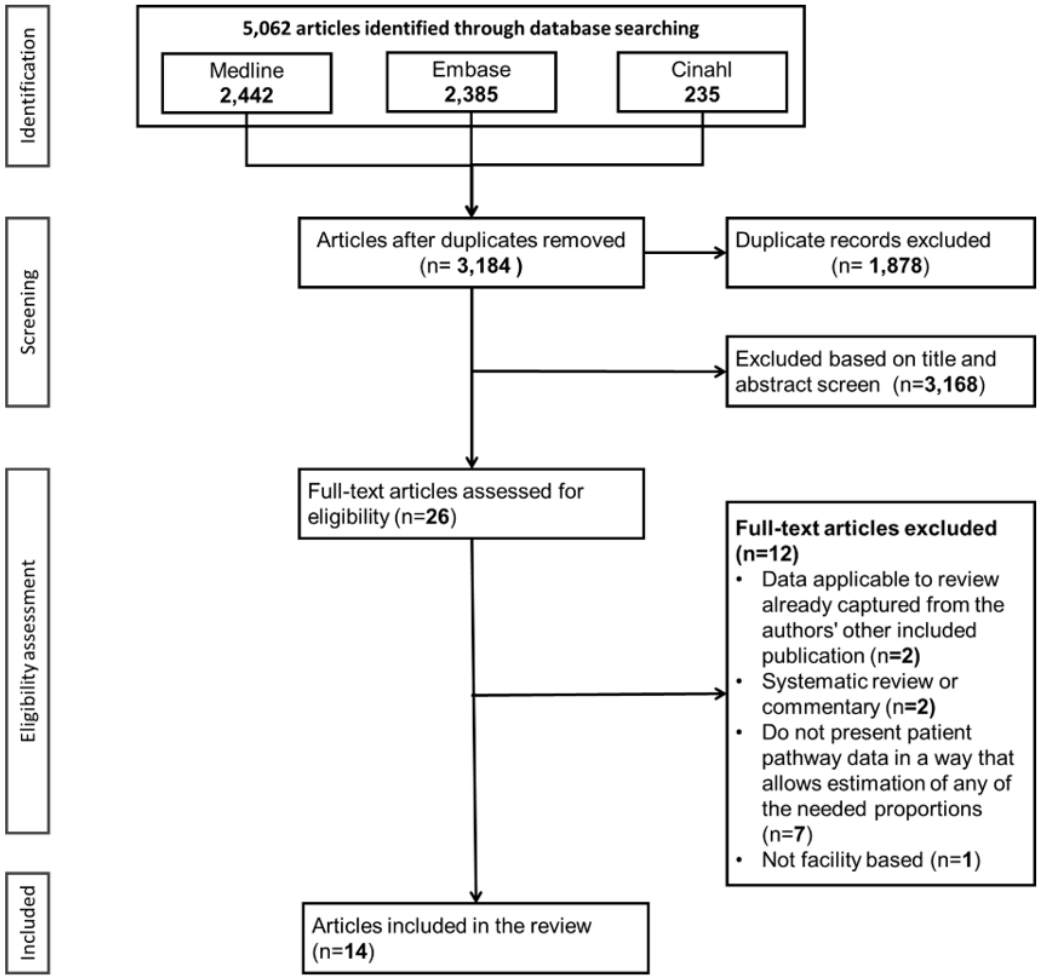

Figure 2

Flowchart for the selection of studies on the diagnostic and care pathway for tuberculosis in high burden countries

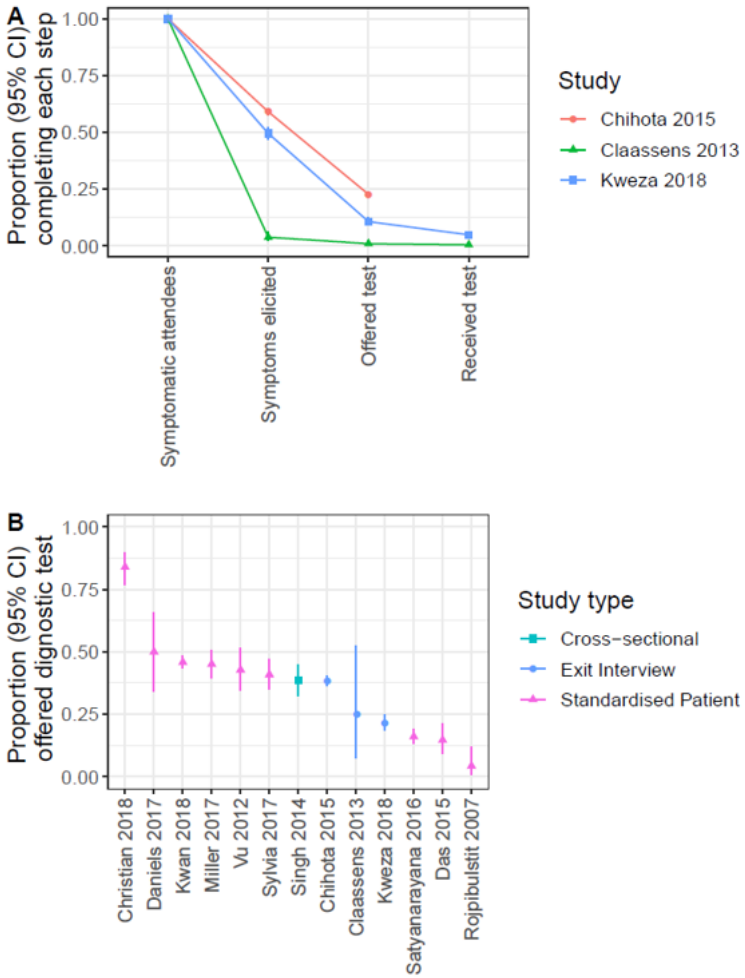

Figure 3

(A) TB diagnostic and care cascade for exit interview studies showing proportion of symptomatic attendees in whom symptoms were elicited, who were offered a diagnostic test and who received test results and (B) proportion of symptomatic attendees who were offered a diagnostic test after being asked about symptoms in all included studies. In all cases exact binomial confidence intervals are shown

Supplementary Files

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